PREFACE

This is in consonance with the objective of the Drugs & Cosmetic Act 1940 and Rules 1945 and other functions of CDSCO wherever applicable.

These guidelines are intended for the guidance of Departmental offices only. It sets out the nature of work that the Zonal, Sub-Zonal and Port offices of the Central Drugs Standard Control Organization generally carry out and the guidelines about the policy that should be followed in disposing of the work & duties.

These guidelines are not to be quoted as a reference in any official communication, except in the communications with the headquarters. The procedure set out therein cannot also be quoted as legal authority.

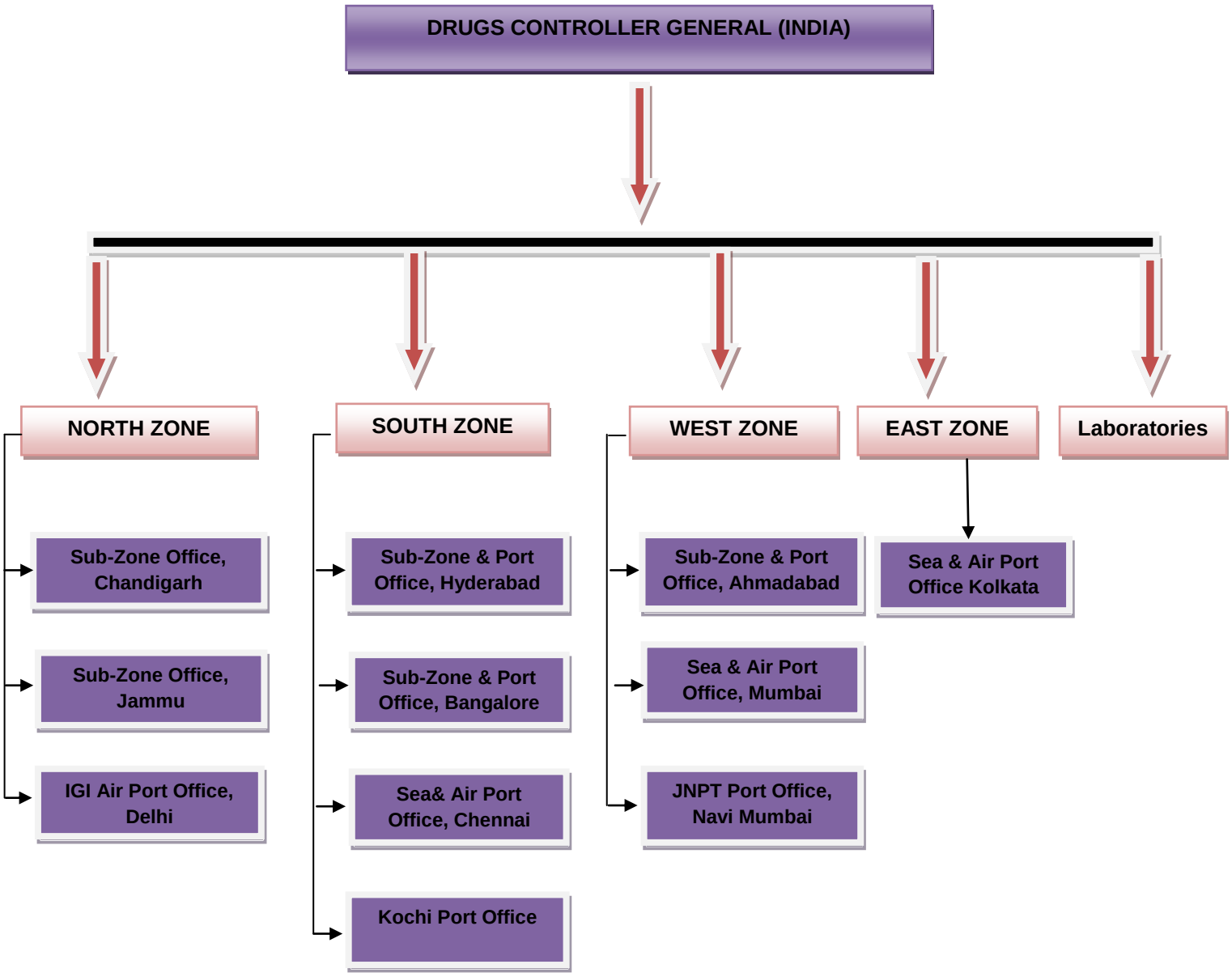
While all conceivable item of work that pass through the Central Drugs Standard Control Organization at the Zone, Sub-Zone & ports, have been included in these guidelines, there may be certain omissions. This guidance documents may be amended from time to time as per requirements after obtaining necessary approval from the competent authority.

INTRODUCTION

It is felt necessary that the activities of all the subordinate offices under the control of the Drugs Controller General (India) should be uniform and all the activities require to be implemented in rational way so that the whole system functions transparently. Accordingly it is necessary to prepare a proper guidance documents for implementation by all zonal, sub-zonal and port offices. It is also required through a network that all the activities of all the aforesaid offices are linked with Head Quarter i.e. FDA Bhawan and the day to day activity is recorded electronically and shared with the office of Drugs Controller General (India) and other subordinate offices.

In view of the above objectives, the following working procedures are suggested to be carried out by all the subordinate offices under the control of the Drugs Controller General (India).

ORGANISATION SET-UP OF CENTRAL DRUGS STANDARD CONTROL ORGANISATION (CDSCO)



BROAD FUNCTIONS & ACTIVITIES OF ZONAL & SUB ZONAL OFFICES

All the Zonal Offices are headed by Dy. Drugs Controller (India) who is assisted by Assistant Drugs Controller (India), Drugs Inspectors, Technical Officers, Senior Technical Assistants & Technical Assistants for the technical work and a group of Ministerial staff including one Head Clerk and other subordinate staff in the Administrative work. Different sub-zonal offices and port offices headed by Assistant Drugs Controller (India) & Technical Officer at Kochi is also under the direct control of the Dy. Drugs Controller (India) of the respective zone for Technical as well as Administrative function. Following are the broad functions, activities and duties of the zonal and sub-zonal offices.

TECHNICAL

1. To participate in the joint inspection for issuance / revalidation of Certificate of Pharmaceutical Products (COPPs) as per WHO certification scheme after receiving the application from the manufacturing firm.
2. To participate in the joint inspection for grant/renewal of Blood Bank license.
3. To participate in the joint inspection for grant/renewal of license for Vaccine / Sera manufacturing units for both human as well as veterinary.
4. To participate in the joint inspection for grant/renewal of license for LVP manufacturing units.
5. To participate in the joint inspection for grant/renewal of license for notified Medical Devices & Critical Diagnostics manufacturing units.
6. To participate in the joint inspection for grant/renewal of license for Bio-Tech & Bio-similar products manufacturing units.
7. To participate in the inspection of Clinical Trial facilities and BA/BE centres as directed by the Drugs Controller General (India) from time to time.

8. To carry out Surprise check/Raid jointly/independently on the basis of complaint received under Whistle Blower scheme and also from other sources.
9. To carry out joint inspection of Drug Testing Laboratory for the purpose of grant of approval for test / analysis of Drugs & Cosmetics.
10. To follow up action on NSQ drugs with State Licensing Authorities in the respective zone as well as with other zonal offices.
11. Drawing of regular drugs samples from the manufacturing & sales / distribution premises including the Govt. establishment.
12. When the samples drawn by the Central Drugs Inspector are declared spurious / adulterated / grossly sub-standard etc., the cases are investigated and prosecution are launched in the appropriate court after obtaining necessary sanction from the Drugs Controller General (India).
13. Information regarding cancellation/suspension of manufacture licenses or withdrawal of product permission by the State Licensing Authority is circulated to other State Licensing Authorities in the zone and other zonal offices.
14. Deputation of Drugs Samplers at various places of suspicious nature and collect samples through them as surrogate patient from the sales premises by way of survey to monitor the quality of drugs. Further surprise check/raid is to be carried out by the Drugs Inspectors in case these samples are declared as NSQ by the testing lab.
15. To pursue the court cases pending in different courts under the zone.
16. Technical survey as and when directed by the Drugs Controller General (India) from time to time.
17. To coordinate with the medical colleges under PvPI falling under the zone in respect of their activities related to PvPI as directed by DCG (I).
18. To discuss the matter with various State Drugs Controllers in the zone in connection with enforcement of

the provisions of D&C Act & Rules there under from time to time.

19. To monitor the statutory work of Drugs Inspector working under the zonal and sub-zonal offices.
20. To co-ordinate for answering the Parliament Questions and for obtaining the data from various State Licensing Authorities under the zone.
21. Preparation of Monthly / Quarterly / Annual Reports.
22. To participate in the joint inspection with respect to grant of NOC on Form 29 as per requirements.
23. To co-ordinate with various international regulatory agencies for inspections conducted by various international regulatory agencies as and when directed.
24. To organise workshop, seminar etc. as directed.
25. To conduct the function of Drugs Controller General (I) as delegated by him under rule 22 (b) & 122L and other rules of the Drugs & Cosmetics Act. Presently (w.e.f. 20.06.2011), the following functions are delegated to respective zonal officers for carrying out on his behalf: -
    a. Renewal of licences for blood banks.
    b. No objection certificates for grant of licence to manufacture drugs for the purpose of examination, test or analysis as provided under Rule 89 of the Drugs and Cosmetics Rules.
    c. No objection certificates for grant of permissions for manufacture for export only of unapproved / approved new drugs and drugs banned under sanction 26-A of the Drugs and Cosmetics Act.
    d. Permit for import of small quantities of drugs for personal use under Form 12B of the Drugs and Cosmetics Rules.
    e. No objection certificates for grant of permissions for import of dual use items, not for medicinal use.
26. Any other functions as assigned by DCG(I) / DDC(I).

ADMINISTRATIVE

1. Maintenance of Service records/leave records of Gazetted and Non-Gazetted Staff.
2. Matters related to confirmation and filling of posts wherein concerned zonal officer is the appointing authority.
3. Promotion of staff, recruitment of staff, relieving of staff and maintenance of seniority of Non-Gazetted employees.
4. To arrange DPC for eligible candidates to give regular promotion and under MACP Scheme to Group C & D Staff.
5. Maintenance of Rosters for Group C & D posts.
6. Preparation of annual budgets /preliminary and final estimate of expenditure etc.
7. Sanction of increments/fixation of Pay etc.
8. Preparation of reports/replies concerning to the above administrative function.
9. Handling of Cash and Accounts and maintenance of its records.
10. Preparation and submission of all types of bills including arrears, loans and advances to Pay & Accounts Office and maintenance of its records.
11. Preparation of Accounts reports-Monthly, Quarterly, Half Yearly and annual and maintenance of its records.
12. Maintenance of G.P.F. Records in respect of Group-D employees and correspondence regarding G.P.F. in respect of other staff.
13. Reconciliation work of Cash & Accounts with concerned PAO.
14. Purchase of perishable and non perishable store items and maintenance of its records.
15. Maintenance of all the documents (through FTS wherever it is installed).
16. To maintain the inventory and account of scientific books and journals etc.

17. Preparation of monthly, half yearly and annual return concerning to income tax through a qualified Chartered Accountant.
18. Annul Maintenance Contract (AMC) of office equipment and machineries etc.
19. All other administrative returns after receiving the queries from Directorate / Ministry from time to time.
20. Preparation of documents and bills in case of superannuation.
21. Reply under RTI Act.
22. Any other functions assigned by DCG(I) / DDC(I) from time to time.

ACTIVITIES OF ZONAL & SUB-ZONAL OFFICES OF CDSCO

The zonal / sub-zonal offices deal with various applications. The targeted time lines and subsequent actions for disposal of the applications received in the office of zonal/sub-zonal offices is as follows: -

Nature of application	Targeted time lines	First response & Action to be taken
Grant or renewal of Blood Bank license.	Targeted time line should be **21 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies are observed in the documents, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Grant or renewal of Vaccine manufacturing licenses	Targeted time line should be **30 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be

		proposed to the State Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Grant or renewal of Medical Devices Manufacturing licenses	Targeted time line should be **21 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Approval of Institution for carrying out Test on Drugs, Cosmetics and Raw materials as prescribed under Rule 150F of Drugs	Targeted time line should be **21 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State

& Cosmetics Rules.		Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Grant or renewal of LVP manufacturing licenses.	Targeted time line should be **21 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Grant or renewal of Bio-Tech/Bio-similar products manufacturing licenses	Targeted time line should be **30 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority

		with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
For approval BA/BE studies and Clinical Trial site.	Targeted time line should be **30 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Grant or revalidation of COPPs	Targeted time line should be **28 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority with a copy endorsed

		to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
Issuance of COPPs for additional products	Targeted time line should be **21 working days** from the date of submission of the application for scrutiny of the documents.	In case some deficiencies in the documents is observed, notice of compliance should be forwarded to the applicants within this time frame otherwise tentative inspection date should be proposed to the State Licensing Authority with a copy endorsed to the applicant. On conformation of the date, inspection to be carried out and the application shall be disposed of.
For any other inspection communicated from the Office of the Drugs Controller General (India)	As directed by DCG(I).	Inspection should be completed as per the requirement.

(The complaints regarding drug products are to be disposed of as early as possible in coordination with concerned agencies.)

The documents required to be submitted for various applications as mentioned above should be displayed in the notice board of the respective zonal office for perusal of the applicants and common public. The required documents for various applications are enclosed as Annexure B to G.

As soon as any document is received, the Zonal officer should mark the documents for scrutiny to the technical staff and the documents should reach to the concerned technical staff after proper noting on file or computerised system like FTS. The concerned technical staff should submit his or her observations on the documents in a specified checklist as enclosed in Annexure H to M following SOP No. 002.

Depending on the work load of the office, the technical staff may be asked to submit either directly his/her observations to the zonal / sub-zonal officer or may be routed through Drugs Inspector or STA. In case notice of compliance (NOC) to be issued to the applicants, the draft for approval (DFA) in this regard should also be prepared by the concerned technical staff and send along with the observations checklist for further necessary action. If after scrutiny, the documents are found in order, the zonal officer should instruct the concerned technical staff to propose for a joint inspection to the State Licensing Authority.

After the inspection date is proposed and the inspection was allotted to a particular inspector, the concerned file along with all the documents including observations checklist should be handed over to the concerned Drugs Inspector for joint inspection. The inspections may be carried out as per SOP No. 001.

After the joint inspection is carried out by the Drugs Inspector following SOP No. 001, inspection report in the prescribed proforma (which are annexed as Annexure N, R, S, T & U respectively) should be prepared. The concerned file along with the copy of joint inspection report should be

submitted by the Drugs Inspector to the zonal / sub-zonal officer as the earliest.

The zonal / sub-zonal officer should go through the report and record his observations on the report in writing and further necessary action as deemed fit shall be initiated by him. After completion of the whole process, the file should be returned back either to STA or person responsible for keeping the files in safe custody.

PROCEDURES FOR SAMPLING BY THE DRUGS INSPECTOR AND DRUGS SAMPLERS IN ZONAL/SUB-ZONAL OFFICE

Sampling of drugs & cosmetics from the marketing place for test/analysis is an essential tool to regulate the quality of the drugs & cosmetics moving in the distribution channel. Therefore, all zonal & sub-zonal office should frame a plan to draw samples of Drugs & Cosmetics under the Act at regular interval from various distribution points. Following sampling plan may be adopted: -

1. Each Drugs inspector shall collect at least 5 samples per month under the Drug and Cosmetics Act for testing. The sample shall be preferably collected from Government dispensaries, hospitals, rural outlets and from manufacturing premises during inspection. Emphasis may be on the collection of drugs samples from Govt. Hospital Medical Stores and CGHS Dispensaries on a routine basis.
2. At least 2 samples of Cosmetics shall be collected per month from retail outlets.

It is pertinent to mention here that the Drugs Inspector shall collect the samples as per the provisions of Drugs & Cosmetics Act only and survey samples may be collected when it is warranted for a specific purpose as directed. In case the samples collected under survey is declared as Not of Standard Quality, no further action can be initiated without drawing the samples under section 23 of the said

Act. Since, the Drugs Inspectors always collect the samples after disclosing his / her identity, hence the drugs samples should be collected only as specified under the Act. Survey samples should be drawn through Drugs Samplers who purchase the samples concealing his identity, which can further be sampled by an inspector under the Act, if requirements.

In CDSCO Drugs Samplers are deputed to purchase the drugs samples from the retail drug store as surrogated patient and get it tested from CDTL / RDTL and in case the products are declared as not of standard quality, steps are taken to draw the particular batch from that shop under Section 23 of the Drugs & Cosmetics Act through a notified Drugs Inspector to curb the menace of spurious/adulterated drugs. To achieve the aforesaid objectives, it is very much essential that the drugs samples collected by the Drug Samplers are tested at least for '**Identification'** and **'Assay'** and report should be sent by the Testing Laboratory as early as possible so that in case of NSQ report the sample of same batch No. can be drawn by the Drugs Inspector under sec 23 of the D&C Act. As a policy matter each drugs sampler may be given a target of purchasing at least 20 samples per month from the fast moving and generic products.

PROCEDURE TO CARRY OUT SURPRISE CHECK/RAID AND INVESTIGATION ON THE BASIS OF THE COMPLAINT.

Zonal & sub-zonal office receive complaints from some agencies and stake holders regarding movement of spurious/sub-standard drugs.

If a spurious or sub-standard is detected by zonal or sub-zonal office, utmost care should be taken to connect the manufacturer through all distribution channel from the source of collection of the impugned drug. The moment manufacturer involvement is established, the documented evidence collected in this regard should immediately be sent to the

concerned zonal officer under whose jurisdiction the manufacturing unit is located for further investigation through the Drugs Inspector of the said zone. It is advisable not to send the Drugs Inspector directly to the manufacturing unit or to the concerned State Licensing Authority for investigation without connecting the manufacturer with proper documented evidence.

Procedures to be adapted by the zonal officers to discharge the following functions that has been delegated recently by the Drugs Controller General of India under Rule 22 of the Drugs & Cosmetic Rules

1. Issue of No. Objection certificate for the grant of licence to manufacture drugs for the purpose of examination, test or analysis and provided under Rule 89 of the Drugs & Cosmetic Rules. (SOP in this regards enclosed in annexure V)
2. Issue of No. Objection certificate for the grant of permission for manufacture for export only of unapproved/ approved new drugs and drugs banned under section 26-A of the Drugs & Cosmetic Act. (SOP in this regards enclosed in annexure W)
3. Issue of Permit for import of small quantities of drugs for personal use under Form-12B of the Drugs & Cosmetic Rules. (SOP in this regards enclosed in annexure X)
4. Issue of No. Objection certificate for the grant of permission for import of dual use items, not for medicinal use. (SOP in this regards enclosed in annexure Y)

Further, Drugs Controller General of India vide Gazette notification GSR 425/E Dated 02nd June 2011 delegated his power under Rule 122 L of the Drugs & Cosmetic Rules relating to renewal of licences for operation of Blood banks, for processing of whole human blood, for components to the respective zonal officers and accordingly the modalities to be performed in this regard have been prescribed by DCG(I) vide OM No. DCGI/Misc./2011 Dated 09/06/2011 which is annexed as Annexure Z.

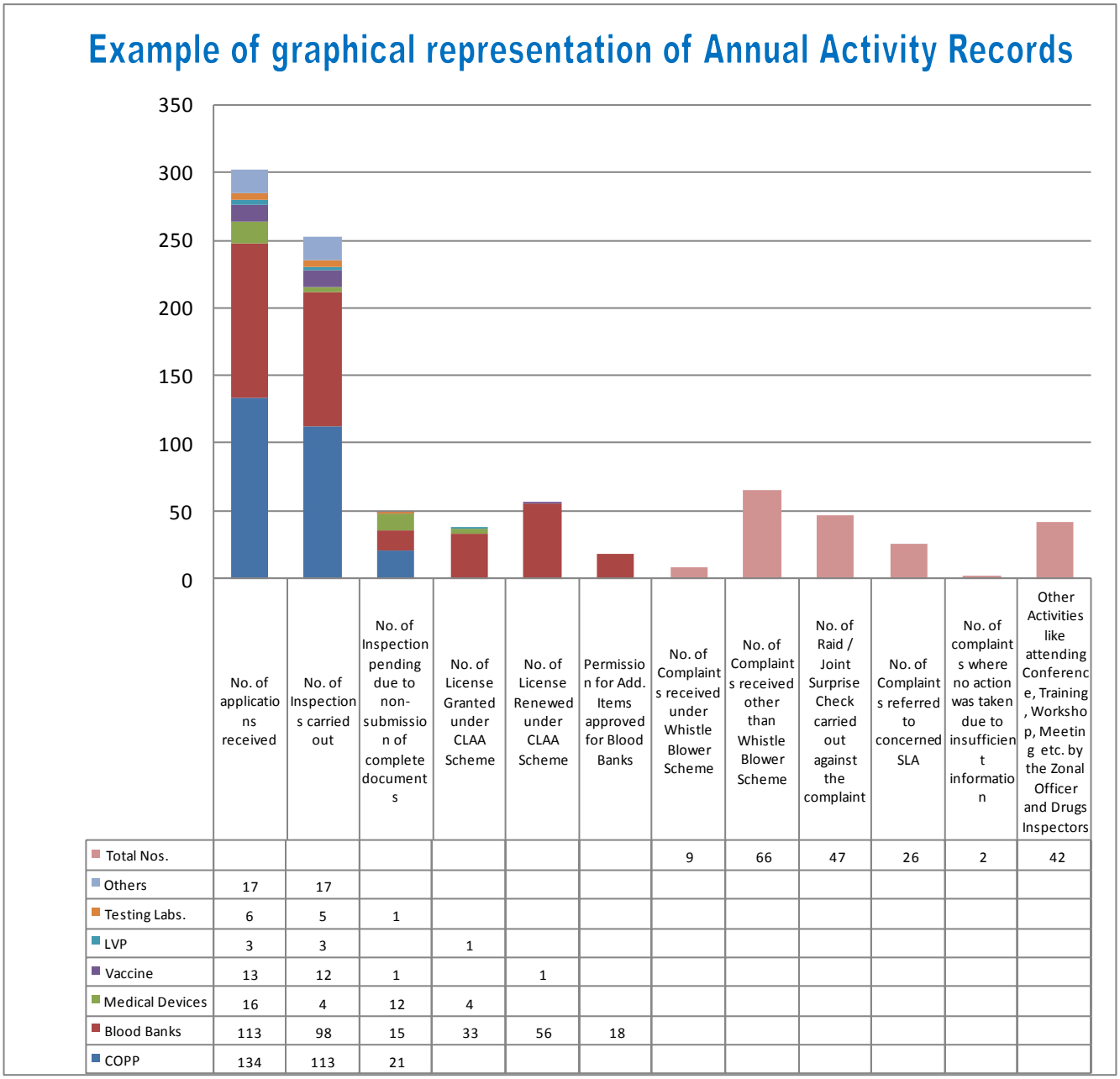
Procedure to be followed to maintain the records of all activities of Zonal & Sub-Zonal office

Following activities of the zonal / sub-zonal office should be recorded and the generated data in this regard should be preserved in graphical representation (as depicted below) and forward to the head quarter as well as the zonal offices at regular interval e.g. monthly and yearly.

Administrative	Technical
i. No. of receipts ii. No. of receipts processed and reply thereof iii. No. of receipt filed where no action is warranted. iv. No. of letters generated by this office v. Monthly expenditure statement. vi. No. of RTI applications received and disposed of.	i. No. of applications received a. For issuance / revalidation of COPPs. b. For grant / renewal of blood bank licenses. c. For grant / renewal of Medical Devices / Critical Diagnostics d. For grant / renewal of Vaccine mfg. units e. For grant / renewal of LVPs units f. For grant of approval for Testing Laboratory g. For grant of approval for Bio-Tech / Bio-Similar Products h. For grant of approval for BA/BE centres and CRO Inspections as directed by DCG(I). i. For grant of NOC to issue test licence in Form 29 j. For grant of permission in Form 12(B) for import

	of drugs for personal use. k. For grant of NOC for export l. For grant of NOC for dual use items m. For grant of COPPs for additional products ii. No. of samples collected under the Act, No. of test reports received, No. of test reports pending. iii. No. of sample collected under the survey, No. of test report received, No. of test reports pending. iv. No. of samples declared NSQ v. No. of complaint received. vi. No. of complaint attended. vii. No. of complaint where action was initiated. viii. No. of inspections carried out a. For issuance / revalidation of COPPs. b. For grant / renewal of blood bank licenses. c. For grant / renewal of Medical Devices / Critical

	Diagnostics d. For grant / renewal of Vaccine mfg. units e. For grant / renewal of LVPs units f. For grant of approval for Testing Laboratory g. other inspections ix. Other activities (workshop, seminar, meetings, trainings organized / attended)



	No. of applications received	No. of Inspections carried out	No. of Inspection pending due to non-submission of complete documents	No. of License Granted under CLAA Scheme	No. of License Renewed under CLAA Scheme	Permission for Add. Items approved for Blood Banks	No. of Complaints received under Whistle Blower Scheme	No. of Complaints received other than Whistle Blower Scheme	No. of Raid / Joint Surprise Check carried out against the complaint	No. of Complaints referred to concerned SLA	No. of complaints where no action was taken due to insufficient information	Other Activities like attending Conference, Training, Workshop, Meeting etc. by the Zonal Officer and Drugs Inspectors
Total Nos.							9	66	47	26	2	42
Others	17	17										
Testing Labs.	6	5	1									
LVP	3	3		1								
Vaccine	13	12	1		1							
Medical Devices	16	4	12	4								
Blood Banks	113	98	15	33	56	18						
COPP	134	113	21									
Total	302	252	50	38	57	18	09	66	47	26	02	42

No. of Drugs Samples drawn for Test / Analysis

Way of taking the samples	No. of samples drawn	No. of Test Reports received	No. of Test Reports Pending in the Laboratory	No. of reports declared as standard quality	No. of reports declared as Not of Standard Quality	Action Taken
Under Sec. 23 of D & C Act	415	199	216	183	16	i. 11 NSQ reports referred to CBI for further necessary action. ii. 5 NSQ reports are under investigation. iii. For 216 pending samples, the matter is taken up with the Govt. Analyst.
Under Survey	1290	1065	225	1057	08	i. 04 reports referred to SLA with a request to collect the sample u/s 23 of the Act. ii. Four shops were jointly raided by the DI of CDSCO & State Drugs Control to collect the sample u/s 23 of the Act.

List of SOPs and Annexure for Zonal & Sub-zonal Offices

SOP for carrying out inspection of Mfg. Units

CENTRAL DRUGS STANDARD CONTROL ORGANISATION
(Directorate General of Health Services)
Ministry of Health & Family Welfare

Title: General Procedure to be followed during On Site Evaluation (OSE) by Drugs Inspectors			
SOP No.:	001	**Department:**	Technical
Effective Date:		**Version:**	00
Review Date:		**Page No.:**	1of 4

1.0 OBJECTIVE:

The Central Drugs Standard Control Organization is responsible for laying down the standards of drugs, cosmetics, diagnostics and devices and enforcing the rules of Good Manufacturing Practice (GMP) in India for manufacturers of Finished Pharmaceuticals Products (FPP) and Active Pharmaceutical Ingredients (API). The objective of this document is to provide uniform enforcement procedures for onsite inspections to evaluate compliance of the quality system and infrastructure with nationally & internationally accepted GMP Standards (based on the reference document as prescribed in the D & C Act & Rules and WHO-GMP/TRS guidelines)

2.0. SCOPE:

This SOP sets out a uniform procedure for carrying out the notified inspections for following
modules under the preview of D & C Act & Rules and WHO-GMP-TRS throughout India.

2.1. Routine Inspection
- 2.1.1. Inspections for grant/renewal of licenses under CLAA Scheme.
- 2.1.2. Inspections for issuance / revalidation of COPPs as per WHO Certification Scheme for use in international commerce only.
- 2.1.3 Inspections for approval of Testing Laboratories.

2.2. Follow up inspection
- 2.2.1. Compliance verification inspection to authenticate the results of corrective actions.

2.3. Special Inspection
- 2.3.1. UNOPS/RITES inspection for NCB/ICB.

3.0 RESPONSIBILITIES:

3.1. It is the responsibility of concerned Drugs Inspector(s)/inspection team member(s) who carry out the aforesaid inspection to follow this SOP.

4.0. EXTERNAL EXPERTS OTHER THAN DRUGS INSPECTORS:

4.0.1. The Field expert may join the team as necessary, for example:-
- 4.0.1.1. For biologicals including vaccines — a biological products specialist;
- 4.0.1.2. A blood Bank Expert for blood Bank inspection.
- 4.0.1.3. Bio-tech expert for products like rDNA, monoclonal etc.

4.0.1.4. Clinical Pharmacologist or other experts for BA/BE centres or CROs.

5.0. PROCEDURES

5.1. PREPARING FOR THE INSPECTION

5.1.1. Receipt of File of the firm to the deputed inspection team member(s).

5.1.2. A review should be made relating to the firm to be visited from the documents available in the office file. This may include:-

5.1.2.1. Drug Manufacturing Licence.

5.1.2.2. The marketing Authorization for the applied products.

5.1.2.3. Site Master File

5.1.2.4. Evaluation of

i. Product records (process validation and stability studies),

ii. Reports of adverse Drugs reaction,

iii. Market complaint,

iv. Product recall record,

v. NSQ reports available in the office file,

vi. Discrepancies pointed out in previous inspection reports.

5.1.3. Preparation of the day wise inspection plan (1-3 days) as per Annexure A

5.1.4. Communication with the Local Authority for access to the site of inspection and regarding the Schedule of inspection.

5.2 CONDUCT OF INSPECTORS DURING INSPECTION

5.2.1 The inspectors are public servant within the meaning of Sec. 21 of IPC and should behave accordingly.

5.2.2. Inspector shall act according to the procedures for handling of confidential information. All information observed or passed to the inspector is confidential and shall not be disclosed to anybody other than his controlling authority.

5.2.3. Inspector shall neither carry with him any written or printed materials relating to other units nor disclose any information relating to another company.

5.2.4. The inspector's task is not only to point out deficiencies but also to provide guidance based on scientific evidence.

5.3. OPENING SESSION

5.3.1. **At the opening session:-**

The inspection usually begins with a meeting between the inspector(s), representatives of the firm or plant management and those responsible for the product or areas to be inspected.

5.3.1.1. The inspectors shall identify themselves and describe their jobs;

5.3.1.2. The inspection team shall give a written day wise plan for the inspection schedule as per Annexure- A

5.3.1.3. The inspector(s) shall inform to the firm management to ensure presence of concerned in-charge of the respective areas as per inspection plan.

5.3.1.4. The inspectors shall state which documents they need to examine once they have completed their preliminary tour of the site.

5.4 CONDUCT OF INSPECTION

5.4.1. There will be a preliminary tour of the site to allow the inspectors to get a general orientation of the site. It is recommended that the inspecting team start the plant tour as soon as possible after arrival. It is advisable to follow the inspection plan as per material flow.

5.4.2. Over the course of the inspection the inspectors shall review all procedures, production and laboratory records, validations and any other record or documentation relating to production and control of the production process.

5.4.3. It is advisable to check the items that are specific to certain areas of the facility, such as, Sampling /Dispensing of RM/PM, in process testing and working documents at the point of operation.

5.4.4. The inspection shall also include detailed tours of all production facilities, laboratories, stores, utilities, the plant's record and documentation centre.

5.4.5. The following specific issues shall be investigated, inter alia:

5.4.5.1 The suitability of the facility for its purpose, including the orderliness of its Lay-out for man and material movement, equipment and cleanliness;

5.4.5.2 The production equipment —its qualification/validation, calibration and cleanliness, preventive maintenance, daily equipment usage logs.

5.4.5.3. Whether production records are fully maintained and in real time.

5.4.5.4. Critical systems: HVAC, water system, filtered compressed air, drainage, ETP and any other relevant systems.

5.4.5.5. The documents such as master formulae, test specifications, Standard Operating Procedures, batch records (including protocols of analysis and documents relating to the control of printed material and labelling operations) requires close verification.

5.4.5.6. The inspection team may adopt the additional and other plan for areas of inspection based on the need of particular inspection for the required purpose.

5.5 CONCLUDING SESSION:-

5.5.1 The inspection shall conclude with a final session between inspectors and firm's representatives. The final session shall cover (at least)

5.5.2. A detailed listing of the findings and deficiencies found by the inspectors during the course of their inspection;

5.5.3. Issues of non-compliance observed during inspections shall be noted, discussed with firm representatives and handed over a copy of the same.

5.6. REPORTING AND SUBMISSION: -

The report of the inspection shall be prepared as per checklists provided for guidance in this document. The checklist for inspection of manufacturing units is a general example and need to be adopted as per specific need of the inspection and the products, e.g. for inspection of LVPs, Biological Products other than Vaccines and for issuance of COPPs. As the said checklist is primarily prepared on the basis of provisions

of Schedule M of the D & C Rules, it is imperative to adopt it as per the current applicable WHO GMP Guidelines in case of inspection for issuance of COPPs.

The report of Inspection shall be completed in all respects as per the checklist and submitted to the Controlling Authority for review, comments and for further necessary action as early as possible.

6.0. RECORDS:-

Annexure-A- Inspection Plan

Annexure-B- List of Documents to be submitted along with the application for grant /revalidation of COPPs.

Annexure-N- Inspection Checklist for GMP inspection

Annexure-R- Inspection Checklist for Blood Bank

Annexure-U-Inspection Checklist for Testing Laboratory

Annexure-T- Inspection Checklist for Medical Devices

Annexure-S Inspection Checklist for Vaccines Plant as per WHO Norms

` **7.0 ABBREVIATION(S)**

D & C ACT & RULE- DRUGS & COSMETICS ACT 1940 & RULES 1945

CDSCO – Central Drug Standard Control Organisation

CLAA-Central Licence Approving Authority

SLA – State Licensing Authority

OSE- On Site Evaluation

DML-Drug Manufacturing Licence

COPP – Certificate of Pharmaceutical Product

TDA- Technical Data Associate

RM/PM- Raw Material/Packaging Material

WHO TRS – World Health Organisation, Technical Report Series

NCB-National Competitive Bidding

ICB- International Competitive Bidding.

HVAC- Heating Ventilation & Air Conditioning System.

ETP- Effluent Treatment Plant

Note: - When the application is made for 'Site Certification' as prescribed in WHO TRS 908, similar procedure as mentioned above for inspection shall be adopted if all the categories of the products licensed for manufacturing on the premises / section applied for, fulfils the WHO GMP requirements with respect to stability, process validation, analytical method validation etc.

Prepared by	Checked by	Approved by

CENTRAL DRUGS STANDARD CONTROL ORGANISATION

(Directorate General of Health Services)

Ministry of Health & Family Welfare

Title: Screening of applications for COPPs, CLAA Items & Approved Testing Laboratories			
SOP No.:	002	**Department:**	Technical
Effective Date:		**Version:**	00
Review Date:		**Page No.:**	1 of 2

1.0 OBJECTIVE:

To lay down the procedure for scrutiny of the documents submitted along with the application in respect of grant/ revalidation of COPP & CLAA items.

2.0 SCOPE:

This procedure is applicable for screening of the documents submitted by the Pharmaceutical companies at respective CDSCO, Zonal and Sub-zonal Offices.

3.0 RESPONSIBILITIES:

3.1. For Scrutnization & Preparation of checklist and draft - Should be done by STA/TA/TDA at CDSCO.

3.2. For review, correction & approval of checklist and draft - Should be done by Technical Head of the Department.

4.0 DEFINITION(S):

COPP:– Certificate issued by the international drug regulatory authority in accordance with the WHO Certification Scheme on the Quality of Pharmaceutical Products moving in international commerce.

5.0 PROCEDURE:

5.1 Receive the documents in the FTS system (soft copy) and physically (hard copy). Trace the file and attach the received application with CD in the corresponding file.

5.2 Scrutinize the content of CD as per annexure no. 1

5.3 After scrutnization, prepare the checklist with details of documents submitted in the CD.

5.4 A draft should be prepared according to the observations listed in the checklist.

5.5 After preparation of Checklist and/or draft, it should be sent to the Technical head for review/ correction and approval through FTS system.

5.6 After approval of the checklist and/ or draft; it should be dispatched by fax or registered post to the manufacturer or SLA accordingly.

5.7 After dispatch, it should be attached to the corresponding file and close in FTS system.

5.8 Max. 15 days time is permitted for the screening of this type of application except Vaccines and Biotech Products for which maximum time limit is permitted 30 days.

6.0 ABBREVIATION(S)

CDSCO – Central Drug Standard Control Organisation

COPP – Certificate of Pharmaceutical Product

FTS – File Tracking System

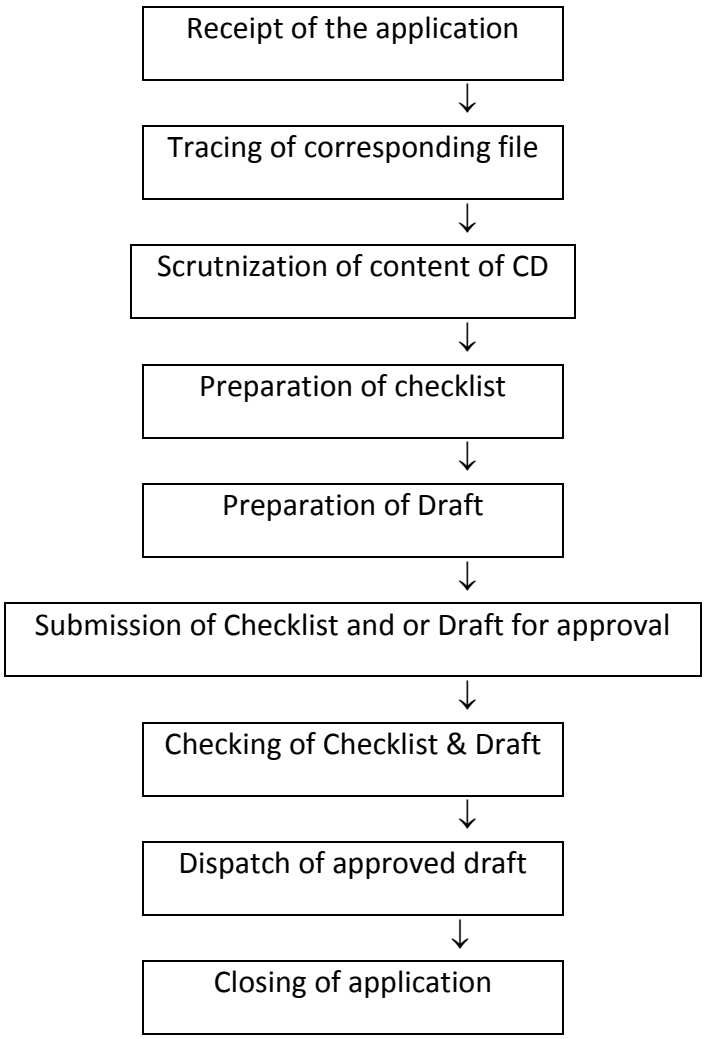
LVP- : Large Volume Parentral

OSD – Oral Solid Dosage

SLA – State Licensing Authority

WHO TRS – World Health Organisation, Technical Report Series

7.0 FLOW CHART:



Prepared by	Checked by	Approved by
Technical Data Associate	**Senior Technical Assistant**	**Deputy Drugs Controller (India)**

CENTRAL DRUGS STANDARD CONTROL ORGANISATION
(Directorate General of Health Services)
Ministry of Health & Family Welfare

Title: Maintenance of Service records/leave records of Gazetted and Non-Gazetted Staff			
SOP No.:	003	**Department:**	Administrative
Effective Date:		**Version:**	00
Review Date:		**Page No.:**	1 of 2

8.0 OBJECTIVE:

To lay down the procedure for maintenance of service records in service book of Gazetted and Non-Gazetted Staff as per FRs, SRs & GFRs rules.

9.0 SCOPE:

This SOP is applicable to all staff (permanent or temporary) at CDSCO.

10.0 RESPONSIBILITIES:

3.1. Head Clerk who supervises all the activities of administrative work.

11.0 DEFINITION(S):

Service Book: Service book is a record of every event occurring in the official life of a government servant. It has to be maintained for every government servant holding a permanent or a temporary post except for those who are not likely to be in service for more than one year or those holding non pensionable service (SRs 196 and 197).

Service book in form MSO (T)-27 (Revised) must be opened for all government servants from the date of entry into service and is to be maintained till his service is ceased.

12.0 PROCEDURE:

5.1 After receiving any order regarding promotion, confirmation, suspension, reduction in rank, withholding of increments, recovery loss, leave without pay, service break, award of President Police Medal/Indian Police Medal etc. for any Gazetted/ Non-Gazetted Staff, the said information to be updated in the service book of the individual and a copy of the order is attached with the service book.

5.2 All the leave details with respect to Earned & Medical should be recorded immediately and verified through HOO half yearly

5.3 Any increment in the salary is to be updated in the service book of the individual and a copy of the order is attached with the service book.

5.4 Any LTC (Leave Travel Concession) taken from home to visiting place is to be updated in the service book of the individual.

5.5 Any encashment of earn leave is to be updated in the service book of the individual

5.6 Any conformation, promotion or suspension in the service period of an individual is to be updated in the service book of the individual.

5.7 Periodic inspection of service book.

13.0 ABBREVIATION(S)

CDSCO – Central Drug Standard Control Organisation
HOO – Head of the Office
HC – Head Clerk

Prepared by	**Checked by**	**Approved by**
Lower Division Clerk	**Head Clerk**	**Deputy Drugs Controller (India)**

CENTRAL DRUGS STANDARD CONTROL ORGANISATION

(Directorate General of Health Services)
Ministry of Health & Family Welfare

Title: Matters related to promotion of Grade C & D posts			
SOP No.:	004	**Department:**	Administrative
Effective Date:		**Version:**	00
Review Date:		**Page No.:**	1 of 2

14.0 OBJECTIVE:

To lay down the procedure for matters related to promotion of posts.

15.0 SCOPE:

This SOP is applicable to all staff (permanent or temporary) at CDSCO.

16.0 RESPONSIBILITIES:

3.1 Head Clerk who supervises all the activities of administrative work.
3.2 Departmental Promotion Committee
3.3 Head of the Office

17.0 DEFINITION(S):

Promotion: Change of designation to higher position from lower position.

18.0 PROCEDURE:

5.1 FOR PROMOTION OF POSTS

5.1.1 Promotion is based on the principles of "Selection cum Seniority" as specified in the respective RR. The DPC should assess the suitability of the employees for promotion on the basis of their Service Records and with particular reference to the CRs for last five preceding years irrespective of the qualifying service prescribed in the Service/Recruitment Rules.

5.1.2 A noting is prepared by HC for the approval for promotion of posts from HOO.

5.1.3 After authorization by HOO, DPC meeting is conducted where its members as specified in the respective RR fix the promotion criteria and decide that the recommended person is fit or unfit for the promotion.

5.1.4 A clearance from the Vigilance by HOO/Department should also be obtained before making actual promotion of officer approved by DPC to ensure that no disciplinary proceedings are pending against the officer concerned.

5.1.5 The panel for promotion drawn up by DPC for 'selection' posts would normally be valid for one year. It should cease to be in force on the expiry of a period of one year or when a fresh panel is prepared, whichever is earlier.

5.1.6 After above procedure, order for promotion and fixation of pay may be issued by HOO.

6.0 ABBREVIATION(S)

CDSCO – Central Drug Standard Control Organisation
HOO – Head of the Office
HC – Head Clerk
DPC - Departmental Promotion Committee
RR – Recruitment Rules

7.0 REFERENCES:

1. Department of Personnel and Training, OM No. 22011/4/91-Estt.(A) dated 14. 9.1992
2. Administrative Services (Recruitment & Promotion) rules, 1991

Prepared by	**Checked by**	**Approved by**
Head Clerk	**Senior Most Drugs Inspector who is the member of the DPC**	**Deputy Drugs Controller (India)**

Annexure: A

GENERAL SHECDULE OF INSPECTION PLAN

(To be adopted for 1-3 Days as per requirements)

Day	Topic	Points to be covered	Average Time
First day	**Opening Meet**	Introduction Describe Purpose of Inspection Firm's presentation Preliminary review of ➢ SMF ➢ Lay out Plan	**9.00 -9.30 Hrs**
	Tea		
	Site Evaluation Tour		
	Raw Material & Packing Material Receipt area & Store	➢ Material Receiving Bay ➢ De-dusting procedure ➢ Assessment of Vendors' qualification ➢ Procedure for receipt of materials ➢ Quarantine / under test / Approved / rejected Area ➢ Sampling Area & procedure ➢ Dispensing Area / booth ➢ Storage Condition ➢ Stock Register & Physical Verification of raw materials along with distribution process	**9.30-1.30 Hrs**
	Lunch Break		**1:30 PM to 2:00 PM**
	Production area	➢ Change Rooms ➢ Gowning Procedure ➢ Internal Finishing of Core Processing area ➢ Air Filtration with Pressure Balancing ➢ Environmental Monitoring System ➢ Production Lay out & Men Material Movement ➢ Drainage system & Service Lines ➢ Equipments placement, Cleaning / sanitization & MOC ➢ Tools & Change Part Storage	**2:00 PM to 5:30 PM**

		➢ IPQC ➢ Bulk Quarantine ➢ Primary Packing ➢ Secondary Packing	
Second Day	**Quality Control & QA** **FGS** **Utilities**	➢ Physico Chemical Laboratory ➢ Instrumental Laboratory ➢ Microbiology laboratory ➢ Control Sample Storage ➢ Stability Study area ➢ Chemical, Glassware & Reagent Store ➢ Quarantine & Approved Store ➢ HVAC System ➢ Water System ➢ Air Compressor ➢ ETP, if any.	**9:00 AM to 11:30 AM**
	Document Evaluation	Drugs Manufacturing Licence Product Permission Site Master File Approved Vendor list SOPs Process Validation Cleaning Validation Qualification of Equipments Stability Study Data Market Complaint Product Recall Trainings Medical Examinations Internal Quality Audit Annual Product Review Master Validation Plan HVAC Validation Water System Validation Preventive Maintenance Programme(PMP)	**11:30 PM to 1:30 PM**
	Lunch Break		**1:30 PM to 2:00 PM**
	Documents evaluation (contd.)	Verification of 1 or 2 specific batch manufacturing record along with supporting documents.	**2:00 PM to 5:30 PM**
Third Day	**Report Preparation**	As per the specified check list.	**9:00 AM to 2:00 PM**
	Lunch Break		**2:00 PM to 2:30 PM**
	Concluding Session	Discussion with the management representative regarding non-compliance observations noted during the inspection and shares the observations with them.	**2:30 PM to 5:30 PM**

Annexure: B

DOCUMENTS REQUIRED FOR GRANT / REVALIDATION OF COPPs

1. Application from Manufacturer
2. Site Master file (as specified under WHO TRS 823)
3. Copy of Manufacturing License
4. List of Approved Products
5. List of products applied for issuance of COPPs
6. List of SOPs and STPs
7. Stability Data (3 batches)

   Accelerated / Real Time
8. List of equipment and Instruments
9. List of Technical staff, their qualification, experience and approval status
10. Manufacturing Layout Plan
11. Process validation for 3 batches of each product
12. Schematic diagram of Water system specifying circulation loop and MOC (Material of Construction)
13. Schematic diagram of HVAC system specifying terminal filter configuration
14. Export data of last 2 years in case of revalidation
15. Product Summery sheet

ANNEXURE: C

DOCUMENTS REQUIRED FOR GRANT/ RENEWAL OF BLOOD BANK LICENSE

1. Application from Blood Bank (Form 27-C).
2. Copy of License/ Last Renewal Certificate (for renewal application).
3. A plan of premises (Layout).
4. List of equipment & machinery.
5. Memorandum of association/ constitution of the firm (List of Directors).
6. Attested copies of certificates of competent technical staff (as per Drugs & Cosmetic Act and Rules 1945).

    6a) Academic Qualification Certificates,
    6b) Experience Certificates.

7. Documents relating to ownership or tenancy of the premises.
8. Licence fee receipt/ Chalan form
9. NOC from SBTC in case of stand-alone Blood Bank.
10. Registration Certificate of charitable trust (if applicable).

Annexure: D

Checklist for the documents required for Grant/Renewal of License for Vaccines

1. Application from Manufacturer
2. Site Master file (as specified under WHO TRS 823)
3.(a) Copy of Manufacturing License

(b) Form 27-D

4. Plan of premises
5. Constitution of the firm
6. List of equipment and Instrument
7. List of technical staff, their qualification, experience and approval status
8. Quality of water & its generation at the site
9. List of SOPs and STPs
10. Details of HVAC system including schematic diagram used for Classified Area
11. Washing arrangements for the components
12. Procurement of Master Cell Bank
13. Preparation of Cell Bank
14. Manufacturing process flow chart
15. Certificate of Analysis
16. Package Insert & Labels

Annexure: E

Check list for documents required for grant of license for Medical Devices.

1. Covering Letter
2. Authorization Letter
3. Form 27
4. Challan (Fess)
5. Constitution Details
6. Manufacturing Premises Plan/Layout
7. Full particulars of competent & regular technical staff
8. Site Master File
9. Specific Requirements
10. Device Master File
11. Product undertaking by manufacturer
12. ISO 13485:2003 Certificate (If any)
13. Full Quality Assurance Certificate (If any)
14. CE Design Examination Certificate (If any)
15. Declaration of Conformity (If any)
16. Any other approval

Annexure: F

Checklist for the documents required for Grant/Renewal of License for Testing Labs.

1. Application from Laboratories
2. License Fees (Treasury Receipt)
3. Form 36
4. List of SOPs and STPs
5. List of equipment and Instrument
6. List of technical staff, their qualification, experience and approval status
7. List of media for microbiology
8. List of reference standard
9. CPCSEA approval for animal house, if applicable
10. Laboratory layout
11. HVAC system for microbiological section, if applicable, in the testing Laboratory
12. NOC from Pollution Control Board for handling Bio-medical Laboratory waste
13. Contact details

Annexure: G

Checklist for the documents required for Grant/Renewal of License for LVP

1.	Application from Manufacturer
2.	Form 27-D
3.	Copy of Manufacturing License in case of renewal of licence
4.	Site Master file
5.	Plan of the premises along with details of the areas of each section
6.	Name, address, qualification and experience of the technical staff responsible for manufacture and testing. The qualification and experience should be backed up with attested proof.
7.	Name and address of the Directors, Partners or Proprietor
8.	Proof of Payment of fee (Challan)
9.	List of drugs intended to be manufactured (along with formula, pack size and details of primary packing material (glass or plastic).
10.	Ownership, rent or lease details of the premises in case of grant of licence
11.	Stability Studies for all products (3 batches, 6 Months) in case of renewal of license
	Accelerated
	Real Time
12.	List of machinery installed/ laboratory equipment
13.	Validation and calibration of essential and critical equipment and instruments
14.	Validation of HVAC system
15.	Copies of procurement documents of machinery and equipments (bills etc) in case of grant of licence
16.	Description of the manufacturing process in case of grant of licence

Annexure: H

Checklist for screening the documents related to COPPs.

Name of the firm: M/s .
Date of receipt of application: ----------
Subject: Revalidation/ Grant of COPP.

S.No.	Parameter	Status	Remark
1.	Application from Manufacturer	Yes/No	
2.	Site Master file (as specified under WHO TRS 823)	Yes/No	
3.	Copy of Manufacturing Licence	Yes/No	
4.	List of approved products	Yes/No	
5.	List of products applied for issuance of COPPs	Yes/No	
6.	List of SOPs and STPs	Yes/No	
7.	Stability Data (3 batches, 6 Months)	Yes/No	
	Accelerated	Adequate/ inadequate	
	Real Time	Adequate/ inadequate	
8.	List of equipment and Instrument	Yes/No	
9.	List of technical staff, their qualification, experience and approval status	Yes/No	
10.	Manufacturing layout	Yes/No	
11.	Process validation for 3 batches of each product	Yes/No	
12.	Schematic diagram of water system specifying circulation loop and MOC	Yes/No	
13.	Schematic diagram of HVAC system specifying terminal filter configuration	Yes/No	
14.	Export data of last 2 years in case of revalidation	Yes/No	
15.	Product summery sheet	Yes/No	

Opinion: The firm has submitted the documents vide Letter no. ……. dated ……. on scrutiny of the documents, it was observed that all aforesaid documents are in order.
The firm is ready for inspection.

Annexure: I

Checklist for screening the documents (Blood Bank)

Name of the firm: M/s

Date of receipt of application: ----------

Subject: Grant / Renewal of licence for the preparation of Whole Human Blood/ Components/ Aphaeresis

S.No.	Parameter	Status	Remark
17	Application from Blood Bank	Yes/No	
18	Licence no. and validity (in case of renewal)	Yes/No	
19	Form 27 C	Yes/No	
20	A plan of premises (Layout)	Yes/No	
21	List of equipment & machinery	Yes/No	
22	Memorandum of association/ constitution of the firm (List of Directors)	Yes/No	
23	Certificates of competent technical staff (academic, experience etc.)	Yes/No	
24	Documents relating to ownership or tenancy of the premises	Yes/No/NA	
25	Licence fee receipt/ Chalan form	Yes/No	
26	Whether inspection carried out	Yes/No	
27	NOC from SBTC in case of stand alone blood bank	Yes/No/NA	
28	Registration Certificate of charitable trust	Yes/No	
29	Letter received from SLA	Yes/No	

Opinion:

The firm has submitted the documents vide Letter no. ---------- Dated ---------- on scrutiny of the documents; it was observed that all

Aforesaid documents are in order/ aforesaid documents are yet to be submitted.

Annexure: J

Checklist for screening the documents for Vaccines

Name of the firm: M/s ----------.

Date of receipt of application: ---------

Subject: Grant of Drugs Manufacturing Licence

S. No.	Parameter	Status	Remark
1.	Application from Manufacturer	Yes/No	
2.	Site Master file (as specified under WHO TRS 823)	Yes/No	
3. (a)	Copy of Manufacturing Licence	Yes/No/NA	
(b)	Form 27-D	Yes/No	
4.	Plan of premises	Yes/No	
5.	Constitution of the firm	Yes/No	
6.	List of equipment and Instrument	Yes/No	
7.	List of technical staff, their qualification, experience and approval status	Yes/No	
8.	Quality of water & its generation at the site	Yes/No	
9.	List of SOPs and STPs	Yes/No	
10.	Details of HVAC system including schematic diagram used for Classified Area	Yes/No	
11.	Washing arrangements for the components	Yes/No	
12.	Procurement of Master Cell Bank	Yes/No	
13.	Preparation of Cell Bank	Yes/No	
14.	Manufacturing process flow chart	Yes/No	
15.	Certificate of Analysis	Yes/No	
16.	Package Insert & Labels	Yes/No	
17.	Letter from SLA	Yes/No	

Opinion: The firm has submitted the documents vide Letter no. ..... dated ..... on scrutiny of the documents, it was observed that

1. All aforesaid documents are in order.

The firm is ready for inspection.

Annexure: K

Checklist for Screening the documents required for Grant of Manufacturing License for Medical Devices

Name of the firm: M/s .
Date of receipt of application: ----------
Subject: Grant of manufacturing license for sterile & non-sterile Orthopaedic Implants

S.No.	Parameter	Status	Remark
1.	Covering Letter	Yes/No	
2.	Authorization Letter	Yes/No	
3.	Form 27	Yes/No	
4.	Challan (Fess)	Yes/No	
5.	Constitution Details	Yes/No	
6.	Approved Manufacturing Premises Plan/Layout	Yes/No	
7.	Full particulars of competent & regular technical staff	Yes/No	
8.	Site Master File	Yes/No	
9.	Specific Requirements	Yes/No	
10.	Device Master File	Yes/No	
11.	Product undertaking by manufacturer	Yes/No	
12.	ISO 13485:2003 Certificate (If any)	Yes/No	
13.	Full Quality Assurance Certificate (If any)	Yes/No	
14.	CE Design Examination Certificate (If any)	Yes/No	
15.	Declaration of Conformity (If any)	Yes/No	
16.	Any other approval	Yes/No	

Opinion: The firm has submitted the documents vide Letter no. ---------- dated ---------- on scrutiny of the documents, it was observed that

1. Aforesaid documents are yet to be submitted.

Annexure: L

Checklist for Screening the documents for Approved Laboratory

Name of the firm: M/s ----------

Date of receipt of application: ----------

Subject: Grant of licence or approval for carrying out test on Drug/Cosmetics or RM used in manufacture.

S.No.	Parameters	Status	Remarks
1.	Application from Laboratories	Yes/No	
3.	License Fees (Treasury Receipt)	Yes/No	
4.	Form 36	Yes/No	
5.	List of SOPs and STPs	Yes/No	
6.	List of equipment and Instrument	Yes/No	
7.	List of technical staff, their qualification, experience and approval status	Yes/No	
8.	List of media for microbiology	Yes/No	
9.	List of reference standard	Yes/No	
10.	CPCSEA approval for animal house, if applicable	Yes/No/NA	
11.	Laboratory layout	Yes/No	
12	HVAC system for microbiological section, if applicable, in the testing Laboratory	Yes/No	
13	NOC from Pollution Control Board for handling Bio-medical Laboratory waste	Yes/No	
14.	Letter received from State	Yes/No	
15.	Contact details	Yes/No	

Opinion:

The firm has submitted the documents vide Letter no. …….. dated ……..

On scrutiny of the documents, it was observed that -

1. Aforesaid documents are yet to be submitted.

Annexure: M

Checklist for screening the documents for Licensing of LVP

Name of the firm: M/s ----------

Date of receipt of application: ----------.

Subject: Grant/ Renewal of Manufacturing Licence for LVP section

S. No.	Parameter	Status	Remark
	Application from Manufacturer	Yes/No	
	Form 27-D	Yes/No	
	Copy of Manufacturing Licence in case of renewal of licence	Yes/No/NA	
	Site Master file (as specified under WHO TRS 823)	Yes/No	
	Plan of the premises along with details of the areas of each section	Yes/No	
	Name, address, qualification and experience of the technical staff responsible for manufacture and testing. The qualification and experience should be backed up with attested proof.	Yes/No	
	Name and address of the Directors, Partners or Proprietor	Yes/No	
	Proof of Payment of fee (Challan)	Yes/No	
	List of drugs intended to be manufactured (along with formula, pack size and details of primary packing material (glass or plastic).	Yes/No	
	Ownership, rent or lease details of the premises in case of grant of licence	Yes/No/NA	
	Stability Studies for all products (3 batches, 6 Months) in case of renewal of license	Yes/No/NA	
	Accelerated	Adequate/ inadequate	
	Real Time	Adequate/ inadequate	
	List of machinery installed/ laboratory equipment	Yes/No	
	Validation and calibration of essential and critical equipment and instruments	Yes/No/NA	
	Validation of HVAC system	Yes/No/NA	
	Copies of procurement documents of machinery and equipments (bills etc) in case of grant of licence	Yes/No/NA	
	Description of the manufacturing process in case of grant of licence	Yes/No/NA	
	Letter from SLA for inspection	Yes/No	

Opinion: On scrutiny of the submitted documents vide letter no. Nil dated 08.12.2010, it was observed that-

Aforesaid documents are yet to be submitted / Ready for inspection.

Annexure: N

Checklist for inspections of manufacturing units

(Based on Schedule –M and Technical Guidance note to the Industry)

1.	***Location and surroundings:***	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1.1	**How factory building is situated and controlled to avoid risk of contamination from external environment including open sewage, drain, public lavatory or any other factory which produces disagreeable or obnoxious, odors, fumes, excessive soot, dust, and smoke, chemical or biological emissions.** ***Pls specify industries / establishments adjoining manufacturing site.***			
1.2	**Building and premises: -**			
1.2.1	**How the building has been designed constructed and maintained to suit the manufacturing operations so as to produce drugs under hygienic conditions.** ***Pls specify nature of construction used in the facility in respect of its maintenance and hygienic conditions.***			

1.2.2	**Whether the building confirm to the conditions laid down in the Factories Act, 1948** ***Pls attach valid factory certificate/ license issued by the competent authority.***			
1.2.3	**Specify how the premises used for manufacturing operations and testing purpose prevents contaminations and cross contamination is:** **a) Compatible with other drug manufacturing operations that may be carried out in the same or adjacent area.** **Pls specify any special criteria for the product manufacturered. e.g. temperature, humidity, air class requirements maintained for aseptic products, etc.**			
1.2.4	**b) Whether adequate working space is provided to allow orderly and logical placement of equipment, materials and movement of personnel so as to avoid risk of mix-up between different categories of drugs and to avoid possibility of the contamination by suitable mechanism.** **Pls specify space left around the machines. Pls attach equipment lay out, men and material movement, waste movement if applicable.**			

1.2.5	**c) Describe the pest, insects, birds and rodents control system followed in the premises.** **Attach copy of pest / rodent control schedule along with contract agreement if any.**			
1.2.6	**d) What measures have been taken to make Interior surface of (walls, floors, and ceilings) smooth and free from cracks, and to permit easy cleaning** ***Specify material of construction and finish for walls, ceiling, floor, coving etc. i.e. whether Epoxy or PU coated, kota / granite stone with epoxy sealed joints, solid / GI / gypsum / cal. Silicate board ceiling with epoxy, PU or any other pre-fabricated panel (GRP, powder coated SS or Aluminum etc.) paint.***			
1.2.7	**e) What measures have been taken so that the production and dispensing areas are well lighted and effectively ventilated, with air control facilities.** **Pls specify the lux level maintained in various parts of the premise.**			
1.2.7.1	**Pls specify the air handling system used in various areas like stores, production, packing, QC areas etc.**			

1.2.8	**f) Specify drainage system which prevents back flow and entry of insects and rodents into the premises.** ***(pls specify number and location of drains installed)***			
1.3	**Water system: -**			
1.3.1	**Whether the unit has validated system for treatment of water drawn from own or any other source to render it potable in accordance with standards specified by BIS or local municipal norms.** **Pls specify source of raw water and give details of treatment processes, sampling points, distribution and storage system for raw and purified water.**			
1.3.1.1	**How bio burden in purified water controlled / reduced.**			
1.3.2	**How water tank are cleaned periodically and records maintained thereof. How water distribution system is sanitized to control microbial contaminations.**			
1.4	**Disposal of waste: -**			
1.4.1	**Specify the system of disposal of sewage, and effluents (solid, liquid, and gas) from the manufacturing site.** **(Enclosed the copy of NOC obtained from State Pollution Control Board in this regard).**			

1.4.2	**Whether provision for disposal of bio-medical waste made as per the provisions of the Bio Medical Waste (Management and Handling) Rules 1996.**			
2.	***Warehousing Area: -***			
2.1	**Whether adequate areas have been allocated for warehousing of Raw Materials, intermediates, Packaging Material, products in quarantine, finish products, rejected or returned products.** **How these areas marked or segregated.** **Please specify the total area provided for warehousing.**			
2.2	**How the warehousing areas being maintained to have good storage conditions. Are they clean and dry and maintained within acceptable temperature limits?**			
	Specify the storage arrangement provided for materials which sensitive to temperature, humidity and light and how the parameters are monitored. **Is cold room or deep freezers required for storage of goods? If yes, how the temperature is monitored.**			

2.2.1	**Whether proper racks, bins and platforms have been provided for the storage.**			
2.3	**Whether receiving and dispatch bays are maintained to protect in coming and out going materials.**			
2.3.1	**How incoming materials are treated and cleaned before entry into the plant.** **Please specify the cleaning system for the outer surface of the container.**			
2.4	**How quarantined materials are segregated from other materials.** **How access to quarantined area is restricted.**			
2.5	**Whether separate sampling area for active Raw Materials and Excipients is provided and maintained.** **If yes, what is the control on entry of material and men into the sampling area. Whether reverse LAF have been provided for sampling. Whether log book for sampling booth maintained.** **If not what provision has been made for sampling so as to prevent contamination, cross contamination and mix-ups at a time of sampling.**			
	Specify the arrangements			

	provided to sample the primary packaging materials foils, bottles, etc which are used as such.			
2.5.1	**Pls specify sampling plan used.** **Which type of sampling tools are used and how they are cleaned, dried and maintained.**			
	How containers are cleaned before and after sampling. Who carries out the sampling? **(Pls specify whether the sampling is carried out as per the current SOP).**			
2.5.2	**What precautions are taken during sampling of photosensitive, hygroscopic materials?**			
2.6	**What provisions have been made for segregated storage of rejected, recalled or returned materials or products.** **How is the access to these areas restricted.**			
2.7	**How highly hazardous, poisonous and explosive materials, narcotics, and psychotropic drugs are handled and stored.** **How these areas are safe and secure.** **Is there certification from competent authority for handling of explosives etc. If any. Pls attach the certificate issued by**			

	the competent authority.			
2.8	**How printed secondary packaging materials are stored in safe, separate and secure manner.**			
2.9	**Specify the arrangement provided for dispensing of starting materials.** **What is the control on entry of material and men into the dispensing area? Whether reverse LAF have been provided for dispensing with back ground clean air supply.** **Whether pressure differential is maintained between the dispensing and adjacent areas.**			
2.9.1	**Which type of dispensing tools are used and how they are cleaned, dried and maintained.** **How containers are cleaned before and after dispensing. Who carries out the dispensing?** **(Pls specify whether the dispensing is carried out as per the current SOP).**			
2.10	**How and where sampling of sterile materials carried out.**			
2.11	**What steps are taken against spillage, breakage and leakage of containers?**			
2.12	**What provisions have been made to prevent the entry of rodents, insects, birds.**			

	Which substance is used for pest control and how it is handled. **(Pls specify whether the pest control is carried out as per the SOP).**			
3.	***Production Area: -***			
3.1	**Please specify the design of the manufacturing area which allow uni-flow and logical sequence of operations so as to prevent product contamination/ mix ups.** **Is there any criss cross of flow of materials and men.** **Specify the position of IPQC lab in the manufacturing area .** **Please specify whether non storage areas used for storage of any material.**			
3.2	**Whether separate dedicated and self-contained facilities have been provided for the production of sensitive pharmaceutical product like Penicillin, Biological preparation with like micro-organism, Beta lactam, Sex Hormones and Cytotoxic substances.** **If yes pls explain how and attach copy of plan of premises of each category of drug.**			
3.3	**Please specify the provisions of storage of dirty, washed and cleaned equipment parts, tool room, in process storage areas**			

	etc. Which provide sequential / logical manner so as to prevent contamination and cross contamination?			
3.4	**Please specify how service lines like pipe work, electrical fittings, ventilation openings etc. are identified by colors for nature of supply and direction of the flow.** **Whether service lines in production areas are through service pendants.** **If not, how they are placed so as to avoid accumulation of dust.**			
4.	***Ancillary areas: -***			
4.1	**Please specify the position of rest and refreshment rooms and mention whether they are separate and not leading directly to the manufacturing and warehouse areas.**			
4.2	**Are there general change rooms in plant?** **Are toilets, change room separate from mfg. Area? Pls specify number of washing station & toilets provided for number of users.** **Whether change facilities separated for both sexes.** **How many sets of protective garments provided for each personnel entering production area.**			

	Is there in house general laundry for garment washing / cleaning? If not how garments washing are carried out and monitored.			
4.3	**Whether maintenance workshop is separate and away from production.**			
4.4	**Whether animals for production or testing are housed in the facility if so whether areas housing animals are isolated from other areas.** **Please specify the provision of air conditioned and ventilation system for the animal house.** **How quarantined, under test and tested animals housed and controlled.** **How animal carcass are disposed of.** **Pls attach copy of CPCSEA.**			
5.	**Quality Control Area: -**			
5.1	**Whether QC area is independent of production area.** **Whether QC carries out its own:** • **physico-chemical testing,** • **biological testing,** • **microbiological testing & sterility testing and** • **Instrumental testing.**			

	Whether firm is outsourcing testing. If yes names of the testing laboratories contacted or approved. Pls give list of test currently outsourced. **In case of contractual testing what are the responsibilities of contract giver and contract acceptor. (Copy of the contract should be enclosed)** **Are there safety installation such as shower, eye washer, fire extinguisher etc in the laboratory.** **Is there separate area for humidity chambers for stability studies. How many humidity chambers have been provided. Pls attach stability calendar.**			
5.2	**Please specify the arrangement provided for handling and storage of test samples, retained samples, reference standards / cultures, reagents.** **Whether separate area for storage of reagents and glassware provided.** **Whether separate records room is provided.**			
5.2.1	**How hazardous or poisonous materials are stored and handled.**			
5.3	**How environmental conditions are met during the course of storage and testing of samples.**			

	Whether separate washing and drying area provided.			
5.3.1	**Which grade of glassware are used in assay procedures.**			
5.3.2	**Whether separate AHU's are provided for biological, microbiological and radio iso-topes testing areas with** **HEPA filter arrangement.**			
5.4	**Whether separate areas provided for sterility testing within microbiology lab.** **Whether support areas are under AHU.** **Whether double door autoclave provided for sterilization of materials.**			
	Whether entry to the sterility area is through three air lock systems. **What is the air class of these testing areas and whether pressure difference is maintained in these areas?**			
	Which types of workbenches are provided in these areas for testing? **When was the last filter integrity tests performed on HEPA filters.**			
	How waste (cultures etc) disposed of. **Whether in case of antibiotic potency testing, statistical proof of the determination of potency and validity of the test carried out.**			

6.	***Personnel: -***			
6.1	**Whether the manufacturing and testing of drugs is conducted under approved technical staff** **Names of Technical Staff alongwith qualification & experience** **<u>For Manufacturing:</u>** **<u>-</u>** **<u>For Analysis:</u>**			
6.2	**Please specify whether head of Q.C. is independent of manufacturing unit**			
6.3	**Name, qualification and experience of the personnel responsible for Quality Assurance function.**			
6.4	**Whether responsibilities for production and QC laid down and followed.**			
6.5	**Whether adequate number of personnel employed in direct proportion to the work load.**			
6.6	**What is the firm's policy on training of personnel at various levels?**			
7.	***Health, clothing and sanitation of workers: -***			
7.1	**Whether personnel handling Beta lactam antibiotics are tested for penicillin sensitivity before employment.**			

7.2	**Whether personnel involved in handling of sex hormones, cytotoxic and other portent drugs are periodically examined for adverse effect.** **(Pls specify whether the current SOP is followed or not).**			
7.3	**Whether all personnel prior to employment have undergone medical examination including eye examination and all free from Tuberculosis, skin and other communicable or contagious diseases**			
	Whether there is a SOP for medical examination.			
	Pls give name and qualification of contracted medical officer for medical examination.			
	Whether investigational reports, films of X rays etc. preserved. **Whether records of such medical examination are maintained thereof**			
7.4	**Whether all personnel are trained to ensure high level of personal hygiene.** **Pls attach training calendar of last two years.**			
7.5	**Whether proper uniforms and adequate facilities for personal cleanliness are provided.** **Pls specify nature and type of dress used by the personnel in**			

	various areas of operation. **How many dress/footwear have been provided to each personnel.** **Please specify whether cross over bench is in place in the change room and if so whether it rule out the possibility of entering dust particle to the clean side.** **Whether arrangements provided for cleaning of outside dust and dirt from foot** **Please specify whether hands are disinfected before entering the production area** **Whether for sterile garments in house clean laundry has been provided.**			
8.	***Manufacturing Operations and Controls: -***			
8.1	**Whether the contents of all vessels and containers used in manufacture and storage is conspicuously labeled with the name of the products. Batch no, Batch Size, and stage of manufacture along with signature of technical staff.**			
8.1.1	**Whether the products not prepared under aseptic conditions are free from pathogens like Salmonella, Escherichia coli, Pyocyanea etc.**			

8.1.2	**If yes, pls give brief account of measures taken to assure freedom from pathogens.**			
8.2	***Precautions against mix-up and cross-contamination: -***			
8.2.1	**Whether proper AHU, pressure differential, segregation, status labeling have been provided to prevent mix-up and cross-contamination in manufacturing area**			
	Pls specify the areas of dust generation and mechanism involved in controlling the dust.			
	Do all the areas have their own independent air locks separately for men and material entry.			
	What criteria of pressure differential has been set for production v/s adjoining areas.			
	Whether various operations are carried out in segregated areas.			
8.2.2	**Whether processing of sensitive drugs like Beta lactum Antibiotics and Sex Hormones is done in segregated areas with independent AHU and proper pressure differentials alongwith demonstration of effective segregation of these areas with records.**			

	Please specify what measures has been taken to prevent contamination of products with Beta Lactum Antibiotics, Sex harmons and cyto toxic substances			
8.2.3	**What measures has been taken to prevent mix-ups during various stages of production.**			
	Whether equipments use for production are labeled with their current status.			
8.2.4 & 5	**Whether packaging lines are independent and adequately segregated.**			
	How line clearance is performed. Whether records of line clearance is maintained according to appropriate checklist.			
8.2.6	**Whether separate carton coding area has been provided or online carton coding is performed** **How carton coding procedure is controlled.**			
8.2.7	**Please specify how temperature, humidity and air filtration are controlled in the areas where raw material and/or products are exposed and handled.**			
8.2.8	**How access of authorized persons to manufacturing areas including packaging is controlled.**			
	Whether separate gowning provision is follows before entering into the procedure.			

8.2.9	**Whether segregated secured areas for recall or rejected materials or for such material which are to be processed or recovered are provided. Please specify the room No. of such areas in the plant.**			
9.	***Sanitation in the Manufacturing areas:-***			
9.1	**Specify the cleaning procedure of the manufacturing areas.** **Whether cleaning procedure is validated.** **Please specify validation protocol No. of the same.**			
9.2	**Whether the manufacturing areas are used as the general thoroughfare and storage of materials not under process.**			
9.3	**Whether a routine sanitation program is in place.** **Please specify detailed account of sanitation proramme specific to various areas, equipment.**			
9.4	**Dose the location facilitate cleaning of equipment as well as the cleaning of the areas in which they are installed.**			
9.5	**Whether production area is adequately lit. If yes.** **Please give lux levels provided in production, visual inspection and other areas.**			

10	***Raw Materials: -***			
10.1	**Whether the hard copies of records of Raw Materials are maintained as per schedule-U.**			
10.2	**Please specify the procedures followed receiving and processing of in-coming materials (Starting materials and packing material).**			
	Whether first in / first out or first expiry principal has been adopted.			
10.3	**How they are labeled and stored as per their status – Under Test, Approved and Rejected**			
10.4	**Whether incoming materials are purchased from approved sources.**			
	What is the procedure for approving the source for incoming materials.			
	Whether the raw materials are directly purchased from the manufacturers.			
	Whether list of approved vendors is available to the user.			
10.4	**How damaged containers are identified recorded and segregated.**			

10.5	**Whether each batch of a consignment is considered for sampling, testing and release.**			
	Whether all the containers of each batch of starting materials is sampled for identification test.			
10.6	**Whether labels of raw material in the storage area have information like** (a) designated name of the product and the internal code reference, where applicable, and analytical reference number; (b) manufacturer's name, address and batch number; (c) the status of the contents (e.g. quarantine, under test, released, approved, rejected); and (d) the manufacturing date, expiry date and re-test date.			
10.7	**Whether separate areas are provided for under test, approved and rejected materials.**			
	How control on temperature and humidity conditions, wherever necessary, maintained in these storage areas.			
10.8	**How the containers from which samples have been drawn labeled.**			
10.9	**Please specify the procedures by which it is ensured that the raw materials which has**			

	been released by the Quality Control Department and which are within their shelf life are going to be used in the product.			
10.10	**How materials are stacked in the Stores i.e on Pallets, racks etc.**			
11	***Equipment: -***			
11.1	**Whether the equipments are designed aiming to minimize risk of error and permit effective cleaning in order to avoid cross contamination, build up of dust.**			
	Whether all equipment are provided with log book.			
	Please specify the procedures to clean the equipment after each batch production.			
	Whether validity period for use after the cleaning of equipment is specified.			
	Whether separate area is provided for storage of machine parts etc.			
11.2	**Whether balances and other measuring equipments with appropriate range are available in the Raw Material stores & production areas and they are calibrated in accordance with SOP maintained.** **Specify the calibration schedule of the balances.**			

11.3	**Please specify material of construction of contact parts of the production equipments.**			
11.4	**Which types of lubricants are used in the equipment.** **Specify the quality and control reference No. of these lubricants.**			
11.5	**Specify the procedures to remove defective equipments from production areas.**			
12	***Documentation and Records: -***			
12.1 **12.1.1** **12.2** **12.3**	**How the documents are designed, prepared, reviewed and controlled to provide an audit trail. Whether documents are approved signed and dated by appropriate and authorized person.** **Whether documents are approved signed and dated by appropriate and authorized person.** **Whether documents specify title, nature and purpose.** **Whether documents are regularly reviewed and kept up to date. If yes. Please specify review period.** **Please attached the list of documents maintained by the firm.**			

12.4	**Whether the records are made at the time of each operation in such a way that all significant activities concerning to the production are traceable.**			
12.5	**Whether data is recorded by electronic data processing system or by other means. If by electronic data processing system then how access is controlled to enter, modify etc. the data.**			
	Whether master formula and detailed operating procedures are maintained as hard copy.			
	Who is responsible for maintenance of these records.			
13	***Labels and Other Printed Materials:***			
13.1	**Whether the printing is in bright colour and legible on labels and other printed materials.**			
	How printed labels (art work) are approved. Is there any SOP for this if yes please give current SOP No.			
	Which colour coding system is used to indicate the status of a product and equipment.			
13.2	**How printed packaging materials, product leaflets etc. are stored separately to avoid chances of mix-up.**			

13.3	**How labels cartons boxes circulars inserts and leaflets are controlled.**			
13.4	**Whether the samples from the bulk are drawn tested, approved and released prior to packaging and labeling.** **How carryout the sampling**			
13.5	**How records of receipt of all labeling and packaging materials are maintained.**			
	Whether re-conciliation of used packaging materials is maintained. **Whether unused packaging materials return to the store or destroyed.**			
	How returned/unused packaging material like foils is controlled so as to prevent contamination and cross- contamination.			
13.6	**How the labels of reference standard and culture maintained.**			
14	***Quality Assurance: -***			
14.1 **(a)**	**Specify the comprehensive quality assurance system maintained by the firm *Inter-alia* to cover deviation, reporting, investigation and change control.** **How the products are designed and developed in accordance with GMP.**			

(b)	**Please specify the arrangements provided to ensure that correct starting and packaging materials are used for manufacture.**			
(c)	**Please specify the mechanism by which all control like IP QC Calibration, Validation etc. are ensured.**			
(d)	**Please specify the mechanisms to ensure that the finished product has been correctly processed and checked in accordance with the established procedures.**			
(e)	**Please specify the mechanisms to ensure that Pharmaceuticals products are released for sale by authorization person.**			
15	***Self Inspection and Quality Audit: -***			
15.1	**Whether the firm has constituted a self inspection team supplemented with a quality audit procedure to evaluate that GMP is being followed. If no. How internal audits are carried out.**			
	What is the system of monitoring, evaluation of self inspection.			
	How conclusion and recommended correcting actions are followed and adopted.			
15.2	**What is the frequency of self-inspection.**			
15.3	**Is there any proforma for carrying out the self-inspection.** **Please indicate the date of last self-inspection.**			

16	***Quality Control System: -***			
16.1 to 16.3	**Please specify the details of quality control system of the unit.**			
	How the reference standards are stored, evaluated and maintained. **Please provide list of reference standard and reference impurities procured from the authentic sources.**			
	Please specify the procedures of preparation of working standard from the reference standards.			
16.4 & **16.5**	**Whether SOPs for sampling, inspecting, testing of Raw Materials, Finish products, Packing Materials and for monitoring environmental conditions are available.**			
	Whether approved specifications for different materials, products, reagents, solvents including test of identity content, purity and quality available.			
16.7	**How reference samples from each batch of the products are maintained.**			
16.6 &	**Who releases batch of the products for sale**			

16.8 **16.9**	**or supply.**			
	Whether there is check list for release of a batch. Please specify current SOP No. for batch release.			
	Please specify the sampling procedures from various stages of production.			
	How it is ensured that the sample collected are representative of the whole batch.			
16.10 **16.11**	**Please specify the procedures for carrying out the stability studies.**			
	Under what condition stability studies of the products are tested. **How many stability chambers have been provided.**			
	How self life is assigned to a product. Please give current stability protocol No.			
	Whether records of stability studies are maintained.			
	Please attach stability calendar of last year.			
	How complaints are investigated.			
16.12	**How instruments are calibrated and at which interval.**			
	How testing procedure validated before they are adopted for routine testing.			
	Specify the validation procedure is responsible for validation of procedures.			

	How validation procedures are documented (Please indicate various protocols/ recoding system applied during validation).			
16.13	**Whether specifications for raw materials intermediates final products and packaging materials are available.**			
	Whether periodic revision of these specifications are carried out. **Please specify No. of STPs being maintained by the firm.**			
16.14	**Which pharmacopoeias in original are available in the plant.**			
17	***Specifications: -***			
17.1	**Whether specification of raw material include.** **(a) the designated name and internal code reference;** **(b) reference, if any, to a pharmacopoeial monograph;** **(c) qualitative and quantitative requirements with acceptance limits;** **(d) name and address of manufacturer or supplier and original manufacturer of the** **material;** **(e) specimen of printed material;**			

	(f) directions for sampling and testing or reference to procedures; **(g) storage conditions; and** **(h) Maximum period of storage before re-testing.** **Whether specification of finished product include** **(a) the designated name of the product and the code reference;** **(b) the formula or a reference to the formula and the pharmacopoeial reference;** **(c) directions for sampling and testing or a reference to procedures;** **(d) a description of the dosage form and package details;** **(e) the qualitative and quantitative requirements, with the acceptance limits for release;** **(f) the storage conditions and precautions, where applicable, and** **(g) the shelf-life.**			
17.2	**Whether the container and closures meet the pharmacopial specifications.** **Whether second hand or used containers and closures used.**			
18	**Master Formula Records: -**			

	How master formula records are prepared, authorized and controlled.			
	Whether head of production, quality control and quality assurance unit endorse this documents. Whether master formula is batch size specific.			
	Whether all products have master formula containing. **(a) the name of the product together with product reference code relating to its specifications;** **(b) the patent or proprietary name of the product along with the generic name, a description of the dosage form, strength, composition of the product and batch size;** **(c) name, quantity, and reference number of all the starting materials to be used. Mention** **shall be made of any substance that may 'disappear' in the course of processing.** **(d) a statement of the expected final yield with the acceptable limits, and of relevant intermediate yields, where applicable.** **(e) a statement of the processing location and the principal equipment to be used.** **(f) the methods, or reference to the methods, to be used**			

	for preparing the critical equipments including cleaning, assembling, calibrating, sterilizing; **(g) detailed stepwise processing instructions and the time taken for each step;** **(h) the instructions for in-process control with their limits;** **(i) the requirements for storage conditions of the products, including the container, labeling and special storage conditions where applicable;** **(j) any special precautions to be observed;** **(k) packing details and specimen labels.**			
19 & 20	**Packaging Records: -**			
	Whether authorized packaging instructions for each products, pack size and type are maintained and complied with. **Whether following are included in the packaging instructions.** **(a) Name of the product;** **(b) description of the dosage form, strength and composition;** **(c) the pack size expressed in terms of the number of doses, weight or volume of the product in the final container;** **(d) complete list of all**			

	the packaging materials required for a standard batch size, including quantities, sizes and types with the code or reference number relating to the specifications of each packaging material.; **(e) reproduction of the relevant printed packaging materials and specimens indicating where batch number and expiry date of the product have been applied;** **(f) special precautions to be observed, including a careful examination of the area and equipment in order to ascertain the line clearance before the operations begin.** **(g) description of the packaging operation, including any significant subsidiary operations and equipment to be used;** **(h) details of in-process controls with instructions for sampling and acceptance; and** **(i) Re-cancellation after completion of the packing and labeling operation.** **(j) Whether line clearance records are part of batch packing records.**			
21	***Batch Processing Records*** **(BPR)**			
21.1	**Whether BPR are based on current master formula record.**			

	How BPR are designed to avoid transcription errors. **Whether the Batch Processing Records for each product on the basis of currently approved master formula is being maintained.** **Whether following information are recorded in BPR** **(a) the name of the product,** **(b) the number of the batch being manufactured,** **(c) dates and time of commencement, significant intermediate stages and completion of production.** **(d) initials of the operator of different significant steps of production and where appropriate, of the person who checked each of these operations,** **(e) the batch number and/or analytical control number as well as the quantities of each starting material actually weighed,** **(f) any relevant processing operation or event and major equipment used,** **(g) a record of the in-process controls and the initials of the person(s) carrying them out,and the results obtained,**			

	(h) the amount of product obtained after different and critical stages of manufacture (yield), **(i) comments or explanations for significant deviations from the expected yield limits shall be given,** **(j) notes on special problems including details, with signed authorization, for any deviation from the Master Formula,** **(k) Addition of any recovered or reprocessed material with reference to recovery or reprocessing stages.** **Specify the procedures for all the entries made in BPR's.**			
22	**Standard Operating Procedure and Records: -**			
22.1 to 22.5	**Whether SOPs and records are being maintained and complied for the following.** **SOP for receipt of in coming material** **(a) SOP for Internal labelling, quarantine, storage, packaging material and other materials** **(b) SOP for each instrument and Equipment** **(c) SOP for sampling** **(d) SOP for batch numbering** **(e) SOP for testing** **(f) SOP for equipment assembly and validation** **(g) SOP for Analytical**			

	apparatus and calibration **(h) SOP for maintenance, cleaning and sanitation** **(i) SOP for training and hygiene for the personal** **(j) SOP for retaining reference Samples** **(k) SOP for handling, re-processing and recoveries** **(l) SOP for distribution of the product** **(m) SOP for warehousing of products.** **Whether applicable SOPs are available in each area where they are required.** **Whether recording formats are referred in SOP.** **Is there SOP for writing an SOP.**			
23	**Reference Samples**			
23.1 & 2	**Specify the procedures for collection of reference samples of active ingredients and finished formulations and how they are stored and maintained.**			
24	**Reprocessing and Recoveries**			
24.1 – 24.3	**Specify the procedures for reprocessing.** **Whether reprocessed batch is subjected to stability evaluation.** **Whether the recoveries are added into the subsequent batches. If yes specify the procedures.**			
25	**Distribution records**			

	Whether pre dispatch inspections are carried out before release.			
	Whether periodic audits of distribution center are carried out to access warehousing practices			
	Whether distribution records are part of the batch record. If not how batch wise distribution record up to retail levels are maintained.			
	Whether instruction for warehousing and stocking of products like LVPs, Heat sensitive etc are available in store.			
26	**Validation and Process Validation: -**			
26.1 to 26.5	**Specify the validation policy of the company.** **Whether validation master plan has been prepared.**			
	Whether validation studies of processing, testing and cleaning procedures are conducted as per pre defined protocol.			
	How records and conclusion of such validation studies are prepared and maintained.			
	Whether master formula is based on approved process validation.			
	Specify how significant changes to the manufacturing process equipments material etc are controlled.			

	Whether DQ,IQ,OQ & PQ are in place for all major equipment and facility.			
	Whether validation records of all utilities and major equipments are available.			
27	***Product Recalls: -***			
27.1 to 27.6	**Specify the product recall system followed by the firm.** **How promptly recall operation at the level of each distribution channel up-to the retail level can be carried out.** **Whether there is a SOP for recall of products clearly defining responsibility, procedure, reporting, re-conciliation etc.**			
28	***Complaints and Adverse Reactions: -***			
28.1	**Specify the review system for complaints concerning the quality of products.**			
	How records of complaint and adverse reactions maintained.			
	Whether reports of serious drugs reaction with comments and documents immediately sent to Licensing Authority			
	Is there any criteria for action to be taken on the basis of nature of complaint / adverse reaction.			

29	***Site Master file: -***			
	Whether all the relevant information have been included in the site master file.			
	Whether quality policy has been included in the site master file. **Please attach the current version.**			

Checklist

	PART-IA **(Specific requirements for manufacture of Sterile products, Parenteral preparations (Small Volume Injectable Large Volume Perenterals) and Sterile ophthalmic preparations)**	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1.	Whether dampness, dirt and darkness is visible in the facility.			
2.	**Building and Civil Works**			
2.1	Whether the building is devoid of cracks especially in the Aseptic solutions preparation rooms, Filling rooms, Sealing rooms			
2.2	Are the location of services like water, steam, gases etc. are such that the servicing or repairs can be carried out without any threat to the integrity of the facility			
2.3	Whether water lines pose any threat of leakage to the aseptic area			
2.4	Whether the manufacturing areas clearly separated into Support Areas (washing and component preparation areas, storage areas etc.) Preparation areas (bulk manufacturing areas, non aseptic blending areas etc) Change areas and Aseptic areas			

2.5	Whether de-cartooning areas to remove outer cardboard wrappings of primary packaging materials segregated from the washing areas			
2.6	Whether particle shedding materials like wooden pallets, fiber board drums, cardboards etc taken into the preparation areas etc			
2.7a	Whether in the aseptic areas: Walls, floors and ceiling are - Impervious - Non-shedding - Non-cracking - Coved at wall and ceiling junction			
2.7b	Whether the walls are flat, smooth and devoid of recesses			
2.7c	Whether the surface joints like electric sockets, gas points flushed with walls			
2.7d	Whether the ceiling is solid and the joints are properly sealed.			
2.7e	the air grills and lights flushed with the walls			
2.7f	**Are the grade A & B areas devoid of sinks and drains**			
2.7g	Are the doors and windows made up of non-shedding materials			
2.7h	Whether doors open towards higher pressure areas and close automatically due to air pressure			

2.7i	**In case fire escapes are provided, whether they are suitably fastened to** the walls without gaps			
2.7j	Whether the quality of the furniture used is smooth & washable and made of stainless steel, or of any other suitable material other than wood			
2.8	Whether the Manufacturing and support areas have the same quality of civil structure as desired for aseptic areas except the environmental standards which may vary in the critical areas			
2.9	Is the change rooms entrance provided with air locks before entry to the sterile product manufacturing areas and then to the aseptic areas.			
2.10	Are the change rooms to the aseptic areas clearly demarcated like 'black', 'gray' and 'white' with different levels of activity and air cleanliness?			
2.11	Are the sinks and drains in the first change rooms (un-classified) kept clean all the time			
2.12	Do the specially designed drains are periodically monitored to check for pathogenic micro-organisms			
2.13	Whether an appropriate inter- locking system with visual and/or audible warning system installed			

	to prevent the opening of more than one door at a time.			
2.14	Do the aseptic and non-aseptic areas provided with intercom telephones or speak phones for communication purposes			
2.15	Whether the aseptic areas and outside areas provided with suitable air-locks or pass boxes with suitable interlocking arrangements for material transfer			
2.16	Are the rest rooms, tea room, canteen and toilets outside the sterile manufacturing area			
2.17	Are the animal houses outside and away from the sterile product manufacturing area with separate AHU.			
3	**Air Handling System (Central Air Conditioning)**			
3.1	Whether the Air Handling Units for sterile product manufacturing area separate from those for other areas			
3.2	**Give the Background Grade of air for following critical areas:**			
	• Aseptic filling area			
	• Sterilized components unloading area for aseptic filling preparations.			

	• Sterilized components unloading area for terminally sterilized products.			
	• Filling room of terminally sterilized products.			
	• Batch manufacturing area for aseptic filling preparations.			
	• Batch manufacturing area for terminally sterilized products.			
	• Component washing and preparation area.			
	• Final change room (Aseptic Area)			
3.3	Whether Aseptic filling area, sterilized component unloading area and changes rooms conforming to Grade B, C and D have separate Air Handling Units.			
3.4	Are the filter configuration in the air handling system suitably designed to achieve the Grade A, B, C and D of air as per designated classified areas.			
3.5	Whether the types of Operations to be carried out in the various Grades for Aseptic Preparations are as under:			
a)	**Grade Type of Operation** Aseptic preparation & filling			
b)	Aseptic Solution preparation to be filtered			

d)	Handling of components after Washing			
3.6	Whether for aseptically filled products the filling room meet **Grade B** conditions at rest, unmanned within a period of about **30 minutes** of the personnel leaving the room after completion of operations			
3.7	Are the filling operations undertaken in **Grade A** conditions and demonstrated under working of simulated conditions			
3.8	Whether the filling room meets **Grade C** conditions at rest in case of terminally sterilized products and these conditions obtainable within a period of about 30 minutes of the personnel leaving the room after completion of the operations			
3.9	Whether the manufacturing and component preparation areas for terminally sterilized products meet Grade C conditions			
3.10	Whether the washed components and vessels for terminally sterilized products protected with Grade C background or if necessary under LAF station.			
3.11	Whether the number of air changes in Grade B and Grade C areas are more than 20 per hour.			

3.12	Whether the Grade A Laminar Air Flow stations meet the criteria of air flow of 0.3 meter per second in case of vertical and that of 0.45 meter per second in case of horizontal flows +/- 20 %			
3.13	Whether the differential pressure between areas of different environmental standards meets the requirements (at least 15 Pascal/ 0.06 inches/ 1.5 mm water gauge)			
3.14	Whether suitable manometers / gauges installed for measurement and verification. Specify type of manometer.			
3.15	Whether the final change rooms have the same class of air as specified for the aseptic area.			
3.16	Whether the pressure differential in the change rooms is in the descending order, from ' white' to' black'. Specify pressures of three change rooms.			
4.	**Environmental Monitoring**			
3.18	Whether temperature and humidity (NMT 27^{C}C and 55 % RH respectively) in the aseptic areas are controlled.			
4.1	Whether the records exist to show that all the environmental parameters were verified at the time of installation and checked periodically thereafter?			

4.2	Are the recommended periodic monitoring frequencies followed			
a)	Particulate counts - 6 Monthly			
b)	HEPA filters integrity testing –Yearly			
c)	Air Change rates - 6 Monthly			
d)	Air pressure differentials - Daily			
e)	Temperature and Humidity - Daily			
f)	Microbiological monitoring by settle plates and/ or swabs in: **Aseptic areas -- Daily,** **Other areas -- Decreased frequency**			
4.3	Does a written Environmental Monitoring Program exist? How long the settle plates are exposed in Grade A and other areas.			
4.4	Are the microbiological results recorded			
4.5	Are these results assessed with recommended limits			
4.6	Do they take action in case particulate and microbiological monitoring counts exceed the limits?			
4.7	In case of major engineering modifications being carried out to the HVAC system of any area, Whether all parameters reassessed and approved before starting production.			

5.	**Garments**			
5.1	Whether Outdoor clothing is allowed in the sterile areas			
5.2	Do they use cotton garments which are not allowed?			
5.3	Are the garments made of non- shedding and tight weaving material?			
5.4	Whether the garments are of suitable design in single piece with fastening at cuffs, neck and at legs to ensure close fit Trouser legs to be tucked inside the cover Boots			
5.5	Whether the garment includes a hood or a separate hood which can be tucked inside the overall.			
5.6	Whether Pockets, pleats and belts are avoided			
5.7	Whether Zips (if any used in garments) are of plastic material			
5.8	Whether the personnel wear only clean, sterilized and protective garments at each work session where aseptic filtration and filling operations are undertaken and at each work shift for products intended to be sterilized, post-filling			
5.9	Are masks and gloves are changed at every work session.			

5.10	Are the gloves used made of latex or other suitable plastic material			
5.11	Are powder free gloves used in clean rooms			
5.12	Are the gloves long enough to cover the wrists completely and allow the over-all cuff to be tucked in			
5.13	Are the foot-wear used made of plastic or rubber material			
5.14	Are the foot-wear daily cleaned with a bactericide			
5.15	Does the safety goggles / numbered glasses worn in side the aseptic areas have side extensions			
5.16	Are safety goggles sanitized by a suitable method			
5.17	Whether the garment changing procedure documented			
5.18	Whether the operators trained in garment changing procedure.			
5.19	Whether a full size mirror been provided in the final change room to ascertain that the operator has appropriately attired in the garments			
6.	**Sanitation**			
6.1	Whether written procedures available for sanitation of sterile processing facilities			

6.2	Whether the employees carrying out the sanitation of aseptic areas specially trained for the purpose			
6.3	Whether more than one sanitizing agent is used in rotation.			
6.4	Whether the concentration of the agent used has been recommended by the manufacturer			
6.5	Whether distilled water is used for the dilution of the disinfectant, if so is it directly collected from the distilled water plant or from re-circulation loop maintained above 70 ^{o}C or sterilized by autoclaving and filtered through membrane filtration			
6.6	Whether alcohol or isopropyl alcohol is used as disinfectant for hand sprays?			
6.7	Whether disinfectant solutions filtered through membrane into suitable sterile containers before use?			
6.8	Whether the diluted disinfectants bear 'use before' labels based on microbiological establishment of their germicidal properties			
6.9	Whether records maintained thereof			
6.10	Whether fumigation carried out in aseptic areas. If yes, specify fumigating agent and its conc. used.			

6.11	Whether an SOP exist for the purpose of fumigation.			
6.12	Whether cleaning of sterile processing facility done using air suction devices non-linting sponges or clothes.			
6.13	Whether air particulate quality monitored on a regular basis			
7.	**Equipments**			
7.1	Whether the unit-sterilizers double ended with suitable inter-locking between the doors			
7.1.1	Whether the initial effectiveness of sterilization process established by using microbial spores indicators			
7.1.2	Whether thermal Mapping of heat sterilizers is carried out on regular basis. Check records.			
7.1.3	Whether suitable vent filters and recording thermographs provided in Autoclaves.			
7.1.4	Whether HEPA filters for cooling air and recording thermographs provided in DHS			
7.1.5	Whether provisions of CIP or SIP available.			
7.1.6	Whether firm has made provisions for pure steam generation and its use.			

7.2	Whether filter integrity test carried out before and after the filtration process			
7.3	Whether the filling machines challenged initially and there after periodically by simulation trials including sterile media fills.			
7.4	Are SOPs with acceptance criteria for media fills been established, validated and documented			
7.5	Whether the material of construction of the parts of equipment which are in direct contact with the product and the manufacturing vessels of stainless steel 316 and of glass containers Boro-silicate glass			
7.6	Whether the tubing used capable of washing and autoclaving			
7.7	Whether the installation qualification been done of all the equipments by the engineers (with the support of production and quality assurance personnel)			
7.8	Whether the critical processes such as aseptic filling and sterilizers suitably validated before these were put to use			
7.9	Whether SOPs available for each equipment for its calibration, operation and cleaning.			

7.10	Whether the measuring devices attached to equipment calibrated at suitable intervals.			
7.11	Whether a written calibration program is available			
7.12	Whether calibration status documented and displayed on the of the equipment and the gauges			
8	**Water & Steam Systems**			
8.1	Whether **potable water** used for the preparation of purified water meets the requirement of not more than 500 cfu/ml			
8.2	Whether potable water tested (100 ml sample) for freedom from pathogenic microorganisms: Escherichia coli, Salmonella, Staphylococcus aurious and Pseudomonas			
8.3	Whether the Purified Water prepared by de-mineralization meet the microbiological specification of not more than 100 cfu/ml			
8.4	Whether Purified Water tested for freedom from pathogenic microorganisms. (Sample size 100 ml)			
8.5	Whether Purified Water meet IP specifications for chemical testing			

8.6	Whether purified water is stored in stainless steel tanks.			
8.7	Are the distribution lines made of stainless steel 316 grades?			
8.8	What is the water source for preparation **Water for Injection (WFI)**:			
8.9	Whether WFI meet microbiological specification of not more than 10 cfu/100ml			
8.10	Whether WFI meet IP specifications for Water for Injection			
8.11	Whether WFI meet the endotoxin level of not more than 0.25 EU/ml			
8.12	Whether WFI used for			
8.12.1	- Bulk preparations of liquid parenterals - Final rinse of product containers			
8.12.2	- Final rinse of machine parts			
8.12.3	- Preparation of disinfectant solutions for use in aseptic areas			
8.13	Whether WFI used for liquid injectables collected freshly from the distillation plant or from a storage / circulation loop kept at above 70^{o}C.			
8.14	Whether the steam condensate meets the microbiological specification of not more than 10 cfu/100ml and IP specifications of WFI			

8.15	Whether steam used in production meet the endotoxin level of not more than 0.25EU/ml			
8.16	What is the schedule for the monitoring of steam quality exist			
9.	**Manufacturing process**			
9.1	Whether the bulk raw materials and bulk solutions monitored for bio-burden periodically (solutions not to contain more than 100 cfu/ml)			
9.2	Whether the principle of minimum possible time between the preparation of the solution and its sterilization or filtration through microorganism retaining filters followed and also specified in Master formula.			
9.3	Whether the filter the gases coming into contact with the sterile product through two 0.22 micron hydrophobic filters connected in series			
9.4	Whether gas cylinders are kept out side of the aseptic areas			
9.5	Whether the washed containers sterilized immediately before use			
9.6	Whether the sterilized containers not used within an established time, rinsed with distilled or filtered purified water and re-sterilized			

9.7	Is each lot of the finished product filled in one continuation operation			
10.	**Terminally Sterilized product**			
10.1	Whether the preparation of Primary packaging material such as glass bottles, ampoules and rubber stoppers is carried out in at least Grade D (grade C in case there is unusual risk of contamination to the product)			
10.2	Whether these processes used for component preparation have been validated.			
10.3	Whether the filling area is **of Grade A** environment with Grade C background			
10.4	Whether the solutions which are sterilized by filtration is prepared in Grade C environment.			
10.5	And if not to be filtered, whether the preparation of materials and products carried out in Grade A environment with Grade B background			
10.6	Whether for aseptic filling, non- fiber releasing sterilizing grade cartridge / membrane filter of nominal pore size of 0.22 micron and 0.45 micron porosity for terminally sterilized products are used.			
10.7	Whether a second filtration with another 0.22 micron sterilizing grade cartridge / membrane filter, performed immediately prior to filling.			

10.8	Whether process specifications indicate the maximum time during which a filtration system may be used (precluding microbial build-up to levels that may affect the microbiological quality of the product)			
10.9	Whether integrity of the sterilizing filter verified and confirmed immediately after use. If so, by which method: Bubble Point, Diffusive Flow or Pressure Hold Test			
	Sterilization (Autoclaving)			
10.10	Whether the sterilizing processes have been validated (Dry heat, Moist heat, filtration, ETO, ionizations whichever applicable.			
10.11	Whether the validity of the process verified at regular intervals (at least annually)			
10.12	Whether records are maintained when significant changes made to the equipment and / or the product.			
10.13	Whether sterilizer double ended			
10.14	Whether the terminal sterilizer's capacity is sufficient to sterilize one batch completely at one time. If not specify controls and measures taken in lot sterilizations.			

10.15	Whether the monitoring of products bio-burden carried out before terminal sterilization.			
10.16	Whether bio-burden controlled to the specified limits in the Master Formula.			
10.17	Whether biological indicators used in monitoring of sterilization.			
10.18	Whether the biological indicators stored and used as per manufacturers instructions. Whether quality of BI's checked by positive controls.			
10.19	Whether a clear means of differentiating 'sterilized' from 'unsterilized' products in place. Specify.			
10.20	Whether the label on the basket / tray or other carrier of product / component clearly states: • Name of the material • Its batch number • Its sterilization status Indicator (in case it has passed through sterilization process)			
10.21	Whether sterilization records including thermographs and sterilization monitoring slips attached with the Batch Production Record			
10.22	**Sterilization (By Dry Heat)**			

10.23	Whether the sterilization cycle recording device of suitable size and precision provided in DHS.			
10.24	Whether the position of temperature probes used for controlling and / or recording determined during validation and (where applicable) been checked against a second independent temperature probe located in the same position			
10.25	Whether the chart forms a part of the batch record.			
10.26	Whether sterilization cycle validated only by biological indicator and chemical indicators or physical validation is also carried out.			
10.27	Whether the time allowed reaching the required temperature before commencing the measurement of sterilizing time, separately determined for each type of load.			
10.28	Are adequate precautions taken to protect the load during cooling after it has gone through the high temperature phase of a heat sterilization cycle			
10.29	In case the cooling is affected with any fluid or gas in contact with the product, is it sterilized.			
10.30	Whether the equipment air inlet and outlets been provided with bacteria retaining filters			

10.31	In the process of sterilization by dry heat, does the equipment has: • Air circulation facility within the chambers • Positive pressure to prevent entry of non-sterile air			
10.32	Whether the process of dry heat sterilization is also intended to remove the pyrogens If so, has the validation been done with challenge tests using endo-toxins			
10.33	**Sterilization (By Moist Heat)**			
10.34	Whether recording of both temperature and pressure carried out to monitor the process			
10.35	Whether the control instrumentation independent of the monitoring instrumentation and recording charts.			
10.36	Whether the equipment has automated control and monitoring system, if so, have these been validated to ensure that critical process requirements are met.			
10.37	Whether the system and cycle faults are recorded inbuilt and also observed by the operator and record maintained.			
10.38	Whether the readings of the thermograph during sterilization cycling are routinely checked by the operator against the reading shown by the dial thermometer fitted with autoclave.			

10.39	Whether the sterilizer fitted with a drain at the bottom of the chamber If so, does the record of temperature at this position is recorded throughout the sterilizing period			
10.40	Are frequent leak tests conducted on the chamber of the autoclave on each day of operation.			
10.41	Whether all items to be sterilized (other than sealed containers) are wrapped for sterilization.			
10.42	Whether the wrapping material allows removal of air and penetration of steam ensuring contact with the sterilizing agent at the required temperature for required time			
10.43	Whether the wrapping prevent contamination after sterilization			
10.44	Whether the steam used for sterilization is of suitable quality and doesn't contain additives at a level which could cause contamination of the product or equipment			
10.45	Whether the minimum time for all unit operations and processes are specified in the manufacture of a batch			
10.46	Whether the shortest validated time being adhered from the start of a batch to its ultimate release for distribution			

10.47	Whether the containers closing methods been validated			
10.48	Whether the containers closed by fusion e.g. glass or plastic ampoules, subjected to 100% leak testing			
10.49	Whether the samples of other containers checked for integrity as per appropriate procedures			
10.50	Whether the containers sealed under vacuum checked for required vacuum conditions			
10.51	Whether the filled containers of parenterals inspected individually for extraneous contamination /other defects			
10.52	Whether the inspection process done visually, if so, are the illumination and background conditions controlled.			
10.53	Whether the workers engaged in inspection activity pass the regular eye- sight test (with spectacles if worn)			
10.54	Whether the visual inspectors allowed frequent rest from inspection			
10.55	If other method of inspection of containers is used,			
	• What is the method-			
	• Has it been validated			

	• Are the equipment used for the purpose checked at suitable intervals			
	• Are the results/ recorded maintained			
11.	**Product Containers & Closures**			
11.1	Whether the containers and closures used comply to pharmacopoeia or other specific requirements			
11.2	To assure suitability of the containers/ closures and other component parts of drug packages, whether they have: Suitable sample sizes, Specifications, Test methods, Cleaning procedures, Sterilizing procedures			
11.3	Whether the container is compatible with the product and affecting its quality and purity.			
11.4	Whether second hand containers and closures used			
11.5	Whether the plastic granules used checked for fulfillment of Pharmacopoeia requirements including physico- chemical and biological tests			
11.6	Whether containers and the closures rinsed with WFI before sterilization			

11.6.1	Whether a written procedure exist for washing process. Do they follow the written schedule for cleaning of the glass bottles			
11.6.2	Whether the design of closures and containers suitable to make cleaning easy, and to make an air tight seal when fitted to the bottles			
11.6.3	Whether the material quality of the stoppers and closures ensures that it does not affect the quality of the product and avoids the risk of toxicity			
11.6.4	In case the bottles are not dried after washing are these rinsed with distilled water or pyrogen free water as the case may be as per written procedure			
12.	**Documentation**			
12.1	Do the manufacturing records pertaining to manufacture of sterile products indicate the following details:			
(1)	Serial number of Batch Manufacturing Record			
(2)	Name of the product			
(3)	Reference to Master Formula Record			

(4)	Batch/ Lot number			
(5)	Batch/ Lot size			
(6)	Date of commencement and completion of manufacture			
(7)	Date of manufacture and assigned date of expiry			
(8)	Date of each step in manufacturing			
(9)	Names of all ingredients with grade given by the quality control department			
(!0)	Quantity of all ingredients			
(11)	Control reference numbers for all ingredients			
(12)	Time and duration of blending, mixing etc. where ever applicable			
(!3)	PH of solutions whenever applicable			
(14)	Filter integrity testing records			
(15)	Temperature and humidity records whenever applicable			
(!6)	Records of plate-counts whenever applicable			
(17)	Results of pyrogen and/ or bacterial endotoxin and toxicity			
(18)	Records of weight or volume of drug filled in containers			

(19)	Bulk sterility in case of aseptically filled products			
(20)	Leak test records			
(21)	Inspection records			
(22)	Sterilization records including leakage test records, load details, date, duration, temperature, pressure etc.			
(23)	Container washing records			
(24)	Total number of containers filled			
(25)	Total number of containers rejected at each stage			
(26)	Theoretical yield, permissible yield, actual yield and variation there of			
(27)	Clarification for variation in yield beyond permissible yield			
(28)	Reference number of relevant analytical reports			
(29)	Details of re-processing, if any			
(30)	Names of all operators carrying out different activities			
(31)	Environmental monitoring records			

(32)	Specimens of different packaging material			
(33)	Records of destruction of rejected containers and packaging material			
(34)	Signature of the competent technical staff responsible for manufacture and testing			
13.	**Notes**			
13.1	Whether products released only after complete filling and testing.			
13.2	Whether result of the tests relating to sterility, pyrogens and bacterial endotoxins are maintained in the analytical records			
13.3	Whether Validation details and simulation trial records maintained separately			
13.4	Whether records of environmental monitoring like temperature, humidity, microbiological data etc., are maintained.			
13.5	Whether records of periodic servicing of HEPA filters, sterilizers and other periodic maintenance of facilities and equipment carried out, are maintained.			

Checklist

	Part-IB **Specific Requirements for manufacture of Oral Solid Dosage Forms (Tablets and Capsules)**	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1.1	**Please specify HVAC and air extraction systems provided to avoid contamination from extraneous particles / dust and other products.** **Whether HVAC and air extraction system is capable of preventing discharging contaminants into the environment? In case of re-circulation of air what is the micron size of final filter.**			
1.1.1	**Are there manometers to monitor pressure differential at all strategic points.**			
1.1.2	**Is there schematic drawing of AHU's available.**			
1.1.3	**Whether dedicated AHU's for different operations are in place.**			
1.2	**Please specify how specific product requirements like temperature, humidity and light are controlled.**			
1.3	**Pls specify the materials of construction of equipments.**			
1.3.1	**Whether metal detector is used to detect metallic contamination.**			
1.4	**Whether dedicated areas for sifting provided.**			
1.5	**Pls give brief account on pressure cascade (differential pressure) being maintained in the various areas of production.**			

1.5.1	**Whether pressure balancing is automatic or manual.**			
1.5.2	**Whether records of this pressure differential reviewed at regular interval. If yes pls specify intervals of monitoring and its review.**			
1.6	**Is Air blowing or vacuum system is used for clearing of powders from the machine parts etc.**			
1.6.1	**In case of vacuum cleaning how it is used to avoid contamination and cross contamination.**			
2	***Sifting, Mixing and Granulation: -***			
2.1	**Whether mixing, sifting and blending operations are carried out in dedicated areas & how generation of dust is controlled.**			
2.1.1	**Whether these operations are closed.**			
2.1.2	**Whether integrity of screens checked before and after operation.**			
2.1.3	**Whether mixing and blending equipment have timers for control.**			
2.2	**Whether personnel in production carry out the verification of the weight of the raw materials used in the manufacturing of each lot.**			
2.2.1	**Whether critical operating parameter likes time and temperature for each mixing and drying operation are recorded in BPR and tally with the master formula.**			
2.2.2	**Whether static or fluid bed dryers are used for drying.**			
2.2.	**Whether FBD and static dryers have arrangements for**			

3	**temperature monitoring and recording.**			
2.4	**Specify the system of using filter bags used in FBD.**			
2.4.1	**How filter bags are identified for various products and stored.**			
2.4.1	**Whether air entering into the dryers is filtered. If yes then specify type of filters installed.**			
2.4.2	**Whether air going out of FBD is also filtered. If yes then specify type of filters installed.**			
2.5	**Whether granulation and coating solutions are made, stored and used in a manner which minimizes the risk of contamination or microbial growth.**			
2.5.1	**Whether the washing facility in the granulation suites takes proper measures to prevent contamination and cross contamination.**			
3	***Compression (Tablets) :-***			
3.1	**Whether each compression machine is installed in separate cubicle.**			
	What type of dust control facilities are provided with the Tablet compressing machine in its cubicle.			
3.2	**How granules and compressed tables stored and controlled to prevent mix ups.**			
3.2.1	**How these containers are cleaned and maintained in a proper condition.**			
3.3	**How tablets are being inspected and checked for suitable pharmacopoeial parameters like appearance, weight variation, disintegration, hardness, friability, thickness and records maintained thereof.**			

3.4	**Whether instruments used in IPQC lab are calibrated and accurate to measure out of specification units.**			
3.5	**How tablets are being de-dusted and monitored for the presence of foreign materials.**			
3.7	**Whether rejected or discarded tablets are isolated in identified container and their quantity recorded in the BMR.**			
3.8	**Which type of lubricating oil is used in compression machine.**			
4	***Coating (Tablets):-***			
4.1	**Which type of tablet coaters are provided for coating.**			
	Whether air supplied to coating pan is filtered. If yes pls specify type of filter and justification for its suitability.			
	Whether coating area is provided with suitable exhaust system and environmental control (temperature, Humidity) measures.			
4.2	**Whether coating solutions are being made afresh and used.**			
5.	**Filling of Hard Gelatin Capsule: -**			
5.1	**How empty gelatin capsules are stored and controlled in the filling area.**			
5.1.1	**Whether capsule filling is carried out manually or by machine.**			
5.1.2	**Whether additional provisions in the AHU's has been made to control humidity. If yes, pleases specify the same.**			
6.	**Printing (tablets and capsules): -**			

6.1	**Whether the tablets / capsules are overprinted. If yes which type of ink is used. Please specify quality of ink.**			
6.1.1	**How printing operation is controlled to avoid mix up of products during printing.**			
6.1.2	**Whether after printing, the products are approved by quality control before release for packaging or sale**			
7	***Packaging (Strip & Blister)***			
7.1	**Whether a system of line clearance is in place and recorded before a new packaging operation is commenced.**			
7.2	**How contamination and cross contamination are prevented during packaging operation of tablets / capsules.**			
7.3	**How the strips/Blister coming out of the machines is inspected for defects such as miss-print, cuts on the foil, missing tablets and improper sealing.**			
7.4	**Whether IPQC tests are performed on strips or blisters? Whether records of these tests maintained.**			

Checklist

	PART-IC **Specific Requirements for manufacture of Oral Liquid**	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1.1 **1.1.1**	***Building and Equipments: -*** **How the facility for liquid oral designed and constructed to prevent cross contamination and mix-ups.**			
	Whether the manufacturing area have entrance through double air lock facility.			
1.1.2	**Whether in the manufacturing area walls, floors and ceiling are impervious, non-shedding, non-cracking, coved at all junctions.**			
	Whether the doors and windows and light fixtures are flushed, made up of non fiber shedding material.			
1.2	**Whether fly catcher and/or air carton has been provided at strategic suitable points.**			
1.3	**Whether the drains are provided with traps to prevent back flow.**			
	How drains are maintained.			
1.4	**Whether the production area is cleaned and sanitized at the end of every production process. If yes, whether records maintained.** **(How the area is sanitized. How sanitization procedures controlled).**			

1.5, 1.6 & 1.8	**What is the material of construction of tanks, containers, Pipe work and pumps?**			
	Whether the tanks have clean in place **facility. If not how tanks are cleaned to prevent accumulation of residual microbial growth and cross-contamination.**			
	How tanks, pipe works and other containers sanitized.			
	Whether the pipelines and services have any dust lodging surface.			
	Whether microbial monitoring of the area is carried out.			
	Whether use of glass containers is restricted.			
	Whether furniture's are of stainless steel and are capable of cleaned effectively.			
1.7	**Whether cleaning of bottles, caps, droppers etc are carried out by suitable machine/devices equipped with high pressure air, water and steam jets.**			
2	**Purified Water: -**			
2.1	**Whether the Microbial quality of purified water is monitored routinely.** **(What is the in house limit of CFU / ml of purified water).**			
	Whether water is tested for freedom from Pathogen on daily basis. If not what is the schedule.			
2.2	**Whether the unit has written procedure for operation and maintenance of purified water system. (Specify the method).**			

3	***Manufacturing: -***			
3.1 **3.2**	**What types of clothing's are worn by personnel in manufacturing area?**			
	Whether materials like gunny bags, or wooden pallets are allowed in manufacturing areas.			
3.3	**Whether suspensions and emulsions are manufactured.** **If yes how homogeneity of the same is ensured throughout the process.**			
3.4	**Whether separate syrup preparation area has been provided,`**			
	Specify the room temperature requirement in the manufacturing area.			
3.5	**Whether the maximum period of storage of product in a bulk stage is validated and mentioned in MFR.**			

Checklist

	PART-ID (Specific Requirements for manufacture of topical products (Ointment, Creams, Lotion & Dusting Powders)	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1	**Whether the entrance to manufacturing area is through an air lock.** **Whether air lock is supplied with filtered air.**			
	Whether insectocutor has been installed out side air lock.			
2 & 3	**Whether HVAC system installed in manufacturing areas. If not how air quality is maintained.** **Which filter is used for air filtration to the mfg. Area.**			
	How temperature in the mfg. Area controlled.			
	How fumes, vapors if generated during the process are controlled.			
4 & 5	**What is the material of construction of tanks, containers, Pipe work and pumps?**			
	Whether the tanks have clean in place facility. If not how tanks are cleaned. **What type of transfer pumps is used. And precaution taken to protect the product from the contamination.**			
	How tanks, pipe works and other containers sanitized.			

6.	**Whether water used in the compounding is purified water IP.**			
7	**Whether the powders whenever used are suitably sieved.**			
	How contamination with metals prevented.			
8.	**How heating of base like petroleum jelly is done in the vessels.** **Whether melting facility is separate / dedicated to the process.**			
9	**Whether a separate packing section is provided for primary packaging of products.**			
	Whether product is filled in tubes or jars. **How jars are cleaned before filling.**			

Checklist

	Validation	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1	Is there a master plan **(Master validation plan)** covering:			
1.1	Resources and those responsible for its implementation.			
1.2	Identification of the systems and processes to be validated			
1.3	Documentation and standard operating procedures (SOPs), Work Instructions and Standards (applicable national and international standards)			
1.4	Validation list: facilities,processes (e.g. aseptic filling), products			
1.5	Key approval criteria			
1.6	Protocol format			

1.7	Each validation activity, including re-validation and reasonable unforeseen events (power failures, system crash and recovery, filter integrity failurer. Please attach validation calendar.			
2.	Pls specify whether the critical processes validated Prospectively, retrospectively or concurrently.			
3.	Whether validation of following performed and documented: Analytical methods, Production and assay equipment, Sterile production processes, Non-sterile production processes, Cleaning procedures, Critical support systems (purified water, water for injections, air, vapor, etc.), Facilities			
4.	Please list reasons considered important for validation or re-validation.			
5.	In case electronic data processing systems are used, are these validated? Please specify whether periodical challenge tests performed on the system to verify reliability.			

6.	Are the validation studies performed according to pre-defined protocols? Is a written report summarized, results and conclusions prepared and maintained? Is the validity of the critical processes and procedures established based on a validation study?			
7.	Are criteria established to assess the changes originating a revalidation? Are trend analyses performed to assess the need to re-validate in order to assure the processes and procedures continue to obtain the desired results?			
8	**WATER SYSTEM** **PURIFIED WATER** **WATER FOR INJECTIONS**			
8.1	Please specify whether waster system qualification (IQ, OQ and PQ) has been carried out as per protocol and repots have been prepared and maintained.			

8.2	Whether IQ protocol include at least facility review, equipment specification vs. design, welding roughness testing on pipelines, absence of dead points / section in the pipelines, pipe and tank passivation, drawings, SOP for operations, cleaning, sanitation, maintenance and calibration of gadgets. Whether its report includes Conclusion / Summary, description of the performed assay, Data tables, Results, Conclusions, Protocol reference, Revision and approval signatures.			
8.3	Whether OQ protocol include at least System production capacity (L/min), Flow type and water rate, Valve operation, Alarm system operation and Controls operation?			
8.4	Whether its report includes Conclusion / Summary, description of the performed assay, Data tables, Results, Conclusions, Protocol reference, Revision and approval signatures.			
8.5	Please specify the water whether Phase 1, Phase 2 and Phase 3 studies carried out in at PQ stages?			

8.5.1	Phase 1 : Whether the operations parameters, cleaning and sanitation procedures & frequencies defined. Whether daily sampling records for every pretreatment point and usage point for a period of 2 to 4 weeks maintained and SOP's prepared.			
8.5.2	**PHASE 2** : Whether daily sampling records for every pretreatment point and usage point for a period of 4 to 5 weeks after Phase 1 maintained and reviewed.			
8.5.3	**PHASE 3 :** Whether weekly sampling records available of every usage point for a one-year period. In the case of water for injections systems, are the daily sampling records of at least one usage point available, with all the usage points sampled weekly? Whether results of these records summarized to show suitability. Are there personnel training records?			

9.	**EQUIPMENT**			
9.1	Are the equipment installation Qualification (IQ) protocols contains followings: Introduction, Installation description, Responsibilities, Performed tests/assays, Qualification acceptance criteria and Data recording and reporting?			
	Whether report contains Summary, Description of performed tests/assays, Obtained data tables, Results, Conclusions, Installation diagrams, Revision and approval signatures.			
9.2	Whether the equipment operation qualification (OQ) protocols contains following: Introduction, Equipment description, Description of the equipment operation steps (SOP's), Responsibilities, Qualification acceptance criteria, Data recording and reporting. Whether report contains Summary, Description of performed tests/assays, Obtained data tables, Results, Conclusions, Revision and approval signatures.			

9.3	Whether equipment performance qualification (PQ) protocols contains followings: Introduction, Responsibilities, Performed assays, Qualification acceptance criteria, Data recording and reporting.			
	Whether report contains Summary, Description of performed tests/assays, Obtained data tables, Results, Conclusions, Revision and approval signatures.			
10.	**Analytical Method Validation**			
10.1	Please specify whether following Characteristics are considered during validation of analytical methods: — specificity — linearity — range — accuracy — precision — detection limit — quantitation limit — Robustness.			
10.2	Whether Paharmocopial methods are also validated. If yes, how.			
10.3	Whether system suitable testing is included in testing protocols e.g. HPLC, GC etc.			

11	**CLEANING**			
11.1	Is a validation performed to confirm cleaning effectiveness?			
	Does the protocol define the selection criteria for products or groups of products subject to cleaning validation?			
	Is data produced supporting the conclusion that residues were removed to an acceptable level?			
11.2	Please specify whether the validation is implemented to verify cleaning of: Surfaces in contact with the product, After a change in product, Between shift batches.			
	Please specify whether the Validation Strategy include contamination risks, equipment storage time, the need to store equipment dry and sterilize and free of pyrogens if necessary?			

11.3	Whether the cleaning Validation Protocol include: a. Interval between the end of production and the beginning of the cleaning SOP's. b. Cleaning SOP's to be used. c. Any monitoring equipment to be used. d. Number of consecutive cleaning cycles performed? e. Clearly defined sampling points.			
11.4	Whether Quality Control responsible of the sampling for cleaning verification?			
11.5	Whether personnel engaged in cleaning, sampling etc. trained.			
11.6	Please specify whether acceptance limits been set for cleaning verification and are based on following criteria: a. Visually clean. b. 10 ppm in another product c. 0.1% of the therapeutic dose?			
11.7	Please specify whether detergent residues investigated and degradation products verified during validation.			

11.7.1	Whether validation records include Recovery study data, Analytical methods including Detection Limits and Quantification Limits, Acceptance Criteria, Signatures of the Quality Assurance Manager, employee in charge of cleaning and the verification from Production and Quality Control.			
12	**HVAC**			
12.1	Please specify whether following parameters have been qualified: — temperature — relative humidity — supply air quantities for all diffusers — return air or exhaust air quantities — room air change rates — room pressures (pressure differentials) — room airflow patterns — unidirectional flow velocities — containment system velocities —filter penetration tests (HEPA) — room particle counts — room clean-up rates — microbiological air and surface counts where appropriate — operation of de-dusting — warning/alarm systems where applicable.			
12.2	Whether strategic tests like Particle count, air pressure differential, air flow volume, air flow velocity etc. included in HVAC qualification.			

13	**Media fill test**			
13.1	Whether medial fill tests carried out twice in a year during normal working conditions.			
	Pls give date of last such test.			
13.2	How many units are filled and tested.			
	What is the criterion for qualification of this test?			
13.3	In case of failure of media fill test, what precautions or actions are taken.			

	Specific Product Information	Self appraisal to be filled by the manufacturer along with all details (yes or no type reply will not be acceptable)	Observations to be noted by the inspecting team at the time of inspection	Rating to be made by the inspecting team as per Benchmarks
1.	Name of product (i) Generic Name (ii) Brand Name (iii) Dosage Form (iv) Strength			
2.	Whether validated master formula is available?			
3.	Whether specific SOP for product processing is available?			
4.	Comments on the above SOP			
5.	No. of Batches Produced			

6.	Stability studies (i) Accelerated (ii) Real Time (iii) Whether the expiry date assigned on the basis of stability study?			
7.	Whether trend analysis was carried out and interpretation thereof?			
8.	Whether Annual product review (APR) is carried out?			
9.	Is there any complaint received for the product and If any, whether the investigation report along with ATR is maintained?			

Technical Guidance Note to the Industry for complying with Schedule M of the Drugs and Cosmetics Act/Rules

1. **Quality Assurance**

1.1 Manufacturers should have a comprehensive Quality Assurance system. This should cover deviation reporting and investigation, and change control.

2. **Good Manufacturing Practices (GMP)**

2.1 The manufacturer should ensure that all manufacturing processes are clearly defined, systematically reviewed in the light of experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications.

2.2. Manufacturers should ensure that qualification and validation are performed; all necessary resources are provided, including appropriately qualified and trained personnel; adequate premises and space; suitable equipment and services; appropriate materials, containers and labels; approved procedures and instructions; suitable storage and transport; adequate personnel, laboratories and equipment for in process controls; instructions and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided; operators are trained to carry out procedures correctly; records are made (manually and/or by recording instruments) during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and quality of the product are as expected; any significant deviations are fully recorded and investigated; records covering manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form; the proper storage and distribution of the products minimizes any risk to their quality; a system is available to recall any batch of product from sale or supply; complaints about marketed products are examined, the causes of quality defects investigated, and appropriate measures taken in respect of the defective products to prevent recurrence.

3. **Sanitation**

3.1 Personnel should be instructed to wash their hands before entering production areas.

3.2. Appropriate hair covering should be worn. Used clothes, if reusable, should be stored in separate closed containers until properly laundered and, if necessary, disinfected or sterilized.

4. **Qualification and validation**

4.1.The key elements of a qualification and validation programme of a company should be clearly defined and documented in a validation master plan.

4.2. Qualification and validation should establish and provide documentary evidence that:

(a) The premises, supporting utilities, equipment and processes have been designed in accordance with the requirements for GMP (design qualification or DQ).

(b) The premises, supporting utilities and equipment have been built and installed in compliance with their design specifications (installation qualification or IQ);

(c) The premises, supporting utilities and equipment operate in accordance with their design specifications (operational qualification or OQ)

(d) A specific process will consistently produce a product meeting its predetermined specifications and quality attributes (process validation or PV, also called performance qualification or PQ)

4.3. Any aspect of operation, including significant changes to the premises, facilities, equipment or processes, which may affect the quality of the product, directly or indirectly, should be qualified and validated.

4.4. Qualification and validation should not be considered as one-off exercise. An on-going programme should follow their first implementation and should be based on an annual review.

4.5. The commitment to maintain continued validation status should be stated in the relevant company documentation, such as the quality manual or validation master plan.

4.6. Validation studies are an essential part of GMP and should be conducted in accordance with predefined and approved protocols.

4.7. A written report summarizing the results recorded and the conclusions reached should be prepared and stored.

4.8. Processes and procedures should be established on the basis of the results of the validation performed.

4.9. It is of critical importance that particular attention is paid to the validation of analytical test methods and automated systems.

5. **Complaints**

5.1 Special attention should be given to establishing whether a complaint was caused because of counterfeiting.

5.2. If a product defect is discovered or suspected in a batch, consideration should be given to whether other batches should be

checked in order to determine whether they are also affected. In particular, other batches that may contain reprocessed product from the defective batch should be investigated.

5.3. Complaints records should be regularly reviewed for any indication of specific or recurring problems that require attention and might justify the recall of marketed products.

6. **Product recalls**

6.1. The authorized person should be responsible for the execution and coordination of recalls. He/she should have sufficient staff to handle all aspects of the recalls with the appropriate degree of urgency.

6.2. All licensing authorities of all states to which a given product has been distributed should be promptly informed of any intention to recall the product because it is, or is suspected of being, defective.

7. **Self-inspection and quality audits**

7.1The frequency at which self-inspections are conducted may depend on company requirements but should be at least once a year. The frequency should be stated in the procedure.

7.2. A report should be made at the completion of a self-inspection. The report should include;

(a) Self-inspection observations;

(b) Evaluation and conclusions;

(c) Recommended corrective actions.

7.3. There should be an effective follow-up programme. The company management should evaluate both the self-inspection report and the corrective actions as necessary.

7.4. There should be a system for qualification of vendor.

8. **Personnel and training**

8.1. Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitizing materials are handled, should be given specific training.

8.2. The duties of responsible staff may be delegated to designated deputies of a satisfactory qualification level. There should be no gaps or unexplained overlaps in the responsibilities of personnel concerned with the application of GMP. The manufacturer should have an organization chart.

8.3. Key personnel include the head of production, the head of quality control and the authorized person. Normally, key posts should be occupied by full-time personnel. The heads of production and quality control should be independent of each other. In large organizations, it may be necessary to delegate some of the functions; however, the responsibility cannot be delegated.

Competent key personnel responsible for supervising the manufacture quality control and Quality Assurance of pharmaceutical products should possess the qualifications of a scientific education and practical experience required by national legislation. Their education should include the study of an appropriate combination of:

(a) Chemistry (analytical or organic) or biochemistry;

(b) Chemical engineering;

(c) Microbiology;

(d) Pharmaceutical sciences and technology;

(e) Pharmacology and toxicology;

(f) Physiology;

(g) Other related sciences.

8.5. They should also have adequate practical experience in the manufacture and quality assurance of pharmaceutical products. In order to gain such experience, a preparatory period may be required, during which they should exercise their duties under professional guidance. The scientific education and practical experience of experts should be such as to enable them to exercise independent professional judgement, based on the application of scientific principles and understanding to the practical problems encountered in the manufacture and quality control or pharmaceutical products.

8.6. The heads of the production and quality control generally have some shared, or jointly exercised, responsibilities relating to quality. These may include, depending on national regulations:

(a) authorization of written procedures and other documents, including amendments;

(b) monitoring and control of the manufacturing environment;

(c) plant hygienic;

(d) process validation and calibration of analytical apparatus;

(e) training, including the application and principles of quality assurance;

(f) approval and monitoring of suppliers of materials;

(g) approval and monitoring of contract manufacturers;

(h) designation and monitoring of storage conditions for materials and products;

(i) performance and evaluation of in-process controls;

(j) retention of records;

(k) monitoring of compliance with GMP requirements;

(l) Inspection, investigation and taking of samples in order to monitor factors that may affect product quality.

8.7. The head of the production generally has the following responsibilities:

(a) to ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality;

(b) to approve the instructions relating to production operations, including the in-process controls, and to ensure their strict implementation;

(c) to ensure that the production records are evaluated and signed by a designated person;

(d) to check the maintenance of the department, premises, and equipment;

(e) to ensure that the appropriate process validations and calibrations of control equipment are performed and recorded and the reports made available;

(f) To ensure that the required initial and continuing training of production personnel is carried out and adapted according to need.

8.8. The head of the quality control generally has the following responsibilities;

(a) to approve or reject starting materials, packaging materials and intermediate, bulk and finished products in relation with their specification;

(b) to evaluate batch records;

(c) to ensure that all necessary testing is carried out;

(d) to approve sampling instructions, specifications, test methods and other quality control procedures;

(e) to approve and monitor analyses carried out under contract;

(f) to check the maintenance of the department, premises and equipment;

(g) to ensure that the appropriate validations, including those of analytical procedures, and calibrations of control equipment are carried out;

(h) to ensure that the required initial and continuing training of quality control personnel is carried out and adapted according to need.

8.9. The authorized person **from Quality Assurance** is responsible for compliance with technical or regulatory requirements related to the quality of finished products and the approval of the release of the finished product for sale.

8.10. The authorized person will also be involved in other activities, including the following;

(a) implementation (and, when needed, establishment) of the

quality system;

(b) participation in the development of the company's quality manual;

(c) supervision of the regular internal audits or self –inspections;

(d) oversight of the quality control department;

(e) participation in external audit (vendor audit)

(f) Participation in validation programmes.

8.11. The function of the approval of the release of a finished batch or a product can be delegated to a designated person with appropriate qualifications and experience who will release the product in accordance with an approved procedure

8.12. The person responsible for approving a batch for release should always ensure that the following requirements have been met:

(a) the marketing authorization and the manufacturing authorization requirements for the product have been met for the batch concerned;

(c) the manufacturing and testing processes have been validated, if different;

(d) all the necessary checks and tests have been performed and account taken of the production conditions and manufacturing records;

(e) any planned changes or deviations in manufacturing or quality control have been notified in accordance with a well defined reporting system before any product is released.

(f) any additional sampling, inspection, tests and checks have been carried out or initiated, as appropriate, to cover planned changes and deviations;

(g) all necessary production and quality control documentation has been completed and endorsed by supervisors trained in appropriate disciplines;

(h) appropriate in process checks and spot-checks are carried out by experienced and trained staff;

(i) Approval has been given by the head of quality control.

8.13. Continuing training should also be given, and its practical effectiveness periodically assessed.

8.14. Training programmes should be available. Training records should be kept.

8.15. The concept of quality assurance and all the measures which aid its understanding and implementation should be fully discussed during the training sessions.

8.16. Visitors or untrained personnel should preferably not be taken into the production and quality control areas. If this is unavoidable,

they should be given relevant information in advance (particularly about personal hygiene) and the prescribed protective clothing. They should be closely supervised.

8.17. Consultant and contract staff should be qualified for the services they provide. Evidence of this should be included in the records.

9. **Premises**

9.1. Electrical supply should be appropriate and such that they do not adversely affect, directly or indirectly, either the pharmaceutical products during their manufacture and storage, or the accurate functioning of equipment.

9.2. Receiving areas should be designed and equipped to allow containers of incoming materials to be cleaned if necessary before storage.

10. **Equipment**

10.1. Washing, cleaning and drying equipment should be chosen and used so as not to be a source of contamination.

11. **Materials**

11.1. Materials dispensed for each batch of the final product should be kept together and conspicuously labelled as such.

11.2. All products and packaging materials to be used should be checked on delivery to the packaging department for quantity, identity and conformity with the packaging instructions.

11.3. The purchase of starting materials is an important operation that should involve staff who has a adequate knowledge of the products and suppliers.

Finished Products

11.4. Finished products should be held in quarantine until their final release, after which they should be stored as usable stock under conditions established by the manufacturer.

12. Returned Products

12.1. Products returned from the market should be destroyed unless it is certain that their quality is satisfactory; in such cases they may be considered for resale or relabeling, or alternative action taken only after they have been critically assessed by the quality control function in accordance with a written procedure. The nature of the product, any special storage conditions it requires, its condition and history, and the time elapsed since it was issued should all be taken into account in this assessment. Where any doubt arises over the quality of the product, it should not be considered suitable for reissue or reuse. Any action taken should be appropriately recorded.

Reagents and culture media

12.2. There should be records for the receipt and preparation of reagents and culture media.

12.3. Reagents made up in the laboratory should be prepared according to written procedures and appropriately labelled. The label should indicate the concentration, standardization factor, shelf-life, the date when re-standardization is due, and the storage conditions. The label should be signed and dated by the person preparing the reagent.

12.4. Both positive and negative controls should be applied to verify the suitability of culture media each time they are prepared and used. The size of the inoculums used in positive controls should be appropriate to the sensitivity required.

12.5. Reference standards prepared by the producer should be tested, released and stored in the same way as official standards. They should be kept under the responsibility of a designated person in a secure area.

12.6. Secondary or working standards may be established by the application of appropriate tests and checks at regular intervals to ensure standardization.

13. **Documentation**

13.1. The reproduction of working documents from master documents must not allow any error to be introduced through the reproduction process.

14. **Good practices in quality control**

14.1. Out-of-specification results obtained during testing of materials or products should be investigated.

14.2. Records demonstrating that all the required sampling, inspecting and testing procedures have actually been carried out and that any deviations have been fully recorded and investigated.

14.3. All tests should follow the instructions and results should be checked by the supervisor before the material or product is released.

14.4. Sampling equipment should be cleaned and if necessary, sterilized, before and after each use and stored separately.

14.5. Replace with 929 requirements.

14.6. Quality control should evaluate the quality and stability of finished pharmaceutical products and, when necessary, of starting materials and intermediate products.

14.7. A written programme for ongoing stability determination should be developed and implemented.

14.8. Stability should be determined prior to marketing and following any significant changes in processes, equipment, packaging materials.

Quality Rating System

Rating	Meaning	Interpretation
2	Good	Item/area/system/knowledge is superior.
1	Adequate	Item/area/system/knowledge meets basic minimum requirements
0	Deficient	Item/area/system/knowledge is weak and not up to acceptable standards.
X	Critical Deficiencies	Item/area/system/knowledge is missing or of such nature to warrant serious quality/compliance concerns.
NA	Not Applicable	Question is not applicable to type of operation or item was unable to be addressed during the audit.

Comment: -

1. **All deficiencies under critical category will be marked as "X" and one critical finding will make the manufacturing site unsuitable for acceptance till rectified irrespective of scores in other points.**

2. **Some users of the checklist find responses to some questions are difficult to quantify on a 0-2 scale and prefer to use a simple "Yes" or "No" approach. In such cases, a "Yes" should be assigned a "1" value and a "No" should be assigned as "0" value.**

Classification of Findings

Type of Findings	Categorization of Deficiencies:
	Critical (To be marked as "X")
Personnel	- Production and / or testing carried out in the absence of approved competent technical personnel. - Personal hygiene not adequate. - Inadequate training system for personnel
Premises	- No air filtration system to eliminate airborne contaminants that are likely to be generated during manufacturing or wherever the product is exposed. - Processing of sensitive drug* is not segregated from other manufacturing areas and testing facilities. - Critical equipment used for manufacturing operations of products not qualified. - Malfunctioning of the ventilation system that could result in possible localized or occasional cross-contamination. - Maintenance such as air filter replacement, monitoring of pressure differentials not performed. - Utilities (steam, air, nitrogen, vacuum etc) not controlled or monitored when necessary. - Damages (holes, cracks or peeling paint) to wall/ceiling immediately adjacent or above manufacturing areas or equipment where the product is exposed. - Un-cleanable surface created by pipes, fixtures or ducts in the manufacturing area wherever products is exposed. - No separate area/sufficient precautions to prevent contamination or cross-contamination during RM sampling and dispensing. - Surfaces finish (floor, walls and ceilings) that do not permit effective cleaning - Insufficient manufacturing space that could lead to mix-ups. - Personnel are directly entering from exterior to manufacturing and primary packaging areas where products are exposed. - Un-screened / Un-trapped floor drains in the manufacturing area. - Receiving and dispatch bay are not covered. - De-dusting is carried out by air blowing.
Sanitation	- Evidence of widespread accumulation of residues / extraneous matter in the manufacturing areas. - Evidence of gross infestation.
Raw Material Testing	- Evidence of falsification or misrepresentation of analytical results. - No validation of test methods
Manufacturing	- No written Master Formula.

Control	- Evidence of falsification or misrepresentation of manufacturing and packaging records. - Incomplete recall procedure - Inadequate checks for incoming materials.
Equipment	- Premises and equipment not maintained to minimize contamination / generation of particles. - Equipment does not operate within its validated parameters. - Clean in Place (CIP) not validated. - Tanks for manufacturing of liquids and ointments not equipped with sanitary clamps. - Insufficient number of samples for room classification/inadequate sampling methods. - Insufficient environmental controls/ insufficient monitoring for viable microorganism during filling for aseptically filled products. - Inadequate maintenance of PW and WFI systems. - Inadequate re-validation of PW and WFI systems after upgrading, out- of-specs trends. - Inadequate training of personnel for operation of equipment. - Inadequate gowning practices for clean area - Inadequate practices / precautions to minimize contamination and prevent mix-ups - Non-validated time lapse between cleaning, sterilization, use of components, containers and equipment - No consideration given to bio-burden prior to sterilization - Non-validated time lapse between start of manufacturing and sterilization by filtration - Inadequate procedures for media-fills insufficient number of units filled during media-fills Media- fills do not simulate actual operations • Insufficient number of units filled during media-fills does not simulate actual operations. • Capability of media to grow a wide spectrum of microorganisms not demonstrated • Misinterpretation of results for media-fills - Absence of leak test for ampoules - PW is not used as the feed water for the WFI system and the clean steam generator. - The WFI used in the preparation of Parenterals is not tested for endotoxins.
Quality Control Department	- QC department not a distinct and independent unit, lacking real decisional power, with evidence that QC decisions are often overruled by production department or management. - Evidence of falsification or misrepresentation of analytical data.
Finished Products	- Finished product not tested for compliance with applicable specifications before release for sale. - Evidence of falsification or misrepresentation of testing

Testing	results. - Evidence of falsification or misrepresentation or records. - Samples for sterility testing not representative of the entire production run. - Insufficient quantity of samples for testing of finished products or active Pharmaceutical ingredient.
Stability	- No data available to establish the shelf-life of products. - Evidence of falsification or misrepresentation of stability data.
Sterile Products	- Sterilization cycles based on probability of survival not validated. - Water for injection (WFI) systems not validated. - No media fills performed (Simulation) to demonstrate the validity of aseptic filling operations. - No environmental controls / No monitoring for viable microorganisms during filing for aseptically filled products. - Aseptic filling operations continued even after unsatisfactory results obtained for media fills without any corrective action. - Batches failing initial sterility test released for sale on the basis of a second test without proper investigation. - Steam used for sterilization not monitored to assure suitable quality and absence of contaminants. - Inadequate control on the number of personnel present in clean and aseptic areas. - Gases used to purge solutions or blanket products not passed through a sterilizing filter - Inadequate inspection for particles and defects.
	Deficient (To be marked as "0")
Premises	- Physical and electronic quarantine accessible to unauthorized personnel / Physical quarantine area not well marked and / or not followed when used. - Outlets for liquids and gases not marked. - Damages to surfaces not directly adjacent or above exposed products - Non-production activities performed in production areas - Inadequate rest, change, wash-up and toilet facilities.
Equipment	- Insufficient distance between equipments and walls to permit cleaning - Base or immovable equipment not adequately sealed at points of contact - Use of temporary means or devices for repair - Defective or unused equipment not removed or appropriately labeled
Sanitation	- Inadequate sanitation/ disinfection program - Incomplete written sanitation program but premises in acceptable state of cleanliness - Sanitation or Health and hygiene programs not properly implemented or followed by em0ployees
Manufacturing	- Incomplete SOPs for handling of materials and

Control	products - Access to production areas not restricted to authorized personnel - Written procedures incomp0lete for packaging operations
Packaging Material Testing	- Multiple lots comprising one consignment not considered as separate lot for sampling, testing and release - Inadequate procedures of transportation and storage - Incomplete testing - Inadequate specification
Finished Product Testing	- Incomplete testing of physical parameters
Records	- Incomplete records / documentation for a product - Incomplete plans and specifications for the manufacturing buildings - Incomplete documentation pertaining to supervisory personnel - Insufficient retention time for evidence and records to be maintained - Incomplete records for the sanitation program - No organization charts
Samples	- Samples of RM not available - Improper storage conditions
Stability	- Insufficient number of lots in continuing stability program - Incomplete testing of parameters - Insufficient quantities for complete testing

* Sensitive drugs: Beta lactum antibiotics, Sex Hormones and cytotoxic substances etc.

BENCHMARKS

1.	*General Observations*	**Quality Rating**			
	Location and surroundings:	2	1	0	X
1.1	**How factory building is situated and controlled to avoid risk of contamination from external environment including open sewage, drain, public lavatory or any other factory which produces disagreeable or obnoxious, odors, fumes, excessive soot, dust, and smoke, chemical or biological emissions.** ***Pls specify industries / establishments adjoining manufacturing site.***	Situated in eco-friendly zone with less than 50% FAR with the surroundings in the campus is free from dust and planned greeneries. Dedicated AHU's are provided for each operation.	Situated in industrial area and not effective by other industries. AHU's also provided.	Situated in industrial area and obnoxious, Fumes, Smoke is produced in the surroundings, although AHU's are provided	No AHU.
1.2	**Building and premises: -**				
1.2.1	**How the building has been designed constructed and maintained to suit the manufacturing operations so as to produce drugs under hygienic conditions.**	Made of RCC and layout is such so that uni-flow system of	Made of RCC and interior surfaces are smooth, free from cracks and permits easy cleaning.	Cracks are seen at many places.	--

	Pls specify nature of construction used in the facility in respect of its maintenance and hygienic conditions.	man and material is maintained and interior surfaces are smooth, free from cracks and permits easy cleaning. Maintenance of hygienic conditions is excellent and proper documents are available. All the manufacturing and surrounding corridors including change rooms are made of epoxy flooring and interior surfaces are free from any cracks or joints.			
1.2.2	**Whether the building confirm to the conditions laid down in the**	--	Yes	No	--

	Factories Act, 1948 ***Pls attach valid factory certificate/ license issued by the competent authority.***				
1.2.3	**Specify how the premises used for manufacturing operations and testing purpose prevents contaminations and cross contamination is:** **a) Compatible with other drug manufacturing operations that may be carried out in the same or adjacent area.** **Pls specify any special criteria for the product manufacturered. e.g. temperature, humidity, air class requirements maintained for aseptic products, etc.**	Totally dedicated facility for each product or multi-products are manufactured on campaign basis after proper cleaning validation. Temperature, humidity and extraneous particles are controlled with the help of AHU.	Multi-products are manufactured after batch clearance by proper cleaning which is validated temperature and humidity are controlled.	No such measures are taken to prevent contamination and cross contamination	--
1.2.4	**b) Whether adequate working space is provided to allow orderly and logical placement of equipment, materials and movement of personnel so as to avoid risk of mix-**	---	Yes	No	--

	up between different categories of drugs and to avoid possibility of the contamination by suitable mechanism. **Pls specify space left around the machines. Pls attach equipment lay out, men and material movement, waste movement if applicable.**				
1.2.5	**c) Describe the pest, insects, birds and rodents control system followed in the premises.** **Attach copy of pest / rodent control schedule along with contract agreement if any.**	--	Agreement copy and SOP in place.	Neither agreement copy nor SOP available.	--
1.2.6	**d) What measures have been taken to make Interior surface of (walls, floors, and ceilings) smooth and free from cracks, and to permit easy cleaning** ***Specify material of construction and finish for walls, ceiling, floor, coving etc. i.e. whether Epoxy or PU coated, kota / granite stone with epoxy sealed joints, solid / GI / gypsum / cal. Silicate board ceiling with epoxy, PU or any other pre-fabricated***	Wall surface and ceiling are made up of GRP Panel, Epoxy/PU painted and the floors are made up of epoxy/PU.	Wall surface and ceiling are made up of washable paints and the floors are made up of Kota stone joints of which are sealed with epoxy.	Kota stone flooring with no sealed joints.	--

	panel (GRP, powder coated SS or Aluminum etc.) paint.				
1.2.7	**e) What measures have been taken so that the production and dispensing areas are well lighted and effectively ventilated, with air control facilities.** **Pls specify the lux level maintained in various parts of the premise.**	Lux level defined. Dispensing booth has separate man and material entry and background of this is a clean area.	Adequate light. Dispensing booth is provided with clean background.	Light is not adequate. No dispensing booth. Only a clean area is provided for dispensing.	--
1.2.7.1	**Pls specify the air handling system used in various areas like stores, production, packing, QC areas etc.**	Totally dedicated AHU for each operation.	Separate AHU for critical area.	No	--
1.2.8	**f) Specify drainage system which prevents back flow and entry of insects and rodents into the premises.** ***(pls specify number and location of drains installed)***	GMP drains with cleaning records and SOP in place. Drawing is also available specifying the number and location of drains.	GMP drains with cleaning records and SOP in place.	GMP drains with SOP only.	No GMP drain.

1.3	**Water system: -**				
1.3.1	**Whether the unit has validated system for treatment of water drawn from own or any other source to render it potable in accordance with standards specified by BIS or local municipal norms.** **Pls specify source of raw water and give details of treatment processes, sampling points, distribution and storage system for raw and purified water.**	IQ, OQ, DQ, PQ avalable. Vent filter and spray ball provided.	OQ, PQ available.	System is not validated.	--
1.3.1.1	**How bio burden in purified water controlled / reduced.**	RO/Mixed bed System	Mixed Bed	No provision	--
1.3.2	**How water tank are cleaned periodically and records maintained thereof. How water distribution system is sanitized to control microbial contaminations.**	Cleaning records available along with cleaning validation. Distribution lines are sanitized by steam or by chemicals with defined validated procedure	Cleaning records available. Distribution lines are sanitized by hot water or by chemicals with defined validated procedure.	Systems is deficient.	--

1.4	**Disposal of waste: -**				
1.4.1	**Specify the system of disposal of sewage, and effluents (solid, liquid, and gas) from the manufacturing site.** **(Enclosed the copy of NOC obtained from State Pollution Control Board in this regard).**	ETP plant available.	NOC from State Govt. available.	No NOC	--
1.4.2	**Whether provision for disposal of bio-medical waste made as per the provisions of the Bio Medical Waste (Management and Handling) Rules 1996.**	SOP in place, followed and records are maintained.	SOP in place and followed accordingly.	No SOP.	--
2.	***Warehousing Area: -***				
2.1	**Whether adequate areas have been allocated for warehousing of Raw Materials, intermediates, Packaging Material, products in quarantine, finish products, rejected or returned products.** **How these areas marked or segregated.** **Please specify the total area provided for warehousing.**	Physically segregated area.	Area in cleaning earmarked.	Not earmarked.	--

2.2	**How the warehousing areas being maintained to have good storage conditions. Are they clean and dry and maintained within acceptable temperature limits?**	Provision for fresh air supply .Centralized system for controlling temperature and humidity if required.	Suitable exhaust provided. Split AC provided if required.	Suffocated	--
	Specify the storage arrangement provided for materials which sensitive to temperature, humidity and light and how the parameters are monitored. Is cold room or deep freezers required for storage of goods? If yes, how the temperature is monitored.	Cold room provided with facility for recording temp. Thermal mapping records available.	Cold room provided and temp. is recorded manually.	No Cold room No record maintained	--
2.2.1	**Whether proper racks, bins and platforms have been provided for the storage.**	--	Yes	No	--
2.3	**Whether receiving and dispatch bays are maintained to protect in coming and out going materials.**	Completely covered	Partially covered	Shed	-
2.3.1	**How incoming materials are treated and cleaned before entry into the plant. Please specify the cleaning system for the outer surface of the container.**	Deducting by tunnel	By vaccum	Wiping	Blowing

2.4	**How quarantined materials are segregated from other materials.** **How access to quarantined area is restricted.**	Physical segregation. only authorised personnel are allowed	Earmarked area	Not earmarked	No defined area
2.5	**Whether separate sampling area for active Raw Materials and Excipients is provided and maintained.** **If yes, what is the control on entry of material and men into the sampling area. Whether reverse LAF have been provided for sampling. Whether log book for sampling booth maintained.** **If not what provision has been made for sampling so as to prevent contamination, cross contamination and mix-ups at a time of sampling.**	Separate area for active and excipient. Sampling is done in classified area(A/D) with separate man and material entry. Suitable pressure difference is maintained.	Separate area with RLAF	Only exhaust provided	--
	Specify the arrangements provided to sample the primary packaging materials foils, bottles, etc which are used as such.	Sampling booth provided	Separate area is earmarked	---	--

2.5.1	**Pls specify sampling plan used.** **Which type of sampling tools are used and how they are cleaned, dried and maintained.**	N.P or R plan. Dedicated washing facility in warehouse only and cleaning procedure is validated	Defined plan. Cleaning procedure is validated	No plan. Cleaning procedure is not validated	-
	How containers are cleaned before and after sampling. Who carries out the sampling? **(Pls specify whether the sampling is carried out as per the current SOP).**	Vaccum	Wiping	None	--
2.5.2	**What precautions are taken during sampling of photosensitive, hygroscopic materials?**	Neon lamps are provided. Sampling area has centralized system for controlling humidity	Lights are switched off in the exposed area. Portable dehumidifier available	No arrangements made	
2.6	**What provisions have been made for segregated storage of rejected, recalled or returned materials or products.** **How is the access to these areas restricted?**	Segregated area and only authorized access.	--	--	--

2.7	**How highly hazardous, poisonous and explosive materials, narcotics, and psychotropic drugs are handled and stored.** **How these areas are safe and secure.** **Is there certification from competent authority for handling of explosives etc. If any. Pls attach the certificate issued by the competent authority.**	In segregated area with all safety features. Certificate from competent authority available.	In segregated area with all safety features	--	--
2.8	**How printed secondary packaging materials are stored in safe, separate and secure manner.**	----	Stored in safe, separate and secured area.	--	--
2.9	**Specify the arrangement provided for dispensing of starting materials.** **What is the control on entry of material and men into the dispensing area?** **Whether reverse LAF have been provided for dispensing with back ground clean air supply.** **Whether pressure differential is maintained between the dispensing and adjacent areas.**	Separate area for active and excipient. Sampling is done in classified area(A/D) with separate man and material entry. Suitable pressure difference is maintained.	Separate area with RLAF	Only exhaust provided	--

2.9.1					
2.9.2	**Which type of dispensing tools are used and how they are cleaned, dried and maintained.** **How containers are cleaned before and after dispensing. Who carries out the dispensing?** **(Pls specify whether the dispensing is carried out as per the current SOP).**	Dedicated washing facility in warehouse only and cleaning procedure is validated	Cleaning procedure is validated	Cleaning procedure is Not validated	-
2.10	**How and where sampling of sterile materials carried out.**	Separate classified area suitable for aseptic sampling conforming to grade A/C within store with separate man and material entry	Dedicated area for sampling within the sterile production area	No dedicated area	-
2.11	**What steps are taken against spillage, breakage and leakage of containers?**	--	Containers are checked and condition of the containers are noted	NO arrangements made	--
2.12	**What provisions have been made to prevent the entry of rodents, insects, birds.**	Agreement copy and SOP in	Agreement copy and SOP in place.	Only SOP available.	No system.

	Which substance is used for pest control and how it is handled. **(Pls specify whether the pest control is carried out as per the SOP).**	place. Further it is ensured by validation that no residue is left.			
3.	***Production Area: -***				
3.1	**Please specify the design of the manufacturing area which allow uni-flow and logical sequence of operations so as to prevent product contamination/ mix ups.** **Is there any criss cross of flow of materials and men.** **Specify the position of IPQC lab in the manufacturing area .** **Please specify whether non storage areas used for storage of any material.**	--	Primary and secondary areas are separated. Separate man and material movement in the production area. IPQC designed in such a manner that may not cause cross contamination.	No measures established	--
3.2	**Whether separate dedicated and self-contained facilities have been provided for the production of sensitive pharmaceutical product like Penicillin, Biological preparation with like micro-**	With isolator technology	Dedicated facility	On campaign basis	--

	organism, Beta lactam, Sex Hormones and Cytotoxic substances. **If yes pls explain how and attach copy of plan of premises of each category of drug.**				
3.3	**Please specify the provisions of storage of dirty, washed and cleaned equipment parts, tool room, in process storage areas etc. Which provide sequential / logical manner so as to prevent contamination and cross contamination?**	Dedicated washing facility within each Productio n suite	Dedicated facility	No dedicated area	--
3.4	**Please specify how service lines like pipe work, electrical fittings, ventilation openings etc. are identified by colors for nature of supply and direction of the flow.** **Whether service lines in production areas are through service pendants.** **If not, how they are placed so as to avoid accumulation of dust.**	Through pendants	Surface mounted	--	--

4.	***Ancillary areas: -***				
4.1	**Please specify the position of rest and refreshment rooms and mention whether they are separate and not leading directly to the manufacturing and warehouse areas.**	--	Separate and outside the manufacturing area	Inside the manufacturing area	--
4.2	**Are there general change rooms in plant?** **Are toilets, change room separate from mfg. Area? Pls specify number of washing station & toilets provided for number of users.** **Whether change facilities separated for both sexes.** **How many sets of protective garments provided for each personnel entering production area.** **Is there in house general laundry for garment washing / cleaning? If not how garments washing are carried out and monitored.**	--	Separate and outside the manufacturing area Separate for male and female	Inside the manufacturing area	--
4.3	**Whether maintenance workshop is separate and away from production.**	--	Yes	No	__

4.4	**Whether animals for production or testing are housed in the facility if so whether areas housing animals are isolated from other areas.** **Please specify the provision of air conditioned and ventilation system for the animal house.** **How quarantined, under test and tested animals housed and controlled.** **How animal carcass are disposed of.** **Pls attach copy of CPCSEA.**	Isolated block with separate AHU's and has certificate from competent authority. Segregated area for quarantine, under test and tested	Yes	No	__
5.	**Quality Control Area: -**				
5.1	**Whether QC area is independent of production area.** **Whether QC carries out its own:** • **physico-chemical testing,** • **biological testing,** • **microbiological testing & sterility testing and** • **Instrumental testing.** **Whether firm is outsourcing testing. If yes names of the testing laboratories contacted or approved. Pls give**	Independent area. Testing is carried out at its own. Contract agreement available. Safety equipments installed at all strategic points.	Yes	No	__

	list of test currently outsourced. **In case of contractual testing what are the responsibilities of contract giver and contract acceptor. (Copy of the contract should be enclosed)** **Are there safety installation such as shower, eye washer, fire extinguisher etc in the laboratory.** **Is there separate area for humidity chambers for stability studies. How many humidity chambers have been provided. Pls attach stability calendar.**				
5.2	**Please specify the arrangement provided for handling and storage of test samples, retained samples, reference standards / cultures, reagents.** **Whether separate area for storage of reagents and glassware provided.** **Whether separate records room is provided.**	Separate space/area provided for each separate records room.	Yes	No	__
5.2.1	**How hazardous or poisonous materials are stored and handled.**	--	Separate area with all safety features	No separate area and no safety features	--

5.3	**How environmental conditions are met during the course of storage and testing of samples.** **Whether separate washing and drying area provided.**	-	Centralized AHUs and/or Air condition provided Separate washing and drying area have been provided	No separate washing and drying area have been provided	--
5.3.1	**Which grade of glassware are used in assay procedures.**	--	Class A certified glassware	Class B with calibrated against Class A	--
5.3.2	**Whether separate AHU's are provided for biological, microbiological and radio iso-topes testing areas with HEPA filter arrangement.**	--	Separate AHU's are provided with HEPA	No AHU	--
5.4	**Whether separate areas provided for sterility testing within microbiology lab.** **Whether support areas are under AHU.** **Whether double door autoclave provided for sterilization of materials.**	--	Yes	No	--
	Whether entry to the sterility area is through three air lock systems. **What is the air class of these testing areas and whether pressure difference is maintained in these areas?**	--	Yes, 15 P difference. Class-A/C	No	--

	Which types of workbenches are provided in these areas for testing? **When was the last filter integrity tests performed on HEPA filters.**	--	Vibration proof benches		Wooden benches	--
	How waste (cultures etc) disposed of. **Whether in case of antibiotic potency testing, statistical proof of the determination of potency and validity of the test carried out.**	--	Autoclaved and sent for disposal as per biomedical waste contract		No proper disposal	--
6.	***Personnel: -***					
6.1	**Whether the manufacturing and testing of drugs is conducted under approved technical staff** **Names of Technical Staff along with qualification & experience** **<u>For Manufacturing: -</u>** **<u>For Analysis:</u>**		Approved and adequate in No.	Approved but not adequate in number	Not approved	--
6.2	**Please specify whether head of Q.C. is independent of manufacturing unit**		--	Yes	No	-
6.3	**Name, qualification and experience of the personnel responsible for Quality Assurance function.**					
6.4	**Whether responsibilities for production and QC laid down and followed.**		--	Yes	No	-
6.5	**Whether adequate number of personnel employed in direct proportion to the work load.**		--	Yes	No	-

6.6	**What is the firm's policy on training of personnel at various levels?**	--	Yes	No	-
7.	***Health, clothing and sanitation of workers: -***				
7.1	**Whether personnel handling Beta lactam antibiotics are tested for penicillin sensitivity before employment.**	--	Yes	No	-
7.2	**Whether personnel involved in handling of sex hormones, cytotoxic and other portent drugs are periodically examined for adverse effect.** **(Pls specify whether the current SOP is followed or not).**	--	Yes	No	-
7.3	**Whether all personnel prior to employment have undergone medical examination including eye examination and all free from Tuberculosis, skin and other communicable or contagious diseases**	--	Yes	No	-
	Whether there is a SOP for medical examination.	--	Yes	No	-
	Pls give name and qualification of contracted medical officer for medical examination.	--	Given	Not given	--
	Whether investigational reports, films of X rays etc. preserved. **Whether records of such medical examination are maintained thereof**	--	Yes	No	-
7.4	**Whether all personnel are trained to ensure high level of personal hygiene.** **Pls attach training calendar of last two years.**	--	Yes	No	-
7.5	**Whether proper uniforms and adequate facilities for personal cleanliness are provided.** **Pls specify nature and type of dress used by the personnel in**	--	Yes	No	-

	various areas of operation. **How many dress/footwear have been provided to each personnel.** **Please specify whether cross over bench is in place in the change room and if so whether it rule out the possibility of entering dust particle to the clean side.** **Whether arrangements provided for cleaning of outside dust and dirt from foot** **Please specify whether hands are disinfected before entering the production area** **Whether for sterile garments in house clean laundry has been provided.**				
8.	***Manufacturing Operations and Controls: -***				
8.1	**Whether the contents of all vessels and containers used in manufacture and storage is conspicuously labeled with the name of the products. Batch no, Batch Size, and stage of manufacture along with signature of technical staff.**	--	Yes	No	-
8.1.1	**Whether the products not prepared under aseptic conditions are free from pathogens like Salmonella, Escherichia coli, Pyocyanea etc.**	--	Yes	No	-
8.1.2	**If yes, pls give brief account of measures taken to assure freedom from pathogens.**	Purified water under recirculation is used	Freshly collected	No validation and control	--

8.2	***Precautions against mix-up and cross-contamination: -***				
8.2.1	**Whether proper AHU, pressure differential, segregation, status labeling have been provided to prevent mix-up and cross-contamination in manufacturing area**	--	Yes	No	-
	Pls specify the areas of dust generation and mechanism involved in controlling the dust.	Centralized dust extraction system	Localized dust extraction system	Exhaust	No dust extraction system
	Do all the areas have their own independent air locks separately for men and material entry.	Separate	Only few	Not separated at all	--
	What criteria of pressure differential has been set for production v/s adjoining areas.	15P	5-15 P	1-5 P	No Pr. Diff.
	Whether various operations are carried out in segregated areas.	-	Yes	No	--
8.2.2	**Whether processing of sensitive drugs like Beta lactum Antibiotics and Sex Hormones is done in segregated areas with independent AHU and proper pressure differentials alongwith demonstration of effective segregation of these areas with records.**	Separate modules/Isolators with independent AHU's	Dedicated areas with independent AHU's	Not dedicated areas	-

	Please specify what measures has been taken to prevent contamination of products with Beta Lactum Antibiotics, Sex harmons and cyto toxic substances	Water system is also separate and independent	Separate distribution lines	-	--
8.2.3	**What measures has been taken to prevent mix-ups during various stages of production.**	--	Physical segregation, labeling etc.	No control	--
	Whether equipments use for production are labeled with their current status.	--	Yes	No	--
8.2.4 & 5	**Whether packaging lines are independent and adequately segregated.**	--	Yes	No	-
	How line clearance is performed. Whether records of line clearance is maintained according to appropriate checklist.	--	Yes	No	-
8.2.6	**Whether separate carton coding area has been provided or online carton coding is performed** **How carton coding procedure is controlled.**	Online carton coding	Separate carton coding area provided	Within packaging section but area is not enclosed	--
8.2.7	**Please specify how temperature, humidity and air filtration are controlled in the areas where raw material and/or products are exposed and handled.**	Centralized system with chemical dehumidification and temp.	Inbuilt. HEPA in plenum	Localized	--

		by heating coils. Air filtration is controlled by HEPA filters located terminally			
8.2.8	**How access of authorized persons to manufacturing areas including packaging is controlled.**	Electronically	Manually. Names of the authorized personnel are displayed	No system	--
	Whether separate gowning provision is follows before entering into the procedure.	--	Yes	No	--
8.2.9	**Whether segregated secured areas for recall or rejected materials or for such material which are to be processed or recovered are provided.** **Please specify the room No. of such areas in the plant.**	--	Yes	No	--
9.	***Sanitation in the Manufacturing areas:-***				

9.1	**Specify the cleaning procedure of the manufacturing areas.** **Whether cleaning procedure is validated.** **Please specify validation protocol No. of the same.**	--	Yes	No	--
9.2	**Whether the manufacturing areas are used as the general thoroughfare and storage of materials not under process.**	--	Yes	No	--
9.3	**Whether a routine sanitation program is in place.** **Please specify detailed account of sanitation proramme specific to various areas, equipment.**	--	Yes	No	--
9.4	**Dose the location facilitate cleaning of equipment as well as the cleaning of the areas in which they are installed.**	--	Yes	No	--
9.5	**Whether production area is adequately lit. If yes.** **Please give lux levels provided in production, visual inspection and other areas.**	--	Yes	No	--
10	***Raw Materials: -***				
10.1	**Whether the hard copies of records of Raw Materials are maintained as per schedule-U.**	--	Yes	No	--
10.2	**Please specify the procedures followed receiving and processing of in-coming materials (Starting materials and packing material).**	-	Deducting is done followed by making GRN & sampling.	No Proper SOP	--
	Whether first in / first out or first expiry principal has been adopted.	--	Yes	No	--

10.3	**How they are labeled and stored as per their status – Under Test, Approved and Rejected**	--	Yes	No	--
10.4	**Whether incoming materials are purchased from approved sources.**	--	Yes	No	--
	What is the procedure for approving the source for incoming materials.	Pre audit is carried and raw materials are validated as per the defined specifications	Purchasing from reputed sources / past exp.	No system	--
	Whether the raw materials are directly purchased from the manufacturers.	Directly	From approved supplier of that manufacturer	No vendor approval system found in place	--
	Whether list of approved vendors is available to the user.	--	Yes	No	--
10.4	**How damaged containers are identified recorded and segregated.**	--	Sop in place and followed	No proper control	--

10.5	**Whether each batch of a consignment is considered for sampling, testing and release.**	--	Yes	No	--
	Whether all the containers of each batch of starting materials is sampled for identification test.	NPR-plan	Defined Sop	No Sop	--
10.6	**Whether labels of raw material in the storage area have information like** (a) designated name of the product and the internal code reference, where applicable, and analytical reference number; (b) manufacturer's name, address and batch number; (c) the status of the contents (e.g. quarantine, under test, released, approved, rejected); and (d) the manufacturing date, expiry date and re-test date.	--	Yes	No	--
10.7	**Whether separate areas are provided for under test, approved and rejected materials.**	--	Yes	No	--
	How control on temperature and humidity conditions, wherever necessary, maintained in these storage areas.	Centralized system for controlling temp. & humidity	Split AC/ Portable dehumidifier	Only AC provided	No system in place

10.8	**How the containers from which samples have been drawn labeled.**	--	Sign. Of sampler in place & number of containers mentioned	NO proper plan	--
10.9	**Please specify the procedures by which it is ensured that the raw materials which has been released by the Quality Control Department and which are within their shelf life are going to be used in the product.**	Electronically controlled system	Bin card system	Manually	No system
10.10	**How materials are stacked in the Stores i.e on Pallets, racks etc.**	Up to 5 stacked or more if load bearing study is in place	Up to 5 stacked	No system	--
11	***Equipment: -***				
11.1	**Whether the equipments are designed aiming to minimize risk of error and permit effective cleaning in order to avoid cross contamination, build up of dust.**	CIP	Designed as such which permits effective cleaning	Improperly designed	--

	Whether all equipment are provided with log book.	--	Yes	No	
	Please specify the procedures to clean the equipment after each batch production.	--	Sop in place	No SOP	--
	Whether validity period for use after the cleaning of equipment is specified.	--	Yes	No	--
	Whether separate area is provided for storage of machine parts etc.	Dedicated area provided with manufacturing area	Stored separately in processing area	No separate area	--
11.2	**Whether balances and other measuring equipments with appropriate range are available in the Raw Material stores & production areas and they are calibrated in accordance with SOP maintained.** **Specify the calibration schedule of the balances.**	--	Calibrations records availabl e	No calibration records available	--

11.3	**Please specify material of construction of contact parts of the production equipments.**	All the contact parts and outer surfaces of the machines and equipments are made up of SS 316.	Yes	No.	--
11.4	**Which types of lubricants are used in the equipment.** **Specify the quality and control reference No. of these lubricants.**	Edible grade and test reports available	Edible grade	Non edible grade	--
11.5	**Specify the procedures to remove defective equipments from production areas.**	--	SOP in place	No SOP	--
12	***Documentation and Records: -***				
12.1	**How the documents are designed, prepared, reviewed and controlled to provide an audit trail.**	--	SOP in plan	No SOP	--
12.1.1	**Whether documents are approved signed and dated by appropriate and authorized person.**	--	Yes	No	--

12.2 12.3	**Whether documents specify title, nature and purpose.** **Whether documents are regularly reviewed and kept up to date. If yes. Please specify review period.** **Please attached the list of documents maintained by the firm.**	--	Yes Yes as per SOP	No No	-- --
12.4	**Whether the records are made at the time of each operation in such a way that all significant activities concerning to the production are traceable.**	--	Yes	No	--
12.5	**Whether data is recorded by electronic data processing system or by other means. If by electronic data processing system then how access is controlled to enter, modify etc. the data.**	--	With authorized persons only	No control	--
	Whether master formula and detailed operating procedures are maintained as hard copy.	--	Yes	No	--
	Who is responsible for maintenance of these records.	QA	QC/QA	QC/QA	--
13	***Labels and Other Printed Materials:***				
13.1	**Whether the printing is in bright colour and legible on labels and other printed materials.**	--	Yes	No	--

	How printed labels (art work) are approved. Is there any SOP for this if yes please give current SOP No.	QA	QC/QA	QC/QA	No approval
	Which colour coding system is used to indicate the status of a product and equipment.	--	As per SOP	No color coding system available	--
13.2	**How printed packaging materials, product leaflets etc. are stored separately to avoid chances of mix-up.**	In pigeon hole almirahs. Room is air conditioned	In pigeonhole almirahs but the area is not air conditioned	Not in pigeonhole almirahs	
13.3	**How labels cartons boxes circulars inserts and leaflets are controlled.**	--	Reconciliation is done	Not done	--
13.4	**Whether the samples from the bulk are drawn tested, approved and released prior to packaging and labeling.** **How carryout the sampling.**	--	QC	Production	--
13.5	**How records of receipt of all labeling and packaging materials are maintained.**	--	Yes	No	--
	Whether re-conciliation of used packaging materials is maintained. **Whether unused packaging materials return to the store or destroyed.**	--	Destroyed	Returned	--

	How returned/unused packaging material like foils is controlled so as to prevent contamination and cross- contamination.	--	By labeling properly	No proper control	--
13.6	**How the labels of reference standard and culture maintained.**	--	With special tapes resistant to temp. & humidity	Not maintained properly	--
14	***Quality Assurance: -***				
14.1 **(a)**	**Specify the comprehensive quality assurance system maintained by the firm *Inter-alia* to cover deviation, reporting, investigation and change control.** **How the products are designed and developed in accordance with GMP.**	Separate head with adequate staff	QC/QA head is same but separate staff for QA	No QA	--
(b)	**Please specify the arrangements provided to ensure that correct starting and packaging materials are used for manufacture.**	--	Specifications available	No specification available.	--
(c)	**Please specify the mechanism by which all control like IP QC Calibration, Validation etc. are ensured.**	--	IPQC in place Proper SOP maintain	No SOP followed	--

(d)	**Please specify the mechanisms to ensure that the finished product has been correctly processed and checked in accordance with the established procedures.**	--	--	All the parameters are reviewed by QA	--
(e)	**Please specify the mechanisms to ensure that Pharmaceuticals products are released for sale by authorization person.**	--	SOP in place	No SOP	--
15	***Self Inspection and Quality Audit: -***				
15.1	**Whether the firm has constituted a self inspection team supplemented with a quality audit procedure to evaluate that GMP is being followed. If no. How internal audits are carried out.**	Self inspection team with external expert	Self inspection team	Team not competent	--
	What is the system of monitoring, evaluation of self inspection.	--	Matrix inspection schedule found in place.	No schedule found in place.	--
	How conclusion and recommended correcting actions are followed and adopted.	--	Sop in place	No SOP in place	--
15.2	**What is the frequency of self-inspection.**	--	Twice a year and in case of exigencies	No schedule.	--

15.3	**Is there any proforma for carrying out the self-inspection.** **Please indicate the date of last self-inspection**	--	Yes	No	--
16	***Quality Control System: -***				
16.1 to 16.3	**Please specify the details of quality control system of the unit.**	--	System in place.	Unorganized QC System	--
	How the reference standards are stored, evaluated and maintained. **Please provide list of reference standard and reference impurities procured from the authentic sources.**	Stored as per requirements. Traceability data available and standards are validated at periodic intervals	Stored as per requirements. Traceability data availabl e	System deficient	No reference standards available
	Please specify the procedures of preparation of working standard from the reference standards.	--	As per SOP	No SOP exist	--
16.4 & 16.5	**Whether SOPs for sampling, inspecting, testing of Raw Materials, Finish products, Packing Materials and for monitoring environmental conditions are available.**	--	Yes	No	--

	Whether approved specifications for different materials, products, reagents, solvents including test of identity content, purity and quality available.	--	Yes	No	--
16.7	**How reference samples from each batch of the products are maintained.**	--	SOP in place for easy traceability. Samples are kept in original containers or simulated containers	No SOP	--
16.6 & 16.8 16.9	**Who releases batch of the products for sale or supply.**	--	Authorised person from QC	Unauthorized person.	--
	Whether there is check list for release of a batch. Please specify current SOP No. for batch release.	QA	QA/QC	Management	
	Please specify the sampling procedures from various stages of production.	--	As per SOP	No sop found in place	--

	How it is ensured that the sample collected are representative of the whole batch.	--	Collected in the beginning and at end or at some interruptive incidents	Improper sampling.	--
16.10 16.11	**Please specify the procedures for carrying out the stability studies.**	Separated area provided with stability chambers	Stability chambers provided	No stability chambers	-
	Under what condition stability studies of the products are tested. How many stability chambers have been provided.	Real as well as accelerated	Real only	No stability studies.	--
	How self life is assigned to a product. Please give current stability protocol No.	--	Using Arrhenious equation	No correlation.	--
	Whether records of stability studies are maintained.	--	Yes	No	--
	Please attach stability calendar of last year.	--	Available.	Not available.	--
	How complaints are investigated.	--	Sop in place	No SOP	--

16.12	**How instruments are calibrated and at which interval.**	--	Sop in place	No SOP	--
	How testing procedure validated before they are adopted for routine testing.	As per ICH	In house and pharmacopeal to a limited extent like ruggedness, selectivity etc.	Not validated.	--
	Specify the validation procedure is responsible for validation of procedures.	--	Yes	No	--
	How validation procedures are documented (Please indicate various protocols/ recoding system applied during validation).	--	Process validation protocol of report found in place.	No PVP & PVR found in place.	--
16.13	**Whether specifications for raw materials intermediates final products and packaging materials are available.**	--	Yes	No	--
	Whether periodic revision of these specifications are carried out. **Please specify No. of STPs being maintained by the firm.**	--	Yes	No	--
16.14	**Which pharmacopoeias in original are available in the plant.**	--	Yes	No	--

17	***Specifications: -***				
17.1	Whether specification of raw material include. (a) the designated name and internal code reference; (b) reference, if any, to a pharmacopoeial monograph; (c) qualitative and quantitative requirements with acceptance limits; (d) name and address of manufacturer or supplier and original manufacturer of the material; (e) specimen of printed material; (f) directions for sampling and testing or reference to procedures; (g) storage conditions; and (h) Maximum period of storage before re-testing. Whether specification of finished product include (a) the designated name of the product and the code reference; (b) the formula or a reference to the formula and the pharmacopoeial reference; (c) directions for sampling and testing or a reference to procedures; (d) a description of the dosage form and package details; (e) the qualitative and quantitative requirements, with the acceptance limits for release; (f) the storage conditions and precautions, where applicable, and (g) the shelf-life.	--	Yes	No	--
17.2	Whether the container and closures meet the pharmacopial specifications. Whether second hand or used containers and closures used.	--	Yes	No	--

18	**Master Formula Records: -**				
	How master formula records are prepared, authorized and controlled.	--	Respon sibility with QA Deptt.	No Assigned responsibility	--
	Whether head of production, quality control and quality assurance unit endorse this documents. Whether master formula is batch size specific. **Whether all products have master formula containing.** **(a) the name of the product together with product reference code relating to its specifications;** **(b) the patent or proprietary name of the product along with the generic name, a description of the dosage form, strength, composition of the product and batch size;** **(c) name, quantity, and reference number of all the starting materials to be used. Mention shall be made of any substance that may 'disappear' in the course of processing.** **(d) a statement of the expected final yield with the acceptable limits, and of relevant intermediate yields, where applicable.** **(e) a statement of the processing location and the principal equipment to be used.** **(f) the methods, or reference to the methods, to be used for preparing the critical equipments including cleaning, assembling, calibrating, sterilizing;** **(g) detailed stepwise processing instructions and the time taken for each step;** **(h) the instructions for in-process control with their limits;** **(i) the requirements for storage conditions of the products, including the container, labeling and special storage conditions where applicable;** **(j) any special precautions to be observed;** **(k) packing details and specimen labels.**	--	Yes	No	--
19 & 20	**Packaging Records: -**				

	Whether authorized packaging instructions for each products, pack size and type are maintained and complied with. **Whether following are included in the packaging instructions.** **(a) Name of the product;** **(b) description of the dosage form, strength and composition;** **(c) the pack size expressed in terms of the number of doses, weight or volume of the product in the final container;** **(d) complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types with the code or reference number relating to the specifications of each packaging material.;** **(e) reproduction of the relevant printed packaging materials and specimens indicating where batch number and expiry date of the product have been applied;** **(f) special precautions to be observed, including a careful examination of the area and equipment in order to ascertain the line clearance before the operations begin.** **(g) description of the packaging operation, including any significant subsidiary operations and equipment to be used;** **(h) details of in-process controls with instructions for sampling and acceptance; and** **(i) Re-cancellation after completion of the packing and labeling operation.** **(j) Whether line clearance records are part of batch packing records.**	--	Yes	No	--
21	***Batch Processing Records*** **(BPR)**				

21.1	**Whether BPR are based on current master formula record.** **How BPR are designed to avoid transcription errors.** **Whether the Batch Processing Records for each product on the basis of currently approved master formula is being maintained.** **Whether following information are recorded in BPR** **(a) the name of the product,** **(b) the number of the batch being manufactured,** **(c) dates and time of commencement, significant intermediate stages and completion of production.** **(d) initials of the operator of different significant steps of production and where appropriate, of the person who checked each of these operations,** **(e) the batch number and/or analytical control number as well as the quantities of each starting material actually weighed,** **(f) any relevant processing operation or event and major equipment used,** **(g) a record of the in-process controls and the initials of the person(s) carrying them out,** **and the results obtained,** **(h) the amount of product obtained after different and critical stages of manufacture (yield),** **(i) comments or explanations for significant deviations from the expected yield limits shall be given,** **(j) notes on special problems including details, with signed authorization, for any deviation from the Master Formula,** **(k) Addition of any recovered or reprocessed material with reference to recovery or reprocessing stages.** **Specify the procedures for all the entries made in BPR's.**	--	Yes	No	--

22	**Standard Operating Procedure and Records: -**				
22.1 to 22.5	**Whether SOPs and records are being maintained and complied for the following.** **SOP for receipt of in coming material** **(n) SOP for Internal labeling, quarantine, storage, packaging material and other materials** **(o) SOP for each instrument and Equipment** **(p) SOP for sampling** **(q) SOP for batch numbering** **(r) SOP for testing** **(s) SOP for equipment assembly and validation** **(t) SOP for Analytical apparatus and calibration** **(u) SOP for maintenance, cleaning and sanitation** **(v) SOP for training and hygiene for the personal** **(w) SOP for retaining reference Samples** **(x) SOP for handling, re-processing and recoveries** **(y) SOP for distribution of the product** **(z) SOP for warehousing of products.** **Whether applicable SOPs are available in each area where they are required.** **Whether recording formats are referred in SOP.** **Is there SOP for writing an SOP.**	--	Yes	No	--
23	**Reference Samples**				

23.1 & 2	**Specify the procedures for collection of reference samples of active ingredients and finished formulations and how they are stored and maintained.**	--	SOP in place	SOP not in place	--
24	**Reprocessing and Recoveries**				
24.1 – 24.3	**Specify the procedures for reprocessing.** **Whether reprocessed batch is subjected to stability evaluation.** **Whether the recoveries are added into the subsequent batches. If yes specify the procedures.**	--	SOP in place	No SOP in place	--
25	**Distribution records**				
	Whether pre dispatch inspections are carried out before release.	--	Yes	No	--
	Whether periodic audits of distribution center are carried out to access warehousing practices	--	Yes, follow GTDP	No	--
	Whether distribution records are part of the batch record. If not how batch wise distribution record up to retail levels are maintained.	--	Yes & SOP in place	No	--
	Whether instruction for warehousing and stocking of products like LVPs, Heat sensitive etc are available in store.	-	Appropriate areas as per requirement provided	No areas as per requirement provided	--

26	**Validation and Process Validation: -**				
26.1 to 26.5	**Specify the validation policy of the company.** **Whether validation master plan has been prepared.**	--	Yes	No	--
	Whether validation studies of processing, testing and cleaning procedures are conducted as per pre defined protocol.	--	Yes	No	--
	How records and conclusion of such validation studies are prepared and maintained.	--	Studies for Justification of each step were made and validation data maintained.	Improper Studies done and validation data maintained not maintained.	--
	Whether master formula is based on approved process validation.	--	Yes	No	--
	Specify how significant changes to the manufacturing process equipments material etc are controlled.	--	Change control procedure are found in place	No change control procedure are maintained	--

	Whether DQ,IQ,OQ & PQ are in place for all major equipment and facility.	--	Yes	No	--
	Whether validation records of all utilities and major equipments are available.	--	Yes	No	--
27	***Product Recalls: -***				
27.1 to 27.6	**Specify the product recall system followed by the firm.** **How promptly recall operation at the level of each distribution channel up-to the retail level can be carried out.** **Whether there is a SOP for recall of products clearly defining responsibility, procedure, reporting, re-conciliation etc.**	Dummy recall conducted	SOP for effective recall up to retail level found in place	No SOP for effective recall up to retail level found in place	--
28	***Complaints and Adverse Reactions: -***				
28.1	**Specify the review system for complaints concerning the quality of products.**	--	SOP in place	No SOP	--
	How records of complaint and adverse reactions maintained.	--	Yes	No	--
	Whether reports of serious drugs reaction with comments and documents immediately sent to Licensing Authority	--	Yes	No	--
	Is there any criteria for action to be taken on the basis of nature of complaint / adverse reaction.	--	Yes	No	--
29	***Site Master file: -***				
	Whether all the relevant information have been included in the site master file.	--	Yes	No	--
	Whether quality policy has been included in the site master file. Please attach the current version.	--	Yes	No	--

BENCHMARKS

	PART-IA **(Specific requirements for manufacture of Sterile products, Parenteral preparations (Small Volume Injectable Large Volume Perenterals) and Sterile ophthalmic preparations)**	Quality Rating			
		2	**1**		
1.	Whether dampness, dirt and darkness is visible in the facility.	--	Yes	No	--
2.	**Building and Civil Works**				
2.1	Whether the building is devoid of cracks especially in the Aseptic solutions preparation rooms, Filling rooms, Sealing rooms	--	Yes	No	--
2.2	Are the location of services like water, steam, gases etc. are such that the servicing or repairs can be carried out without any threat to the integrity of the facility	Through pendants	Surface mounted.	Surface mounted may cause problems for servicing	--
2.3	Whether water lines pose any threat of leakage to the aseptic area	--	NO	Yes	--

2.4	Whether the manufacturing areas clearly separated into Support Areas (washing and component preparation areas, storage areas etc.) Preparation areas (bulk manufacturing areas, non aseptic blending areas etc) Change areas and Aseptic areas	--	Segregated area is provided	No	--
2.5	Whether de-cartooning areas to remove outer cardboard wrappings of primary packaging materials segregated from the washing areas	--	Yes	No	--
2.6	Whether particle shedding materials like wooden pallets, fiber board drums, cardboards etc taken into the preparation areas etc	--	No	Yes	--
2.7a	Whether in the aseptic areas: Walls, floors and ceiling are - Impervious - Non-shedding - Non-cracking - Coved at wall and ceiling junction	Floors are epoxy/PU coated walls and ceiling are made of GRP or similar type of panel.	Yes	No	--
2.7b	Whether the walls are flat, smooth and devoid of recesses	--	Yes	No	--
2.7c	Whether the surface joints like electric sockets, gas points flushed with walls	--	Yes	No	--
2.7d	Whether the ceiling is solid and the joints are properly	--	Ceiling are made	No	--

	sealed.		of GRP or similar panel which are solid and walk able or made up of RCC		
2.7e	the air grills and lights flushed with the walls	--	Yes	No	--
2.7f	Are the grade A & B areas devoid of sinks and drains	--	Yes	No	--
2.7g	Are the doors and windows made up of non-shedding materials	Doors and windows are made of double glass with GRP or similar panel and flushed with the wall surface.	Yes	No	--
2.7h	Whether doors open towards higher pressure areas and close automatically due to air pressure	--	Yes	No	--
2.7i	In case fire escapes are provided, whether they are suitably fastened to the walls without gaps	--	Yes	No	--
2.7j	Whether the quality of the furniture used is smooth & washable and made of stainless steel, or of any other suitable material other than wood	--	Yes	No	--
2.8	Whether the Manufacturing and support areas have the same quality of civil structure as desired for aseptic areas except the environmental standards which may vary in the critical areas	--	Yes	No	--

2.9	Is the change rooms entrance provided with air locks before entry to the sterile product manufacturing areas and then to the aseptic areas.	4 Air locks.	3 Air locks	Less than 3 Air locks	--
2.10	Are the change rooms to the aseptic areas clearly demarcated like 'black', 'gray' and 'white' with different levels of activity and air cleanliness?	1st air lock - Grade D 2nd , 3rd and 4th air lock – Grade –C	1st air lock - Grade D 2nd and 3rd Grade –C	Air locks are not classified .	--
2.11	Are the sinks and drains in the first change rooms (un-classified) kept clean all the time	--	Yes	No	--
2.12	Do the specially designed drains are periodically monitored to check for pathogenic micro-organisms	--	Yes	No	**--**
2.13	Whether an appropriate inter-locking system with visual and/or audible warning system installed to prevent the opening of more than one door at a time.	Automatic interlocking with audio & visual display	Appropriate interlocking system with audio/visual display.	No interlocking system.	--
2.14	Do the aseptic and non-aseptic areas provided with intercom telephones or speak phones for communication purposes	--	Yes	No	--
2.15	Whether the aseptic areas and outside areas provided with suitable air- locks or pass boxes with suitable interlocking arrangements for material transfer	--	Yes	No	--
2.16	Are the rest rooms, tea room, canteen and toilets outside the sterile manufacturing area	--	Yes	No	--

2.17	Are the animal houses outside and away from the sterile product manufacturing area with separate AHU.	--	Yes	No	
3	**Air Handling System (Central Air Conditioning)**				
3.1	Whether the Air Handling Units for sterile product manufacturing area separate from those for other areas	Totally dedicated AHU for each operation.	Separate AHU for critical area.	No	--
3.2	**Give the Background Grade of air for following critical areas:**				
	• Aseptic filling area	Grade B with particulate monitoring during operation.	Grade B	No Grade B	--
	• Sterilized components unloading area for aseptic filling preparations.	Grade B, with an arrangement of mobile LAF bench.	Grade B	No Grade B	--
	• Sterilized components unloading area for terminally sterilized products.	Grade C, with an arrangement of mobile LAF bench.	Grade C	No Grade C	--
	• Filling room of terminally sterilized products.	LAF. Grade C	Grade C	No Grade C	--
	• Batch manufacturing area for aseptic filling preparations.	Grade B, with an arrangement of mobile LAF bench with provision of	Grade B	No Grade B	--

		constant particle count during production.			
	• Batch manufacturing area for terminally sterilized products.	Grade C, with an arrangement of mobile LAF bench with provision of constant particle count during production.	Grade C	No Grade C	--
	• Component washing and preparation area.	Grade D under LAF with provision of constant particle count during production.	Grade D	No Grade D	--
	• Final change room (Aseptic Area)	Grade C with provision of constant particle count during production.	Grade C	--	--
3.3	Whether Aseptic filling area, sterilized component	--	Yes	No	--

	unloading area and changes rooms conforming to Grade B, C and D have separate Air Handling Units.				
3.4	Are the filter configuration in the air handling system suitably designed to achieve the Grade A, B, C and D of air as per designated classified areas.	--	Yes	No	--
3.5	Whether the types of Operations to be carried out in the various Grades for Aseptic Preparations are as under:				
a)	**Grade Type of Operation** Aseptic preparation & filling	--	A/B	A/C	Not under Grade A
b)	Aseptic Solution preparation to be filtered	--	Grade C	No Grade C	--
d)	Handling of components after Washing	Grade C (2 air locks) with LAF to protect washed components with Epoxy flooring	Grade D (one air lock) with protection of washed components under LAF. Flooring is of Kota stone with Epoxy joints.	Grade D without protection of washed components. Flooring is Kota Stone without Epoxy joints.	--
3.6	Whether for aseptically filled products the filling room meet **Grade B** conditions at rest, unmanned within a period of about **30 minutes** of the personnel leaving the room after completion of operations	Grade B at rest and the condition shall be obtained with in 15 min. after completion of	Grade B at rest and the condition shall be obtained with in 30 min after completion of	The room condition at rest is not obtained with in 30 min after completion of operation	--

		operation and this time period is validated.	operation and this time period is validated.	.	
3.7	Are the filling operations undertaken in **Grade A** conditions and demonstrated under working of simulated conditions	--	The filling operation are simulated under similar conditions and records maintained.	Filling operations are not simulated under similar condition.	No simulation
3.8	Whether the filling room meets **Grade C** conditions at rest in case of terminally sterilized products and these conditions obtainable within a period of about 30 minutes of the personnel leaving the room after completion of the operations	Grade C at rest and the condition shall be obtained with in 15 min. after completion of operation and this time period is validated.	Grade C at rest and the condition shall be obtained with in 30 min after completion of operation and this time period is validated.	The room condition at rest is not obtained with in 30 min after completion of operation.	--
3.9	Whether the manufacturing and component preparation areas for terminally sterilized products meet Grade C conditions	--	Yes	No	--
3.10	Whether the washed components and vessels for terminally sterilized products protected with Grade C background or if necessary under LAF station.	Class C (2 air locks) with LAF to protect washed components with Epoxy flooring	Grade D (one air lock) with protection of washed components. Flooring is of Kota stone with Epoxy joints.	Grade D without protection of washed components. Flooring is Kota Stone without Epoxy joints.	--

3.11	Whether the number of air changes in Grade B and Grade C areas are more than 20 per hour.	> 60	> 20	< 20	< 20
3.12	Whether the Grade A Laminar Air Flow stations meet the criteria of air flow of 0.3 meter per second in case of vertical and that of 0.45 meter per second in case of horizontal flows +/- 20 %	--	Yes	No	--
3.13	Whether the differential pressure between areas of different environmental standards meets the requirements (at least 15 Pascal/ 0.06 inches/ 1.5 mm water gauge)	--	Yes	No	--
3.14	Whether suitable manometers / gauges installed for measurement and verification. Specify type of manometer.	MAGHNELIC gauges with proper calibration.	Suitable manometers with proper calibration	No manometers	--
3.15	Whether the final change rooms have the same class of air as specified for the aseptic area.	--	Yes	No	**--**
3.16	Whether the pressure differential in the change rooms is in the descending order, from ' white' to' black'. Specify pressures of three change rooms.	--	Yes	NO	**--**
4.	**Environmental Monitoring**				
3.18	Whether temperature and humidity (NMT 27^{C}C and 55 % RH respectively) in the aseptic areas are controlled.	--	Yes	NO	**--**

4.1	Whether the records exist to show that all the environmental parameters were verified at the time of installation and checked periodically thereafter?	--	Yes	NO	**--**
4.2	Are the recommended periodic monitoring frequencies followed	--	Yes	NO	**--**
a)	Particulate counts - 6 Monthly	--	At least once in a 6 months	Beyond 6 months	--
b)	HEPA filters integrity testing – Yearly	--	At least once in a Year.	Beyond 1 year.	--
c)	Air Change rates - 6 Monthly	--	At least once in a 6 months	Beyond 6 months	--
d)	Air pressure differentials - Daily	--	Daily	Not done daily	--
e)	Temperature and Humidity - Daily	--	Daily	Not done daily	--
f)	Microbiological monitoring by settle plates and/ or swabs in: **Aseptic areas -- Daily, Other areas -- Decreased frequency**	--	Daily in aseptic area and at decreased frequency for others.	Not done daily in aseptic area and No written programme.	--
4.3	Does a written Environmental Monitoring Program exist? How long the settle plates are exposed in Grade A and other areas.	--	Not < 30 min. in Grade A area and not less than 2 hours in other areas.	< 30 min. in Grade A area and less than 2 hours in other areas.	--
4.4	Are the microbiological results recorded	--	Yes	No	--
4.5	Are these results assessed with recommended limits	--	Yes, SOP is being maintained for CAPA	No	--
4.6	Do they take action in case	--	Alert and	Alert and	--

	particulate and microbiological monitoring counts exceed the limits.		action limit defined.	action limits not defined.	
4.7	In case of major engineering modifications being carried out to the HVAC system of any area, Whether all parameters reassessed and approved before starting production.	--	Yes	No	--
5.	**Garments**				
5.1	Whether Outdoor clothing is allowed in the sterile areas	--	No	Outdoor clothing is not fully covered.	--
5.2	Do they use cotton garments which are not allowed?	--	No	Yes	--
5.3	Are the garments made of non- shedding and tight weaving material?	--	Yes	No	--
5.4	Whether the garments are of suitable design in single piece with fastening at cuffs, neck and at legs to ensure close fit Trouser legs to be tucked inside the cover Boots	--	Yes	No	**--**
5.5	Whether the garment includes a hood or a separate hood which can be tucked inside the overall.	--	Yes	No	**--**
5.6	Whether Pockets, pleats and belts are avoided	--	Yes	No	**--**
5.7	Whether Zips (if any used in garments) are of plastic material	--	Yes	No	**--**
5.8	Whether the personnel wear only clean, sterilized and protective garments at each work session where aseptic	--	Yes	No	**--**

	filtration and filling operations are undertaken and at each work shift for products intended to be sterilized, post-filling				
5.9	Are masks and gloves are changed at every work session.	--	Yes	No	--
5.10	Are the gloves used made of latex or other suitable plastic material	--	Yes	No	--
5.11	Are powder free gloves used in clean rooms	--	Yes	No	--
5.12	Are the gloves long enough to cover the wrists completely and allow the over-all cuff to be tucked in	--	Yes	No	--
5.13	Are the foot-wear used made of plastic or rubber material	--	Yes	No	--
5.14	Are the foot-wear daily cleaned with a bactericide	--	Yes	No	--
5.15	Does the safety goggles / numbered glasses worn in side the aseptic areas have side extensions	--	Yes	No	--
5.16	Are safety goggles sanitized by a suitable method	--	Yes	No	--
5.17	Whether the garment changing procedure documented	--	Yes	No	--
5.18	Whether the operators trained in garment changing procedure.	--	Yes	No	--

5.19	Whether a full size mirror been provided in the final change room to ascertain that the operator has appropriately attired in the garments	--	Yes	No	**--**
6.	**Sanitation**				
6.1	Whether written procedures available for sanitation of sterile processing facilities	--	Yes	Inadequate procedure	--
6.2	Whether the employees carrying out the sanitation of aseptic areas specially trained for the purpose	--	Yes	No	**--**
6.3	Whether more than one sanitizing agent is used in rotation.	--	Yes	No	**--**
6.4	Whether the concentration of the agent used has been recommended by the manufacturer	--	Yes	No	**--**
6.5	Whether distilled water is used for the dilution of the disinfectant, if so is it directly collected from the distilled water plant or from re-circulation loop maintained above 70 ^{o}C or sterilized by autoclaving and filtered through membrane filtration	--	From recirculation loop maintained above 70 deg. C or freshly collected and sterilized by Autoclaving and dilution is carried out in "white change room".	No	--
6.6	Whether alcohol or isopropyl alcohol is used as disinfectant for hand sprays?	--	Yes	No	**--**

6.7	Whether disinfectant solutions filtered through membrane into suitable sterile containers before use?	--	Yes	No	**--**
6.8	Whether the diluted disinfectants bear 'use before' labels based on microbiological establishment of their germicidal properties	--	Yes	No	**--**
6.9	Whether records maintained thereof	--	Yes	No	**--**
6.10	Whether fumigation carried out in aseptic areas. If yes, specify fumigating agent and its conc. used.	By Ozonization through AHU ducts and regular sanitization with different sanitizing agents.	Generally no fumigation is carried out, however in case of major civil modification the same is carried out by using formalin vapor.	Fumigation is carried out routinely without any justification by using a mixture of formalin and potassium permanganate.	--
6.11	Whether an SOP exist for the purpose of fumigation.	--	Yes	No	--
6.12	Whether cleaning of sterile processing facility done using air suction devices non-linting sponges or clothes.	--	Yes	No	**--**
6.13	Whether air particulate quality monitored on a regular basis	--	Yes	No	**--**
7.	**Equipments**				
7.1	Whether the unit- sterilizers double ended with suitable inter-locking between the doors	--	Yes	No	**--**

7.1.1	Whether the initial effectiveness of sterilization process established by using microbial spores indicators	--	Yes	No	--
7.1.2	Whether thermal Mapping of heat sterilizers is carried out on regular basis. Check records.	--	Yes, at least once in a year	No	--
7.1.3	Whether suitable vent filters and recording thermographs provided in Autoclaves.	--	Yes	No	--
7.1.4	Whether HEPA filters for cooling air and recording thermographs provided in DHS	--	Yes	No	--
7.1.5	Whether provisions of CIP or SIP available.	Yes	Arrangement for proper washing and sterilization is in place	No	--
7.1.6	Whether firm has made provisions for pure steam generation and its use.	--	Yes	No	--
7.2	Whether filter integrity test carried out before and after the filtration process	--	Yes	No	--
7.3	Whether the filling machines challenged initially and there after periodically by simulation trials including sterile media fills.	Half yearly and after any major modification.	Yearly and after any major modification.	No	--
7.4	Are SOPs with acceptance criteria for media fills been established, validated and documented	--	Yes	No	--

7.5	Whether the material of construction of the parts of equipment which are in direct contact with the product and the manufacturing vessels of stainless steel 316 and of glass containers Boro-silicate glass	All the contact parts and outer surfaces of the machines and equipments are made up of SS 316.	Yes	No.	--
7.6	Whether the tubing used capable of washing and autoclaving	--	Yes	No	**--**
7.7	Whether the installation qualification been done of all the equipments by the engineers (with the support of production and quality assurance personnel)	Yes as per DQ and the results are documented.	Yes	No	--
7.8	Whether the critical processes such as aseptic filling and sterilizers suitably validated before these were put to use	--	Yes	No	**--**
7.9	Whether SOPs available for each equipment for its calibration, operation and cleaning.	--	Yes	No	**--**
7.10	Whether the measuring devices attached to equipment calibrated at suitable intervals.	--	Yes	No	**--**
7.11	Whether a written calibration program is available	--	Yes	No	**--**
7.12	Whether calibration status documented and displayed on the of the equipment and the gauges	--	Yes	No	**--**
8	**Water & Steam Systems**				

8.1	Whether **potable water** used for the preparation of purified water meets the requirement of not more than 500 cfu/ml	--	Yes and documented	No records	**--**
8.2	Whether potable water tested (100 ml sample) for freedom from pathogenic microorganisms: Escherichia coli, Salmonella, Staphylococcus aurious and Pseudomonas	--	Yes and documented	No records	**--**
8.3	Whether the Purified Water prepared by de-mineralization meet the microbiological specification of not more than 100 cfu/ml	Also has conductivity < 1 and provisions to monitor TOC (<500ppb) online and offline with records.	Yes and records are found maintained.	No records available	--
8.4	Whether Purified Water tested for freedom from pathogenic microorganisms. (Sample size 100 ml)	--	Yes	No	**--**
8.5	Whether Purified Water meet IP specifications for chemical testing	--	Yes	No	**--**
8.6	Whether purified water is stored in stainless steel tanks.	--	Yes	No	**--**
8.7	Are the distribution lines made of stainless steel 316 grades?	SS 316L and in recirculation loop.	SS 316	Other than SS and not justified.	--
8.8	What is the water source for preparation **Water for Injection (WFI)**:	--	Purified water	Potable water	--
8.9	Whether WFI meet microbiological specification of not more than 10 cfu/100ml	--	Yes, with records maintained.	No records	**--**
8.10	Whether WFI meet IP specifications for Water for Injection	--	Yes	No records	**--**

8.11	Whether WFI meet the endotoxin level of not more than 0.25 EU/ml	--	Yes	No records	--
8.12	Whether WFI used for				
8.12.1	- Bulk preparations of liquid parenterals - Final rinse of product containers	--	Yes	No	--
8.12.2	- Final rinse of machine parts	--	Yes	No	--
8.12.3	- Preparation of disinfectant solutions for use in aseptic areas	--	Yes	No	--
8.13	Whether WFI used for liquid injectables collected freshly from the distillation plant or from a storage / circulation loop kept at above 70^{o}C.	--	Yes	No	--
8.14	Whether the steam condensate meets the microbiological specification of not more than 10 cfu/100ml and IP specifications of WFI	--	Yes	No	--
8.15	Whether steam used in production meet the endotoxin level of not more than 0.25EU/ml	--	Yes	No records	--
8.16	What is the schedule for the monitoring of steam quality exist	Sampling and testing is carried out on the basis of a validated study and records maintained.	Sampling and testing is carried out as per SOP of the firm without any validated study and records maintained.	No record	--

9.	**Manufacturing process**				
9.1	Whether the bulk raw materials and bulk solutions monitored for bio-burden periodically (solutions not to contain more than 100 cfu/ml)	--	Yes	No	**--**
9.2	Whether the principle of minimum possible time between the preparation of the solution and its sterilization or filtration through microorganism retaining filters followed and also specified in Master formula.	--	Yes	No	**--**
9.3	Whether the filter the gases coming into contact with the sterile product through two 0.22 micron hydrophobic filters connected in series	--	Yes	No	**--**
9.4	Whether gas cylinders are kept out side of the aseptic areas	--	Yes	No	**--**
9.5	Whether the washed containers sterilized immediately before use	--	Yes	No	**--**
9.6	Whether the sterilized containers not used within an established time, rinsed with distilled or filtered purified water and re-sterilized	--	Yes	No	**--**
9.7	Is each lot of the finished product filled in one continuation operation	--	Yes	No	**--**
10.	**Terminally Sterilized product**				
10.1	Whether the preparation of Primary packaging material	Grade C with LAF	Grade D with	No classified	--

	such as glass bottles, ampoules and rubber stoppers is carried out in at least Grade D (grade C in case there is unusual risk of contamination to the product)	to protect washed components	protection of washed components	area	
10.2	Whether these processes used for component preparation have been validated.	--	Yes	No	**--**
10.3	Whether the filling area is **of Grade A** environment with Grade C background	--	Yes	No	**--**
10.4	Whether the solutions which are sterilized by filtration is prepared in Grade C environment.	--	Yes	No	**--**
10.5	And if not to be filtered, whether the preparation of materials and products carried out in Grade A environment with Grade B background	--	Yes	No	**--**
10.6	Whether for aseptic filling, non- fiber releasing sterilizing grade cartridge / membrane filter of nominal pore size of 0.22 micron and 0.45 micron porosity for terminally sterilized products are used.	--	Yes	No	**--**
10.7	Whether a second filtration with another 0.22 micron sterilizing grade cartridge / membrane filter, performed immediately prior to filling.	--	Yes	No	**--**
10.8	Whether process specifications indicate the maximum time during which a filtration system may be used (precluding microbial build-up to levels that may affect the microbiological quality of the product)	--	Yes	No	**--**

10.9	Whether integrity of the sterilizing filter verified and confirmed immediately after use. If so, by which method: Bubble Point, Diffusive Flow or Pressure Hold Test	Bubble point, Diffusive flow and pressure hold test	Any one of the said method	No	--
	Sterilization (Autoclaving)				
10.10	Whether the sterilizing processes have been validated (Dry heat, Moist heat, filtration, ETO, ionizations whichever applicable.	--	Yes	No	**--**
10.11	Whether the validity of the process verified at regular intervals (at least annually)	Once in a three months	Once in a year	Not carried out	**--**
10.12	Whether records are maintained when significant changes made to the equipment and / or the product.	--	Yes	No	**--**
10.13	Whether sterilizer double ended	--	Yes	No	**--**
10.14	Whether the terminal sterilizer's capacity is sufficient to sterilize one batch completely at one time. If not specify controls and measures taken in lot sterilizations.	One complete batch Is sterilized in one cycle.	One complete batch is sterilized not in one cycle but specific controls and measures taken at the time of	One complete batch is sterilized not in one cycle and no specific control and measures are taken.	**--**

			sterilization as per SOP prepared in this regard.		
10.15	Whether the monitoring of products bio-burden carried out before terminal sterilization.	--	Yes	No	--
10.16	Whether bio-burden controlled to the specified limits in the Master Formula.	--	Yes	No	--
10.17	Whether biological indicators used in monitoring of sterilization.	--	Yes	No	--
10.18	Whether the biological indicators stored and used as per manufacturers instructions. Whether quality of BI's checked by positive controls.	--	Yes	No	--
10.19	Whether a clear means of differentiating 'sterilized' from 'unsterilized' products in place. Specify.	--	Each carrier of the sterile product is properly labeled.	No	--
10.20	Whether the label on the basket / tray or other carrier of product / component clearly states: • Name of the material • Its batch number • Its sterilization status Indicator (in case it has passed through sterilization process)	--	Yes	No	--
10.21	Whether sterilization records including thermographs and sterilization monitoring slips attached with the Batch Production Record	--	Yes	No	--

10.22	**Sterilization (By Dry Heat)**				
10.23	Whether the sterilization cycle recording device of suitable size and precision provided in DHS.	PLC	Inbuilt recorder	No recorder	
10.24	Whether the position of temperature probes used for controlling and / or recording determined during validation and (where applicable) been checked against a second independent temperature probe located in the same position	--	Yes	No	**--**
10.25	Whether the chart forms a part of the batch record.	--	Yes	No	**--**
10.26	Whether sterilization cycle validated only by biological indicator and chemical indicators or physical validation is also carried out.	--	Yes	No	**--**
10.27	Whether the time allowed reaching the required temperature before commencing the measurement of sterilizing time, separately determined for each type of load.	--	Yes	No	**--**
10.28	Are adequate precautions taken to protect the load during cooling after it has gone through the high temperature phase of a heat sterilization cycle	--	Yes	No	**--**
10.29	In case the cooling is affected with any fluid or gas in contact with the product , is it sterilized.	--	Yes	No	**--**
10.30	Whether the equipment air inlet and outlets been provided with bacteria retaining filters	--	Yes	No	**--**

10.31	In the process of sterilization by dry heat, does the equipment has: • Air circulation facility within the chambers • Positive pressure to prevent entry of non-sterile air	--	Yes	No	**--**
10.32	Whether the process of dry heat sterilization is also intended to remove the pyrogens If so, has the validation been done with challenge tests using endo-toxins	--	Yes	No	**--**
10.33	**Sterilization (By Moist Heat)**				
10.34	Whether recording of both temperature and pressure carried out to monitor the process	PLC	Recordin g/Data logger provided	-	
10.35	Whether the control instrumentation independent of the monitoring instrumentation and recording charts.	--	Yes	No	**--**
10.36	Whether the equipment has automated control and monitoring system, if so, have these been validated to ensure that critical process requirements are met.	--	Yes	No	**--**
10.37	Whether the system and cycle faults are recorded inbuilt and also observed by the operator and record maintained.	--	Yes	No	**--**

10.38	Whether the readings of the thermograph during sterilization cycling are routinely checked by the operator against the reading shown by the dial thermometer fitted with autoclave.	--	Yes	No	**--**
10.39	**Whether the sterilizer fitted with a drain at the bottom of the chamber** If so, does the record of temperature at this position is recorded through out the sterilizing period	--	Yes	No	**--**
10.40	Are frequent leak tests conducted on the chamber of the autoclave on each day of operation.	--	Yes	No	**--**
10.41	Whether all items to be sterilized (other than sealed containers) are wrapped for sterilization.	--	Yes	No	**--**
10.42	Whether the wrapping material allows removal of air and penetration of steam ensuring contact with the sterilizing agent at the required temperature for required time	--	Yes	No	**--**
10.43	Whether the wrapping prevent contamination after sterilization	--	Yes	No	**--**
10.44	Whether the steam used for sterilization is of suitable quality and doesn't contain additives at a level which could cause contamination of the product or equipment	--	Pure steam and test performed regarding its purity and documented.	No records are available.	--

10.45	Whether the minimum time for all unit operations and processes are specified in the manufacture of a batch	--	Yes	No	**--**
10.46	Whether the shortest validated time being adhered from the start of a batch to its ultimate release for distribution	--	Yes	No	**--**
10.47	Whether the containers closing methods been validated	--	Yes	No	**--**
10.48	Whether the containers closed by fusion e.g. glass or plastic ampoules, subjected to 100% leak testing	--	Yes	No	**--**
10.49	Whether the samples of other containers checked for integrity as per appropriate procedures	--	Yes	No	**--**
10.50	Whether the containers sealed under vacuum checked for required vacuum conditions	--	Yes	No	**--**
10.51	Whether the filled containers of parenterals inspected individually for extraneous contamination /other defects	--	Yes	No	**No**
10.52	Whether the inspection process done visually, if so, are the illumination and background conditions controlled.	--	Yes	No	**--**
10.53	Whether the workers engaged in inspection activity pass the regular eye-sight test (with spectacles if worn)	--	Yes	No	**--**

10.54	Whether the visual inspectors allowed frequent rest from inspection	--	Yes	No	**--**
10.55	If other method of inspection of containers is used,				
	• What is the method-	Automatic (laser beam technique)	Semi-automatic /visual	No	No
	• Has it been validated	--	Yes	No	**--**
	• Are the equipment used for the purpose checked at suitable intervals	--	Yes	No	**--**
	• Are the results/ recorded maintained	--	Yes	No	**--**
11.	**Product Containers & Closures**				
11.1	Whether the containers and closures used comply to pharmacopoeia or other specific requirements	--	Yes	No	**--**
11.2	To assure suitability of the containers/ closures and other component parts of drug packages, whether they have: Suitable sample sizes, Specifications, Test methods, Cleaning procedures, Sterilizing procedures	--	Yes	No	**--**

11.3	Whether the container is compatible with the product and affecting its quality and purity.	--	Yes	No	**--**
11.4	Whether second hand containers and closures used	--	No	Yes	Yes
11.5	Whether the plastic granules used checked for fulfillment of Pharmacopoeia requirements including physico- chemical and biological tests	--	Yes	No	**--**
11.6	Whether containers and the closures rinsed with WFI before sterilization	--	Yes	No	**--**
11.6.1	Whether a written procedure exist for washing process. Do they follow the written schedule for cleaning of the glass bottles	--	Yes	No	**--**
11.6.2	Whether the design of closures and containers suitable to make cleaning easy, and to make an air tight seal when fitted to the bottles	--	Yes	No	**--**
11.6.3	Whether the material quality of the stoppers and closures ensures that it does not affect the quality of the product and avoids the risk of toxicity	--	Yes and documented.	No document.	--
11.6.4	In case the bottles are not dried after washing are these rinsed with distilled water or pyrogen free water as the case may be as per written procedure	--	Yes	No	**--**

12.	**Documentation**				
12.1	Do the manufacturing records pertaining to manufacture of sterile products indicate the following details:	--	Yes	No	**--**
(1)	Serial number of Batch Manufacturing Record	--	Yes	No	**--**
(2)	Name of the product	--	Yes	No	**--**
(3)	Reference to Master Formula Record	--	Yes	No	**--**
(4)	Batch/ Lot number	--	Yes	No	**--**
(5)	Batch/ Lot size	--	Yes	No	**--**
(6)	Date of commencement and completion of manufacture	--	Yes	No	**--**
(7)	Date of manufacture and assigned date of expiry	--	Yes	No	**--**
(8)	Date of each step in manufacturing	--	Yes	No	**--**
(9)	Names of all ingredients with grade given by the quality control department	--	Yes	No	**--**
(!0)	Quantity of all ingredients	--	Yes	No	**--**
(11)	Control reference numbers for all ingredients	--	Yes	No	**--**
(12)	Time and duration of blending, mixing etc. where ever applicable	--	Yes	No	**--**
(!3)	PH of solutions whenever applicable	--	Yes	No	**--**

(14)	Filter integrity testing records	--	Yes	No	--
(15)	Temperature and humidity records whenever applicable	--	Yes	No	--
(!6)	Records of plate-counts whenever applicable	--	Yes	No	--
(17)	Results of pyrogen and/ or bacterial endotoxin and toxicity	--	Yes	No	--
(18)	Records of weight or volume of drug filled in containers	--	Yes	No	--
(19)	Bulk sterility in case of aseptically filled products	--	Yes	No	--
(20)	Leak test records	--	Yes	No	--
(21)	Inspection records	--	Yes	No	--
(22)	Sterilization records including leakage test records, load details, date, duration, temperature, pressure etc.	--	Yes	No	--
(23)	Container washing records	--	Yes	No	--
(24)	Total number of containers filled	--	Yes	No	--
(25)	Total number of containers rejected at each stage	--	Yes	No	--
(26)	Theoretical yield, permissible yield, actual yield and variation there of	--	Yes	No	--
(27)	Clarification for variation in yield beyond permissible yield	--	Yes	No	--
(28)	Reference number of relevant analytical reports	--	Yes	No	--
(29)	Details of re-processing, if any	--	Yes	No	--

(30)	Names of all operators carrying out different activities	--	Yes	No	--
(31)	Environmental monitoring records	--	Yes	No	--
(32)	Specimens of different packaging material	--	Yes	No	--
(33)	Records of destruction of rejected containers and packaging material	--	Yes	No	--
(34)	Signature of the competent technical staff responsible for manufacture and testing	--	Yes	No	--
13.	**Notes**				
13.1	Whether products released only after complete filling and testing.	--	Yes	No	--
13.2	**Whether result of the tests relating to sterility, pyrogens and bacterial endotoxins are maintained in the analytical records**	--	Yes	No	--
13.3	Whether Validation details and simulation trial records maintained separately	--	Yes	No	--
13.4	**Whether records of environmental monitoring like temperature, humidity, microbiological data etc., are maintained.**	--	Yes	No	--
13.5	**Whether records of periodic servicing of HEPA filters, sterilizers and other periodic maintenance of facilities and equipment carried out, are maintained.**	--	Yes	No	--

BENCHMARKS

Part-IB **Specific Requirements for manufacture of Oral Solid Dosage Forms (Tablets and Capsules)**		**Quality Ratings**			
		2	**1**	**0**	**X**
1.1	**Please specify HVAC and air extraction systems provided to avoid contamination from extraneous particles / dust and other products.** **Whether HVAC and air extraction system is capable of preventing discharging contaminants into the environment? In case of re-circulation of air what is the micron size of final filter.**	Class 100,000 with terminal HEPA filters (H-13). Centralized dust extraction system with scrubber.	Class 100,000 with HEPA filters (0.3 micron) in Plenum/terminal with re-circulation of air through riser or 5 micron filter at terminal with 100% exhaust through 5 micron filter and or scrubber (for potent products). Localized dust extraction system is in place.	AHU with 3-5 micron in recirculation. No dust extraction system.	No AHU and No dust extraction system.
1.1.1	**Are there manometers to monitor pressure differential at all strategic points.**	Maghnelic gauges are provided at all strategic points	Manometers are provided at strategic points.	Manometers not provided at strategic points.	--

		and are controlled by BMS.			
1.1.2	**Is there schematic drawing of AHU's available.**	--	Drawings available.	Drawings not available	--
1.1.3	**Whether dedicated AHU's for different operations are in place.**	Dedicated AHU's in place for each and every operation.	AHU's are provided for all the areas where products are exposed but not dedicated for individual operation.	Some of the areas where products are exposed, are not covered under AHU`s	--
1.2	**Please specify how specific product requirements like temperature, humidity and light are controlled.**	In built within AHU provided with chemical dehumidification for maintaining humidity and temperature control arrangement on the basis of thermal mapping. Appropriate lux level based on requirement and regular monitoring of the same.	In built within AHU by heating and cooling method for maintaining humidity and temperature. Area is well lighted but not defined.	Split AC and portable dehumidifier. Light is insufficient (normal text is not readable).	No provision to control temperature and humidity. Part of the area was found dark.
1.3	**Pls specify the materials of construction of equipments.**	All contact and exposed portion of the machine and utensils are made of SS 316.	All the contact portion of the machine and utensils are made of SS.	Not all the contact portion of the machine and utensils are made of SS.	Wooden or any other particle shedding materials are used in production.

1.3.1	**Whether metal detector is used to detect metallic contamination.**	Metal detector is used online with sensor.	Metal detector is used.	No metal detector is used	--
1.4	**Whether dedicated areas for sifting provided.**	Enclosed dedicated area with proper dust control.	Dedicated area	No dedicated area.	No provision for shifting of powder.
1.5	**Pls give brief account on pressure cascade (differential pressure) being maintained in the various areas of production.**	--	5-20 pascals difference of pressure is maintained between the powder generated and the adjacent area. The powder generated area is negative in comparison to the adjacent area but positive in comparison with the ambient.	No pressure differential	--
1.5.1	**Whether pressure balancing is automatic or manual.**	Automatic	Manual	No pressure balancing	--
1.5.2	**Whether records of these pressure differential reviewed at regular interval. If yes pls specify intervals of monitoring and its review.**	Daily.	Weekly.	Records not available.	--

1.6	**Is Air blowing or vacuum system is used for clearing of powders from the machine parts etc.**	---	Under vacuum	Air blowing	-
1.6.1	**In case of vacuum cleaning how it is used to avoid contamination and cross contamination.**	--	Dedicated Vacuum Cleaner is used for each operation	No dedicated Vacuum Cleaner is used for each operation	--
2	***Sifting, Mixing and Granulation: -***				
2.1	**Whether mixing, sifting and blending operations are carried out in dedicated areas & how generation of dust is controlled.**	Enclosed dedicated area having centralized provision for dust control with scrubber.	Dedicated area having localized provision for dust control.	No dedicated area.	--
2.1.1	**Whether these operations are closed.**	--	Yes	No	--
2.1.2	**Whether integrity of screens checked before and after operation.**	--	Yes	No	--
2.1.3	**Whether mixing and blending equipment have timers for control.**	--	Yes	No	--
2.2	**Whether personnel in production carry out the verification of the weight of the raw materials used in the manufacturing of each lot.**	--	Yes	No	--

2.2.1	**Whether critical operating parameter likes time and temperature for each mixing and drying operation are recorded in BPR and tally with the master formula.**	--	Yes	No	--
2.2.2	**Whether static or fluid bed dryers are used for drying.**	--	FBD and/or tray drier made up of SS.	Tray drier with metallic tray other than SS	--
2.2.3	**Whether FBD and static dryers have arrangements for temperature monitoring and recording.**	--	Yes	No	--
2.4	**Specify the system of using filter bags used in FBD.**	--	Product dedicated for highly potent or sensitizing products and for other general products washed as per qualified procedure in between use of different products.	Bags are neither product dedicated nor properly washed by any qualified method between uses of different products.	Bags are neither product dedicated nor washed between uses of different products.
2.4.1	**How filter bags are identified for various products and stored.**	--	Stored in a separate room with ID number.	Stored in a separate room with no ID number.	--

2.4.1	**Whether air entering into the dryers is filtered. If yes then specify type of filters installed.**	0.3µ filter	5µ filter	> 5µ filter	--
2.4.2	**Whether air going out of FBD is also filtered. If yes then specify type of filters installed.**	0.3µ filter	5µ filter	> 5µ filter	--
2.5	**Whether granulation and coating solutions are made, stored and used in a manner which minimizes the risk of contamination or microbial growth.**	--	Yes	No	--
2.5.1	**Whether the washing facility in the granulation suites takes proper measures to prevent contamination and cross contamination.**	--	Yes	No	--
3	***Compression (Tablets) :-***				
3.1	**Whether each compression machine is installed in separate cubicle.**	--	Yes	No	--
	What type of dust control facilities are provided with the Tablet compressing machine in its cubicle.	--	Centralized/localized dust control arrangement is provided.	No dust control arrangement.	-
3.2	**How granules and compressed tables stored and controlled to prevent mix ups.**	--	SS containers with proper labeling of each container with product details.	No proper labeling	Stored in particle shedding containers

3.2.1	**How these containers are cleaned and maintained in a proper condition.**	--	Cleaned following a validated procedure and stored in cleaned and dedicated area with proper record.	Neither cleaning procedure is established nor any records maintained.	--
3.3	**How tablets are being inspected and checked for suitable pharmacopoeial parameters like appearance, weight variation, disintegration, hardness, friability, thickness and records maintained thereof.**	--	Separate I.P.Q.C. area provided	I.P. Q.C. is done in processing area only.	--
3.4	**Whether instruments used in IPQC lab are calibrated and accurate to measure out of specification units.**	--	Yes	No	--
3.5	**How tablets are being de-dusted and monitored for the presence of foreign materials.**	--	De duster provided and inspection is carried out on inspection unit/belt.	De dusting is done manually and there is no provision of inspection unit/belt.	--
3.7	**Whether rejected or discarded tablets are isolated in identified container and their quantity recorded in the BMR.**	--	Yes	No	--

3.8	**Which type of lubricating oil is used in compression machine.**	--	Edible grade	Non edible grade.	--
4	***Coating (Tablets):-***				
4.1	**Which type of tablet coaters are provided for coating?**	Auto coata with closed system.	SS Coating pan with proper dust extraction system	SS coating pan without dust extraction system	--
	Whether air supplied to coating pan is filtered. If yes pls specify type of filter and justification for its suitability.	Blower with scrubber. (HEPA filter). Flame proof area.	Hot air blower with filters (5 micron otherwise HEPA filter). Flame proof area.	Hot air blower without filter.	-
	Whether coating area is provided with suitable exhaust system and environmental control (temperature, Humidity) measures.	--	Yes	No	--
4.2	**Whether coating solutions are being made afresh and used.**	--	Yes	No	--
5.	**Filling of Hard Gelatin Capsule: -**				
5.1	**How empty gelatin capsules are stored and controlled in the filling area.**	--	Under controlled condition of temperature and humidity.	No controlled condition.	-

5.1.1	**Whether capsule filling is carried out manually or by machine.**	--	Automatic/Semi Automatic machine.	Hand filling machine	--
5.1.2	**Whether additional provisions in the AHU's has been made to control humidity. If yes, pleases specify the same.**	In built within AHU provided with chemical dehumidification for maintaining.	In built within AHU by heating and cooling method for maintaining humidity.	No provision to control humidity.	--
6.	**Printing (tablets and capsules): -**				
6.1	**Whether the tablets / capsules are overprinted. If yes which type of ink is used. Please specify quality of ink.**	--	Edible grade.	Non edible grade.	--
6.1.1	**How printing operation is controlled to avoid mix up of products during printing.**	--	Under dedicated area with proper segregation of each machine.	No proper segregation in between the machines.	-
6.1.2	**Whether after printing, the products are approved by quality control before release for packaging or sale.**	--	Yes	No	--
7	***Packaging (Strip & Blister)***				

7.1	**Whether a system of line clearance is in place and recorded before a new packaging operation is commenced.**	--	Yes	No	--
7.2	**How contamination and cross contamination are prevented during packaging operation of tablets / capsules.**	--	Separate area having AHU facility.	No Separate area.	-
7.3	**How the strips/Blister coming out of the machines is inspected for defects such as miss-print, cuts on the foil, missing tablets and improper sealing.**	Automatically	Manually	Not done.	-
7.4	**Whether IPQC tests are performed on strips or blisters? Whether records of these tests maintained.**	--	Yes	No	--

BENCHMARKS

PART-IC **Specific Requirements for manufacture of Oral Liquid**		**Quality Ratings**			
		2	**1**	**0**	**X**
1.1	***Building and Equipments: -*** **How the facility for liquid oral designed and constructed to prevent cross contamination and mix-ups.**	Class 100,000 with terminal HEPA filters (H-13) with temperature control for whole liquid section.	AHU with 5 micron filter at terminal and temperature control for manufacturing & primary packaging and FDV (5 micron) for syrup preparation and bottle washing area.	AHU without 5 micron filter at terminal in the primary packaging area.	No AHU.
1.1.1	**Whether the manufacturing area have entrance through double air lock facility.**	--	Yes	No	--

1.1.2	**Whether in the manufacturing area walls, floors and ceiling are impervious, non-shedding, non-cracking, coved at all junctions.**	Floors are epoxy/PU coated, walls are made of GRP or similar type of panel and ceiling is solid slab/monolithic without beams. All junctions are coved with epoxy.	Floors are of Kota stone with epoxy joints, walls are monolithic and painted with washable paint and false ceiling made up of epoxy coated aluminum/ cemented ceiling. All junctions are coved.	Kota stone without epoxy joints, walls surface are not smooth and washable. False ceiling made up of fiber shedding material. All junctions are not coved.	**--**
	Whether the doors and windows and light fixtures are flushed, made up of non fiber shedding material.	No ledges, flushed, opening on positive pressure side made of SS or modular	No ledges, flushed, open on positive Al coated doors.	Ledges, not flushed, open on positive Al un-coated doors.	**Wooden Doors**
1.2	**Whether fly catcher and/or air carton has been provided at strategic suitable points.**	--	Yes	No	--
1.3	**Whether the drains are provided with traps to prevent back flow.**	--	Yes	No	--
	How drains are maintained.	--	Sanitized as per schedule and recorded.	No records.	--

1.4	**Whether the production area is cleaned and sanitized at the end of every production process. If yes, whether records maintained.** **(How the area is sanitized.** **How sanitization procedures controlled).**	--	Yes	No	--
1.5, 1.6 & 1.8	**What is the material of construction of tanks, containers, Pipe work and pumps?**	All contact and exposed portion of the machine and utensils are made of SS 316.	All the contact portion of the machine and utensils are made of SS.	Not all the contact portion of the machine and utensils are made of SS.	--
	Whether the tanks have clean in place **facility. If not how tanks are cleaned to prevent accumulation of residual microbial growth and cross-contamination.**	CIP facility.	Cleaning as per validated SOP.	No validated SOP has been followed	--
	How tanks, pipe works and other containers sanitized.	--	Sanitization is carried out as per validated SOP	No validated SOP.	--
	Whether the pipelines and services have any dust lodging surface.	--	No	Yes	--

	Whether microbial monitoring of the area is carried out.	--	Yes	No	--
	Whether use of glass containers is restricted.	--	Yes	No	--
	Whether furniture's are of stainless steel and are capable of cleaned effectively.	--	Yes	No	--
1.7	**Whether cleaning of bottles, caps, droppers etc are carried out by suitable machine/devices equipped with high pressure air, water and steam jets.**	--	Yes	No	--
2	**Purified Water: -**				
2.1	**Whether the Microbial quality of purified water is monitored routinely.** **(What is the in house limit of CFU / ml of purified water).**	--	Yes	No	--
	Whether water is tested for freedom from Pathogen on daily basis. If not what is the schedule.	--	Water is tested as per pre-defined schedule.	Tested randomly.	--
2.2	**Whether the unit has written procedure for operation and maintenance of purified water system. (Specify the method).**	--	Yes	No	--

3	***Manufacturing: -***				
3.1 **3.2**	**What types of clothing's are worn by personnel in manufacturing area?**	--	Non-fiber shedding.	Fiber shedding.	--
	Whether materials like gunny bags or wooden pallets are allowed in manufacturing areas.	--	No	Yes	--
3.3	**Whether suspensions and emulsions are manufactured.** **If yes how homogeneity of the same is ensured throughout the process.**	--	Due care has been taken to ensure that product is Homogenous during filling with the help of Homogenizer / Stirrer.	No care has been taken to ensure that product is Homogenous during filling.	--
3.4	**Whether separate syrup preparation area has been provided,`**	Separate sugar handling by pneumatic system and separate syrup preparation room.	Separate syrup preparation room.	No separate syrup preparation room	--
	Specify the room temperature requirement in the manufacturing area.	--	Less than 30^0C.	> 30^0C	--
3.5	**Whether the maximum period of storage of product in a bulk stage is validated and mentioned in MFR.**	--	Yes	No	--

BENCHMARKS

	PART-ID (Specific Requirements for manufacture of topical products (Ointment, Creams, Lotion & Dusting Powders)	Quality Ratings			
		2	**1**	**0**	**X**
1	**Whether the entrance to manufacturing area is through an air lock.** **Whether air lock is supplied with filtered air.**	Air lock with filtered air.	An air lock provided.	No air lock.	--
	Whether insect catcher has been installed out side air lock.	—	Installed	Not Installed	--
2 & 3	**Whether HVAC system installed in manufacturing areas. If not how air quality is maintained.** **Which filter is used for air filtration to the mfg. Area.**	5 Micron AHU with 100% exhaust.	20 Micron AHU with 100% exhaust.	No AHU.	--
	How temperature in the mfg. Area controlled.	In built within AHU provided with temperature control arrangement on the basis of thermal mapping.	In built within AHU by heating and cooling method for maintaining and temperature.	Split AC	No provision to control temperature.

	How fumes, vapors if generated during the process are controlled.	With exhaust	With exhaust	With exhaust	No exhaust
4 & 5	**What is the material of construction of tanks, containers, Pipe work and pumps?**	All contact and exposed portion of the machine and utensils are made of SS 316.	All the contact portion of the machine and utensils are made of SS.	Not all the contact portion of the machine and utensils are made of SS.	Wooden or any other particle shedding materials are used in production .
	Whether the tanks have clean in place facility. If not how tanks are cleaned. **What type of transfer pumps is used? And precaution taken to protect the product from the contamination.**	CIP facility is available.	Cleaning as per validated SOP.	Cleaning as per convenie nce	--
	How tanks, pipe works and other containers sanitized.	----	-----	-----	-----
6.	**Whether water used in the compounding is purified water IP.**		less than 500 CFU/ml.	More than 500 CFU/ml.	--
7	**Whether the powders whenever used are suitably sieved.**	In an enclosed area having provision for Drugs Control.	In an enclosed area.	No an enclosed area.	
	How contamination with metals prevented.	Metal detector is used.	Metal detector is used.	No metal detector is used	--

8.	**How heating of base like petroleum jelly is done in the vessels.** **Whether melting facility is separate / dedicated to the process.**	Melting facility in dedicated area with 5 micron AHU.	Melting facility in dedication area together with 20 micron AHU.	No dedicated facility.	--
9	**Whether a separate packing section is provided for primary packaging of products.**	5 Micron filtration with temperature control.	20 micron with temperature control.	No AHU.	--
	Whether product is filled in tubes or jars. **How jars are cleaned before filling.**	Cleaned by filtered air (5 micron)	Cleaned by filtered air (20 micron)	Cleaned by filtered air	Not cleaned by filtered air.

BENCHMARKS

	Validation	Quality Ratings			
		2	1	0	X
1	Is there a master plan **(Master validation plan)** covering:				
1.1	Resources and those responsible for its implementation.	--	Yes	No	--
1.2	Identification of the systems and processes to be validated	--	Yes	No	--
1.3	Documentation and standard operating procedures (SOPs), Work Instructions and Standards (applicable national and international standards)	--	Yes	No	--
1.4	Validation list: facilities,processes (e.g. aseptic filling), products	--	Yes	No	--
1.5	Key approval criteria	--	Yes	No	--
1.6	Protocol format	--	Yes	No	--

1.7	Each validation activity, including re-validation and reasonable unforeseen events (power failures, system crash and recovery, filter integrity failurer. Please attach validation calendar.	--	Yes	No	--
2.	Pls specify whether the critical processes validated Prospectively, retrospectively or concurrently.	Prospective	Concurrent	Retrospective	No validation
3.	Whether validation of following performed and documented: Analytical methods, Production and assay equipment, Sterile production processes, Non-sterile production processes, Cleaning procedures, Critical support systems (purified water, water for injections, air, vapor, etc.), Facilities	--	Yes	No	--

4.	Please list reasons considered important for validation or re-validation.	--	Reason and justification for each step listed	No justification listed	--
5.	In case electronic data processing systems are used, are these validated? Please specify whether periodical challenge tests performed on the system to verify reliability.	--	Yes	No	--
6.	Are the validation studies performed according to pre-defined protocols? Is a written report summarized, results and conclusions prepared and maintained? Is the validity of the critical processes and procedures established based on a validation study?	--	Yes	No	--

7.	Are criteria established to assess the changes originating a revalidation? Are trend analyses performed to assess the need to re-validate in order to assure the processes and procedures continue to obtain the desired results?	--	Yes	No	--
8	**WATER SYSTEM** **PURIFIED WATER** **WATER FOR INJECTIONS**				
8.1	Please specify whether waster system qualification (IQ, OQ and PQ) has been carried out as per protocol and repots have been prepared and maintained.	--	Yes	No	--

8.2	Whether IQ protocol include at least facility review, equipment specification vs. design, welding roughness testing on pipelines, absence of dead points / section in the pipelines, pipe and tank passivation, drawings, SOP for operations, cleaning, sanitation, maintenance and calibration of gadgets. Whether its report includes Conclusion / Summary, description of the performed assay, Data tables, Results, Conclusions, Protocol reference, Revision and approval signatures.	--	Yes	No	--
8.3	Whether OQ protocol include at least System production capacity (L/min), Flow type and water rate, Valve operation, Alarm system operation and Controls operation?	--	Yes	No	--

8.4	Whether its report includes Conclusion / Summary, description of the performed assay, Data tables, Results, Conclusions, Protocol reference, Revision and approval signatures.	--	Yes	No	--
8.5	Please specify the water whether Phase 1, Phase 2 and Phase 3 studies carried out in at PQ stages?	--	Yes	No	--
8.5.1	Phase 1 : Whether the operations parameters, cleaning and sanitation procedures & frequencies defined. Whether daily sampling records for every pretreatment point and usage point for a period of 2 to 4 weeks maintained and SOP's prepared.	--	Yes	No	--

8.5.2	**PHASE 2** : Whether daily sampling records for every pretreatment point and usage point for a period of 4 to 5 weeks after Phase 1 maintained and reviewed.	--	Yes	No	--
8.5.3	**PHASE 3 :** Whether weekly sampling records available of every usage point for a one-year period. In the case of water for injections systems, are the daily sampling records of at least one usage point available, with all the usage points sampled weekly? Whether results of these records summarized to show suitability. Are there personnel training records?	--	Yes	No	--
9.	**EQUIPMENT**				

9.1	Are the equipment installation Qualification (IQ) protocols contains followings: Introduction, Installation description, Responsibilities, Performed tests/assays, Qualification acceptance criteria and Data recording and reporting?	--	Yes	No	--
	Whether report contains Summary, Description of performed tests/assays, Obtained data tables, Results, Conclusions, Installation diagrams, Revision and approval signatures.	--	Yes	No	--

9.2	Whether the equipment operation qualification (OQ) protocols contains following: Introduction, Equipment description, Description of the equipment operation steps (SOP's), Responsibilities, Qualification acceptance criteria, Data recording and reporting. Whether report contains Summary, Description of performed tests/assays, Obtained data tables, Results, Conclusions, Revision and approval signatures.	--	Yes	No	--
9.3	Whether equipment performance qualification (PQ) protocols contains followings: Introduction, Responsibilities, Performed assays, Qualification acceptance criteria, Data recording and reporting.	--	Yes	No	--

	Whether report contains Summary, Description of performed tests/assays, Obtained data tables, Results, Conclusions, Revision and approval signatures.	--	Yes	No	--
10.	**Analytical Method Validation**	--	Yes	No	--
10.1	Please specify whether following Characteristics are considered during validation of analytical methods: — specificity — linearity — range — accuracy — precision — detection limit — quantitation limit — Robustness.	--	All parameters covered	All parameters are not covered	--
10.2	Whether Paharmocopial methods are also validated. If yes, how.	--	Yes	No	--

10.3	Whether system suitable testing is included in testing protocols e.g. HPLC, GC etc.	--	Yes	No	--
11	**CLEANING**				
11.1	Is a validation performed to confirm cleaning effectiveness?	--	Yes	No	--
	Does the protocol define the selection criteria for products or groups of products subject to cleaning validation?	--	Yes	No	--
	Is data produced supporting the conclusion that residues were removed to an acceptable level?	--	Yes	No	--
11.2	Please specify whether the validation is implemented to verify cleaning of: Surfaces in contact with the product, After a change in product, Between shift batches.	--	Yes	No	--

	Please specify whether the Validation Strategy include contamination risks, equipment storage time, the need to store equipment dry and sterilize and free of pyrogens if necessary?	--	Yes	No	--
11.3	Whether the cleaning Validation Protocol include: f. Interval between the end of production and the beginning of the cleaning SOP's. g. Cleaning SOP's to be used. h. Any monitoring equipment to be used. i. Number of consecutive cleaning cycles performed? j. Clearly defined sampling points.	--	Yes	No	--
11.4	Whether Quality Control responsible of the sampling for cleaning verification?	--	Yes	No	--

11.5	Whether personnel engaged in cleaning, sampling etc. trained.	--	Yes	No	--
11.6	Please specify whether acceptance limits been set for cleaning verification and are based on following criteria: d. Visually clean. e. 10 ppm in another product f. 0.1% of the therapeutic dose?	--	Exhaustive data available	No study conducted	--
11.7	Please specify whether detergent residues investigated and degradation products verified during validation.	--	Yes	No	--
11.7.1	Whether validation records include Recovery study data, Analytical methods including Detection Limits and Quantification Limits, Acceptance Criteria, Signatures of the Quality Assurance Manager, employee in charge of cleaning and the verification from Production and Quality Control.	--	Yes	No	--
12	**HVAC**				

12.1	Please specify whether following parameters have been qualified: — temperature — relative humidity — supply air quantities for all diffusers — return air or exhaust air quantities — room air change rates — room pressures (pressure differentials) — room airflow patterns — unidirectional flow velocities — containment system velocities —filter penetration tests (HEPA) — room particle counts — room clean-up rates — microbiological air and surface counts where appropriate — operation of de-dusting — warning/alarm systems where applicable.	--	Yes	No	--

12.2	Whether strategic tests like Particle count, air pressure differential, air flow volume, air flow velocity etc. included in HVAC qualification.	--	Yes	No	--
13	**Media fill test**				
13.1	Whether medial fill tests carried out twice in a year during normal working conditions.	--	Yes	No	--
	Pls give date of last such test.				
13.2	How many units are filled and tested.				
	What is the criterion for qualification of this test?				
13.3	In case of failure of media fill test, what precautions or actions are taken.	--	Adequate action taken to prevent future failure	No action taken	--

BENCHMARKS

	Specific Product Information	Quality Ratings			
		2	1	0	X
1.	Name of product (v) Generic Name (vi) Brand Name (vii) Dosage Form (viii) Strength				
2.	Whether validated master formula is available?	--	Yes	No	--
3.	Whether specific SOP for product processing is available?	--	Yes	No	--
4.	Comments on the above SOP	--	Satisfactory	Not satisfactory	
6.	Stability studies (iv) Accelerated (v) Real Time (vi) Whether the expiry date assigned on the basis of stability study?	-- -- __	Yes Yes Yes	No No No	--
7.	Whether trend analysis was carried out and interpretation thereof?	--	Yes	No	--
8.	Whether Annual product review (APR) is carried out?	--	Yes	No	--
9.	Is there any complaint received for the product and If any, whether the investigation report along with ATR is maintained?	__	Investigation Report along with ATR is maintained	Not maintained	__

Annexure: Q

Proposed Format for Writing summarized Inspection Report on the basis of Observations made in the above check list

On the basis of application furnished by the authorized signatory, vide letter ref. No. xxxxxxx dated xxxxxxxx for issuance of xxxxxxxxxxxx for certain items of xxxxxxx (list of which enclosed) and subsequent instructions received from xxxxxxxxxxxxxxxxxxxxxxx. and the xxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxx the under signed team members inspected the manufacturing site of M/s xxxxxxxxxxxxxxxxxxxxxxxx on xxxxxxxx.

The following technical personnel were present throughout the inspection and all the technical queries and discussions were made with them by the inspecting team.

1.

2.

3.

4.

The observations made during the inspection were noted in the enclosed inspection checklist, which may be summarized as follows:

Summarized Observations:

Manufacturing License No and its Validity

- **xxxxxxx (form 25)** dated xxxxxx, valid up to xxxxxxx
- **xxxxxxx (form 28)** dated xxxxxx, valid up to xxxxxxx

Categories of Products Permitted to manufacture

Tablet,

Capsule

Dry Syrup

Ointment

Oral liquids

External preparation

Sterile preparations

Location and Surroundings

The whole manufacturing site was found located in an eco-friendly environment and free from open sewage, drain public lavatory or any other activities which may contaminate the final product.

The whole plant was found covering a total area of around xxx acres of land at xxxx with the facilities include raw and packaging materials warehouses, dedicated and total segregated areas for manufacture of xxxxxx, Utility Block and ETP.

A well-equipped stability cell along with Quality Control and Process Development Laboratory was also found in place. No Toxic or Hazardous substances were found used / manufactured in the facility. The over all locations and surroundings was found fit and satisfactory for the manufacture of Pharmaceutical Dosage Formulations.

Building and Layout

Xxxxxx were found manufactured at a dedicated facility. Total covered area for the aforesaid activity including Process Development Laboratory, Stability Testing Laboratory and Quality Control Laboratory along with Administrative wing was found around xxxxxx sq. meters.

The whole building was found well built and capable of preventing the entry of pest and birds etc. The floors, walls and ceiling of manufacturing and storage areas were found smooth, washable and impervious. Buildings are constructed with bricks and RCC structure with xxxxxxxxxxxx flooring (joint of which are sealed with xxxxxxx, in the general area). **The walls and ceiling in the manufacturing facility was found plastered to have smooth finish following PU surface painting.** The floors of the whole manufacturing area was found made up of xxxxxxxxx with double glass panel window and doors flushed with the wall and all joints and corners are coved. All service lines were found coming to the processing area from the ceiling (solid). Light fittings and air grills were found flushed with ceiling to prevent ingress of dust and dirt. MOC of all the equipments and furniture (contact surface) placed in the manufacturing area were found made up of SS 316 grade.

Man entry from outside were found through suitable airlocks provided with cross over the bench (however the same should be placed in such a manner so that the possibility of entering dust particle to clean side is ruled out). The material transfer was found through pass boxes with internal locking arrangements. Flow of man and material was appropriate. The following specified areas were found in place.

1. .
2. .
3. .
4. .
5.

(Total build up area for aforesaid operations were found around XXXX sq. mtr.)

The manufacturing bock is a xxxxxxxxx storied building. The ground floor is used for storage of raw material, dispensing, sampling manufacturing operation of XXXX and the xxxxxx floor is used for XXXX.

The overall cleanliness maintained by the firm in the said area and the layout were found satisfactory and suits the requirement of GMP guidelines. The production areas as well as storage areas were found under xxx AHUs of assorted capacity with terminally fitted HEPA Filter with return duct through riser.

Plant and Machineries

The List of Plant and Machineries submitted by the firm along with the application were verified at the time of inspection and found that capacity of each machine is commensurate with the batch size. DQ, IQ and PQ of some of the machines were examined by the inspecting team at the time of inspection and found satisfactory.

All the machines were found installed in such a manner so that proper cleaning after each batch production could be done. The Process equipment like xxxx was found fitted with HEPA filter to prevent any extraneous contamination and the bags used for the FBD were found all products dedicated.

CIP and SIP was found inbuilt in the system.

HVAC System

A total number of xxx independent Air Handling Units (AHUs) were found in place to control the Production areas and Warehousing Areas. Each process operation has its own AHU to control temperature, humidity and particulate matter. The internal corridors were found at a positive pressure in comparison with the adjacent production rooms (Powder generated) to prevent cross as well as the extraneous contamination of the products. Magnehelic manometers to indicate the pressure differential were found in all strategic places.

Each AHU was found fitted with 10 micron filters, chilled water stroke brine coil, Hot water coil, 5 micron filters and finally through 0.3 micron HEPA filters provided at terminal. Separate return air ducts were found provided in each room at a height of 30 cm from the floor and were fitted with 10 micron filters in the return grills. The HVAC system was found BMS (Building Management System) controlled. Dust extraction systems with proper hoods were found provided in granulation and compression areas. Temperature is maintained at comfort condition.

Some of the records related to AHUs for supplying air for compression area was examined regarding DOP testing, particle count, humidity and temperature, air change rates, pressure balancing etc. by the inspecting team during inspection and found satisfactory.

The environmental monitoring system by settle plate method and non viable particle count through XXXX was found in place (the inspecting team checked the operation of particle count machine during inspection and the printed data obtained is enclosed). The present practice followed by the firm for HVAC system is found xxxxxxxxxxxxx.

Water System

It was observed that the firm maintained a pre specified water system for the whole plant. Raw water was found collected by deep tube well (xxxxx feet) and after passing through Multi-grade filter, cartridge filter, RO system, EDI (Electro Deionization) and finally through ultra filtration and stored in a SS316L storage tank of capacity of xx KL and then circulated through circulation loop into production area.

The microbiological analysis report showed that the said water is complying with the standard norms and the CFU is less than 100/ml and free from pathogenic organisms like s.aurious, s.tiphy and e.colli.

The inspecting team checked the whole system and the present function were compared with the technical manual supplied by the RO, EDI and UF system supplier. From the test report of this purified water submitted by the firm it was observed that the water generated from this system is complying with the standard of purified water as specified in IP'96 and USP.

Personnel and Hygiene

A total of xxxx employees were found engaged in the plant. As per the training SOP placed by the firm, all employees should be trained on various aspects including hygienic requirements at the time of induction and at regular intervals there after. Training record of some of the employees were checked by the inspecting team and found satisfactory.

All the technical personnel were found possessing proper academic background and competent enough to perform the duty assigned to them. The list of approved technical personnel is enclosed as Annexure-xxx. The medical examination of all the employees was found carried out by Dr. XXXXXX. Registered number XXXXX. In XXXX.

Two sets of aprons, caps and foot wares were found provided to the employees authorized to enter into the general areas. Non fiber shedding garments with full covering were found provided (two sets) to all employees authorized to enter in to the manufacturing area. Auto IPA dispenser was found provided at the entry point of the production area to sanitize hands.

The firm has their own laundry system for cleaning and washing the used linen. The cleaning validation of the linen was found in place and the residual limit of the detergent was found maintained at the level of not more than XXXX ppb calculated on the basis of wash water analysis.

Rest room and cafeteria for employees were found well outside the manufacturing.

The present practice to maintain hygiene of the personnel is acceptable.

Qualification and Validation

Qualification and validation were found performed for critical equipment and process like XXXXXX, XXXX machines and process validation of mixing blending, cleaning etc. The documents reviewed during the inspection revealed satisfactory level of implementation and compliance with current requirements. AHU (number – XXX) qualification, temperature mapping of certain area of the raw material store and cleaning validation of the garments were verified by the inspecting team at the time of inspection and found in the level of compliance of current requirement.

Self-Inspection and Quality Audits

Self-inspection and quality audit was found carried out by a team consists of the Head of the Plant, QA, Production and other departmental Heads once in every xxxxx months. Additionally, Quality audits were also found performed by the Corporate Quality Assurance team once in a year, which involves audit of facilities, systems, procedure and documentation.

Vendor Development

All starting and primary packaging materials were found procured from the approved vendors who were pre qualified through regular audits and review of satisfactory vendor assessment questionnaire.

Training

It was observed that the firm meticulously follows a structured training program, which covers all employees. Functional managers mainly carry out training within the plant itself. Managers were also found exposed to different training programs conducted by various professional bodies. The in-house training program consists of

- Induction programme
- cGMP Requirements
- Safety
- Hygiene
- Training on use of equipment (on the job training)
- Risk analysis

Some of the records regarding training were examined at the time of inspection and found satisfactory.

Manufacturing Operation and Control

It was observed that all the critical parameters of the manufacturing operations were found carried out under the active supervision of competent technical personnel following the Standard Master Formula (properly validated). All the documents related to the batch manufacturing were found scrutinized by the QA before releasing the finished product in the market.

Product Recall

A validated product recall system was found in place covering details to initiate promptly recall operation at the level of each distribution channel up to the retail level.

Records

All necessary records starting from receipt of material to the distribution of finished goods were found maintained by the firm. In addition, around xxx SOPs were found maintained. Some of the records were verified by the inspecting team at the time of inspection and found satisfactory.

Quality control

It was observed that the firm established its own QC laboratory (headed by XXXX and assisted by XXX technical personnel) with the arrangement for testing of raw material, packing material and finished products by chemical, instrumental and microbiological analysis. The QC area is completely separated from the manufacturing area and the QC personnel enter the production area after following the specified dress code and other precautions as per the SOP no. XXXXX.

The instrument laboratory was found under central AC with all relevant instruments including HPLC, FTIR, Liquid particle Counter, TOC Analyzer, Conductivity Analyzer, UV-Spectrophotometer etc. required for the analysis of all the raw materials and finished products applied for except GC (required for one of the test of XXXX). The firm made arrangements with approved laboratories to carry out some test on their behalf (contract in this regard was verified by the inspecting team at the time of inspection and found in compliance WHO – TRS 908). List of instruments as submitted with the application were verified by the inspecting team at the time of inspection and found all are operational. However, for HPLC testing, the firm should procure C-18 column (10cmx4.6mm & 15cmx4.6mm) to carry out all test in house.

The microbiological laboratory was found under dedicated AHU's to control the testing procedures as well as to protect the environment from microbiological contaminants. The design and layout of the microbiology laboratory were found satisfactory. The entry to the microbiology area is restricted through three air locks of desired air classification and LAF stations were found provided on all the rooms for carrying out different microbiological tests. The competency of the microbiologist was examined by the inspecting team at the time of inspection and found satisfactory.

The chemical laboratory was found provided with proper fuming chamber with adequate space for storage of tests samples, retained samples, reference standards, reagents and records.

QA Function

It was observed that the QA function is headed by XXXXXX and assisted by XXX more technical personnel. The QA head is responsible for release of finished product after verification of all relevant documents from production, QC and other related departments.

Stability Studies

It was observed that the firm has made arrangements for stability studies on each product for accelerated as well real time for which XXXX Stability chambers (controlling humidity and temperature) were found in place. The data of stability studies of the following products were verified at the time of inspection by the inspecting team and found satisfactory.

1. **:**
2. **.**
3. **.**

All the critical parameters of the manufacturing process were found validated by **prospective** as well as **concurrent** validation method.

Utility Services

Following utility services were found provided by the firm:

1. Air Compressor (Oil free)- 150 CFM
2. DG set – 750 KV
3. Boiler, husk fired – 5 tons
4. Chiller -150 TR (Ton Refrigeration)

Annual product review and trend analysis

A System in this regard is found in place. Some of the products as detailed below was verified at the time of inspection.

1.

2.

3.

Remarks and recommendation

Annexure: R

BLOOD BANK INSPECTION CHECK LIST

(use separate sheets ,if necessary)
(Collect specimen forms, documents, labels, record copies whenever necessary)

Name of Institution			Date of Inspection	
Address of the Institution				
Telephone No.: Fax No.: E-mail:				
Licence number and date of issue				
Inspected By				
Institution represented by				
Purpose of inspection				
Type of Institution	Government	Charitable	Red Cross	Others (specify) Registered Society & attached with Hospital.
Constitution Details				
Product(s)				

Technical staff *(Attach sheet, if reqd.)*	Name	Qualification *(check documents)*	Experience *(check testimonials)*
Doctor			
Registered Nurse			
Technician			

A	Total Collection *(Last two calendar years)*	Year	New Case	
		Voluntary		
		Replacement		
		Professional		
		Total		
	Distribution	Used in own hospital		
		Issued to others		
		Discarded		
B	**Premises**	Total area		
	Details of areas		**Comments**	
1	Registration and Medical Examination			
2	Blood Collection (A/C ?)			
3	Refreshment & Rest Room (A/C ?)			
4	Serology Lab. (A/C ?)			
5	Transmissible diseases Lab. (A/C ?)			
6	Sterilization & washing			
7	Stores and Records			

	General comments on Area		
1	Standard Books? (obtain list)		
2	Blood Bank Manual		
3	Standard operating procedures		
a	Criteria to determine donor suitability	Yes/No/NA	
b	Method of donor selection	Yes/No/NA	
c	Preparation of phlebotomy site	Yes/No/NA	
d	Product to Donor traceabllity	Yes/No/NA	
e	Collection procedures, precautions etc.	Yes/No/NA	
f	Method of components preparation	Yes/No/NA	
g	Test methods	Yes/No/NA	
h	Pre-transfusion testing	Yes/No/NA	
i	Adverse reaction management	Yes/No/NA	
j	Storage temperature & its control	Yes/No/NA	
k	Expiry date assignment	Yes/No/NA	
l	Returned Blood management	Yes/No/NA	
m	QC for reagents & supplies	Yes/No/NA	

n	Maintenance, calibration & validation of equipment	Yes/No/NA	
o	Labeling procedures	Yes/No/NA	
p	Apheresis procedures	Yes/No/NA	
q	Any other SOPs	Yes/No/NA	
D	Procedure for disposal of blood (expired, clotted, improperly collected, HIV + etc.	Yes/No/NA	
E	Donor education/ motivation material	Yes/No/NA	
F	Donor selection	Yes/No/NA	
1	Donor record	Yes/No/NA	
2	Selection/rejection manual	Yes/No/NA	
3	**Donor record details:**		
a	Age	Yes/No/NA	
b	Interval between donations	Yes/No/NA	
c	Last pregnancy/delivery/ abortion	Yes/No/NA	
d	Immunization details	Yes/No/NA	
e	Recent drug intake	Yes/No/NA	
f	Major surgery	Yes/No/NA	
g	Malaria	Yes/No/NA	
h	Jaundice	Yes/No/NA	
i	Other viral infection	Yes/No/NA	
j	Fever & common cold	Yes/No/NA	

k	History-cancer, TB, Diabetes, Drug addiction, etc.	Yes/No/NA	
l	Alcohol intake	Yes/No/NA	
m	Transfusion history	Yes/No/NA	
4	Donor Examination	Yes/No/NA	
a	Weight	Yes/No/NA	
b	Venipuncture site	Yes/No/NA	
c	haemoglobin	Yes/No/NA	
d	Blood pressure	Yes/No/NA	
e	Pulse	Yes/No/NA	
f	Temperature	Yes/No/NA	
G	**Collection of Blood**		
a	Preparation of phlebotomy site	Yes/No/NA	
b	Type and amount of anti-coagulant used	Yes/No/NA	
c	Amount of blood collected (random wt.)	Yes/No/NA	
d	Blood collected in bags/bottles	Yes/No/NA	
e	Pediatric Bags?	Yes/No/NA	
f	Is mixing done during collection? How?	Yes/No/NA	
g	Is new bag used in case of 2nd puncture?	Yes/No/NA	
h	How is sample tubes labelled?	Yes/No/NA	
i	Emergency kit available?	Yes/No/NA	
H	**Storage of blood**		
a	Temperature recording graph preserved?	Yes/No/NA	
b	Alarm system checks done?	Yes/No/NA	
c	Physical Verification done? Frequency?	Yes/No/NA	
d	How is blood transported? Outside, to wards?	Yes/No/NA	

I	**Blood Testing**		
a	Sterility Testing	Yes/No/NA	
b	Haemoglobin estimation-method	Yes/No/NA	
c	Method for ABO grouping	Yes/No/NA	
d	Procedure for grouping	Yes/No/NA	
e	Method of pooled cell preparation	Yes/No/NA	
f	Du test done on D-samples?	Yes/No/NA	
g	Test for unexpected antibodies done?	Yes/No/NA	
H	Hepatitis test done? Describe method and Name of kit manufacturer	Yes/No/NA	
I	Syphilis test done? Describe method and Name of kit manufacturer	Yes/No/NA	
J	HIV test done? Describe method and Name of kit manufacturer	Yes/No/NA	
K	HCV test done? Describe method and Name of kit manufacturer	Yes/No/NA	
L	Malaria test done? Describe method	Yes/No/NA	
M	Donor informed in case of +ve results?	Yes/No/NA	
N	In case of HbsAg/HIV +ve results Donor debarred permanently	Yes/No/NA	
O	Are HbsAg/HIV +ve donors followed up?	Yes/No/NA	
P	Cross matching. (Describe method)	Yes/No/NA	
J	**Testing of reagents etc.**		
a	Antisera tested?	Yes/No/NA	

b	Method of Antisera testing	Yes/No/NA	
c	CPDA solution testing	Yes/No/NA	
K	**General equipment and Instruments**		
a	Refrigerators for Blood Storage Type, capacity and number		Yes / No / NA
b	Temperature recorder in refrigerator		
c	Audible alarm system in refrigerator		
d	Balance for bag weighing		
e	Autoclave with temp. & pressure display		
f	Incinerator		
g	Emergency power supply (generator)		
h	Donor beds, chairs, tables		
i	Bedside table		
j	Sphygmomanometer & stethoscope		
k	Recovery bed for donors		
l	Donor weighing scale		
L	**Emergency equipment**		
a	Oxygen cylinder, mask, gauge and pressure regulator		
b	5% Dextrose or Normal Saline Inj.		
c	Sterile Disposable Syringes and needles (various sizes)		
d	Sterile disposable I.V.sets		
e	Adrenaline. Noradrenaline, Mephentin, Betamethasone (or dexamethasone),Metochlorpropamide injections		
M	**Accessories**		
a	Blankets, emesis basins, haemostats, set clamps, sponge forceps, gauze, dressing jars, waste cans etc.		
b	Medium cotton balls, 1.25 cm adhesive tapes		
c	Denatured spirit, Tinc. Iodine, green or liquid soap		
d	Paper napkins or towels		

N	Laboratory Equipment	
a	Refrigerator for kits and reagents storage Refrigerator make and Capacity Temperature display provided	
b	Compound microscope with low & high power objectives	
c	Table centrifuge	
d	Water bath- 37°& 57°	
e	Rh viewing box	
f	Incubator with thermostat	
g	Mechanical shakers for serological test of syphilis test	
h	Hand lens	
i	Serological graduated pipettes of various sizes	
j	Pasteur pipettes	
k	Glass slides	
l	Test tubs of various sizes/ microplates	
m	Precipitating tubes (6x50 mm) of various sizes	
n	Test tube racks	
o	Interval timer	
p	Material and equipment for glassware cleaning	
q	Blood transporting containers	
r	Wash bottles	
s	Filter papers	
t	Dielectric tube sealer	
u	Plain and EDTA vials	
v	Chemical balance	
w	Elisa reader with printer, washer and micro-pipettes	
x	Colorimeters / haemoglobinometer (strike off which is not applicable) for haemoglobin determination.	

O	**Records and Reports**		
			Comments on records, if any
a	Blood Stock/master Register	Yes / No / NA	
b	Blood donor record	Yes / No / NA	
c	Issue register	Yes / No / NA	
d	Record of Blood bags	Yes / No / NA	
e	Cross matching records	Yes / No / NA	
f	Register of diagnostic reagents and kits	Yes / No / NA	
g	Adverse reaction records	Yes / No / NA	
h	Stock register of other consumable articles	Yes / No / NA	
i	Are records destroyed?	Yes / No / NA	
j	Labels of Blood containers as per Schedule F of the d & C act	Yes / No / NA	
P	**Outdoor camps**		
a	Eligible to hold outdoor camps	Yes / No / NA	
b	Average number of camps held per month	Yes / No / NA	
c	Vehicle available?	Yes / No / NA	
d	How are blood bags transported	Yes / No / NA	
f	Proof sanitary conditions of camps	Yes / No / NA	
g	Detailed statement of blood collected in camps	Yes / No / NA	

PROCESSING OF BLOOD COMPONENTS FROM WHOLE BLOOD.

Q.	ACCOMMODATION/ PREMISES		COMMENTS
1.	Area provided for component preparation.		
2.	Does an additional 10-sq. meter area provided for aphaeresis procedures .	**YES/NO/NA**	
(a)	Is Blood component room Air-conditioned?	**YES/NO/NA**	
(b)	Is Blood component room well lighted?	**YES/NO/NA**	
(c)	Are walls and floors are smooth & washable?	**YES/NO/NA**	
(d)	Is overall hygienic conditions maintained in the premises.	**YES/NO/NA**	
(h)	Comments on Area		

R	PERSONNEL Whether Technical Supervisor with adequate basic qualification and experience is available with the blood bank.	**YES/NO**	**Comments**
	Name, Qualifications & Experience		

S1	**Equipment** **(As per GSR 245(E) dt.05.08.99)**		**Make/Model/ Capacity**
(i)	Air Conditioner.	YES/NO/NA	
(ii)	Laminar air flow bench.	YES/NO/NA	

(iii)	Suitable refrigerated centrifuge.	YES/NO/NA	
(iv)	Plasma expresser	YES/NO/NA	
(v)	Clipper and clips and or dielectric sealer.	YES/NO/NA	
(vi)	Weighing device.	YES/NO/NA	
(vii)	Dry rubber balancing material.	YES/NO/NA	
(viii)	Artery forceps, scissors.	YES/NO/NA	
(ix)	Refrigerator maintaining a temperature between 2 degree centigrade to 6 degree centigrade, a digital dial thermometer with recording thermograph and alarm device, with provision for continuous power supply.	YES/NO/NA	
(x)	Platelet agitator with incubator (wherever necessary)	**YES/NO/NA**	
(xi)	Deep freezers maintaining a temperature between minus 30 degree centigrade to minus 40	YES/NO/NA	

	degree centigrade and minus 75 degree centigrade to minus 80 degree centigrade.		
(xii)	Refrigerated water bath for plasma Thawing.	YES/NO/NA	
(xiii)	Insulated blood bag containers with provisions for storing at appropriate temperature for transport purposes.	YES/NO/NA	
(xiv)	Whether components are prepared only in a closed system using single double triple or quadruple plastic bags.	YES/NO/NA	
S2	**EQIPMENT (GMP)**		**COMMENTS**
1.	Are equipment located in logical sequence and permit effective cleaning?	YES/NO/NA	
2.	Are equipment calibrated/validated periodically?	YES/NO/NA	

T	**PREPARATION OF BLOOD COMPONENTS.**		
1.	**Concentrated Human RBC's** **(Packed Red Blood Cells)**		**COMMENTS**
a	**Whether SOP is available for preparation of PRC?** ***Specify: Source material*** Method RCF Speed Time	**YES/NO/NA**	
b	**Is blood collected from suitable donor? (check the donor record).**	**YES/NO/NA**	
c	**Are the packed red cells confirmed to the standard of I.P.1996**	YES/NO/NA	
d	**How the Pilot tubes / samples are numbered?**	YES/NO/NA	
e	**Whether pilot tube is attached in a tamper proof manner to the unit?**	YES/NO/NA	
f	**Who is responsible for filling of pilot samples?**	YES/NO/NA	
g	**Whether pilot samples are filled immediately after the blood is collected or at the time the final product is prepared?**	YES/NO/NA	
h	**Whether expiry is assigned as per norms? (specify the period)**	YES/NO/NA	
2	Platelets concentrates		COMMENTS

a	**Whether SOP is available for preparation of Platelets concentrates?** ***Specify: Source material*** Method RCF Speed **Time**	YES/NO/NA	
b	**Whether the whole Blood / source material is stored at 20 degree to 24 degree centigrade after collection, before processing to platelet concentrates?**	YES/NO/NA	
c	**Whether Platelet Concentrates are separated within 6 hours after the time of collection whole blood /source material**	**YES/NO/NA**	
d	**Whether platelet concentrates are tested:** **Platelet count (Note the count)** **pH (not less then 6)** **measurement of Plasma volume** **sterility (1% of total platelets prepared shall be tested for sterility,** **'functional viability' (swirling movement)**	**YES/NO/NA**	
e	**Whether compatibility test prepared on every unit before issue**	**YES/NO/NA**	

f	**Whether platelet yield is calculated (1% of total platelets prepared shall be tested of which 75% of units shall confirm to standards)**	**YES/NO/NA**	
3.	FRESS FROZEN PLASMA		COMMENTS
a	**Whether SOP is available for preparation of FFP?** ***Specify: Source material*** Method RCF Speed **Time**	**YES/NO/NA**	
b	**Whether deep freezers capable of maintaining temp between 75^0c to 80^0c and minus 30^0 c to minus 40^0 c are available**	YES/NO/NA	
c	**Whether the source material/human blood stored at 4^0 c till processed**	YES/NO/NA	
d	**Whether thawing facilities are provided (note the thawing temperature)**	YES/NO/NA	

e	**Lag time between collecting of blood and processing of FFP (check records)**	YES/NO/NA	
4.	CRYOPRECIPITATE		COMMENTS
a	**Whether SOP is available for preparation of CRYOPRECIPITATE?** ***Specify: Source material*** Method ***RCF*** Speed **Time**	**YES/NO/NA**	
b	**Whether thawing facilities are available (note the temperature)**	YES/NO/NA	
c	**Whether anti-hemophiliac factor activity is tested. (NLT 80 units/bag), (1% of total cryo prepared shall be tested of which 75% shall conform to specification)**	YES/NO/NA	
5.	APHERESIS PROCEDURE		*COMMENTS*
a	**Whether cell separator facility is provided?**	YES/NO/NA	
b	**Whether donor is certified fit for apheresis (check the record)**	YES/NO/NA	
c	**Time allowed between successive aphaeresis on a single donor**	YES/NO/NA	

d	**Whether protein estimation of donor carried out if serial apheresis is to be conducted.**	YES/NO/NA	
e	**Whether inquiries about aspirin intake made before platelet apheresis.**	YES/NO/NA	
f	**Whether RBC's are re-transfused during platelet apheresis or leucopheresis. If not, what precautions are taken.**	YES/NO/NA	
g	**Whether following tests are carried out before apheresis procedures** Name of the test Acceptance criteria		
	(i) Hemoglobin/Hematocrit **(ii) Platelet count** **(iii) WBC count** **(iv) Differential count** **(v) Serum protein**		**COMMENTS**
h	How much quantity of plasma is to be collected (Plasma apheresis)		
	DURATION **(I) single sitting** **(II) Per months**	LIMIT Not exceeding 500 ml./1 sitting Not exceeding 1000 ml./1 months)	***COMMENTS***

U	STORAGE OF BLOOD COMPONENTS		
S.No.	BLOOD COMPONENT	**TEMPERATIRE**	**DURATION/EXPIRY PERIOD**
1.	**FFP**		
2.	**Cryoprecipitate**		
3.	**Platelets concentrate**		
4.	**Red Cell concentrate**		
5.	**Granulocytes concentrate**		
V	**RECORDS AND LABELS**		**COMMENTS**
1.	Whether details of quantity supplied, compatibility report, details of receipts and signature of issuing person mentioned in the component record.	**YES/NO/NA**	
2.	Whether master record for component and issue register is mentioned as per norms (GSR 245 E dated 05.04.1999)	**YES/NO/NA**	
3.	Whether labels for components are prepared as per norms (GSR 245 E dated 05.04.1999)	**YES/NO/NA**	
4.	Whether all details on labels are filled by the responsible person on the final container	**YES/NO/NA**	

Observations, irregularities and Recommendations
Signature and Designations of Inspecting Persons

Name of Technical Personnel to be Endorsed on the Licence Copy:-

Personnel	Name	Qualification	Experience	Testimonials
Medical Officer In-Charge(s)				
Registered Nurse (s)				
Blood Bank Technician(s)				
Technical Supervisor(s)				

Sign Of Inspection Team Members

Annexure: S

Inspection Checklist for Vaccine Manufacturing Unit as per WHO Norms

SUMMARY OF COMPANY ORGANIZATION AND SELF INSPECTION

Inspection of M/s **Date :**

Full Address of Company:	**Products manufactured:**	**Location of Production:**
_____ _	_____ _____	
_____ _	_____ _____	
_____ _	_____ _____	
_____ _	_____ _____	

Inspection type: mark all that apply	Name of inspectors:	Affiliation of inspectors:
External [ ]	_____ _____	
Routine [ ]		
Concise [ ]	_____ _____	
Special [ ]		
Internal [ ]		
Annual [ ]	_____ _____	
Semi-annual [ ]		
Announced [ ]	_____	

Unannounced [ ] Follow-up, re-inspection [ ] Pre-licensing [ ]	_____ _____ _____ _____ _____ _____ _____	
<u>Department(s) being inspected:</u> _____ _ _____ _ _____ _ _____ _ _____ _	Date(s) of inspection From : To : Normal working hours: _____ AM to _____ PM	**<u>Date of most recent previous routine inspection (internal or external):</u>** _____ _ Type: _____ _____ QA audit report # : _____ _
Floor plans of facility available **<u>Y [ ] N [ ]</u>**	**<u>Airflow patterns, differential pressures, and classification of production areas indicated?</u>** **<u>Y [ ] N [ ]</u>**	**<u>Flow patterns for personnel, supplies, raw materials, product, and waste for production areas indicated?</u>** **<u>Y [ ] N [ ]</u>**

SUMMARY OF SENIOR PERSONNEL, A: (use next page if these departmental divisions are not appropriate, or for other department designations)

ADMINISTRATION **Position Title**	**Name**
_____ _ _____ _	
PRODUCTION DEPARTMENT **Position Title**	**Name** **Qualifications**
_____ _ _____ _ _____ _ _____ _ _____ _ _____ _	_____ _____ _____ _____ _____ _____ _____ _____ _____ _____
ANIMAL FACILITIES **Position Title**	**Name** **Qualifications**
_____	_____ _____

ENGINEERING/MAINTENANCE **Position Title**	**Name** **Qualifications**
_____ _ _____ _	_____ _____ _____ _____
QUALITY CONTROL DEPT **Position Title**	**Name** **Qualifications**
_____ _ _____ _ _____ _ _____ _	_____ _____ _____ _____ _____ _____ _____ _____
QUALITY ASSURANCE DEPT **Position Title**	**Name** **Qualifications**
_____ _ _____ _ _____	_____ _____ _____ _____ _____ _____

SUMMARY OF SENIOR PERSONNEL, B: (use for additional departments or different organizational divisions)

_____ Department Position Title _____ _ Others department _____ _	Name Qualification _____ _____ _____ _____ _____ _____ _____ _____ _____
_____ Department Position Title _____ _ Others department	Name Qualification _____ _____ _____ _____ _____ _____ _____

_____ _	_____ _____ _____ _____
_____ Department Position Title _____ _ Others department _____ _	Name Qualification _____ _____ _____ _____ _____ _____ _____ _____
_____ Department Position Title _____	Name Qualification _____ _____ _____ _____

_ Others department _____ _	_____ _____ _____ _____ _____ _____
_____ Department Position Title _____ _ Others department _____ _	Name Qualification _____ _____ _____ _____ _____ _____ _____ _____ _____ _____

1.0 A: General

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is there an organizational chart? What departments are identified? Production department(s) Typho-Vi Oral Polio Vaccine Rabies Filling [ ] Labeling/Packaging [ ] Quality Control [ ] Engineering/Maintenance [ ] Quality Assurance [ ] Receiving/Warehousing [ ] Shipping/Distribution [ ] Purchasing [ ] Animal Procurement/Care [ ]				
2	Are there job descriptions for key personnel? Are they appropriate to the activities of the department?				
3	Number of engineering staff ____ Number sufficient? Qualifications adequate? Experience sufficient?				

	Number of production staff ____ Number sufficient? Qualifications adequate? Experience sufficient? Number of quality control staff _ Number sufficient? Qualifications adequate? Experience sufficient? Number of quality assurance staff ____ Number sufficient? Qualifications adequate? Experience sufficient? Number of animal care staff ____ Number sufficient? Qualifications adequate? Experience sufficient?				
4	Is there a clear separation of responsibility for production from QC?				
5	Is there a clear separation of personnel from different areas handling animals, microorganisms, and product? By written procedure?				
6	Are the names and qualifications of those responsible for approving the lot processing records registered with the NCA?				

1.0 B: Key Personnel

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there sufficient key personnel to supervise assigned functions? Production Filling Labeling/Packaging Quality Control Engineering Maintenance Quality Assurance Marketing & Supply General Administration & Account Procurement & Stores				
2	Are they skilled/trained in fields such as biology, microbiology, chemistry veterinary medicine, chemical or industrial engineering, etc.? Engineering Production Department(s) Filling Quality Control Quality Assurance Animal Care				

1.0 C: Training

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there on the job training procedures for new employees?				
2	Are training and education records available? Are they current? Are they filed with the supervisor? Engineering/Maintenance Production Department(s) Filling Quality Control Quality Assurance Animal Care				
3	Does a GMP training programme exist? For new employees? Annual update for all staff? Are records maintained?				
4	Is there training in containment procedures? By written procedures? Are records maintained?				

1.0 D: Personal Hygiene

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are appropriate protective apparel required? Is there a gowning SOP for production staff? For other staff entering production areas? (Engineering/Maintenance; Cleaners; QC samplers; QA auditors) For staff in the Quality Control Lab?				
2	Are staff instructed to report health or medical problems that may have an adverse effect on the product?				
3	Is there a medical monitoring programme to ensure protection of staff and product? Vaccination where applicable? For all employees? For contractors?				
4	Do controlled entry requirements exist for: Production areas? Testing areas? Animal areas? Do procedures exist for preventing unauthorized entry into: Production areas? Storage areas? Quality control areas? Animal areas? Are the procedures in writing?				

2.0 A: General

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the building used for manufacturing of product suitably located and constructed, and of adequate size to facilitate cleaning, maintenance and proper operation?				
2	Are areas clearly defined and appropriately controlled:				
a	For quarantine and storage of starting materials?				
b	For storage of in-process material?				
c	For manufacturing and processing operations?				
d	For control and laboratory operations?				
e	For quarantine and storage of finished products?				
f	For holding of rejected material?				
g	For ancillary usage, e.g. rest rooms, maintenance workshops?				

2.0 A: General, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
h	For animal housing?				
3	Does the building design prevent the entry of insects, vermin and other animals?				
4	Plumbing				
a	Do adequate drains exist? Are they designed with an atmospheric break to prevent back-siphonage from sewer?				
b	Are traps being maintained to ensure adequate performance?				
5	Does the design of the facility achieve a unidirectional flow of materials, personnel, product and waste so as to avoid cross-over of clean and dirty (infectious) material?				
6	Is the lighting provided adequate for the conditions necessary for the work being conducted in the area?				
7	Are facility layout drawings including mechanical, electrical and architectural kept up-to-date following changes? Is revalidation of facilities performed following refurbishment?				
8	**Campaign production**				
a	Is the facility designed and constructed to permit production in campaigns?				

2.0 A: General, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
b	Has campaign changeover been validated (effectiveness of changeover)?				
c	Is there a documented procedure for changeover that described decontamination, removal of equipment, etc.? Is the procedure followed?				
d	It there a campaigning schedule available?				
9	**Do washing facilities include:**				
a	Hot and cold water?				
b	Soap or detergent?				
c	Clean toilet facilities that are easily accessible to working area?				
d	Clean hand drying facilities?				
10	**Are the premises satisfactory with respect to:**				
a	Neatness and cleanliness?				
b	State of repair, e.g. paint work, cracks in floors, ceilings or walls, door seals etc.?				
c	Exposed piping or electrical wiring?				
d	Blocking of air ducts?				
e	Equipment blocking corridors or exits?				

2.0 B: Support Systems

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**Support systems, including those identified below :**				
a	Support systems, including those identified below:				
b	Is there a planned maintenance program on each system? Is it followed?				
c	Are there specs and written procedures for the operation of the systems, sampling plan, sites monitored and alert and action levels defined?				
d	Are definitive action steps taken to resolve conditions that are out of specification?				
2	**HVAC System:**				
a	Are pre-filters present in heating, ventilation and air-conditioning (HVAC) systems and replaced on a routine basis?				
b	Are high-efficiency particulate air (HEPA) filters tested for integrity, at least annually?				
c	Are HEPA Filters terminally located?				

2.0 B: Support Systems, Continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
d	Are duct work materials impervious to disinfectants that may cause corrosion?				
e	Are duct work and filters located outside the clean rooms?				
f	If fumigation procedures are used, is the facility designed to permit effective fumigation?				
g	Is the number of air changes per hour adequate for defined areas?				
h	Is the airflow adequate? {minimal pressure differential (1.21 mm H_2O) maintained?}				
i	Is room temperature and humidity effectively controlled?				
3	**Compressed air**				
a	Is the air supply free from oil?				
b	Is the air supply filtered through a sterilizing grade air filter?				
c	Is humidity controlled?				

2.0 B: Support Systems, Continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
4	**Clean steam**				
a	Is clean steam used for sterilization product contact surfaces?				
b	Is the distribution system constructed of stainless steel treated to prevent corrosion and sloped for drainage?				
5	**Water for injection (WFI) system**				
a	Is the design of the WFI system				
b	Is there a holding tank for the WFI system, is it fitted with a sterilizing grade vent filter that is integrity tested?				
c	If WFI is stored on a continuous circulation, is it held at $\geq$ 80^{o}C? If not circulated, is it discarded every 24 hours or diverted for suitable use?				
d	Is WFI used as a lubricant on the re-circulating pumps?				
e	Are all the dead-legs within acceptable length?				

2.0 C: Sterile Processing

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are the aseptic manufacturing areas and operations consistent with the WHO guidelines for sterile pharmaceutical products provided in TRS 823, Section 17, page 59ff?				
2	**Does the aseptic manufacturing area include:**				
a	Smooth, hard non-particulate generating cleanable floors, walls and ceiling? Able to withstand cleaning, disinfecting reagents?				
b	No horizontal pipes or conduits located over exposed components, in-process material, production or product contact surfaces?				
c	Environmental controls, e.g. temperature, humidity and viable and non-viable particles? Are there specifications for these controls? Has the system been validated?				
d	Air supplied through HEPA filters? (terminal filters should be employed for final formulation and filling activities)				

2.0 C: Sterile Processing, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
f	Fixtures (electrical outlets and lighting, etc.) flush mounted and sealed to prevent air leakage, water access?				
g	Identification of all pipes or conduits for air, clean steam or liquids?				
h	Properly equipped gowning area/air-lock?				
i	The ability to achieve appropriate air standards (Grade A, B, C, D) during operation?				
j	Appropriate air flow design including segregated air systems for different aspects of the processing, e.g. fermentation and filling?				
k	Appropriate air flow design so that the area is flushed by HEPA filtered air exhausted through return ducts (not blocked by equipment)?				
l	The ability to maintain the appropriate pressure differentials between work areas with different Grades of air?				
3	**Does the aseptic manufacturing area exclude:**				
a	Access doors for servicing equipment				

	and fixtures? (Should only be from outside area)				
b	Drains?				
c	Sinks?				
4	Is the vaccine processing area isolated and independent of any space used for any other purpose?				

2.0 C: Sterile Processing, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
5	Are the facilities appropriately designed and validated to comply with relevant containment levels assigned to organisms involved in the manufacturing process?				
6	Is the aseptic manufacturing area cleaned according to a validated procedure? Is it followed? Is the cleaning data recorded?				

3.0 A: Adequacy

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the equipment appropriately designed, constructed and maintained?				
2	Are steps taken to prevent any substances required for operation, such as				

	lubricants or coolants, from coming in contact with in-process or finished products?				
3	Are equipment surfaces that contact components or products of a non-interactive nature?				
4	Are process pipe lines or service lines whose contents come in contact with products or product contact surfaces sloped to allow proper drainage?				

3.0 B: Cleaning and Maintenance

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the equipment suitably located to facilitate its use, cleaning and maintenance?				
2	Are equipment and utensils cleaned, maintained and sanitized as appropriate to prevent malfunction or cross-contamination?				
3	Are piping systems, valves and vent filters properly designed to facilitate cleaning and sterilization? NOTE: Maintaining closed systems through the use of “clean in place” and “ sterilize in place” is preferable.				
4	Are the valves on primary containment vessels (e.g. fermenters) steam sterilized?				
5	Are non-fiber releasing filters used for filtration?				
6	Are filters used for sterile filtration integrity tested before and after use?				

3.0 B: Cleaning and Maintenance, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
7	Are calibrations and validation being performed adequately?				
8	Are autoclaves and sterilizing ovens fitted with effective, proper air filters and are these integrity tested? Are HEPA filters used for the ovens?				
9	Are supplies and equipment which are exposed to pathogens during processing kept separate from unused items to prevent cross-contamination?				

3.0 C: SOPs and Records

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there written procedures (SOPs) for cleaning and maintenance of equipment and utensils and are they followed?				
2	**Do these SOPs include:**				
a	Assignment of responsibility for cleaning?				
b	Defined schedules for cleaning and materials used?				
c	Descriptions of methods, equipment and materials used?				

3.0 C: SOPs and Records, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
d	Instruction for protection of clean equipment from contamination?				
e	Inspection of equipment for cleanliness immediately before use?				
f	Assignment of identification number?				
g	Documentation in record books?				
3	Are cleaning and sanitizing agents validated and approved for use by QC?				
4	Is clean equipment identified as such?				
5	Are calibrations and qualifications properly recorded?				
6	Are all certifications within date?				
7	Are there preventive maintenance programs and consistent records of work performed?				

4.0 A: Adequacy of starting materials

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there approved specifications for all starting material or raw material used in the manufacturing process and				

	are they released by Quality Control?				
2	**To ensure the quality of raw materials:**				
a	Is there a quarantine and release system?				
b	Are the conditions of storage evaluated?				
c	Do the contracts with vendors ensure quality and stability, including reporting of changes in manufacture?				
3	**For raw material of animal origin:**				
a	Are the details of source, origin, and method of manufacture documented?				
b	Are they stored in controlled environments?				
c	Are expiry dates given and is there a retest policy?				
d	Are rejected materials properly segregated form acceptable material?				
e	Have viral removal and inactivation procedures been validated?				
4	Are biological materials that may contain infectious organisms screened or tested prior to entry into laboratories or manufacturing sites?				

4.0 A: Adequacy of starting materials, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
5	**Do Master/Working Cell Banks and Seed Stocks have detailed records of:**				
a	History of cells including the number of generation doublings or passages of virus? Is there a maximum limit?				
b	Characterization according to the WHO TRS relevant to the product?				
c	Demonstration of purity?				
d	Manufacturing procedures?				
e	Appropriate storage and security with continuous monitoring of temperature, alarms and backup power supply?				
f	Inventory log?				
g	Adequately segregated storage to avoid mix-up or cross-contamination with other material?				
h	Storage split into 2 separate locations?				
i	Routine monitoring of stability (viability/purity)?				
j	Demonstration of identity?				

4.0 B: Processes

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**Master Formula (MF):**				
a	Does the MF adequately describe the complete production process?				
b	Is the MF up-to-date and approved by QC/QA?				
c	Is the Batch Production Record form and adequate representation of the MF?				
2	**Process validation:**				
a	Has each phase of the production process been validation protocol?				
b	Is re-validation done when required, and performed appropriately?				
3	**Aseptic fill:**				
a	Are suitable precautions taken to maintain aseptic conditions during the filling process?				
b	Is each filling process validated by a simulated media fill?				
c	Does the simulation use suitable medium, fill sufficient numbers of vials, and cover the full complexity of operations?				
4	Are time and temperature limits established for the completion of production phases?				

5	Are viral removal and inactivation processes validated, if applicable?				

4.0 B: Processes, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
6	Are in-process intermediate materials tested for identity, quality, strength and purity? Alternatively, are there valid certificates of quality issued from the suppliers?				
7	Is there bio-burden monitoring of starting, raw, and in-process materials before sterilization?				
8	Are alert and action limits established for environmental monitoring, and are effective measures taken when limits are exceeded?				
9	Are criteria for microbial limits, physico-chemical characteristics and endotoxins established for water systems and are effective measures taken when limits are exceeded?				

4.0 C: Sterilization/Depyrogenation

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are all sterilization/depyrogenation processes and				

	cycles validated and current?				
2	Is there a sufficient supply of pure steam to assure the simultaneous and proper operation of the validated number of autoclaves?				
3	Are systems for filter sterilization validated and are conditions still the same as when validation was performed?				
4	Is an expiry date given to sterilized items and is there a maximum time period established between washing and sterilization? Are storage conditions for sterilized items specified and appropriate?				

4.0 C: Sterilization/Depyrogenation, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
5	Are the filters tested immediately before and after use for integrity by an appropriate method such as the bubble point test?				
6	Are in-line sterilizing filters used for routine addition of gases, media, solutions, etc. to fermenters?				

4.0 D: Identification

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**If a component/material is transferred to a new container, is the new container identified with:**				
a	Component/material name or item come?				
b	Receiving or control number?				
c	Amount in container?				
2	**Are dispensing/addition operations adequately supervised in that each component/material dispensed is examined by a second person to ensure:**				
a	The component/material was released by QC?				
b	The amount agrees with the batch record?				
c	The container is properly identified?				
d	The components/material are added in the batch by one person and verified by a second person?				
3	Are actual yield and percentages of theoretical yield determined at the conclusion of each phase of operation with documentation of any losses?				
4	Are the yield calculations verified by a second person?				

4.0 D: Identification, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
5	Are all containers, lines and major equipment identified at all times during production for content and phase of operations/				
6	Is major equipment identified with an identification number which is recorded in the batch processing records (BPR0 during production?				
7	Are all deviations from SOPs documented and subject to review by QA/QC for approval or corrective action?				
8	Are there written procedures established to specify action taken with regard to the identification and disposition of material in the environmentally controlled room and in the autoclave if the automatic system fails or malfunctions?				
9	Are records made of the mode, date, duration, temperature and other conditions relating to each sterilization cycle of equipment ad supplies used in production. Are they maintained in a manner that permits identification of the product with the				

	particular manufacturing and sterilization process?				
10	Are sterilized items identified by a sterilization reference number?				
11	Are inspections of areas undertaken immediately prior to use to ensure that all materials from previous operation have been removed and are these procedures adequate?				
12	Are all autoclave and dry heat sterilized items marked with heat sensitive indicators/				

5.0 A: Adequacy

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are specifications, standards, sampling plans, test procedures or other laboratory control mechanisms including any revision, reviewed and approved by Quality Assurance?				
2	Are any deviations from these specs, standards, etc. recorded and justified?				
3	Do laboratory controls include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, test procedures				

	and reference substances, designed to assure that tested materials conform to appropriate standards of identity, strength, quality and purity?				
4	**Do these laboratory controls include:**				
a	Determination of compliance with written specifications for acceptance of each lot within each shipment of materials of holding of products?				
b	Description of sampling and testing procedure for in-process materials?				
c	Retest policy, identifying the rationale and criteria for retests, number of samples, and the documentation required?				
d	A comprehensive calibration/certification intervals, acceptance criteria and provisions for remedial action?				
5	Are reagents, culture media, etc. properly labeled, preparation recorded in lab books and expiry dates given?				
6	Is appropriate testing done on each batch of product required to be free of objectionable microorganisms?				

5.0 A: Adequacy, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
7	Are there written sampling and testing plans for raw materials, intermediates, and final product that include method of sampling and the number of units per batch to be testes and are they followed?				

5.0 B: Reference Reagents

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are all reference reagents kept secure, properly stored, identified and their integrity maintained?				
2	Are the tests results of all references and standards analyzed at appropriate intervals for statistical variation from the expected value?				

5.0 C: Validation, Calibration and Stability Programme

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are the accuracy, sensitivity, specificity and reproducibility of test methods established, documented, validated and subject to regular review and updating?				
2	Is there a written				

	testing programme designed to assess the stability characteristics of each product to determine the appropriate storage conditions and expiration dates?				
3	Is there a retention sampling system?				
4	Does the retention sample quantity consist of at least twice the quantity needed to perform all required tests (except for sterility and pyrogens)?				
5	Are retention samples of each lot of final product stored under conditions consistent with product labeling?				
6	Are these samples at least visually examined annually for evidence of deterioration? Is this recorded?				

6.0 A: General

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**Are there records for :**				
a	All materials used?				
b	All standard operating procedures?				
c	Each lot and/or batch processing and distribution?				
d	All complaints and their investigation?				
e	All equipment, including cleaning, maintenance and validation?				

f	Cleaning, maintenance and environmental control of the premises?				
2	**Are all records"**				
a	Dated?				
b	Signed by the person performing the task (and, for all critical steps, by the person checking it)?				
c	Kept at the work station during the entire operation?				
d	Retained and available for inspection at least 2 years after the expiry date of the lot/batch?				

6.0 B: Lot/Batch Processing Records (BPR)

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**Does the BPR indicate:**				
a	The name, strength and dosage of the product?				
b	The date of manufacture?				
c	The lot and batch identification no.?				
d	Assurance that the copy of the master processing record is accurate?				
e	Changes in the master processing record approved by QA prior to starting the operation?				

6.0 B: Lot/Batch Processing Records (BPR), continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
f	The complete formulation of the lot/batch?				
g	The batch number of each component or other in-process material and, when applicable, the sterilization number				
h	The SOPs used?				
i	The yield obtained at different stages of manufacture, both actual measured values and as a percentage of the expectation?				
j	A record of each step followed?				
k	A record of all major equipment used?				
1	**A record of all in-process control samples taken and of the results obtained?**				
m	A sample of the label on the final container?				
n	Identification of packaging materials, containers, closures used?				
o	Inspection of the processing area before and after use?				
p	Precautions taken and special or unusual observations made throughout the manufacture of the lot?				

q	Investigation of all unusual observations for the batch and, where relevant, from samples of other batches of the product?				
r	For rejected lots/batches, a record of disposal or reprocessing?				
2	**Are all batch processing records reviewed and signed appropriately as indicated by:**				
a	A BPR review document or checklist describing the review process?				
b	A dated signature of the person responsible for approving the manufacturing operations?				

6.0 B: Lot/Batch Processing Records (BPR), continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
c	An analytical report, dated and singed by the responsible person, showing whether the lot/batch complies with the specifications?				
d	Decision on release or rejection of the lot/batch by the quality control department?				
3	Are the BPRs maintained on file for 2 years past the expiry date?				

6.0 C: Documentation of Equipment Used

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are records on the use, cleaning, sterilization and maintenance of equipment kept in individual logs for each piece of equipment?				
2	Are these records dated and signed in chronological order?				
3	Do the records include information of lot/batch including identification numbers and dates?				

7.0 A: Procurement

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there SOPs for animal procurement?				
2	Is a specific individual in department, authorized to order animals?				
3	Do contracts with suppliers assure the quality and consistency of the animals provided?				
4	If the animals come from the manufacturer's own breeding colony, are there SOPs for the maintenance and testing of the colony?				

7.0 B: Receipt and Evaluation

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there SOPs covering the receipt of animals, including identification of the responsible person and required documentation?				
2	Are the newly received animals placed in quarantine?				
3	Are there SOPs for evaluating the health status of animals prior to use?				

7.0 C: Care

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there SOPs covering housing, feeding, handling and care of the animals?				
2	Are there SOPs for identification and isolation of any sick animal?				
3	Are any sicknesses of animals, treatment and preventive measures recorded?				

7.0 D: Allocation of Animals to Use

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are the specifications for animals used in production or quality control tests written in the respective SOPs?				
2	Is there a clear system of identification of animals allocated for each test or use?				

7.0 E: Facilities

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**Are there enough animal rooms of appropriate design to allow separate housing of:**				
a	The breeding colony?				
b	Different animal species?				
c	Animals in quarantine?				
d	Sick animals?				
e	Animals on-test including tests with hazardous infectious and non-infectious materials?				
2	Are there facilities and SOPs for collection and disposal of animal waste and of dead animals, to minimize disease hazards and environmental contamination?				
3	Are there facilities and SOPs for cleaning, sanitizing, sterilizing and maintaining supplies and equipment including animal cages and racks?				
4	Are there specially designated areas for animal inoculation and sample taking, aseptic surgery, autopsy, radiography, histology and other laboratory tests?				
5	Are there separate storage areas for equipment, animal feed and bedding which are protected from infection/contamination, and with refrigeration where needed?				

7.0 E: Facilities, continued

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
6	Is equipment suitably located for operation, inspection, cleaning and maintenance?				
7	Is there separate space for locker, shower, toilet and washing facilities for staff working in the animal facilities?				
8	Is there an appropriate functioning environmental control system?				
9	Is there an implemented pest control system that is documented, validated and approved by QA showing absence of interference with the tests and maintaining animal welfare?				
10	Is the HVAC system appropriate with temperature and humidity control, and adequate air changes/hour?				
11	Is there a time-controlled lighting system?				
12	Is there an appropriate noise control system?				
13	Is emergency power available in the event of power failure?				

8.0 A: General

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there records on suppliers, contractors and consultants?				
2	Are there records of their qualification?				
3	Are there records on up-dating documents?				

8.0 B: SOPs

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there SOPs written and approved for all manufacturing and testing activities?				
2	Are the SOPs reviewed on a regular and defined schedule? At least annually?				
3	Are revisions of SOPs approved by an authorized person?				
4	Is there a system for distribution of SOPs and for revocation of outdates SOPs?				
5	Is it clear that SOPs are used and followed in both production and QC?				

8.0 C: Equipment

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is there a system for validation and regular re-validation of all equipment, including revalidation after repairs?				

2	Is there a system for calibration of all instruments?				
3	Is there a system to report, investigate and record all deviations from specifications or malfunctioning of equipment?				

8.0 D: Environmental Monitoring

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is there monitoring of air for microbes?				
2	Is there monitoring of air for particulates?				
3	Is there monitoring of surfaces for microbes?				
4	Is there monitoring of compressed gas for microbes?				
5	Is there monitoring of compressed gas for particulates?				
6	Is there monitoring of water for microbes and endotoxins?				
7	Is there a defined schedule for environmental monitoring? Is it appropriate to each stage of the production process? Do the records indicate the schedule is followed?				

8.0 E: Intermediates and Final Products

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the stability of the final products and, if applicable, of the intermediates monitored?				
2	Is there a quarantine and release system for intermediates and final products, including clear identification of the status (quarantine, released, rejected, etc.)?				
3	Is there a system for reprocessing of unsatisfactory and returned products, subject to prior approval by quality control?				
4	Is there a system for rapid evaluation and investigation of complaints received from the field?				
5	Is there a system for rapid and effective recall of products? Is there provision for the notification of the national control authority (NDCA)?				

8.0 F: Quality Control

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the QC department independent from production?				
2	Are all QC tests validated?				
3	Does the QC Laboratory have SOPs describing sampling, testing, documentation and precise criteria for release?				

4	Is the QC monitoring consistency of production using trend analysis?				
5	Is the QC Laboratory involved in all decisions that may concern the quality of the product?				

8.0 G: Inspections

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is there a system for regular self-inspection of each manufacturing and test area?				
2	Are the inspections followed up to ensure that appropriate action was taken to correct deficiencies?				
3	Following the national control authority's (NCA) inspection of the manufacturer, is there a system to follow up any recommendations received from NCA?				
4	Is there a system for inspection of contractors in respect of any manufacturing or testing activities contracted out?				

9.0 A: Packaging Materials

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Do primary and printed packaging materials have specification describing qualitative and quantitative requirements?				
2	Are standard operating procedures for the receipt, sampling and testing of packaging materials available?				

3	Are incoming materials stored in controlled areas until released from quarantine?				
4	Are released material secured in controlled areas and is inventory maintained?				
5	Are control or reference numbers assigned to each lot for traceability and control purposes?				
6	Are all label texts approved by the national control authority prior to use and is there a master file of approved labeling held by the responsible person?				

9.0 B: Labelling and Packaging Operations

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are SOPs available for the labeling and packaging operations for equipment and material delivery to the floor and are these easily accessible to the operators?				
2	Are labeling and packaging operations properly physically segregated to prevent mix-up of product or packaging materials?				
3	Is reconciliation performed to ascertain the number of labels issued, used and, if applicable, returned to stock? Is the data recorded on the packaging batch records?				
4	Is there a specification for permissible reconciliation limits and action to be taken in the event of exceeding these?				
5	Is all labeled product accounted for including those destroyed during and at the completion of the operation?				
6	Is there an inspection of the line made before and				

	after each labeling and packaging operation? Is it documented and signed by the responsible person?				
7	Is the name, strength and batch number prominently displayed at each operation?				
8	Is there adequate on-line control of the labeled or packaged product including the quality of printed text?				
9	Are the pieces of equipment used during labeling operations calibrated and certified as operating correctly before and during labeling operations?				
10	Are there documented time and temperature limitations for the labeling and packaging operations?				
11	Are incidents and deviations recorded and appropriate QA actions taken?				
12	Is there a quality control mechanism for assigning lot numbers and expiry dating prior to labeling operations?				
13	Are samples of printed labels and packaging material used for the batch kept with the records				
14	Is there a segregated and secure quarantine storage area for finished goods awaiting QC release?				

9.0 C: Storage and Distribution

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Do records allow rapid identification of all customers who have received any amount of an identified lot/batch?				
2	Are records kept on the time, temperature and other conditions of storage before distribution?				
3	Do records show the date, quantity, mode of package and dispatch of each lot/batch to the customer?				
4	Are there standard operating procedures for the storage of released finished product to the dispatch area?				
5	Are standard procedures available for warehousing?				
6	Are standard procedures available that describe the shipping, final transit conditions and instruction for storage through the distribution chain, especially the cold chain?				
7	Are the shipping methods, especially the cold chain, validated and routinely monitored?				

8	Are records detailed and retrievable so that a rapid recall of any particular lot is achievable? Is the recall process delegated to the responsible person?				
9	Are records maintained for 2 years after the expiry date?				

10.0 A: Facility Design

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the air handling system capable of maintaining the designed containment level (e.g. are supply and exhaust systems adequate for the level of containment required)?				
2	Where applicable, are HEPA filters installed in the exhaust system?				
3	Can the HEPA filters be tested in situ?				
4	Is the air pressure in the manufacturing area appropriate to the surrounding areas?				
5	Are the rooms designed to permit satisfactory cleaning and decontamination?				
6	If the procedure requires the availability of a wash sink, is it close to the exit of room?				
7	Are all conduits, piping and duct work properly				

	sealed in the area to maintain containment?				
8	Are all liquid and gas services protected by backflow prevention devices to prevent contamination?				
9	Are all traps protecting drains maintained properly?				

10.0 B Equipment

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Is the primary containment equipment designed to limit or prevent contact between operators and microorganisms?				
2	Is the equipment designed, constructed and installed to permit ease of decontamination and cleaning?				
3	Are the appropriate classes of Biosafety Cabinets used for the relevant microorganisms, and are they certified annually?				
4	Is the process equipment designed to minimize aerosol generation (including sampling devices)?				
5	Is the process equipment designed to contain organisms within a closed system (e.g. fermenters or other culture vessels)?				

	Are seals and mechanical devices associated with the equipment designed to prevent leakage and do exhaust gases pass through HEPA filtration and/o incineration?				
6	Is the process equipment capable of being decontaminated using a validated inactivation procedure?				

10.0 C Operational Practices and Procedures

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	Are there standard operating procedures for decontamination of process equipment and facilities? Have these procedures been validate and is the performance monitored?				
2	Is the equipment tested regularly for integrity of containment capability?				
3	Are standard operating procedures available and displayed outlining emergency procedures in the event of a spill or accidental release of contaminant?				
4	Is there a list displayed of responsible individuals to be contacted in the event of an emergency?				
5	Do personnel have specific training in the				

	procedures for handling the pathogenic agents used and the method of using containment equipment?				
6	Are there SOPs for dress codes specified for containment levels applicable and is access controlled and secured? Is there a health and medical surveillance program?				
7	Are showers available where applicable?				
8	Is there a health and medical surveillance program?				
9	Are biohazard signs used and posted where applicable?				
10	Are SOPs available for the transport of microorganisms in closed systems or container to and from the area?				

11.0 A: General

#	Audit Item	Yes	No	NA	Observations (Indicate N.O. if not observed)
1	**Pest control programme :**				
a	Is there a pest control programme? Is it in writing and is it followed?				
b	Are pesticides used?				
c	Is their use controlled so as to avoid product contamination?				
d	Are there records of pesticide usage?				
e	Is pesticide storage controlled/				

f	Has QA approved the pesticides and the programme?				
2	Are sewage, refuse, trash controlled and/or disposed of in a safe, timely and sanitary manner?				
3	Are adequately constructed waste containers located in appropriate areas?				
4	Are bagged/boxed items stored off the floor and spaced to allow for cleaning and proper identification?				
5	**Do written procedures for cleaning and sanitation include :**				
a	Assignment of responsibility for sanitation?				
b	Details of cleaning schedules, methods equipment and material?				
c	Routine evaluation of the effectiveness of disinfectants and cleaning agents, and chronological record of the agents used?				
d	Information to be recorded?				
e	Validation for effectiveness of cleaning/sanitation, and validation of removal of residual cleaning/sanitizing agents?				
f	Are the procedures followed and are records maintained?				
6	Are equipment and chemicals used in cleaning appropriately maintained and stored?				

12.0 A: Inspection Team

Sl. No.	**Name of the person**	Designation	Signature	*Date*

Annexure: T

Checklist for inspection of Medical Devices Manufacturing Unit

(Based on Schedule M III & for sterile product Schedule M Part IA)

1.	***Location and surroundings:***	Observations to be noted by the inspecting team at the time of inspection	Remark
1.1	How factory building is located whether sanitary place and hygienic conditions are maintained in the premises. Whether the Premises used for residence or inter-connected with residence. Specify the Level of Cleanliness and ventilation.		
1.2	**Building and premises: -**		
1.2.1	How the building has been designed constructed and maintained to suit the manufacturing operations so as to produce devices under hygienic conditions. What are the measures employed to prevent the entry of insects, rodents, flies, *etc.* Specify the nature of construction used in the facility in respect of its maintenance and hygienic conditions. What measures have been taken to make Interior surface of (walls, floors, and ceilings) be smooth, even and washable, water-proof and capable of being kept clean and shall be such as not to permit retention or accumulation of dust. Specify material of construction and finish for walls, ceiling, floor, coving etc. i.e. whether Epoxy or PU coated, kota / granite stone with epoxy sealed joints, solid / GI / gypsum / cal. Silicate board ceiling with epoxy, PU or any other pre-fabricated panel (GRP, powder coated SS or Aluminum etc.) paint.		

1.2.2	**Whether the firm is registered under the Factories Act, 1948 if yes,** ***Pls. attach valid factory certificate/ license issued by the competent authority.***		
1.2.3	**Specify how the premises used for manufacturing operations and testing purpose to facilitate the unidirectional flow of man and material** **Pls. specify any special criteria for the product manufacture required. e.g. temperature, humidity, air class requirements maintained for assembly and packing of the Medical Devices.**		
1.2.4	**b) Whether adequate working space is provided to allow orderly and logical placement of equipment, materials and movement of personnel so as to avoid risk of mix-up between different categories of medical devices, specify the mechanism used to prevent the mix up.** **Pls specify space left around the machines. Pls attach equipment lay out, men and material movement, waste movement if applicable.**		
1.2.5	**c) Describe the pest, insects, birds and rodents control system followed in the premises.** **Attach copy of pest / rodent control schedule along with contract agreement if any.**		
1.2.6	**e) What measures have been taken so that the processing areas are well lighted and effectively ventilated, with air control facilities?** **Pls specify the lux level maintained in various parts of the premise.**		
1.2.7	**Pls specify the air handling system used in various areas like stores, production, packing, QC areas etc.**		

1.2.8	**Specify drainage system which prevents back flow and entry of insects and rodents into the premises.**		
2.	**Water system: -**		
2.1	**Whether the unit has specified system for treatment of water drawn from own or any other source to render it potable in accordance with standards specified by BIS or local municipal norms.** **Pls specify source of raw water and give details of treatment processes, sampling points, distribution and storage system for raw and purified water.**		
2.2	**How bio burden in purified water controlled / reduced.**		
2.3	**How water tank are cleaned periodically and records maintained thereof. How water distribution system is sanitized to control microbial contaminations.**		
3.	**Disposal of waste: -**		
3.1	**Specify the system of disposal of sewage, and effluents (solid, liquid, and gas) from the manufacturing site.** **(Enclosed the copy of NOC obtained from State Pollution Control Board in this regard).**		
3.2	**Whether provision for disposal of bio-medical waste made as per the provisions of the Bio Medical Waste (Management and Handling) Rules 1996**		
4.	***Health, clothing and sanitation of workers: -***		
4.1	**Whether all personnel prior to employment have undergone medical examination including eye examination and all free from**		

	Tuberculosis, skin and other communicable or contagious diseases		
4.2	**Whether there is a SOP for medical examination.**		
4.3	**Pls. give name and qualification of contracted medical officer for medical examination.**		
4.4	**Whether investigational reports, films of X rays etc. preserved.** **Whether records of such medical examination are maintained thereof**		
4.5	**Whether** clean uniforms, masks, headgears and gloves wherever required **and adequate facilities for personal cleanliness are provided.** **Pls specify nature and type of dress used by the personnel in various areas of operation.** **How many dress/footwear have been provided to each personnel.**		
4.6	**Whether adequate** Medical facilities for first-aid are provided.		
4.7	**Please specify whether cross over bench is in place in the change room and if so whether it rule out the possibility of entering dust particle to the clean side.** **Whether arrangements provided for cleaning of outside dust and dirt from foot** **Please specify whether hands are disinfected before entering the production area** **Whether for sterile garments in house clean laundry has been provided.**		
5	**Warehouse**		
5.1	**Whether adequate areas have been allocated for warehousing of Raw Material, Packaging Material, products in quarantine (for sterilization), finished product rejected or returned products.** **How these areas marked or**		

	segregated. **Please specify the total area provided for warehousing and quarantine storage.**		
5.2	**How the warehousing areas being maintained to have good storage conditions. Are they clean and dry and maintained within acceptable temperature limits where ever required.**		
5.3	**Specify the storage arrangement provided for materials which requires temperature and humidity control.**		
5.4	**Whether proper racks, pallets, bins and platforms have been provided for the storage.**		
5.5	**Whether receiving and dispatch bays are maintained to protect incoming and outgoing materials.**		
5.6	**How quarantined materials are segregated from other materials.** **How access to quarantined area is restricted.**		
5.7	**Whether separate sampling area for Raw Materials is provided and maintained.** **For sampling. Whether log book for sampling booth maintained.** **If not what provision has been made for sampling so as to prevent mix-ups at a time of sampling.**		
5.8	**Specify the arrangements provided to sample the primary packaging materials foils, packaging papers, etc which are used as such.**		
5.9	**Pls. specify sampling plan used Any SOP followed for the sampling.** **Which type of sampling tools are used and how they are maintained.**		
6.	**Raw Materials*: -***		

6.1	Whether an inventory of all raw materials to be used at any stage of manufacture of devices and records are maintain as per Schedule U. Whether All such raw materials shall be identified and assigned control reference number.		
6.2	**Please specify the procedures followed for receiving and processing of in-coming materials (Starting materials and packing material). Pls. Specify SOP No.**		
6.3	**Whether first in / first out or first expiry principal has been adopted.**		
6.4	**Whether incoming materials are purchased from approved sources.**		
6.5	**What is the procedure for approving the source for incoming materials?**		
6.6	**Whether the raw materials are directly purchased from the manufacturers.**		
6.7	**Whether list of approved vendors is available to the user.**		
6.8	**Whether each batch of a consignment is considered for sampling, testing and release.**		
6.9	**Whether labels of raw material in the storage area have information like** (a) designated name of the product and the internal code reference, where applicable, and analytical reference number; (b) manufacturer's name, address and batch number; (c)The status of the contents (e.g. quarantine, under test, released, approved, rejected); and (d) The manufacturing date, expiry date and re-test date.		
6.10	**Please specify the procedures by which it is ensured that the raw materials which has been released by the Quality Control Department and which are within their shelf life are going to be used in the product.**		

6.11	**What provisions have been made for storage of rejected, recalled or returned materials or products.** **How is the access to these areas restricted?**		
6.12	**How highly hazardous, poisonous and explosive materials, are handled and stored if applicable.**		
6.13	**How printed secondary packaging materials are stored in safe, separate and secure manner.**		
6.14	**Specify the arrangement provided for transferring of starting materials to processing area.**		
7.	***Production Area: -***		
7.1	**Moulding Area /Device fabrication**		
7.1.1	(a) Please specify the design of the moulding/fabrication area in case of the manufacture of medical devices is to start from granules/metals which allow uni-flow and logical placement of machines & sequence of operations so as to prevent product mix ups. (b) Is there any criss cross of flow of materials and men? (c) Specify the air classification and exhaust system provided. (d) Specify the cleanliness of area and schedule for cleaning. (e) Specify the position of IPQC lab in the manufacturing area. (f) Please specify the Area allotted for moulding/fabrication operation & different process to be followed in the moulding/fabrication area.		
7.1.2	Please specify the provisions of storage of equipment parts, tool room, in process areas etc. Which provide sequential / logical manner for easy identification?		

7.1.3	Specify the arrangements for storage and accountability of semi finished devices.		
7.2	**Assembly Area**		
7.2.1	Specify the different process to be carried out in the Assembly area. How many Change rooms/Air Locks found provided to enter into the assembly area. What are the air classifications of the change rooms? Whether separate gowning provision is follows before entering into the procedure. What Measures employed to achive the required environmental conditions. What is the air class of this areas and whether pressure difference is maintained in these areas? Whether AHU is fitted with terminally fitted with 0.3 µHEPA. Specify the nature of floor, ceiling, fixtures and service lines to meet the clean room requirements as per design qualification. Specify the nature of work benches whether the top of which are smooth impervious & capable of being washed. Specify the total area provided for these operations. Specify the arrangement for in and out of materials including device parts, primary packaging materials and primary packed device from this area, any material transfer pass box provided?		
8.	**Ancillary Area**		
8.1	**Please specify the position of rest and refreshment rooms and mention whether they are separate and not leading directly to the manufacturing and warehouse areas.**		

8.2	**Are there general change rooms in plant?** **Are toilets, change room separate from mfg. Area? Pls specify number of washing station & toilets provided for number of users.** **Whether change facilities separated for both sexes.**		
8.3	**Whether maintenance workshop is separate and away from production.**		
8.4	**Whether animals for testing are housed in the facility if so whether areas housing animals are isolated from other areas.** **Please specify the provision of air conditioned and ventilation system for the animal house.** **How quarantined, under test and tested animals housed and controlled.** **How animal carcass are disposed of.** **Pls attach copy of CPCSEA.**		
9.	**Sterilization Procedure for Medical devices**		
9.1	What method of sterilization followed by the firm for the manufactured medical devices Whether requisite equipments with required controls and recording device for sterilization of medical devices by Ethylene Oxide Gas in his own premises. If the firm do not have in-house facility for sterilization then- Specify the details of the arrangements with some Institution approved by the Licensing Authority for sterilization either ETO or ionizing radiation sterilization. Whether the products sterilized in this manner shall be monitored to assure acceptable levels of residual		

	gas and its degradation products. Specify the total area provided for basic installation of such facility:- Whether adequate space provided for quarantine & sterilized items. Whether the Space for storage of ETO cylinders provided if yes specify the location. What safety measures employed to encounter against any leakages of ETO gas. Whether the Sterilization cycle validated with the use of physic-chemical parameters and biological indicators. Specify the details of sterilization validation and mention the protocol No.		
10.	**Testing facilities: -**		
10.1	**Whether QC area is independent of production area.** **Whether QC carries out its own:** • **physico-chemical testing,** • **biological testing such as toxicity, BET** • **Biocompatibility testing (skin irritation, genotoxicity, systemic toxicity, etc.** • **Microbiological testing & sterility testing.** • **Instrumental testing.** **Plz. Enclosed the list of Instruments in Physicochemical and microbiology laboratory.** **Whether firm is outsourcing testing. If yes names of the testing laboratories contracted or approved. Pls give list of test currently outsourced.** **In case of contractual testing what are the responsibilities of contract giver and contract acceptor. (Copy of the contract should be enclosed)** **Are there safety installations such as, fire extinguisher, first aid box, etc in the laboratory?**		

10.2	**Please specify the arrangement provided for handling and storage of test samples, retained samples,** **Whether separate records room is provided.**		
10.3	**Whether SOPs for sampling, inspecting, testing of Raw Materials, Finish products, Packing Materials and for monitoring environmental conditions are available.**		
10.4	**How hazardous or poisonous materials are stored and handled.**		
10.5	**How environmental conditions are met during the course of storage and testing of samples if required.** **Whether separate washing and drying area provided.**		
10.6	**Whether the instruments used in the physical QC of the medical devices are calibrated against certified reference instruments from appropriate authority such as NPL.**		
10.7	**Whether separate AHU's are provided for biological, microbiological testing areas with** **HEPA filter arrangement.**		
10.8	**Whether separate areas provided for sterility testing within microbiology lab.** **Whether support areas are under AHU.** **Whether autoclave provided for sterilization of materials.**		
10.9	**Whether entry to the sterility area is through three air lock systems of desired air classification. Plz specify.**		
10.10	**Which types of workbenches are provided in these areas for testing?** **Whether LAF/Biosafety cabinets provided for microbiology and sterility testing.** **When was the last filter integrity tests performed on HEPA filters?**		

10.11	**How Biomedical waste (cultures etc) disposed off, any third party contract made, enclose the copy of the same.**		
11.	***Personnel: -***		
11.1	**Whether the manufacturing and testing of devices are conducted under the supervision of approved technical staff** **Names of Technical Staff along with qualification & experience** **<u>For Manufacturing: -</u>** **<u>For Analysis:</u>**		
11.2	**Please specify whether head of Q.C. is independent of manufacturing unit**		
11.3	**Name, qualification and experience of the personnel responsible for Quality Assurance function.**		
11.4	**Whether responsibilities for production and QC was laid down and followed.**		
11.5	**Whether adequate number of personnel employed in direct proportion to the work load.**		
11.6	**What is the firm's policy on training of personnel at various levels?**		
12.	***Manufacturing Operations and Controls: -***		
12.1	**Whether all the critical stages of manufacturing are carried out under active supervision of the competent approved staff following validated master formula.**		
12.2	**Whether equipments use for production is labeled with their current status.**		

12.3	**Whether packaging lines are independent and adequately segregated if more than one for different types of packaging.**		
12.4	**What criteria of pressure differential have been set for production v/s adjoining areas?**		
	Whether various operations are carried out in segregated areas.		
12.5	**What measures has been taken to prevent mix-ups during various stages of production.**		
12.6	**How line clearance is performed. Whether records of line clearance is maintained according to appropriate checklist.**		
12.7	**Whether separate carton coding area has been provided or online carton coding is performed** **How carton coding procedure is controlled.**		
12.8	**How access of authorized persons to manufacturing areas including packaging is controlled.**		
13.	***Sanitation in the Manufacturing areas:-***		
13.1	**Specify the cleaning procedure of the manufacturing areas.**		
13.2	**Whether the manufacturing areas are used as the general thoroughfare and storage of materials not under process.**		
13.3	**Whether a routine sanitation program is in place.** **Please specify detailed account of sanitation program specific to various areas, equipment.**		
13.4	**Dose the location facilitate cleaning of equipment as well as the cleaning of the areas in which they are installed.**		

13.5	**Whether production area is adequately lit. If yes.** **Please give lux levels provided in production, visual inspection and other areas.**		
14	***Equipment: -***		
14.1	**Whether the equipments are designed aiming to minimize risk of error and permit effective cleaning in order to avoid cross contamination, build up of dust.**		
14.2	**Whether DQ, IQ, OQ & PQ are in place for all major equipment and facility.**		
14.3	**Whether all equipment is provided with log book.**		
14.4	**Please specify the procedures to clean the equipment after each batch production.**		
14.5	**Whether separate area is provided for storage of machine parts etc.**		
14.6	**Whether balances and other measuring equipments with appropriate range are available in the Raw Material stores & production areas and they are calibrated in accordance with SOP maintained.**		
14.7	**Specify the procedures to remove defective equipments from production areas.**		
15	***Documentation and Records: -***		
15.1	**How the documents are designed, prepared for different activities,** in-process controls, assembling, packing, batch records for the quantity of devices manufactured **in medical device manufacturing,** **Reviewed and controlled to provide an audit trail.**		

15.2	**Whether the record prepared and maintained for** duration of work, hourly quantum of production in respect of each item as well as record of each sterilizing cycle of the gaseous method employed.		
15.3	**Whether documents are approved signed and dated by appropriate and authorized person.**		
15.4	**Whether documents specify title, nature and purpose.**		
15.5	**Whether documents are regularly reviewed and kept up to date. If yes. Please specify review period.** **Please attach the list of documents maintained by the firm.**		
15.6	**Whether the records are made at the time of each operation in such a way that all significant activities concerning to the production are traceable.**		
15.7	**Whether data is recorded by electronic data processing system or by other means. If by electronic data processing system then how access is controlled to enter, modify etc. the data.**		
15.8	**Whether master formula and detailed operating procedures are maintained as hard copy.**		
15.9	**Who is responsible for maintenance of these records?**		
15.10	**How long the record/documents preserved.**		
16	***Labels and Other Printed Materials:***		
16.1	**Whether the printing is in bright colour and legible on labels and other printed materials.**		
16.2	**How printed labels (art work) are approved. Is there any SOP for this if yes please give current SOP No.**		
16.3	**Which colour coding system is used to indicate the status of a product and equipment?**		

16.4	**How printed packaging materials, product leaflets etc. are stored separately to avoid chances of mix-up.**		
16.5	**How labels cartons boxes circulars inserts and leaflets are controlled.**		
16.6	**Whether the samples are drawn tested, approved and released prior to packaging and labeling.**		
16.7	**How records of receipt of all labeling and packaging materials are maintained.**		
16.8	**Whether re-conciliation of used packaging materials is maintained.** **Whether unused packaging materials return to the store or destroyed.**		
16.9	**Whether package insert prepared for information & guidance for use of the medical device**		
16.10	**Label of the medical device are printed with all the information as per D & C Rule and BIS standards.**		
17	***Quality Assurance: -***		
17.1 **(a)**	**Specify the comprehensive quality assurance system maintained by the firm *Inter-alia* to cover deviation, reporting, investigation and change control.** **How the products are designed and developed in accordance with QMS.**		
(b)	**Please specify the arrangements provided to ensure that correct starting and packaging materials are used for manufacture.**		
(c)	**Please specify the mechanism by which all control like IPQC Calibration, Validation etc. are ensured.**		
(d)	**Please specify the mechanisms to ensure that the finished product has been correctly processed and checked in accordance with the established procedures.**		

17.2	***Self Inspection and Quality Audit: -***		
17.2.1	**Whether the firm has constituted a self inspection team supplemented with a quality audit procedure to evaluate that QMS is being followed. If no. How internal audits are carried out.**		
17.2.2	**What is the system of monitoring, evaluation of self inspection?**		
17.2.3	**How conclusion and recommended correcting actions are followed and adopted.**		
17.2.4	**What is the frequency of self-inspection?**		
17.2.5	**Is there any proforma for carrying out the self-inspection?** **Please indicate the date of last self-inspection.**		
18	**Quality Management System: -**		
18.1	**Please specify the details of quality Management system of the unit.**		
18.2	**Specify the validation policy of the company.** **Whether validation master plan has been prepared.**		
18.3	**How the finished medical Devices evaluated whether the device is manufactured as per pre established specification, specify the standard followed such as ISO 13485 ,etc** **Please provide list of reference product specifications. Any Device Master file or files are prepared.**		
18.4	**Whether test specifications for different raw materials, finished products for conformity of product to determined requirements are available.**		
18.5	**Whether stability study performed in case of critical medical devices such as drug eluting cardiac stents, etc.**		

18.6	**How reference samples from each batch of the products are maintained.**		
18.7	**Who releases batch of the products for sale or supply.**		
18.8	**Whether there is check list for release of a batch. Please specify current SOP No. for batch release.**		
18.9	**Please specify the sampling procedures from various stages of production.**		
18.10	**How it is ensured that the sample collected are representative of the whole batch.**		
18.11	**How complaints are investigated.**		
18.12	**How instruments are calibrated and at which interval.**		
18.13	**How testing procedure validated before they are adopted for routine testing.**		
18.14	**How validation procedures are documented (Please indicate various protocols/ recoding system applied during validation).**		
18.15	**Whether specifications for raw materials intermediates final products and packaging materials are available.**		
18.16	**Whether periodic revision of these specifications are carried out.** **Please specify No. of STPs being maintained by the firm.**		
18.17	**Whether adequate reference literature/Books are available with the firm , plz. Enclosed the list.**		
19.	**Standard Operating Procedure and Records: -**		
19.1	**Whether SOPs and records are being maintained and complied for the following. Is there SOP for writing an SOP.** **SOP for receipt of incoming material** **(aa) SOP for Internal labeling, quarantine, storage, packaging material and other materials.** **(bb) SOP for sampling** **(cc) SOP for batch numbering** **(dd) SOP for testing**		

	(ee) SOP for equipment assembly and validation **(ff) SOP for Analytical apparatus and calibration** **(gg) SOP for maintenance, cleaning and sanitation** **(hh) SOP for training and hygiene for the personal** **(ii) SOP for retaining reference Samples** **(jj) SOP for each instrument and Equipment** **(kk) SOP for distribution of the product** **(ll) SOP for product release.** **Whether applicable SOPs are available in each area where they are required.** **Whether recording formats are referred in SOP.**		
20	**Product Recalls: -**		
20.1	**Specify the product recall system followed by the firm.** **How promptly recall operation at the level of each distribution channel up-to the retail level can be carried out.** **Whether there is a SOP for recall of products clearly defining responsibility, procedure, reporting, re-conciliation etc.**		
21	***Complaints and Adverse Reactions: -***		
28.1	**Specify the review system for complaints concerning the quality of products.**		
	How records of complaint and adverse reactions maintained.		
	Whether reports of serious reaction with comments and documents immediately sent to Licensing Authority		
	Is there any criterion for action to be taken on the basis of nature of complaint / adverse reaction?		
29	**Site Master File:-**		
	Whether all the relevant information has been included in the site master file.		
	Whether quality policy has been included in the site master file. **Please attach the current version.**		

Annexure: U

CHECK LIST FOR INSPECTION OF APPROVED TESTING LABORATORIES

01.	**General**		
1.1	Date of Inspection		
1.2	Name & address of the Laboratory:		
1.3	Telephone Number	**Fax Number**	**E-mail Number**
1.4	Names and designation of the Inspection Team Members		
	Name	**Designation**	
1.5	Constitution of the firm :		
1.6	(i) Approval Number and Date:-		
	(ii) Validity:-		
1.7	Name and designation of the Responsible Persons of Laboratory present during Inspection:		

Name		**Designation**
1.8	Organization Structure of the Laboratory (Please attach annexure, if required)	
1.9	Name of Approved Staff with Qualification, Experience and approval status.	
1.10	List of the provided equipment and Instruments	
1.11	Whether the management of the laboratory has prepared validation Master Plan/ Quality Manual to ensure	

	that the laboratory carry out its testing, calibration, validation, and all other technical activities in such a way as to meet Good Laboratory Practices (GLP) requirements.		
1.12	Whether the laboratory has appointed Technical or Quality Manager if yes specify the responsibilities of the same.		
S. No.	**Categories**	**Compliance Y/N/N.A.**	**Remark/Comments**
2.	Whether approval has been granted for carrying out testing on the following Categories of Drugs Items and Cosmetics		
2.1	Drugs other than those specified in Schedule C & C (1) including/excluding Homeopathic Medicine.		
2.1.1.	Crude, Vegetable Drugs		
2.1.2.	Mechanical contraceptives (Schedule R) Contraceptives (sterility test only)		
2.1.3.	Surgical Dressings (Schedule F-II)		
2.1.4.	Drugs requiring to use U.V./I.R. or Chromatography		
2.1.5.	Disinfectants		
2.1.6.	Other Drugs (Indicate Category)		
(a)	Medicinal Gases		
(b)	Diagnostics		
(c)	Medical Devices		
2.2	Drugs other than those specified in Schedule C & C (1)		

2.2.1.	Sera, Vaccines, Antigens, Toxins, Antitoxins, Toxoids, Bacteriophages & similar Immunological products		
2.2.2.	Antibiotics		
2.2.3.	Vitamins (excluding electrophoresis)		
2.2.4.	Parenteral Preparations		
2.2.5.	Sterilised Surgical Ligature/Suture		
2.2.6.	Drug requiring the use of animals for their test		
2.2.7.	Drugs requiring microbiological tests		
2.2.8.	Drugs requiring to use U.V./I.R. or Chromatography		
2.2.9.	Other Drugs (Indicate Category)		
(a)	Diagnostics		
2.3.	Homeopathic Drugs		
2.4.	Cosmetics		
3.	**PERSONNEL**		
3.1	Name of the Person In-charge(s)		
3.2	Details of the Analysts appointed by the firm (attach List with qualification and experience)		
3.3	Indicate any change in the Person In-charge and Expert Staff		
3.4	Medical examination of Staff		
3.5	Record of Periodicity of Medical		

	examinations available		
3.6	Is education/experience of Personnel adequate		
	Is there any system of imparting training to staff:		
	(a) Internal: (b) External		
4.	**PERSONNEL SAFETY:**		
4.1	Are protective steps against likely damage to health due to occupational hazards being taken as follows:		
4.2	Is there adequate provision for water shower		
4.3	Is there washing shower provision for eye wash		
4.4	Is there an exclusive overhead water tank for shower		
4.5	Are First Aid Medical Facilities made available at appropriate point?		
4.6	Are Safety personal appliance like Safety gloves, glass face shields, gas masks and proactive clothing be made available to persons engaged in handling hazardous items.		
4.7	Are adequate numbers of fire extinguishers of appropriate type with their status labels installed at the required places and people trained in operating the extinguishers?		
4.8	Whether proper safety measures have been taken to protect staff handling		

	hazardous/contaminated articles.		
4.9	Are SOP's provided for safety of personal and for waste disposal.		
5.	**PREMISES:**		
5.1	Are there any sources of pollution in the neighbourhood of the building?		
5.2	Is there any open drain, blocked sewer or public lavatory nearby		
5.3	Site plan showing area allotted for each section		
5.4	Is plan lay out already approved by the Licensing Authority? Indicate any change in the approved premises.		
5.5	Are the premises have adequate space not only for equipment to carry out necessary test but also for samples tested/proposed in the laboratory and utilities like water, power and gas;		
5.6	Is there any evidence of entry of birds, rodents and insects in the Laboratory? Specify the measure employed to prevents it.		
5.7	Is lighting and ventilation adequate for work.		
5.8	Is the Air conditioning facility provided to control the temperature and relative humidity for testing conditions and storage of drug samples if required		
	Whether The drainage system facilitate proper maintenance and prevent water logging in the laboratory.		
	Whether workbenches are constructed with acid, alkali and		

	solvent resistant material and are smooth and free from crevices		
6.	**ANIMAL HOUSE**		
	Animal House have the approval of the Committee for the Purpose of Controland Supervision on Experiments on Animals (CPCSEA)		
6.1	Is the animal house separate from other activities		
6.2	Is the animal house air conditioned		
6.3	Are the animals kept in hygienic surroundings, specify the provision for clean corridor and dirty corridor.		
6.4	Is there proper arrangements for cleaning of animal house		
6.5	Is there suitable arrangements for preparation of animal feed		
6.6	Is there suitable arrangements for quarantining of animals		
6.7	Is there separate arrangement for housing the animals under test ?		
6.8	Are the sick animals isolated?		
6.9	Are the animals being periodically examined for their physical fitness by a veterinary doctor, are the records available?		
	Whether any Standard Operating Procedure are available for breeding and care of animals, maintenance, cleaning or sanitation with suitable		

	schedule for cleaning of animal Cages, racks, floor and other equipments.		
6.10	Is the firm complying with the requirements of the Prevention of Crudely to animal act 1960(59/of 1960) as amended from time to time.		
6.11	Whether proper arrangements for disposal of carcasses of animals in a manner as not to cause hazard to public health being followed.		
7.	**MICROBIOLOGICAL AREA**		
7.1	Is microbiological section separate from other activities (with proper air-lock)		
7.2	Whether Sterile area properly designed to kept it free from outside contaminations		
7.3	Sterile area is provided with proper working table with absolute Aseptic conditions		
7.4	Are LAF tables properly validated to class 100 requirements		
7.5	Are proper SOP's provided for maintenance of sterile area		

7.6	Whether Standard Operating Procedure for maintenance of microbial culture and sub-culture are available with the laboratory.		
7.8	In case when cultures have become non-viable or mutant, proper procedure are followed to destroy these cultures by autoclaving under an authorised personnel for biological testing. Preferably not more than five passages are prepared. Specify the SOP No.		
8	Instruments required for testing of Drugs other than those specified in Schedule C & C1		
8.1	Crude Vegetable Drugs		
	i) General glassware ii) Balance (Analytical) iii) Microscope iv) Soxhlet Extractor v) Water Bath vi) Refractometer vii) Oven viii) Hot Plate ix) TLC Kit x) U.V. Chamber xi) Any Other Specialized equipment		
8.2	Mechanical Contraceptives (Schedule R)		
	i) Leakage tester ii) Bursting col., Pressure tester iii) Vernier Caliper iv) Micrometer v) Balance (Analytical) vi) Aging Oven vii) Equipment's for Package integrity test.		
8.3	Surgical Dressing (Schedule F11)		
	i) U.V. Cabinet ii) Soxhlet extractor		

	iii) Oven iv) Scale v) Absorbency Tester vi) Balance (Analytical) vii) All equipment required for Sterility testing		
8.4	Drug requiring Instrumental Analysis		
	i) UV/VIS Spectrophotometer ii) I.R. Spectrophotometer a) Pallet maker and holder b) Liquid Cell Holder iii) HPLC (**Gradient**) Type of detector Required Columns		
	a) Required columns b) Type of detector iv) AAS v) HPTLC vi) Fluorometer vii) Poteniometric Titrator viii) Flame Photometer ix) Balance (Analytical) x) Microscope xi) KF Titrator xii) Oven xiii) Furnace xiv) Water Bath xv) Fridge xvi) Dissolution Test Apparatus a) Basket Type b) Paddle Type xvii) Disintegration Test Apparatus xviii) Melting Point Apparatus xix) Refractometer xx) Polarimeter xxi) General Glassware xxii) Chemicals xxiii) Stop watch xxiv) Water Distillation Plant xxv) Particle Counter (Specially for LVP's) xxvi) Any other instrument required for Specialized testing		
9.	Drugs requiring use of Microbiological Testing		

9.1	General		
	i) Clean room. ii) Laminar Flow iii) Autoclave iv) PH Meter v) Gas Burner vi) Water Bath vii) Incubator viii) Filtration unit ix) Vacuum Pump x) BOD Incubator xi) Refrigerator xii) Balance (Analytical) xiii) Glass wares xiv) Centrifuge xv) Microscope xvi) Other general equipment required for general day to day activity xvii) Cultures		
9.2	Special requirements other than General for:		
(a)	Disinfectants		
	i) Platinum loop ii) Proper Culture iii) Stop Watch iv) Oven up to $35^{o}C$		
(b)	Antibiotics		
	i) Spectrophotometer ii) Vernier Caliper/Zone Reader iii) Proper Culture iv) Borer v) Media		
(c)	Vitamins (excluding electrophoresis) i) Spectrophotometer ii) Vernier Caliper/Zone Reader iii) Vortex Mixer iv) Culture v) Media vi) Borer		

(d)	Sterility		
	i) Filtration Unit ii) Vacuum Pump iii) Media iv) 0.45m Pore Filter Paper Sterile v) Sterile forceps, Scissors & Bone cutter, Surgical blade, Ampoule Cutter vi) Sterile Gloves vii) Face Masks viii) Caps ix) Sterile garments		
(e)	Endotoxins		
	i) LAL Reagents ii) Heating block iii) Sterile test tubes iv) Vortex mixer v) Sterile tips vi) Pipettes (Pyrogen free) vii) Stop watch viii) LAL Water/Pyrogen free Sterile distilled water		
(f)	Pyrogen		
	i) Animal House ii) Pyrothermometer/Rectal thermometer iii) Sterile syringes, needles iv) Pyrogen free glassware v) Pyrogen free Sodium Chloride Solution/Water vi) Animal Holding Stands		
(g)	Sterilized surgical Sutures and Ligatures		
	i) Sterility testing facilities ii) Tensile Strength Tester		
(h)	Sera Vaccines		
	i) Sterility testing facilities and Other specialized testing facilities required for Testing Sera vaccines		

(i)	Pharmacological Testing:		
	i) Operation Table ii) Kymograph iii) Water Bath iv) Manometer v) Cannula vi) Oxygen Cylinder vii) Other equipments required for Pharmacological testing		
10.	**RECORD/DOCUMENTS**		
10.1	Whether the details of sample booking are available		
10.2	Whether the details of Certificate & Reports are maintained		
10.3*	Whether the details of sample distribution are available		
10.4	Whether the documents list with retention period is available		
10.5	Whether the Chemist Raw data records are available		
10.6*	Whether equipments details are recorded		
10.7*	Is G.L.P. manual and SOP's are available and being followed		
11.	**EQUIPMENT**		
11.1*	Whether logbooks of equipment are maintained?		
11.2*	Whether the equipment records are proper such as Name of equipment, Manufacturer's name, Serial No. etc. (attach details)		

11.3*	Whether the condition of equipment is recorded when received (new, used, reconditioned)		
11.4	Whether the instruction manual of all major equipment are available		
11.5	Whether the calibration records are properly maintained		
11.6	Whether the next calibration date is recorded		
11.7	Whether the details of damage malfunction, repair (if any) of major equipment recorded		
11.8	Whether SOP's for equipment use, maintenance, preventive maintenance & Calibration are available		
12.	**CERTIFICATAE & REPORTS**		
12.1	Whether test reports are issued on prescribed Form 39 containing the required information as prescribed (attached photocopy of Form 39)		
12.2	Whether description of sample received for testing are available including receipt identification		
12.3*	Whether statement of method used for each test is maintained and available		

12.4	Whether complete records of all raw data including graphs, charts etc. are available		
12.5	Whether records of all calculations performed are available. Check calculation on random basis.		
12.6	Whether statement of test results and how they compare with specification are available		
12.7	Whether initials or signature along with date of person performing each tests are available in the records.		
12.8	Whether initials or signature along with date of second person showing that the records have been reviewed for accuracy, completeness and compliance with the specifications are available in the records.		
12.9	Whether records of preparation of laboratory reference standards, reagents and standard solution are available.		
12..10	**Standard Operating Procedures** Whether the SOPs are prepared by the laboratory as follows.		

	(i) sample handling and accountability; (ii) receipt identification, storage, mixing and method sampling of the test and control articles; (iii) record keeping, reporting, storage and retrieval of data; (iv) coding of different studies, handling of data including use of computerized data system; (v) operation of technical audit personnel in performing and reporting audits, inspections and final report reviews; (vi) routine inspection of cleaning, maintenance, testing, calibration and standardisation of instruments; (vii) action to be taken in respect of equipment failure; (viii) analytical data methods; (ix) the raw data; (x) data handling and storage retrieval; (xi) health and safety protection; (xii) animal room preparations; (xiii) animal care; (xiv) storage and maintenance of microbial cultures; (xv) maintenance of sterility room (i.e. constant maintenance and monitoring of Aseptic condition of sterility room); (xvi) use and storage of reference standards (xvii) procurement of stores and equipment; (xviii) monitoring of testing of samples; (xix) method of retention of unexpended samples, their location, maintenance and disposal; (xx) document control; 9		

	(xxi) redressal of technical complaints; (xxii) housing-keeping; (xxiii) corrective and preventing action; (xxiv) working procedure (test methods); (xxv) calibration Manual; and (xxvi) Training manual.		
13.	**LABORATORY REAGENTS & SOLUTION**		
13.1	Whether properly labelled along with concentration/titer and expiration date		
13.2	Whether proper storage facilities are available		
13.3	Whether period for reuse and scientific basis for this period is available.		
13.4	Whether calibration certificates of weights from authorised agencies are available		
13.5	Whether the logbooks for standardization are maintained		
13.6	Whether standardization is within permissible limit (10% of stated value)		
14.	**REFERENCE/WORKING STANDARD**		
14.1	Whether list of available reference standards being maintained		
14.2	Whether lab has adequate arrangements for proper storage, security and labelling of reference standard and working standard		
14.3*	Whether the lab maintain the records of procurement/source of reference standard (trace ability)		

14.4*	Whether lab maintains record of preparation of working standard for daily use.		
14.5	Whether the lab has written procedure for handling and storage of reference standards		
14.6	Are SOP's for testing of working standards available if so, records thereof		
15.	**SPECIFICATIONS/METHODS**		
15.1	Whether Analytical Method Validation records are available to cover important parameters like linearity, precision, accuracy etc. For in house methods other than the compendia methods		
15.2	Whether specification/standards are authentic and original		
15.3	Whether details of Drugs/Cosmetics reported not of standard quality forwarded to the respective Drug Controller and the Licensing Authority. Whether records maintained in this regard		
15.4	Whether standard reference books available (attach list)		
15.5	a) For how long the sample declared of standard quality preserved.		

	b) For how long the sample declared not of standard quality preserved.		
15.6	Whether the comparison is available that the in-house method is equivalent or superior, in case in-house method is used instead of compendial method		
15.7	Whether the record of study that non interference of placebo has been confirmed, is available		
16.	**HANDLING & RETENTION**		
16.1	SAMPLE		
(a)	Whether samples are right from receiving till disposal are being handled properly		
(b)	After completion of test samples of standard quality and not of standard quality are being kept up to declared time period in proper condition		
(c)	The retrieval of control sample is effective or not		
(d)	Average work load of testing during the year		
(e)	No. of samples received		
16.2	RECORDS		
(a)	Whether records in case of substance for which an expiry date is assigned are being retained for a period of two		

	years form the expiry of such date. Whether in case of other substances such records are being maintained for six years.		
17	**DISPOSAL**		
17.1	SAMPLE		
(a)	Whether disposal of samples after retention period is proper and documented (Standard Quality and not of Standard Quality)		
(b)	Whether manner of disposal of carcasses of animals is proper and according to regulatory requirements		
c)	Whether adequate arrangements for disposal of sewage and effluent made		
17.2	RECORDS		
(a)	Whether disposal of records is being done in proper manner and with proper authorization		

Summary Report for Joint Inspection Report of M/s. XXXXXXXXXX

On the basis of the application on form 36 submitted by the authorized signatory of

M/s.xxxxxxxxxxx
vide letter no. XXXXXXXXXX dated and the letter Ref. No.XXXXX date XXXX received from the State Drug Controlling cum Licensing Authority, of XXXX and the subsequent instruction received from Dy. Drugs Controller (I), XXXX Zone, the undersigned officers jointly inspected the aforesaid testing facility for grant/renewal of approval for carrying out Analysis of drugs & pharmaceuticals by instrumental, chemical and microbiological tests on Form 37.

Fallowing technical personnel were present throughout the inspection.

Name	Designation
1.	
2.	
3.	

The detailed observations about the infrastructure, technical personnel and other set up of the testing facility applied for instrumental, chemical and microbiological analysis of Drugs and pharmaceuticals or raw materials used in the manufacture there of on behalf of licensees for manufacture for sale of Drugs were noted and summarized in aforesaid checklist.

Following observations were made by the joint inspection team during the course of inspection.

Observations

Conclusion & Recommendation :-

On the basis aforesaid inspection checklist and summarized observations it may be concluded that M/s.XXXXXXXXXXXX found to have provided premises , technical staff, equipments, recording systems as per rule 150 C &E of Drugs & Cosmetics Rule.

In the view of above the inspecting team is of the opinion that the application furnished by the subject firm as per Form 36, for approval to carry out test on Drugs & pharmaceuticals or raw materials used in the manufacture thereof on behalf of

licensees for manufacture for sale of Drugs or raw material on Form-37 for following categories of Drugs by Chemical, Instrumental & Microbiological testing may be granted for the followings category of the drugs & Cosmetics:

Drugs other than those specified in schedule C & C(1) excluding Homeopathic Drugs

- Drugs requiring the use of ultraviolet spectroscopy or chromatography
- Disinfectants
- Cosmetics

b. Drugs specified in schedule C and C (1)

- Antibiotics
- Vitamins &
- Parenteral preparations
- Drugs requiring the use of ultraviolet/IR spectroscopy or chromatography
- Drugs requiring microbiological tests.

Signatures of Inspection Team Members

Annexure: V

Guidance Document

Requirement for the Submission of an application for issue of "No Objection Certificate" (NOC) for the manufacture of unapproved/approved New Drugs in Form-29 for the purpose of examination, test & analysis (Excluding for clinical trial purpose) for drugs other than Biologicals/Medical Devices/Diagnostic Kits

Introduction

A manufacture can obtain license in Form – 29 from the concerned State Drug Department, under whose jurisdiction the manufacturing facility lies for the manufacture of any drug in small quantities for the purpose of examinations, test or analysis only, if the person proposing to manufacture a drug for the purpose of examination, test or analysis does not hold a license in Form – 25 or Form – 28 in respect of such drugs he shall, before commencing such manufacture, obtain a license in Form – 29.

Purpose

Requirement for the Submission of an application for issue of "No Objection Certificate" (NOC) for the manufacture of unapproved/approved new drugs in Form – 29 for the purpose of examination, test & analysis (Excluding clinical trial purpose) for drugs other than Biologicals/ Medical Devices/ Diagnostic Kits). This guideline will corroborate various commonly found aspect of granting licence in Form – 29 for the manufacture of specific quantities of drugs under the provisions made in Part – VIII of Drugs & Cosmetics Act & Rules 1945.

Scope

This document is applicable only for the applications for obtaining Form – 29 NOC from Zonal/Sub-Zonal offices for Form – 29 manufacturing licence from State Licensing Authority for drugs excluding Biological/Medical Devices/Diagnostic Kits.

Procedure

Under the provision of Rule – 89 it is mentioned that **"in the case of a drug, the composition of which is such that the drug is not generally recognized among experts qualified by scientific training and experience to evaluate the safety of drugs as safe for use, no licence in Form – 29 shall be granted unless the applicant produces a certificate from the "Licensing Authority" mentioned in Rule 21, to the effect that there would be No Objection to such license being granted".**

In light of the above, it is desirable that the application should be submitted to the respective Zonal/Sub-Zonal offices of CDSCO where the actual manufacturing site is located. The applicant (Manufacturer) should submit document as per the following three categories;

(I) Manufacture of API (Bulk) for examination, test & analysis only;

(1) Name of Drugs
(2) Class of Drugs
(3) Indication of Drugs
(4) Address of the facilities where drugs is to be manufactured

(5) List of equipments
(6) Details of premises (layout plan) & manufacturing process
(7) SOP of Analytical procedure & manufacturing process
(8) Flow Chart of manufacturing Process.
(9) List of Staff their qualification & experience.
(10) Details of raw materials
(11) Details of the test are to be performed with the drug
(12) Published Literature
(13) Status of Drug whether approved/unapproved

(II) Manufacture finished formulation for examination, test & analysis only;

(1) Name of Drugs
(2) Class of Drugs
(3) Indication of Drugs
(4) Dosages & Strength of the formulation
(5) Route of administration
(6) Composition of product
(7) SOP of Analytical procedure & manufacturing process
(8) Flow Chart of manufacturing Process.
(9) List of Staff their qualification & experience.
(10) Details of raw materials
(11) Details of the test are to be performed with the drug
(12) Address of the facilities where drug is to be manufacture
(13) List of equipments
(14) Details of premises & manufacturing process
(15) Published literature of the proposed formulations

(III) Manufacture of Investigational New Drugs (IND) for examination, test & analysis only;

(1) Name of Drugs

(2) Class of Drugs
(3) Indication of Drugs
(4) Dosage & strength of the formulation
(5) Route of administration
(6) Composition of product
(7) SOP of Analytical procedure & manufacturing process
(8) Flow Chart of manufacturing Process
(9) List of Staff their qualification & experience
(10) Details of raw materials
(11) Details of the test are to be performed with the drug
(12) Address of the facilities where drug is to be manufacture
(13) List of equipments
(14) Details of premises & manufacturing process
(15) Published literature for the proposed formulations /Bulk
(16) INN (International Non-proprietary Nomenclature)
(17) Material safety data sheet
(18) Structural Formula & Molecular Formula

Note:-

(*) If the drugs covered under NDPS Act or for veterinary use, the permission from Narcotics Commissioner of India or permission from Department of Animal Husbandry, Ministry of Agriculture & Fisheries, Govt. of India respectively has to enclose along with applications.

(*) Only actual manufacturer has to apply for NOC along with all relevant documents as mentioned above.

(*) Undertaking stating that the product to be manufacture under Form – 29 licence will not be utilised for any Clinical Trial or any commercial purpose.

Annexure: W

Guidance Document on common submission format for issuance of No Objection Certificate for export of Unapproved/Approved New drugs/Banned drugs.

INTRODUCTION

A manufacturer holding valid license copy in Form -25 and Form- 28 can obtain No Objection Certificate from Zonal offices of Central Drugs Standard Control Organisation (CDSCO) for export purpose only for Approved / Unapproved New drug / Banned drug in India.

PURPOSE

Requirement for the common submission format for issuance of No Objection Certificate for export of unapproved/approved new drugs/Banned drugs from India. This document made as per guidelines issued by Ministry of Health and Family Welfare for Export purpose and Rule 94 of the Drugs and Cosmetic Act, 1940.

SCOPE

This document is applicable for the manufacturer to obtain No Objection certificate Zonal offices of Central Drugs Standard Control Organisation (CDSCO) for export purpose.

PROCEDURE

Requirement for Common submission Format for issuance of No Objection Certificate for export of unapproved / approved new drugs / Banned drugs from India

The Following documents are required to be submitted in the following manner and order for issue of the No Objection Certificate for export of drugs from India: -

1. **Covering Letter: -** The covering letter is an important part of the application and should clearly specify the intent of the application. The list of documents that are being submitted (Index with page no's) as well as any other important and relevant information may be provided in the covering letter. The covering letter mentioning list of products to be exported clearly indicating name of the drug, dosage form, composition and strength pack size along with quantity and country to be exported duly signed and stamped by the authorized signatory, indicating the name & designation of the authorized signatory along with the name and address of the firm. Each application should be made by the manufacturer only.

2. **Purchase Order: -**

a. Order from the foreign buyer either in the name of manufacturer or in the name of trader mentioning list of products to be exported clearly indicating name of the drug, dosage form, composition and strength pack size duly signed by the competent authority with specific destination point of the importing country. In case of purchase order in the name of trader further a letter from the trader in the name of manufacturer is required to be submitted along with the application

b. It should be signed by the competent authority/person with a valid purchase order no. and recent date not more than 6 month prior to the application made by the firm.

3. **Manufacturing License: -** License issued by the State Licensing Authority should be enclosed along with each application for the required location to manufacture the drug for export purpose.

4. **Performa Invoice: -**

a. A copy of Performa invoice from the importing country should accompany with application for import of unapproved Active Pharmaceutical Ingredients, used in the drug formulation.

b. A copy of Performa invoice duly signed by the competent authority should be addressed to the manufacturer mentioning the required quantity of the bulk drug.

5. **Registration Certificate: -**

a. For the export of drugs which are banned in India by Central government, which coming under list of drugs prohibited for manufacture and sale through gazette notifications under section 26a of drugs & cosmetics act 1940 by the ministry of health and family welfare.

b. A copy of registration certificate from the specific importing country along with composition and strength of the drug should accompany with the application

c. Registration certificate should be provided in the name of manufacturer.

While processing such applications the following conditions shall be taken into consideration:

1. The application shall provide copy of valid export order and NOC will be issued on a case by case basis against each such order.
2. The applicant shall identify the premises where the drug will be manufactured for export.

3. The applicant should mention whether the batch to be exported has undergone Quality control testing or shall be tested at the destined site.
4. The applicant shall ensure that the drug(s) manufactured on the basis of —NOC given as per (1) above its exported and that no part of it is diverted for domestic sale in India.
5. The applicant shall make available for inspection of the appropriate authorities, on completion of the export orders, information regarding each consignment despatched, remaining stock of drug and related raw materials and intermediates in hand.
6. The applicant shall ensure physical destruction of all un exported quantity of drugs. This should be included as a condition of manufacturing license issued to the applicant by the State licensing authority.
7. The applicant shall ensure that the drug for which NOC has been given shall cease to be manufactured or exported if the drug is prohibited in future in the country or in the importing country.

Annexure: X

CENTRAL DRUGS STANDARD CONTROL ORGANISATION

(Directorate General of Health Services)

Ministry of Health & Family Welfare

Title: SOP to permit for import of small quantities of Drugs for personal use under Form 12 B of the Drugs & Cosmetic Rules.			
SOP No.:	----	**Department:**	Technical
Effective Date:		**Version:**	00
Review Date:		**Page No.:**	1 of 3

1.0 OBJECTIVE:

To lay down the procedure for scrutiny of the documents submitted along with the application in respect of grant of permit to import small quantities of drugs for personal use in Form 12 B.

2.0 SCOPE:

This procedure is applicable for screening of the documents submitted by the Patients at respective CDSCO, Zonal and Sub-zonal Offices.

3.0 RESPONSIBILITIES:

3.1. For Scrutiny & Preparation of checklist and draft - Should be done by STA/TA/TDA at CDSCO.

3.2. For review, correction & approval of checklist and draft - Should be done by Technical Head of the Department.

4.0 DEFINITION(S):

Personal use – use of the imported drugs by the patient only.

5.0 PROCEDURE:

5.1 Receive the documents in the FTS system.

5.2 Scrutinize the content of documents as per annexure no. ----

5.3 After scrutiny, prepare the checklist with details of documents submitted.

5.4 If all documents are in order, permit may be issued on the same day.

5.5 In case of doubtful documents, investigation may be got carried out for verification of the facts before issuance of the permit.

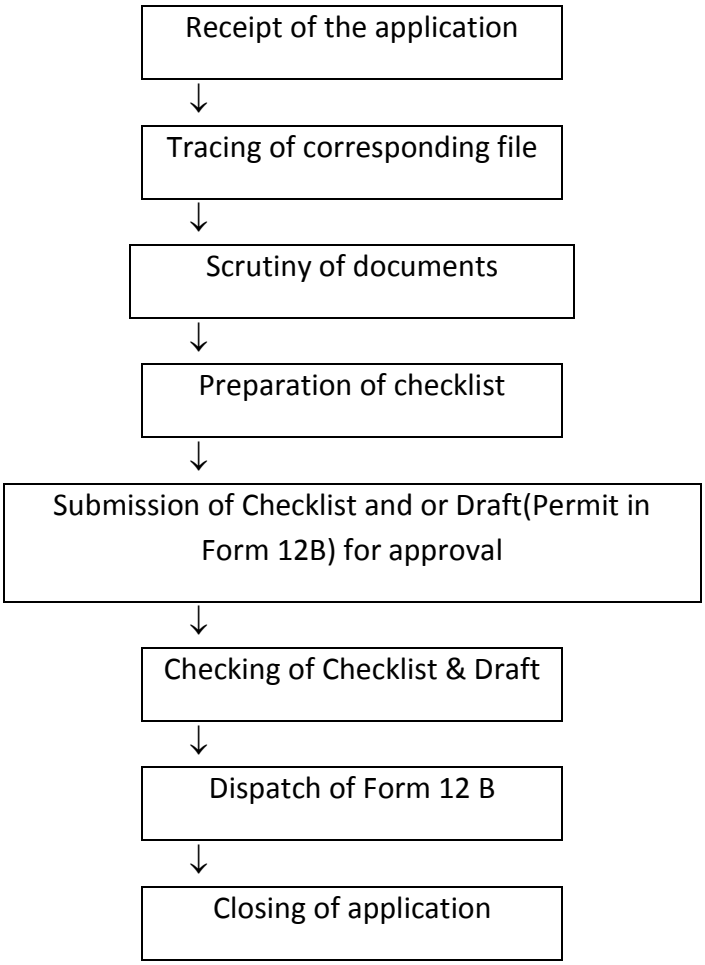
6.0 ABBREVIATION(S)

CDSCO – Central Drug Standard Control Organisation

FTS – File Tracking System

LVP- : Large Volume Parenterals

7.0 FLOW CHART:



Prepared by	**Checked by**	**Approved by**
Technical Data Associate	**Senior Technical Assistant**	**Deputy Drugs Controller (India)**

Checklist for screening the documents related to issuance of Form 12 B

Name of the Patient :
Date of receipt of application: ----------
Subject: Import of Drugs for Personal use

S.No.	Parameter	Status	Remark
1.	Application from Patient in Form 12 A	Yes/No	
2.	Copy of Prescription	Yes/No	
3.	Whether prescription bears Registration No. of M.O.	Yes/No	
4.	Whether quantity required is reasonable	Yes/No	
5.	Name of the Drug	Yes/No	
6.	Whether the required drug is approved/ registered in India	Yes/No	
7.	Whether the applied drug was also supplied earlier to the same patient, if yes, Quantity	Yes/No	

Opinion: The patient/ relative of the patient has submitted the documents vide Letter no. ……. dated ……. on scrutiny of the documents, it was observed that all aforesaid documents are in order.

Form 12 B may be issued to the patient.

Annexure: Y

Guidance Document for grant of permission for Drugs imported in Bulk for Non-Medicinal Use as per Rule 43 of Drugs and Cosmetics Rules 1945.

Introduction

This document provides guidance for the grant of permission for Drugs imported in Bulk for Non-Medicinal Use as per Rule 43 of Drugs and Cosmetics Rules 1945. The purpose of this guidance document is to ensure uniform implementation of Rule 43 of Drugs and Cosmetics Rule 1945 by CDSCO. It also specifies requirements to be fulfilled by the Importer for grant of such permissions. Efforts are also made to identify the list of drugs intended for Non- medicinal use with the help of stakeholders which can be amended from time to time.

The dual use permissions are usually requested by the manufacturer of bulk drug using one of the bulk drugs as starting material based on the approval of State Licensing Authorities. The dual use permission may also be sought by the other industries like food industries etc. which uses raw bulk substance in lower strength than approved as drug by this organisation. Similarly, the Animal feed Industry makes application for the import of raw materials for the exclusive use as animal feed.

The list is enclosed with this guidelines is only for reference purpose. The disposal of application is purely dependent on the intended use and its technical examination keeping in view the applicability of the status of drug.

The importers of dual use have a responsibility to undertake due diligence before making application for import of material for which following points may be important for consideration:

- The drugs already registered for import,
- Approval status of usages of imported item in the country (alone or in combination with other drugs),
- International status (e.g. in most of the countries multivitamins are not considered as drugs hence regulated differently),

- Technical survey through Martindale extra pharmacopeia etc.

The application for dual use import may be made well in advance before the actual import to facilitate technical review for consideration. The permission for dual use items will be granted by Dy. Drugs Controller (India) of the respective Zones.

For the purpose of this Guidance Document

1. "Drug" includes

(i) all medicines for internal or external use of human beings or animals and all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals, including preparations applied on human body for the purpose of repelling insects like mosquitoes;

(*ii*) Such substances (other than food) intended to affect the structure or any function of the human body or intended to be used for the destruction of [vermin] or insects which cause disease in human beings or animals, as may be specified from time to time by the Central Government by notification in the Official Gazette;

(iii) All substances intended for use as components of a drug including empty gelatin capsules; and

*(iv)*Such devices intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, as may be specified from time to time by the Central Government by notification in the Official Gazette, after consultation with the Board.

2. **Rule 43**

The drugs specified in Schedule D shall be exempt from the provisions of Chapter III of the Drugs and Cosmetics Act and of the Rules made

there under to the extent, and subject to the conditions specified in that Schedule.

3. Schedule-D

Class of drugs	Extent and conditions of exemption
Substances not Intended for Medicinal Use	All provisions of Chapter III of the Act and rules there under subject to the condition that if the substance is imported in bulk, the importer shall certify that the substance is imported for non-medicinal uses, and if imported otherwise than in bulk, each container shall bear a label indicating that the substance is not intended for medicinal use or is of commercial quality.

Based on the intended use of the product, the drugs that are falling under Schedule-D of Drugs and Cosmetic Rules have been categorised into:

1. Drugs meant for Non- medicinal use.
2. Drugs meant for Animal feed supplement, Feed premix.
3. Drugs meant for further processing / conversion to other drug.

1. Drugs Meant for Non- Medicinal Use:

The following documents are required to be submitted for the items specified in **Table No. 1** to the Zonal Office for grant of necessary permission under Schedule - D, preferably before importing the consignment.

i. Covering letter- The applicant should submit covering letter by clearly specifying purpose of application, the drugs to be imported, the intended use of the drug, quantity to be imported, name and address of the manufacturer and list of documents that

are being enclosed (Index with page numbers). The covering letter should be duly signed and stamped by the Authorised Signatory, indicating name and Designation of the Authorised Signatory. The pages of the application should be numbered and should be accompanied with index.

ii. Legal Undertaking- The applicant has to submit Legal Undertaking on Rs. 100 stamp paper as per the proforma given under **Annexure-I**. (If the drug is imported by the actual User, Legal Undertaking as per the proforma provided in **Annexure-II** should be obtained from the Trader. The Trader has to retain such undertaking issued by the actual user for any inspection carried out by the regulators).

iii. A copy of valid Manufacturing Licence from Actual User for the products to be manufactured, issued by the Competent Authority wherein the imported drug will be used.

iv. A copy of valid trade licence / Excise Registration Certificate from importer.

v. A copy of letter (notarised) issued by the Competent Authority stating that the imported drug will be used in the manufacture of said finished product and not as an active principle.

vi. A copy of Certificate of Analysis of the drug to be imported, issued by the manufacturer in the country of origin (not by exporter).

vii. Detailed Technical Literature of the drug to be imported.

viii. For subsequent permission, Reconciliation data of previously permitted quantity in addition to above details.

Table No.-1

S.NO	Drugs Names
1.	Aluminium Hydroxide
2.	Benzoyl peroxide
3.	Calcium Carbonate

4.	Cinchonine
5.	Citric acid
6.	Coumarin
7.	Cysteamine HCl
8.	Di calcium phosphate
9.	Diflorasone Base
10.	Disodium carbonate
11.	Disopyramide base
12.	Empty hard gelatine Capsules with TSE/BSE free certificate and GMP declaration of the manufacturing firm.
13.	Estrone
14.	Glycerine with pharmacopeial grade
15.	Guanidine hydrochloride
16.	Heavy Magnesium Carbonate
17.	Hesperidine
18.	Hydrogen Peroxide Pharmacopeial grade
19.	Isoxepac
20.	Magnesium hydroxide
21.	Magnesium oxide
22.	Magnesium Sulphate
23.	Mannitol (non for parenteral use)
24.	Mixed tocopherols 50%
25.	Monensin Sodium
26.	Simethicone Emulsion

27.	Triacetin
28.	Zinc Gluconate
29.	Manganese Sulphate
30.	Alpha Lipoic Acid
31.	Zinc Oxide
32.	Any Other Drug having Dual Use which may find suitable to be included in list.

2. Drugs meant for Animal feed supplement, Feed premix

Before grant of NOC for release of items stated in **Table no.-2**, the concerned Port Officer should verify / examine following documents-

i. Legal Undertaking- The applicant has to submit Legal Undertaking on Rs. 100 stamp paper as per the proforma given under Annexure I. (If the drug is imported by the actual User, Legal Undertaking as per the proforma provided in **Annexure-II** should be obtained from the Trader. The Trader has to retain such undertaking issued by the actual user for any inspection carried out by the regulators).

ii. Purchase order / Proforma invoice of the material to be imported.

iii. NOC from the Ministry of Animal Husbandry in favour of importer / manufacturers, if any.

iv. A copy of valid trade licence / Excise Registration Certificate from importer.

v. A copy of letter (notarised) issued by the Competent Authority stating that the imported drug will be used in the manufacture of said finished product and not as an active principle but as feed.

vi. A copy of Certificate of Analysis of the drug to be imported, issued by the manufacturer in the country of origin (not by exporter).

vii. Detailed Technical Literature of the item to be imported.

viii. For subsequent permission, Reconciliation data of previously permitted quantity in addition to above details.

Table No. - 2

List of the feed grade items which requires NOC from Port Office (CDSCO) for exclusive use in animal feed industry as an animal feed supplement, feed premix.

I. Amino Acids (granular)

1) L-Lysine Mono HCL 99% Feed grade
2) L-Lysine Sulphate 65% Feed grade
3) DL-Methionine 99% Feed grade
4) L-Threonine Feed Grade

II. Vitamin Premix

1) Vitamin AD3 Feed grade 1000:200
2) Vitamin E 50% Feed grade
3) Vitamin D3 0.5 miu/gm feed grade
4) Vitamin B2 80% feed grade
5) Biotin 2% Feed grade
6) Vitamin mineral Premix feed grade (as per formula)
7) Choline Chloride 50% & 60% on Corn Cob carrier

III. Phosphates

1) Mono Calcium Phosphate (MCP) 22% Feed grade
2) Di Calcium Phosphate (DCP) 18% feed grade.

IV. Antibiotic / Antibacterial Feed Additives

1) Chlortetracycline 15% Feed grade
2) Dichlozuril 1% feed grade
3) Zinc Bacitracin 10% feed grade
4) BMD-Bacitracin Methyl Disalicylate 15% Feed grade
5) Tylosin Phosphate 10% premix feed grade
6) Colistin Sulphate - % Premix Feed Grade
7) Clopidol 25% Feed Grade

V. Anticoccidiostats

1) Maduramycin 1% Feed grade
2) Salinomycin 12% Feed grade

Any other product included in the list of poultry/ Animal Feeds shall be included after approval from the Animal Husbandry Department.

3.Drugs meant for further processing / conversion to other drug

For the import of any substance which attracts the definition of “Drug” as per the Drugs and Cosmetics Act 1940 for further processing / conversion to manufacture of other drugs, shall require NOC from Zonal Office for each consignment.

e.g.:- Erythromycin Thiocyanate for the manufacture of Erythromycin salts, Penicillin G Potassium for the manufacture of Penicillin drugs. Such permissions are considered for those manufactures which does not have manufacturing permission in the country for imported drug, however they got permission for manufacture of other drug using imported drug.

The following documents are required to be submitted to the Zonal Office for grant of necessary permission under Schedule- D, preferably before importing the consignment.

i. Covering letter- The applicant should submit covering letter by clearly specifying purpose of application, the drugs to be imported, quantity to be imported, name and address of the manufacturer and list of documents that are being enclosed (Index with page numbers). The covering letter should be duly signed and stamped by the Authorised Signatory, indicating name and Designation of the Authorised Signatory.

ii. A copy of Valid Drug Manufacturing Licence for the Drug to be manufactured, issued by the Drug Licensing Authority wherein the imported drug will be used.

iii. A copy of Master Formula Record of the product to be manufactured Signed and Stamped by the Authorised Signatory of the Firm.

iv. A copy of Certificate of Analysis of the drug to be imported, issued by the manufacturer.

v. Detailed Justification of the quantity of Drug to be imported.

vi. Brief Manufacturing Process including Flowchart wherein the imported product will be used.

vii. Detailed Technical Literature of the drug to be imported.

viii. For Subsequent permission, Reconciliation data of previously permitted quantity in addition to above details.

(List of bulk drugs already registered is annexed as Annexure III)

(The import of drug under dual use for purification or rendering it sterile will not be considered under dual use)

Annexure I

Legal Undertaking for the Import of Drugs as per provisions of Schedule D of Drugs and Cosmetic Rules 1945 to be submitted by the Actual Users to The Central Drugs Standard Control Organisation (CDSCO) Zonal office.

I/We.....S/o..... having premises at .....aged about .....do hereby solemnly affirm state and undertake as under:

1. That I am the importer of..... (Name of the drug) from..... (Name and full address of the Manufacturer) of..... (Quantity) vide Bill of Entry No.....dated.....

2. That I undertake to use..... (Quantity) of above said drug for Non-Medicinal purpose/ as a phrama aid / as a drug intermediate to manufacture other drugs only.(delete whichever not applicable).

3. That I undertake to maintain books and records of transaction of above said drug for which NOC will be granted.

4. That I undertake to allow the Drug Inspectors from the CDSCO to inspect the books and records as well as the actual usage of (Name of the drug) as and when required.

5. I state that that consignment document like Certificate of Analysis, Bill of Entry, invoice etc. clearly mentions “Not for Medicinal Use” or (“for use as pharma aid”).

6. That the bags/containers carrying (Name of the drug) along with other requirements of labelling and packaging also mentions –“Not For Medicinal Use” or (“for use as pharma aid”).

DEPONANT

VERIFICATION

Verified on this .....day of..... (Month & Year) that the contents of my above undertaking are true and that no part it is false and that nothing material has been concealed here from.

DEPONANT

Annexure II

Legal Undertaking for the import of Drugs as per provisions of Schedule D of Drugs and Cosmetic Rules 1945 to be submitted by the Importer/Trader to The Central Drugs Standard Control Organisation (CDSCO) Zonal Office.

I/We.....S/o.....
having premises at .....aged about .....do hereby solemnly affirm state and undertake as under:

1. That I am the importer/trader of..... (Name of the drug) from..... (Name and full address of the Manufacturer) of..... (Quantity) vide Bill of Entry / Purchase order no.....dated.....

2. That I undertake to sell..... (quantity) of above said drug for Non-Medicinal purpose / as a phrama aid / as a drug intermediate to manufacture other drugs only (delete whichever not applicable).

3. That I undertake to maintain books and records of transaction of above said drug for which NOC will be granted.

4. That I undertake to allow the Drug Inspectors from the CDSCO to inspect the books and records as well as the actual usage of said drug as and when required.

5. That the bags/containers of the said drug along with other requirements of labelling and packaging also mentions “Not For Medicinal Use”.

6. That the data of my previous transaction is annexed with this undertaking (Optional in cases of subsequent transaction).

DEPONANT

VERIFICATION

Verified on this .....day of..... (Month & Year) that the contents of my above undertaking are true and that no part it is false and that nothing material has been concealed here from.

DEPONANT

Important Points for consideration

- The application should be complete before submission to the authorities.
- Application for dual use clearance is advised to be made by the manufactures or its authorised agent or importer to the authorities well in time for technical review for consideration preferably before the actual import to avoid demurrages. It may be advised that a period of two months before the actual import will be effective for smooth clearance of consignment.
- The consignment label, bills, invoices etc. in respect of imported items should clearly have indelible marking for its intended use.
- The applicant for manufacture of a drug using imported drug must have Master Formula Record duly attested by the Licensing authority for import application.
- The import of drug under dual use for purification or rendering it sterile will not be considered under dual use.
- The import permission for dual use item can be considered to actual users for the period of one year.
- If application is made to the Port officer, it will be forwarded with remarks to the Zonal head of CDSCO for review and consideration preferably by e mail / fax. The NOC from Zonal Head via e mail / fax will be sufficient for release.
- The Zonal office will maintain data for such releases.

Annexure: Z

CENTRAL DRUGS STANDARD CONTROL ORGANISATION

(Directorate General of Health Services)

Ministry of Health & Family Welfare

Title: SOP for the Blood Bank renewal License under Rule 122F			
SOP No.:	----	**Department:**	Technical
Effective Date:		**Version:**	00
Review Date:		**Page No.:**	1 of 2

8.0 OBJECTIVE:

To lay down the procedure for scrutiny of the documents submitted along with the application in respect of Certificate of renewal of license to operate a Blood Bank for processing of Whole Human Blood and /or for preparation for sale or distribution of its Component in Form 26-G.

9.0 SCOPE:

This procedure is applicable for screening of the documents submitted by the Blood Bank at respective CDSCO, Zonal and Sub-zonal Offices.

10.0 RESPONSIBILITIES:

3.1. Scrutinize & Preparation of checklist and draft - Should be done by STA/TA/TDA at CDSCO.

3.2. For review, correction & approval of checklist and draft - Should be done by Technical Head of the Department.

11.0 DEFINITION(S):

Blood Bank renewal License on Form- 26G.

12.0 PROCEDURE:

5.1 Receive the documents in the FTS system .

5.2 Scrutinize the content of documents as per annexure no. ----

5.3 After scrutnization, prepare the checklist with details of documents submitted.

5.4 If all documents are in order, permit may be issued within 5 days.

5.5 In case of doubtful documents, investigation may be got carried out for verification of the facts before issuance of the license.

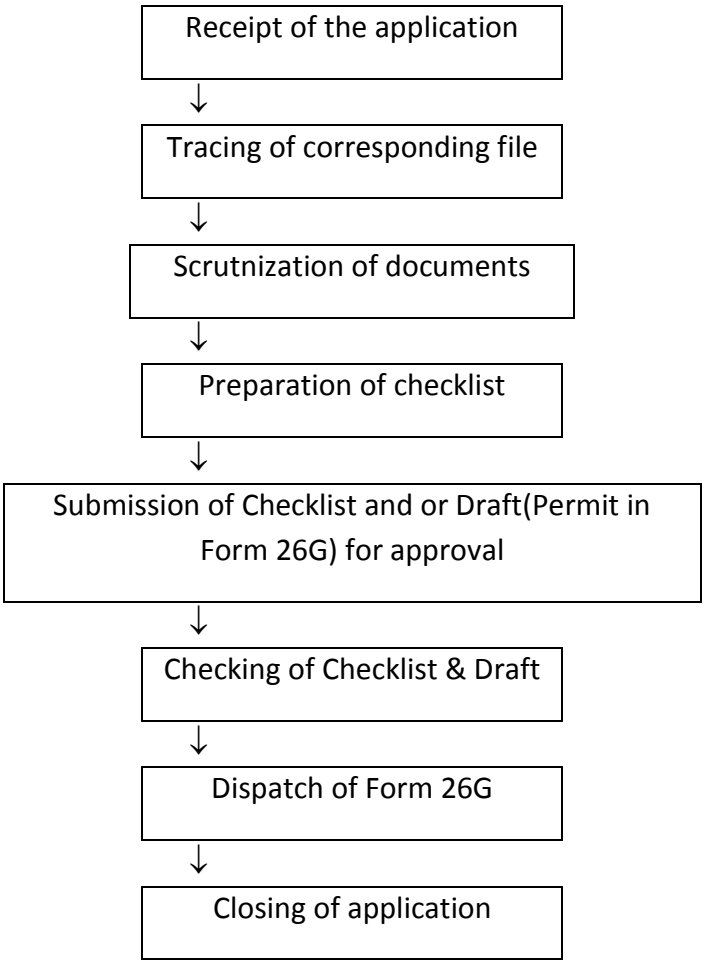
13.0 ABBREVIATION(S)

CDSCO – Central Drug Standard Control Organisation

FTS – File Tracking System

LVP- : Large Volume Parentral

14.0 FLOW CHART:



Prepared by	**Checked by**	**Approved by**
Technical Data Associate	**Senior Technical Assistant**	**Deputy Drugs Controller (India)**

Checklist for screening the documents for approval of CLAA in Form 26 G

Name of the Blood Bank: - M/s……..

Date of receipt of forwarding letter from SLA……..

Subject: Renewal of Blood Bank License for the period ……..

S.No.	Parameter	Status	Remark
1.	Forwarding letter from S.L.A.	Yes/No	
2.	Renewal Certificate in Form 26-G in triplicate duly signed by S.L.A.	Yes/No	
3.	Joint Inspection Report	Yes/No	
4.	Recommendations of the inspecting team	Yes/No	
5.	Compliance verification report, if any	Yes/No	
6.	Other relevant documents as prescribed in note 1 of Form 27C	Yes/No	

Opinion:

All the relevant documents submitted along with the forwarding letter of S.L.A. were scrutinized & found in order / not in order.

Form 26 G is ready for signature / following documents are required.

Activities of the Port Offices

THE BROAD FUNCTIONS AND ACTIVITIES OF PORT OFFICES

All the port offices of central Drugs standard control organization (CDSCO) are under the control of Drugs controller General (India). The CDSCO through the officers posted at the port, exercise control over drugs and cosmetics, which are imported / exported in the country. This control is exercise under chapter III of the Drugs & Cosmetics Act. The port officers function in an advisory capacity to the customs Authorities. Any action for contravention of section 10 of the Drugs and Cosmetics Act is resorted to by advising the Commissioner of Customs to take action under section 11 of Drugs & Cosmetics Act, read with relevant provisions of customs Act 1962.

All the port offices are headed by Assistant Drugs Controller (India) and assisted by Technical Officers/Drugs Inspectors along with some ministerial staff members. Following are the main activities of the port offices

Functions of Port Offices

(1) Scrutiny of the Bills of entry with a view to ensure that the imported drugs comply with the provisions of Chapter III of the Drugs & Cosmetic Act and Rules there under and Drugs and Magic Remedies (Objectionable Advertisements) Act and Rules & Narcotic Drugs and Psychotropic Substances Act(NDPS) & Rules there under and any other law for the time being in force.

(2) To check the shipping bills for export for compliance of Drugs & Cosmetics Act and keep control under Narcotic Drugs and Psychotropic Substances Act & Rules.

(3) In the case of Narcotic Drugs and Psychotropic Substances Act & Rules, a certificate issued by Narcotics commissioner must be checked for import/export and details furnished to Drugs Controller General (India) through the Deputy Drugs controller (India) of the respective Zones.

(4) To ensure that no New Drug is imported into the country unless its import permitted by the Drugs Licensing Authority under Rules (Rules 122 A & 30-AA.

(5) To ensure that small quantities of drugs imported for Test, Examination and Analysis or clinical trials or for personal use are duly covered by Test License (11 or 11-A) or Permit License as (12 B) as the case may be.

(6) Maintenance of Statistics data regarding imports/export of all Drugs/cosmetics/medical devices and submit the same on monthly basis to the Deputy Drugs Controller (India) of the respective zones and to other authorities as and when required.

(7) Co-ordination with the Commissioner of Customs – The Port Officers should have enough knowledge of the relevant portions for Customs Act and DGFT policies.

(8) Import of raw materials under Advance Licenses/100% EOU cases must be intimated to the concerned State Drugs Controller to examine proper post-import check with a copy marked to the DDC(I) of the concerned Zone.

(9) Assist members of the trade with the information required.

(10) Preparation and forwarding of Quarterly and Annual Reports.

(11) Examination of post parcels couriers for import and export of drugs, cosmetics and medical devices.

(12) Coordination with the customs and other investigating agencies for the matters of violation of import/export under intimation to the DDC(I) of the concerned zone.

(13) To examine the re-import/re-export consignment as per the procedures.
(14) To draw samples from import/export and re-import consignment as per laid down procedures.
(15) To examine unclaimed/seized cargo when referred by customs and offer opinion as per procedure laid down.
(16) In case of drugs and cosmetics of not of standard quality/spurious, to be informed to all the port offices directly with a copy marked to the Deputy Drugs controller of the concerned zone.

Requirements and check list for import of drugs

(The documents required to be submitted by the importer and exporter should be displayed in the official notice board for perusal of the applicants and common public.)

1. All the bulk drugs and formulations, notified medical devices, critical diagnostics manufacturing site should be registered in India and Registration Certificate in **Form 41** to be obtained **(GSR 604 (E) dated 24.8.2001.w.e.f.1.1.2003).**
2. If the drugs are imported under DEEC Scheme, Port Officer to verify for ITC Policy Circular No.9 dated 30.6.2003 and/or ITC Policy Circular No.15 dated 17.9.2003 endorsement on the DEEC License for giving benefit of exemption from Drug registration. Registration Certificate & Import License in Form 10 are exempted for DEEC/100% EOU as per DCGI circular dated 11.09.2003.The details of import to be informed to State DC/Zonal Officer immediately for post import check Copies of ITC Policy. Circulars are attached **(Annexure: P-1 to P-2).**
3. If the drugs are imported under 100% EOU/EPZ/SEZ and as are exempted from the condition of registration

as per the above ITC Policy Circulars. To control misuse, as a precautionary measure an undertaking from the importer also to be taken and the details of import to be informed to the State Drug Controller / Zonal Officer / DCGI immediately for post import check.

4. No registration certificate is required for non-critical in-vitro diagnostic kits and reagents (Rule 24(2)) and inactive bulk substances (Rule 24 A (8)) However Form 10 is required for non critical invitro diagnostic kits and reagents.
5. If the drugs are imported under **import for export** policy, all the provisions of Chapter III of Act are exempted provided; the drugs are exported from the import shed itself without physically clearing the goods out of Customs area.
6. A Registration Certificate (Form 41), unless, it is sooner suspended or cancelled, shall be valid for a period of three years from the date of issue: provided that if the application for a fresh Registration Certificate is made nine months before the expiry of the existing certificate, the current registration certificate shall be deemed to continue in force until orders are passed on the application.
7. An import license in Form 10 or 10 A or NOC in case of pending application, as the case may be for import of drug issued by the Licensing Authority / DCGI.
8. Small quantities of new drugs the import of which is otherwise prohibited under section 10 of the said ACT may be imported for the purpose of examination, test or analysis under a license in Form 11 (Rule 33).
9. Small quantities of new drugs the import of which is otherwise prohibited under section 10 of the act may be imported by a Govt. Hospital or Autonomous Medical Institution for the treatment of patients under a license in form 11-A(Rule 33-A).

10. Patent and proprietary medicines shall be imported only in containers intended for retail sale. In case, a firm holds a manufacturing license can import such medicines in bulk for repacking against Rule 37 permission issued by DCGI.
11. No drug having the shelf life of less than 60% is allowed for the import: provided that in exceptional cases the licensing authority may, for the reasons to be recorded in writing, allow the import of any drug having lesser shelf life period, but before the date of expiry as declared on the container of the drug (Rule 31).
12. No drug, the manufacture, sale or distribution of which is prohibited in the country of origin shall be allowed to be imported under the same name or under any other name (Rule 30 B).
13. All the drugs imported in India are required to be stored at drug/product specific temperature conditions.
14. All the drugs imported should comply to the standards as specified in the Second Schedule to the Act and Rules there under.
15. Drugs which are under test and released by LG shall be stored in licensed premises.
16. All the drugs/formulations imported into the India shall fulfil the labelling requirements as prescribed in Drugs and Cosmetics Rules1945.(Part XI)

Documents to be scrutinized by Port Office for Import

1. Self Certified copy of Form10 or 10A and Registration Certificate (Form 41) as the case may be
2. Particulars of information in the Form of ADC import sheet **(Annexure: P-3)**
3. Original license in Form 11/11-A to make the debit for the quantity imported under respective bill of entry.

4. Self Certified copy of the licensed premises where drugs are to be stored.
5. Self Certificate of analysis and Batch release Certificate of each batch.
6. Copy of invoice, packing list, certificate of country of origin (if necessary)
7. Other documents like linked documents CCPIT (China council for promotion of international trade) to be verified by the port office to ensure the authenticity of the consignments.
8. If goods are not directly supplied from the manufacturer then the port officer may verify the authenticity of goods at manufacturer's end through e-mail/fax or his authorized registered agent in India.

Examination of Bill of Entry

1. After scrutiny of the aforesaid documents and making the necessary entry in the records/computer, the technical staff to put up the Bill of entry (B/E) to the port officer. All Bills of Entry received in the office must be disposed of on the same day with ADC(I) remarks as delay in disposal would result in not only making the importer pay demurrages but would cause accumulation in the air sheds/docks. The Port officer should examine B/E and should decide at this stage whether:-

a) Labelling & marking need to be checked by the port officers and samples may be drawn (If the drug imported is in small container of 5 kg or less than the original container may be called for to check the markings/label)
b) When required Samples to be sent for testing / analysis to the Government / Approved testing lab.
c) The consignment may be recommended for release.

General Principles for drawal of samples for testing

1. Normally a drug of a particular manufacturer is tested once or twice a year. However, the port officer may draw more samples depending on the previous test reports, number of consignments and the reputation of the manufacturer/ importer.
2. The drug imported is from a new source from which it was not previously imported.
3. The quantity imported is large.
4. There are no proper labels/markings or no markings on the containers or the markings are illegible.
5. Drugs imported from a supplier/manufacturer have been reported to be not of standard quality/spurious etc at this port or any other port in India.
6. The price of the drug imported is abnormally low as compared with the previous imports.
7. Customs HS number on the invoice is not tallying with the declared item HS number.
8. On request from the Customs etc. based on certain information

Note: When sampling is to be done in case of expensive drugs, the minimum quantity required for test may be drawn and the duplicate and the unutilized sample may be returned to the importer later if everything is in order.

Letter of Guarantee

1. Pending testing report, to avoid demurrage if the importer gives an undertaking (Rule 40 (1)) in writing not to dispose of the drugs without the consent of Customs commissioner etc., the goods can be released on L/G for test (on Stamp Paper). A proforma is attached. **(Annexure: P-4).**
2. Drugs requiring cold storage such as sera, vaccines, may be released forthwith conditionally on L/G for test etc., for

proper storage pending the completion of the formalities. A proforma is attached **(Annexure: P-5).**

3. If there are any labelling defects and importer desire to rectify the defects at their place, they may be allowed to be clear the consignment on L/G for rectification of labelling and/or test. A proforma is attached **(Annexure: P-6)**

Note:

1. Goods on L/G should not be permitted to be taken out of the city of import unless otherwise directed by the DDC(I) of the concerned Zone as a special case.

2. Drugs should not be released on L/G for producing Registration Certificate or Drug Import License unless otherwise directed by the DDC (I) of the concerned Zone.

Procedure for drawing of sample

Samples are drawn in duplicate. Quantity required for test has been specified by the Director, CDL/CRI/CDTL/NIB/NIV/ NARI/NICD/IVRI etc. time to time. Samples are drawn as far as possible under the direct supervision of a technical representative of the port office. Also, sampling should invariably be carried out in the presence of the importer's representative. In case of drugs requiring special precautions due to their hygroscopic, thermo labile nature etc., samples to be drawn invariably under proper conditions. If the drug is sterile, the importers should be asked to make arrangement for drawing of samples under sterile conditions. If the manufacturer premise is located outside the city, Govt. approved private testing laboratories facilities to be utilized and the technical staff from the port offices may be deputed to supervise the drawing of samples. Usually $\sqrt{n}+1$ number of

samples may be drawn, where n is number of containers / batches as per requirements.

Testing guidelines

1. Any bulk drug/formulation imported for the first time to be sent to CDL/CDTL/RDTL
2. Any bulk drug/formulation on routine to be sent to CDL/CDTL or any local Government Approved Private Testing Laboratory.
3. Condoms 100% to be sent for test to CDTL, Chennai
4. Vaccines formulations 100% to be sent for test to CRI, Kasauli
5. Veterinary Vaccines/Sera/Toxoids 100% to IVRI, Izzatnagar
6. Certain Blood Products and Biotech Products, diagnostic kits and reagents etc., to NIB, Noida
7. 100% blood products for HIV and Hepatitis testing to NIV / NARI, PUNE or CMC Vellore or NICD, Delhi etc. depending on the area of import.
8. Homoeopathic medicines to Homeopathic pharmacopeial laboratories (HPL) , Ghaziabad
9. Intra –utrine devices and Falope Rings are to be sent for test to CDTL, Mumbai.
10. Medical Devices are to be sent for test as directed by the DCG (I).
11. Drug intermediates to be cleared as per batch test certificate or sometimes to be tested to establish the identity of the goods in local CDTL or Private Labs.
12. No samples should be drawn from the consignments imported for the purpose of registration only.

Despatch of Samples

1. It is responsibility of the Port Officer to ensure that all samples intended for test, are sent to laboratory as early as possible.

2. The first part of the sample (original) is for test, the second part (Duplicate) is to be retained in the Port Office.
3. Samples drawn from bulk containers to be sent to the laboratories with a code number in order to maintain secrecy. Only the name of the drug shall be mentioned.
4. Port officer should ensure that the seal of the samples should remain intact at required temperature / cold chain shall be maintained during the transportation.

Procedure to be followed on receipt of Test Reports

1. If the goods on test by the laboratory are found to be of standard quality and are labelled as prescribed, they may be released.
2. If the goods, on test, are declared to be not of standard quality, the Customs Commissioner is informed about this along with 2 copies of the test Report. The proforma of the Communication for action under Rule 41(1) used is given in **Annexure: P-7,** intimation about such imports are made to the Deputy Drugs Controller (India) with copies to the other Port Offices, the proforma used for such communication is given in **Annexure: P-8.**
3. On the basis of the advice of the Port Officers the Customs will issue a show Cause memo to the firm concerned. Proforma of show Cause memo generally used is given in **Annexure: P-9**. On the basis of the party's reply the case will be finally adjudicated after ascertaining views of the Port Officers.
4. In case the importers appeal for a retest by submitting sufficient evidence like manufacturer's protocols of test on the items in question, the case should be referred to the Deputy Drugs Controller (India) for orders along with comments of the Port Officer. If the Deputy Drugs Controller (India) so directs, a fresh sample shall be drawn, should be sent for retest to the laboratory. Test report so received should be sent to the Deputy Drugs Controller (India). The orders passed by the Deputy

Drugs Controller (India) on the basis of such retest are final.

5. Where the defect is such, that the importers undertake to recondition the goods up to the required standard, they must submit along with their appeal -

a) The method that will be adopted for re-processing of Bulk Drugs.

b) A declaration to the effect that in the event after the reconditioning failing to comply with the prescribed standards of the quality, the material to be surrendered for destruction.

c) If the Deputy Drugs Controller (India) agrees to the party's request for re-processing, the importers must be asked to execute a Letter of Guarantee to the Commissioner of Customs to that effect (**Annexure: P-4)**.

6. In case of grossly substandard / spurious / adulterated drugs, Commissioner of customs is to be informed stating that the import of these goods constitutes an offence u/s.10 (bb) etc. of Drugs & Cosmetics Act, read with Section 11 ibid read with 11 (k) of the Customs Act 1962 and liable for absolute confiscation u/s. 111 (d) and shall punishable u/s. 135 and prosecution can be launched u/s. 137 of Customs Act 1962 by the Customs Authority under intimation to DDC(I). A proforma used for such communication is given in (**Annexure: P-10).**

7. In case of not of standard quality, other than those mentioned in point 6 above, the importers may be given the option to reship the goods to the country of origin if they so desire or forfeit them to the Central Government for destruction.

Medical Devices & Diagnostics

Medical Devices:

The Ministry of Health and Family Welfare, Govt. of India has notified the following devices to be considered as Drugs under Section 3 (b) (iv) of Drugs and Cosmetics Act 1940. -

a. Disposable Hypodermic Syringes
b. Disposable Hypodermic needles
c. Disposable Perfusion sets
d. Cardiac Stents
e. Drug Eluting Stents
f. Catheters.
g. Intra ocular Lenses.
h. I.V. Cannulae
i. Bone Cement
j. Heart Valves
k. Scalp Vein set.
l. Orthopaedic Implants.
m. Internal Prosthetic replacements.
n. In vitro diagnostic Devices for HIV, HBsAg and HCV

Diagnostics

a) Blood Grouping Reagents

For the import of above devices (S.no. a to n) and Blood grouping reagents only, Registration Certificate in Form-41 and import license in Form-10 are required.

For the import of non-notified diagnostic kits/reagents, only import license in Form-10 is required.

The product label should comply with Rule 96 of Drugs and Cosmetics Rules including name and address of the manufacturer as stated in the Form-10, import license number.

For the import of assembled above notified devices for further processing in India (for sterilization, labelling and packing), Form -10 is necessary.

Drugs having dual use

1. Import of Drugs having “Dual use” and drugs, which are used as Raw Material for the manufacturing of other drugs requires permission from DDC (I) (No. 6-2/2004 dated 13/12/2005).
2. There are substances which are covered under the definition of the drug but are not used for medicinal purpose and are used in other industries like textile industries, chemical industries and food industries etc. or are used as a starting material / intermediate for synthesis of other drugs.
3. At the time of import all the importers are required to submit certified copy of DDC (I) permission for waiver of site registration and import license. (Original License may be asked to make the debit quantity, if quantity based permission is granted by the DCGI.)
4. After release of the goods, the same to be informed to the concerned State Drug Controller and the Zonal officer for post import check.
5. The port office shall inform the applicants requiring NOC for drug items under dual use that they should apply to Zonal officers along with undertaking with other documents as NOC from DDC(I) is compulsory for release of such goods.

The procedure to be followed in case of imports for personal use is detailed under Rule 36 of Drugs & Cosmetics Rule 1945. DDC (I) of the respective Zon is authorized by the Drugs Controller General (I) to issue permits in Form 12 – B.

Gifts for free distribution

1. Import of drugs by Charitable Trusts / NGOs / UNICEF etc. when exempted from payment of duty by the Ministry of Finance for free distribution to the needy and poor people in India are to be released insisting for Drug Import License / Drug Registration / Testing etc. after inspection of the goods and after obtaining an undertaking from the importer regarding status and function of their activities after obtaining the NOC from the DCG(I)
2. Date expired medicines/banned drugs and items covered under NDPS Act should not be permitted.

Homeopathic Medicines

1. No new Homeopathic medicine shall be imported except under Rule 30 AA and in accordance with the permission in writing of the Licensing Authority / DCGI
2. No Homeopathic medicine shall be imported unless it is labelled in conformity with the Rules in Part XI A.
3. As regards to testing, details are already covered above.

Ayurvedic Drugs

1. In case of import of ayurvedic drugs also, invoice , packing list, manufacturer's test report, mfg, license, specimen sample, label may be examined before giving "NOC" by port office, samples may be drawn from import consignment ayurvedic drugs and tested for the presence of heavy metals like, lead,arsenic,cadmium,mercury as per ayush guideline in case of dought. Labelling of imported ayurvedic drugs should comply with rule 161(part VII,

labelling,packing, and limit of alcohol in ayurvedic including siddha or unani drugs) of D&C Rule.

HERBAL MEDICINES

Herbal drugs other than ayurvedic medicine are to be treated as modern drugs as prescribed under sec.3b for the purpose of import.

Cosmetics

1. Import of Cosmetics items should be complied with Part XII (Rule No. 129 to 136) and standard laid down in Schedule 'S' of Drugs & Cosmetics Act and Rules there under.
2. All the cosmetics should comply with the labelling requirements as prescribed in rules under Part XV of Drugs & Cosmetics Rules 1945.

- Port Officer should insist for Free Sale Certificate and Certificate of Analysis.
- If consignment is not directly supplied form the manufacturer, then the Port Officer may verify the authenticity of goods thoroughly, as there is a possibility of import of counterfeit cosmetics into the country, may be referred to the IPR Department of customs.(IPR=Intellectual properties rights)

3. Other documents may be asked by the port officer to ensure the authenticity and quality of the cosmetics
4. Sample to be drawn at random and sent for test to Government appoved Testing Laboratories only.
5. As regard to testing and follow up action is provided under Rule 131, the guidelines

and protocols to be followed is very much similar to the Drugs, only sections and rules to be changed.

6. In case the cosmetic are not having defined standards by BIS, in such cases port officers shall test at least for heavy metals , arsenic, hexachlorophene

Re-Imports

In case of re-import of drugs and cosmetics of Indian origin by the manufacturer / exporter due to certain reasons, samples may be drawn for complete test including specific test in which the consignment was reported to have failed and release the goods thereafter if found to be standard.

Sample to be sent to the Government / approved laboratories. In case the re-imported material is found to be NSQ, then based on the under taking of the manufacturer, the consignment may be released for reprocessing provided it shall be done in the presence of the Drugs Inspectors or representative of Port Office. The decision of release for reprocessing or not to release shall be taken by the concerned DDC(I). Simultaneously, the matter to be informed to the concerned State Drug Controller / Zonal Officer for the re-import check.

BIOLOGICAL SAMPLES

The biological samples for import shall be advised for referral to ICMR for getting NOC.

Export of Drugs & Cosmetics

1. Even though there is no chapter in the Act covering the export of Drugs & Cosmetics, but there is a reference about the ADC's role in the Customs Appraising Manual which is reproduced below:-

   Customs Appraising Manual V – Export of Drugs & Cosmetics

   In case of export consignments also, before the Shipping Bills are finally passed, ADC's No Objection should be obtained for consignments of Drugs & Cosmetics, he should also follow all the instructions given by the ADC prior to the actual export of the goods.

2. In addition to the above, DGFT Public Notice 173 (RE-2008)/2004-2009 dated 13th April 2009 also mentions the ADC's Role. A copy of Public Notice is attached herewith in the (**Annexure: P-11).**

DOCUMNTS TO BE SERUTINIZED FOR SHIPPING BILLS

1. Particulars in the form of ADC Export Sheet (**Annexure: P-12** for format)
2. Compliance to Rule 94 and 147 of Drugs and Cosmetics Rules
3. Compliance to the Drugs & Magic Remedies (OA) Act and Rules
4. Export permissions issued by the Deputy Drugs Controller for / fixed dose combinations / medicines beyond Schedule V limits / unapproved/approved new drugs/banned drugs under 26-A / without labels etc. which are not permitted for marketing in India.

5. Export permits issued by the Narcotic Commissioner for Narcotic and Psychotropic substances and precursor chemicals and forward quarterly and annual statements of exports to DCGI / Narcotic Commissioner for onward transmission to International Agencies.
6. Certificate of analysis issued by the manufacturer for the subject product or a copy of certificate of analysis issued by approved laboratory of the importing country / FDA; or a copy of Certificate of Analysis issued by a laboratory approved by Drugs Controller under Drugs & Cosmetics Act 1940 and the rules made there under.

7. The permission from DCG(India) is required for the schedule P drugs for which shelf life more than mentioned in Schedule P is claimed.

8. Rule 94 violations – In case of export by loan licensee, the name and any address of manufacturer mentioned on the license may be acceptable.

9. In case of neutral code, the consignment may be allowed as long as the identity of the manufacturer is ascertained with licence / code number available on the label.

Aurvedic Drugs

In case of export of ayurvedic drugs following documents are to be examined before release i) shipping bill, ii) Invoice, iii) packing list , iv) Mfg's test report of ayurvedic items for presence of heavy metals, Pb As, Sb, Hg within permissible limits (as per ayush guidline),specimen label/specimen sample, valid mfg. Licence with list of approved items labelling provision of ayurvedic drugs for export should comply with Rule 161A of D&C Rule.

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BIOLOGICAL SAMPLES

In case of export of biological sample other than related to clinical trial and specifically permitted by DCG (India) for export shall be adviced for referral to ICMR for getting NOC.

HERBAL MEDICINES

Herbal drugs other than ayurvedic medicine are to be treated as modern drugs as prescribed under sec.3b for the purpose of export.

List of Annexure for Port Offices

Annexure – P-1

GOVERNMENT OF INDIA

MINISTRY OF COMMERCE & INDUSTRY
DEPARTMENT OF COMMERCE
DIRECTORATE GENERAL OF FOREIGN TRADE
UDYOG BHAVAN, NEW DELHI-110011

POLICY CIRCULAR NO. 9(RE-2003)/2002-2007 Dated :30 .6.2003

To
All Licensing Authorities
All Commissioners of Customs

Sub : Imports of approved & unapproved drugs under the Advance Licensing Scheme – Exemption from Registration procedure.

Attention is invited to Notification No.2(RE-2003)/2002-2007 dated 31.3.2003 vide which certain types of drugs & pharmaceuticals have been placed under free category and their imports have been subjected to the registration and other requirements administered by the Drugs Controller General of India under the provisions of Drugs & Cosmetics Act.

2. Subsequent to the above Notification, representations have been received from various Drug Manufacturers Associations requesting for exemption from registration requirements of the Drugs & Cosmetics Act for imports under the Advance Licensing Scheme. The requests have been considered and It has been decided that import of approved & unapproved drugs under the Advance Licensing Scheme will not be subjected to the Registration procedure and the imports will be permitted subject to the following conditions:

i. Import license will only be given against an existing valid export order and to the extent raw material is required as per that order.
ii. The Drug Controller would be a member of the Advance Licensing Committee.
iii. A copy of the license would be endorsed to the Drug Controller and the concerned State Drug Controller.
iv. Drug Controller along with the State Drug Controller would make random checks.
v. Any violation is punishable under the Foreign Trade Development and Regulation Act and the Customs Act. The Drug Controller could also make provisions for penalizing the Drug Manufacturing Units in terms of suspension or cancelling of his license.
vi. Pre import condition will have to fulfilled.
Export obligation will be fulfilled within a period of six months from the date of issuance of the license.

3. Similarly, 100% EOU/EPZs & SEZs would also be exempted from the condition of registration. However, if they make supplies to the domestic market, they will have to follow the formalities of registration as under the Drugs & Cosmetics Act.

4. Representations have also been received regarding issuance of Form-10 under the Drugs & Cosmetics Act for manufacturers. It is clarified that Form -9 issued by the registered manufacturers should also be accepted for the purpose of issuing Form-10 license under the Drugs & Cosmetics Act.

5. In addition as far as imports of drugs/raw materials for purposes of (i) clinical trials & (ii) for formulation development is concerned, it is clarified that exemption in such cases will be permitted on case to case basis.
This issue with the approval of the DGFT.

(DR. PRATIMA DIKSHIT)
JT.DIRECTOR GENERAL OF FOREIGN TRADE

Annexure – P-2

GOVERNMENT OF INDIA
MINISTRY OF COMMERCE & INDUSTRY
DEPARTMENT OF COMMERCE
DIRECTORATE GENERAL OF FOREIGN TRADE
UDYOG BHAVAN, NEW DELHI-110011

POLICY CIRCULAR NO. 15
(RE-2003)/2002-2007 Dated: 17.09.2003

To
All Licensing Authorities
All Commissioners of Customs

Sub: Exemption from registration procedure for import of all types of approved and unapproved drugs under the Advance Licensing Scheme

A number of representations have been received from members of the exporting community and Trade Bodies/Associations, after the issuance of Policy Circular No.9 dated 30.6.2003. The following clarifications are made in this regard:

2. The exemption from registration procedure of the Drugs & Cosmetics Act will not only cover those drugs listed in Notification No.2 dated 31.3.2003 but all drugs.

3. (a) Applicants wishing to avail of the benefit of exemption from registration procedure under the Drugs & Cosmetics Act will apply for an Advance Licence in accordance with the instructions contained in Policy Circular No.9 dated 30.6.2003. The Licensing Authority will make an endorsement on the licence that the exemption has been granted in terms of Policy Circular No.9 dated 30.6.2003.

(b) Other applicants who comply with the registration procedure under the Drugs & Cosmetics Act may apply for a Advance licence as per the existing EXIM Policy provisions & procedures.

4. For ratification of advance licences issued under Para 4.7 of the Handbook of Procedure (Vol. I), the representative of the Drugs Controller General of India (DCGI) will be a member of the ALC at DGFT Hqrs. For items where SION is fixed, the existing prescribed procedure will be followed and a copy of the Advance Licence will be endorsed to DCGI & State Drugs Controller Office. Copies of advance licences issued under Para 4.7 and amendments recommended by ALC will also be endorsed to the State Drugs Controller's office.

5. The exemption from Registration formalities does not cover Advance Licence under deemed exports, Advance Licence for annual requirements, DFRC & DEPB.

6. All importers making imports against advance licences, which have not been issued in terms of Policy Circular No.9, will either follow the registration procedure and utilise the licence OR get a fresh licence issued in terms of Policy Circular No.9 to clear their consignments.

7. The export obligation period for the advance licences issued as per Policy Circular No.9 dated 30.6.03 will be fulfilled within a period of six months from the date of import of the first consignment (and not from date of issuance of licence as laid down in Policy Circular No.9 dated 30.6.03). Para 4.22.1 of Handbook of Procedures (Vol. I) shall however be applicable for advance licences issued under Policy Circular 9 dated 30.09.2003 for the purpose of extension in export obligation period.

This issues with the approval of the DGFT.

(DR. PRATIMA DIKSHIT)
JT. DIRECTOR GENERAL OF FOREIGN TRADE

Annexure – P-3

ADC SHEET FORMAT FOR IMPORT

B/E No. & Date	**:**
Invoice No. & Date	**:**
Importer's Name & Address	**:**
Supplier Name & Address	**:**
Import License No. & Valid Date	
(Form-10/Form-11/Adv.Lic.No/	
100% EOU) Number	**:**
Any Permission / Endorsement letter	**:**
From The SCG(I)	
Exchange Rate(FC=INR)	**:**

Sr. No.	**Product Name & Batch No.**	**D/M (A)**	**D/E (B)**	**Date of Landing (c)**	**Total shelf Life in days (D)=(B-A)**	**Residual Shelf Life in days (E)=(B-C)**	**Residual Shelf Life in %age (F)=E/D x 100**	**Quantity Batch wise**	**Unit Price**	**Total Amount (FC & INR)**

Annexure - P-4

The President of India Date :
Through the Collector of Customs,

LETTER OF GUARANTEE

(Vide Provision to Rule 40 of the Drugs and Cosmetic Rules, 1945)

1. Bill of Entry No. Date.

2. I.G.M. No. Lines No. Date.

3. Steamer Name /Flight Name S.S. / Flight Name No. Date

4. Description of goods.

5. Marks and Numbers.

6. Packing and Quantity.

7. Country of Origin.

8. C.I.F. Value Rs.

9. Name & Address of Supplier

10. Name & Address of Manufacturer

LETTER OF UNDERTAKING FOR TEST

In consideration of the Collector of Customs or any Officer on his behalf having permitting to clear the above goods not withstanding his decision to detain the same goods under the above mentioned Rule 40 of the Drugs and Cosmetics Rules 1945 on having reason to doubt whether the above mentioned goods comply with the provisions of Chapter III of the Drugs & Cosmetics Act 1940 and rules there under.

We hereby undertake :-

1. That we shall arrange for inspection of the goods as soon as they arrive in the go-down and follow the instructions of representative of the O/o. Assistant Drugs Controller (I), with regard to drawing of samples for test, rectification of labelling defects etc., if any.

2. That we shall not dispose of the said goods without the consent of the Collector of Customs or any Officer on his behalf in writing.

3. That we shall return the said goods in whole or in part as the Collector of Customs or any officer on his behalf may direct within ten days of receipt of a notice from the Collector of Customs or any officer on his behalf to return the goods.

4. That we shall reship or surrender the said goods within two months of the receipt of any order to that effect from the Collector of Customs or any officer in his behalf.

5. That we shall forthwith pay such find and / or penalty and be liable for such punishment as the collector of Customs or any Officer on his behalf or magistrate may impose under Section II of the drugs & Cosmetics Act, 1940 as read with the relevant provisions of the Customs Act, 1962 and Under Section 13 of the Drugs & Cosmetics Act, 1940.

Any amount due under this bond may be recovered in the manner laid down in the subsection of the Section 142 of the Customs Act, 1962 without prejudice to any other mode or recovery.

The undertakings referred to above is given in view of rule 40 of the drugs and Cosmetics Rules 1945. The goods will be stored in our

Go-down at: _____

Signature of the Importer

WITNESS:

(1)

(2)

ACCEPTED ON BEHALF OF THE
PRESIDENT OF INDIA.

Annexure – P-5

The President of India Date :
Through the Collector of Customs,

LETTER OF GUARANTEE (Direct Delivery)
(Vide Provision to Rule 40 of the Drugs and Cosmetic Rules, 1945)

1. Bill of Entry No. Date.

2. I.G.M. No. Lines No. Date.

3. Steamer Name /Flight Name S.S. / Flight Name No. Date

4. Description of goods.

5. Marks and Numbers.

6. Packing and Quantity.

7. Country of Origin.

8. C.I.F. Value Rs.

9. Name & Address of Supplier

10. Name & Address of Manufacturer

LETTER OF UNDERTAKING FOR TEST

In consideration of the Collector of Customs or any officer on his behalf having permitting to clear the above goods no with standing his decision to detain the same goods under the above mentioned Rule 40 of the Drugs and Cosmetics Rules 1945 on having reason to doubt whether the above mentioned goods comply with the provisions of Chapter III of the Drugs and Cosmetics Act 1940 and the Rules there under.

We hereby undertake:

1) That we shall arrange for inspection of the goods as soon as they arrive in our go-down by a representative of Asst. Drugs Controller (India) and obey his instructions as regards drawing samples under proper conditions and rectification of labelling defects if any etc

2) That we shall not dispose of the said goods without the consent of the Collector of Customs or any officer on his behalf in writing.

3) That we shall return the said goods in whole or in part us the Collector of Customs or any officer on his behalf nay direct within ten days of receipt of a notice from the Collector of Customs or any officer on his behalf to return the goods.

4) That we shall reship or surrender the said goods within two months of the receipt of any order to that effect from the Collector of Customs or any Officer on his behalf.

5) That we shall forthwith pay such fine and /or penalty and be liable for such Punishment as the collector of Customs or any Officer on his behalf or Magistrate may impose under Section II of the Drugs and Cosmetics Act, 1940 as red with the relevant provisions of the customs Act, 1962 and under Section 13 of the Drugs and Cosmetics Act, 1940.

Any amount due under this bond may be recovered in the, manner laid down in subsection of the Section 142 of the Customs Act, 1962 without prejudice to any other mode of recovery.

The undertakings referred to above is given in view of Rule 40 of the Drugs and Cosmetics Rules, 1945. The goods will be stored in our

Go-down at ……

Signature of Importers.

WITNESS:
(1)

(2)

ACCEPTED ON BEHALF OF THE
PRESIDENT OF INDIA.

Annexure – P-6

The President of India Date :
Through the Collector of Customs,
Custom House

LETTER OF GUARANTEE
(Vide Provision to Rule 40 & 96 of the Drugs and Cosmetic Rules, 1945)

1. Bill of Entry No. Date.

2. I.G.M. No. Lines No. Date.

3. Steamer Name /Flight Name S.S. / Flight Name No. Date

4. Description of goods.

5. Marks and Numbers.

6. Packing and Quantity.

7. Country of Origin.

8. C.I.F. Value Rs.

9. Name & Address of Supplier

10. Name & Address of Manufacturer

LETTER OF GUARANTEE FOR LABELING

In consideration of the Collector of Customs or any officer on his behalf having permitting to clear the goods mentioned above, although the same have contravened the following provisions of the Drugs & Cosmetics Act, 1940 and the Rules there under, namely Rules 40 & 96

We hereby undertake:

1. That we shall label the goods mentioned above as required under the above rules within a month or such extended period as the Collector of Customs or any officer on his behalf may allow.

2. That we shall not dispose of the said goods without the consent of the Collector of Customs or any officer on his behalf in writing.

3. That we shall return the said goods in whole or in part us the Collector of Customs or any officer on his behalf nay direct within ten days of receipt of a notice from the Collector of Customs or any officer on his behalf to return the goods.

4. That we shall reship or surrender the said goods within two months of the receipt of any order to that effect from the Collector of Customs or any Officer on his behalf.

5. That we shall forthwith pay such fine and /or penalty and be liable for such Punishment as the collector of Customs or any Officer on his behalf or Magistrate may impose under Section II of the Drugs and Cosmetics Act, 1940 as red with the relevant provisions of the customs Act, 1962 and under Section 13 of the Drugs and Cosmetics Act, 1940.

Any amount due under this bond may be recovered in the, manner laid down in subsection of the Section 142 of the Customs Act, 1962 without prejudice to any other mode of recovery.

The undertakings referred to above is given in view of Rule 40 & 96 of the Drugs and Cosmetics Rules, 1945. The goods will be stored in our

Go-down at ……

Signature of Importers.

WITNESS:

(1)

(2)

ACCEPTED ON BEHALF OF THE
PRESIDENT OF INDIA.

Annexure – P-7

File No.

Office of the
Assistant Drugs Controller (India)
Mumbai / Kolkata / Chennai / Delhi
Ahmadabad / Hyderabad/Cochin

Date:

1. Name and address of the Importer.
2. Name and address of the Manufacturer.
3. Description of Goods.
4. Quantity Imported
5. C.I.F. Value
6. Bill of Entry No Date :
7. I.G.M. No. Line No. Date.
8. Steamer Name / S.S. / Flight Name No. Date

……..

The Sample drawn from the above consignment and forwarded for test to the Director, Central Drugs Laboratory, Kolkata /Central Research Institute, Kasauli / NIB Noida / NARI –NIV Pune / IVRI –Izzat Nagar, CDTL, Mumbai, Chennai, Chandigarh has since reported to be "NOT OF STANDARD QUALITY" as defined in the Drugs and Cosmetics Act, 1940 and the Rules there under for the reasons given below:-

"The Sample does not conform to…….. in respect of ……(state the reasons)"

Reasons:

1)

2)

As such the import of the subject drug is prohibited under Section 10 (a) of the Drugs and Cosmetics Act and the goods are liable to absolute confiscation under Section 111(d) of the Customs Act, 1962. The importers, may however please be given the option to have the goods wither reshipped to the country of origin or have them destroyed in the presence of Assistant Drugs Controller (India) or a Custom Officer, provided under Rule 41 (1) of the Drugs and Cosmetics Rules.

In this connection two copies of the relevant test report received from the Director, Central Drugs Laboratory, Kolkata /Central Research Institute, Kasauli / NIB Noida / NARI –NIV Pune / IVRI –Izzat Nagar, CDTL, Mumbai, Chennai, Chandigarh are enclosed, one of which may please be retained for your record and the other forwarded to the importer along with the show cause memo to be issued to them.

The goods are lying in the docks /air-shed/ were cleared on a Letter of Undertaking for test pending the receipt of the test report.

Party's reply when received may please be forwarded to this office.

A.D.C.(India) / Dy. Commissioner of Customs

Annexure – P-8

File No.

Office of the
Assistant Drugs Controller (India)
Mumbai / Kolkata / Chennai / Delhi
Ahmadabad / Hyderabad/Cochin
Dt.

To
The Drugs Controller (India),
Dte. General of Health Services,
New Delhi .

Subject: - Testing of ……..Manufactured by M/s……

MEMORANDUM

Reference B/E No. ……..Date…….

A sample of the subject drug sent for test under Rule 40 of the Drugs and cosmetics Rule from a consignment imported by M/s……
(Name and full address of the importers), has since been reported by the Director, C.D.L. Kolkata / C.R.I. Kasauli / NIB Noida / NARI –NIV Pune / IVRI –Izzat Nagar, CDTL, Mumbai, Chennai, Chandigarh as "NOT OF STANDARD QUALITY" as defined in the Drugs and Cosmetics Act and the Rules there under for the reasons given below :

"The Sample does not conform to ……..
in respect of ……..

State the Reasons:

(1)

(2)

(Vide Test Report No. Dt. Refers)

The quantity imported is ……and the C.I.F. Value ……
The Customs authorities have been advised to take necessary action under Rule 41(1) of the Drugs and Cosmetics Rules in respect of the above goods which are lying in the Docks / were cleared on Letter of undertaking for test.

The action taken may please be approved.

Asstt. Drugs Controller (India)

Copy forwarded for information to: The A.D.C.(India) , Mumbai / Kolkata / Chennai / Delhi /Ahmadabad / Hyderabad Technical Officer , Cochin .

Annexure – P-9

No.

Subject: Dated:

……

1. The goods specified above have on test been found to be not of standard quality. A copy of the test report is attached herewith for your information. The import of these goods are prohibited under Section 10(a) of the Drugs and Cosmetics act read with Section 11 of the same act and liable to absolute confiscation under Section 111 (d) of the Customs act, 1962.

2. You are hereby required to show cause why action should not be taken to confiscate the goods under Section……of the Customs Act.

3. You are required to indicate whether you would like to re-export the goods to the country of origin as per option given in rule 41 (1) of the Drugs and Cosmetics Rules, 1945.

4. You are further required to show cause why a personal penalty should not be imposed on you under the aforesaid section.

5. Your written explanation should be presented within ……day hereof to the undersigned along with all the documentary evidence. You should also indicate in the written explanation whether you wish to be heard in person before the case is adjudicated.

6. If you fail to submit the written explanation in time or do not appear before the adjudicating authority when the case is posted for hearing, the case will be adjudicated on the basis of the evidence on record without any further reference to you.

Appraising Department
Dated…….

DY. COMMISSIONER OF CUSTOMS,
APPRAISING DEPTT.

To,
……..
……..

Annexure – P-10

File No.

Office of the
Assistant Drugs Controller (India)
Mumbai / Kolkata / Chennai / Delhi
Ahmadabad / Hyderabad/Cochin

Dt.

1. Name and address of the Importer

2. Name and address of the Manufacturer

3. Description of Goods.

4. Quantity Imported

5. C.I.F. Value

6. Bill of Entry No Date :

7. I.G.M. No. Lines No. Date.

8. Steamer Name / S.S. / Flight Name No. Date

The import of these goods are prohibited under Section 10 (bb) --- of the Drugs & Cosmetics Act, read with Section 11 of the same Act and the goods are liable to absolute confiscation u/s. 111-D and punishable u/s. 135 of Customs Act, 1962. In terms of Section 10 (bb) etc. etc. and Section 11 of Chapter III of Drugs & Cosmetics Act, 1940, prosecution can be launched by Customs after sanctioning the same under Section 137 of the Customs Act, 1962.

ASSTT. DRUGS CONTROLLER (INDIA) /
DY. COMMISISONER OF CUSTOMS

Annexure – P-11

DGFT PUBLIC NOTICE

-COPY OF-
PUBLIC NOTICE NO.173 (RE-2008)/2004-2009
Dated 13th April, 2009

1. In exercise of the power conferred under Paragraph 2.4 of the Foreign Trade Policy, 2004-2009, as amended from time to time, it has been decided to notify, with immediate effect, procedure /guidelines to strengthen the enforcement mechanism available under the Drugs and Cosmetics Act, 1940, to ensure that counterfeit drugs do not get exported out of the country.

2. Export of Drugs & Pharmaceuticals covered under the provisions of Drugs & Cosmetics Act 1940 and the rules made there under , which is being regulated by Drugs Controller General of India (DCGI) in the Ministry of Health & Family Welfare , shall be as per the requirements given hereunder :

Every exporter of Drugs & Pharmaceuticals at the time of shipment shall submit, along with other required documents, the following:

(i) A copy of Certificate of Analysis issued by the manufacturer for the subject product; Or

(ii) A copy of Certificate of Analysis issued by approved laboratory of the importing country/FDA; Or

(iii) A copy of Certificate of Analysis issued by a laboratory approved by Drugs Controller under Drugs & Cosmetics Act 1940 and the rules made there under.

Wherever required the officials of the Drugs Control Department posted at the port offices shall retain a sample of the subject consignment for the purpose of reference and tracking of the manufacturer / exporter of the subject product.

1. This issue in Public Interest.

sd/-
(R.S.Gujral)
Director General of Foreign Trade
& Ex-Officio Additional Secretary to the
Govt.of India

F.No. 01/91/180/648/AM09/Export Cell

Issued by:
Ministry of Commerce and Industry
Department of Commerce
Director General of Foreign Trade
New Delhi

Annexure – P-12

ADC SHEET FORMAT FOR EXPORT

PORT OF LOADING			ADC SHEET FOR EXPORT				
ENTRY NO	S/B NO & Date	INVOICE NO & DATE	DETAILS OF ITEM & CATEGORY. WITH MFG. DATE, EXP. DATE & BATCH NO.	NAME & ADDRESS OF EXPORTER WITH DSL/ DMI. NO.	NAME & ADDRESS OF CONSIGNEE	FOB VALUE INR	REMARKS / CHA DETAILS
				DULY SIGNED & STAMPED BY THE EXPORTER			

CLINICAL TRIAL & BA/BE INSPECTION PROCEDURES (FOLLOWING GUIDELINES HAS ALREADY BEEN PUT ON CDSCO WEB SITE)

OBJECTIVES

The aims of the programme are:

a. To verify GCP compliance to protect the rights, safety and well being of the subjects involved in clinical trial
b. To verify the credibility and integrity of clinical trial data generated
c. To verify the compliance with various regulatory provisions as per Drugs & Cosmetics Rules

The purpose of this programme is to provide direction to inspectors/CDSCO officers for conducting inspection of site of clinical trial, sponsor / CRO's facilities involved in clinical trial and information to investigators, sponsor/ CRO'S about procedures for inspection and follow up of action.

SCOPE AND EXTENT OF THE PROGRAMME:

Clinical trial inspection programme covers all clinical trial sites and sponsor / CRO's facilities involved in clinical trial of drugs including biological and medical device covered under Drugs & Cosmetics Act. **CLINICAL TRIAL INSPECTION Effective Date: 01-11-2010 Page 5 of 17**

PLANNING FOR INSPECTION

Inspection can be conducted before, during or after a clinical trial is completed.

Selection of studies

Inspection can be carried out as a routine surveillance or for any specific cause(s).Study may be selected for inspection based on, but not restricted to the following criteria:

- Nature of study
- For regulatory decision based on clinical trial data
- Data irregularities
- Complaints

- Vulnerability of subjects
- Number of CT including number of subject enrolled at a particular site

INSPECTION ASSIGNMENTS

CDSCO HQ will issue instruction to the CDSCO Officers /Inspectors to conduct the inspection identifying the Clinical trial, name, address, contact number of clinical trial site, sponsor / CRO's facilities to be inspected. It may also identify the type and purpose of the inspection and provide background materials like study protocol, CRF etc.

PREPARING FOR INSPECTION

The inspector shall go through the information provided by CDSCO HQ and develop a plan for conducting the inspection.

SCHEDULING THE INSPECTION

Inspection of clinical trial site would generally be pre-announced to ensure availability of the Investigator / Sub- Investigator and other personnel along with study records at the time of the inspection.

The date of inspection and other arrangements would be finalised by the CDSCO Officers / Inspector(s) in coordination with the investigator /sponsor/ CRO.

Under some specific circumstances unannounced inspection of clinical trial sites can be carried out as per the direction of CDSCO HQ.

Inspection of CRO/Sponsor can be conducted without prior notice.

CONDUCTING THE INSPECTION

CLINICAL TRIAL SITES

The inspection includes verification of essential documents to determine whether the trial related activities were in accordance

with the protocol, GCP guidelines published by DGHS, Govt. of India and Schedule Y as well as other applicable regulatory requirements. When inspection is carried out after completion of the clinical trial, it will include comparison of data generated by the sponsor with source documents at the clinical trial sites and Case Record Form (CRF) in the investigator's files. If it is a routine surveillance or "for cause" inspection of an ongoing clinical trial, the comparison will generally include source documents and CRF.

OPENING INTERVIEW

Inspector should meet investigator / key person of Sponsor and present his / her identity card. The inspector should provide verbal summary of methods and procedures to be followed during the inspection.
During opening interview following main activities should be found out:

- Investigator prior education and GCP experience, GCP training provided by the sponsor.
- Who did what, when, where and how with respect to following:

- Obtaining Informed consent of subjects,
- Screening and admission of subjects to the study,
- Receipt, handling, administration, return of investigational product,
- Collection and analysing of data,
- Recording, transcribing and reporting of data to sponsor,
- Archiving the data

- How did the investigator identify the subjects for the study,
- Date of enrolment first and last subject
- About Ethics Committee the site is using

- Whether the investigator has copies of protocol, permission from CDSCO, undertaking by the investigator etc.
- Information about unexpected and serious adverse events (if any) occurred at the site,
- Information about monitoring/auditing of the site by sponsor/CRO.

ORGANIZATION & DELEGATION OF RESPONSIBILITIES

Inspector shall verify / obtain following:

- Brief about study site.
- Status of the study.
- Whether investigator has agreement with sponsor for the study.
- Whether financial & Confidentiality agreement with Investigator and concerned laboratory (ies) in place.
- In Investigator undertaking protocol title, Investigator's name, address, telephone no of site, qualification, Name & address of laboratories, Name of Sub-Investigator etc are in-compliance with Schedule Y of Drugs & Cosmetics Rules 1945.
- Obtain list of all clinical trials performed by investigator. The list should have information such as

  - Protocol Number
  - Protocol Title
  - Name of Sponsor/CRO
  - Study date

- Determine whether authority for conducting various Clinical trial related activities were delegated properly by the Investigator to the competent personnel so that investigator was able to supervise the study adequately. Obtain a list of personnel with delegated activity.

- Documents following;

- Date of EC / IEC approval including initial review of protocol, amendment, ICD etc.
- Date of screening of first subject,
- Date of signing ICF by the first subject
- Date of first administration of IP,
- Date of last follow up of any subject,

- List the name and address of facilities involved in laboratory test required by protocol. Verify accreditation status and adequacy of these facilities to perform the specified test,
- Obtain a copy of site enrolment log,
- Determine whether SOP's for various activity are established and documented,

STUDY PROTOCOL

- Determine if, there are any difference between protocol provided to CDSCO and the protocol in the Investigator's file with respect to following

  - Version number and effective date
  - Eligibility of Subject (Inclusion/ Exclusion Criteria)
  - No of Subject
  - Dosage
  - Route of administration
  - Frequency of dosage
  - Randomisation & Blinding process
  - Verify whether Investigator follow the protocol as approved
  - Version number and EC approval of amendments

SUBJECT RECORD & INFORMED CONSENT

- Review the Informed Consent Form (ICF) signed by the subjects. If the number of subjects at site is relatively

small (e.g.20or less) 100% of the ICF can be reviewed. Determine the following:

- whether ICF have all the elements enlisted in Appendix V of Schedule Y,
- whether IC has been obtained from each subjects prior to participation of the subject in the study,
- whether signature/thumb impression of the subjects have been affixed with date,
- whether in case of illiterate subjects or illiterate representative of a subject, there are signature and details of an impartial witness,
- Have witness/ signature been personally dated,
- Have patient signature been personally dated?
- Has the dated signature of the designated person for administering informed consent (IC) been affixed?
- Is the designated person for administering IC medically qualified?
- If IC has been administered by a designated person who is not medically qualified, is there evidence that subject's queries of a medical nature were answered by a medically qualified person or the investigator?
- Is the completed ICF signed and dated by the investigator?

SOURCE DOCUMENTS AND CASE RECORD FORM

- Verify condition, completeness, legibility, accessibility of the investigators source data file.
- Determine whether subjects who were enrolled and /or completed the study meet inclusion and exclusion criteria;
- Determine whether subject received the test drug with respect to dose and frequency specified according to the protocol;
- Determine whether safety/ efficacy end point data was collected and reported in accordance with the protocol;

- Does medical record mentions subject ID/ name /hospital registration number / and indication that subjects are participating in a clinical trial
- Whether all adverse events were reported in CRF;
- Compare the source document with CRF and determine whether source data have been correctly transcribed in CRF;
- Verify whether all SAE's have been reported to the sponsor (within 24 hours) and EC (within 7 working days);
- Verify whether adequate medical care have been given to the subject especially in the event of inter current illness, adverse events including abnormal lab parameters.
- Verify the causality assessment report of serious adverse events (SAEs) including deaths.
- Report details of SAE including deaths which are related to clinical trials.
- Verify and report details of compensation provided in case of study related injuries or deaths. In case of no compensation has been paid, reason for the same should be obtained and documented from both the Sponsors and Ethics Committee.

ETHICS COMMITTEE (EC) / INDEPENDENT ETHICS COMMITTEE (IEC)

- Identify the name , address of the EC/ IEC in the approval letter and compare it with that stated in investigators undertaking;
- Verify if IEC approval letter mention study code , Protocol title and version number of the protocol, list of other documents reviewed, list of members present at the meeting, quorum of five members as specified in Schedule Y satisfied, date, time , venue of the meeting, signature and date of member secretary / Chairman;
- In case the site does not have an IEC, verify whether following are in place:

- Statement of the investigator / institution that approval granted by another IEC would be abided by & statement from the approving IEC that they would take responsibility for ongoing supervision of the site;
- Has the investigator submitted reports of all SAEs to the IEC and appraised the EC/IEC about the trial progress?

SPONSOR

VERIFY/ DETERMINE:

- Whether a clinical trial Investigators agreement has been signed for this study with the sponsor;
- Whether investigator maintains copies of all reports submitted to the sponsor;
- Whether all SAE are reported to sponsor within 24 hours;
- Whether all CRFs were submitted to sponsor after completion of study;
- Whether all dropouts and reasons thereof were reported to sponsor;
- The method and frequency of monitoring the progress of the study by the sponsor;
- Whether a log of onsite monitoring visit is maintained at the site;

TEST DRUG ACCOUNTABILITY

- Review individual subject record to verify the correct dose administration with respect to dose, frequency, route of administration;
- Determine whether unqualified /unauthorised persons administered/dispensed the test drug
- Determine whether adequate record of qty. of test drug received , dispensed/ destroyed/returned is maintained ;
- Determine whether storage condition/monitoring method are as per protocol/recommendation;
- Whether trial medication are maintained under controlled access;
- Have un-used trial medications been returned to the sponsor or disposed of according to protocol? In case of destruction at site, is there a certificate of destruction on file?
- Are the drugs dispensing records being maintained properly?

- Are the records for reconciliation of all IPs received from the sponsor maintained?

RECORD RETENTION

- Is adequate space available at the site for retention of documents
- Determine whether documents are maintained properly and for the period as specified and necessary measures have been taken for accidental and premature destruction;
- Determine who maintained custody of the documents and means for assuring prompt action;

CONCLUDING THE INSPECTION

The inspector should conclude the inspection with final discussion with the Investigator. During discussion the inspector should explain inspection finding .The inspector may also issue a list of observation at the conclusion of inspection.

INSPECTION OF CRO/SPONSOR

The inspection includes verification of essential documents to compare practice and procedure followed by the CRO/Sponsor to that committed in the clinical trial application and GCP guidelines published by DGHS, Govt. of India and Schedule-Y as well as other applicable regulatory requirements. Inspection of CRO/Sponsor can be conducted without prior notice.
During inspection following aspects may be verified.

DOCUMENTS SUBMITTED TO CDSCO AND REGULATORY APPROVALS OBTAINE.

- Clinical Trial application and DCGI approval letter
- Import license application(Form 12) and import licence obtained (Form 11)Copy of license in Form 29 from (State Licencing Authority) SLA (in case of manufacture of test drugs)
- Export NOC for biological samples
- List of investigators
- Investigator Undertaking (as per Appendix VII of Schedule Y)
- Investigator's brochure
- Protocol and Protocol amendments
- Patient Information Sheet and Informed Consent Form
- Case Record Form
- Ethics Committee approval and notifications to CDSCO
- Unexpected and Serious Adverse Event Reports
- Study report

ORGANISATION AND PERSONNEL

- Company profile and overall structure,
- Organization chart for management of the clinical trial, Structure and responsibilities for all activities involving investigational products. Departments, functions, and key personnel responsible for Protocol development,

Investigator's brochure, Case Record Form, Informed consent form (ICF), translations and amendments ,Selection of investigators, Regulatory approval, Ethics Committee (EC) approval, Monitoring, Quality assurance Adverse Event (AE) Reporting, Data Management , Statistical Analysis, Electronic Records/Clinical Database, Clinical Supplies-Investigational Products (IP) Archival.

- Identify and determine the personnel responsible for following

- Authority to review and approve study documents
- For final evaluations and decisions in the review of study
- For obtaining & reviewing adverse events and reporting to CDSCO
- Monitors/CRO(s) with job descriptions and qualifications
- Job description of key stake holders
- Verify clinical personnel training record
- To obtain a list of external service providers and contractors and documentation of the service they provide.
- Verify that SOPs followed for various responsibilities and clinical trial related activities.

SELECTION AND MONITORING OF INVESTIGATORS

- Obtain list of all investigators along with Investigator Undertaking, Signed Investigator Agreements
- Criteria for selection of sites
- Information provided to sites viz.

Informed consent form, Protocol, Reports/publications of previous trials, Investigator's Brochure, Product labelling, Training, All versions and updates etc.

- Investigator’s non-compliance (If any)

- Deviations from CDSCO regulations
- Deviations form protocol
- How sponsor handles serious deviations from approved protocol or Schedule Y /Indian GCP Guidelines.

STEPS FOR CORRECTION

- Verify whether any investigators terminated? Review monitoring reports reported to CDSCO,
- Any Non-compliant investigator /terminated? Reasons?

SELECTION OF MONITOR

- List all monitors for study duration
- Selection criteria for monitors
- Job descriptions/responsibilities
- Qualifications
- Training Records and CVs
- Reporting structure
- Monitoring SOP Frequency, scope and process, Obtain a copy of SOP and check compliance, If no SOPs, interview monitors to check how monitoring was done , Monitoring Plan, Monitoring Reports

➢ Review the Pre trial and periodic trial visit report in respect of following content:

- Process of verifying compliance to protocol
- Process of verifying investigator responsibilities
- Ethics Committee Approvals Amendments/Re-approval Communication-progress reports/SAEs etc Validity / Completeness.
- Informed Consents, Confirmation of consent and process of consent.

- Use of IEC approved forms.
- Adequacy of consent documentation, completeness
- Which CRFs were compared to source docs? When and who verified CRFs against source data (hospital records, office charts, laboratory reports, etc.) at the study site. Form for data verification
- Check copy of any SOPs and guidelines for data verification
- Data correction handling, Compliance to Monitoring Plan, Frequency, Follow up etc.

QUALITY ASSURANCE (QA)

- Verify SOP for QA audits and operation of quality assurance unit
- Describe how the audit and monitoring are separated
- Obtain list of audited trial

ADVERSE EVENTS REPORTING

- Verify sponsor's method for following up of adverse events and for dissemination of AE information to others Investigators:
- Obtain list of SAE reported, Including death
- Verify the timeline for reporting the SAE to CDSCO and other Investigators /EC;
- Verify the causality assessment report of serious adverse events (SAEs) including deaths.
- Report details of SAE including deaths which are related to clinical trials.
- Verify and report details of compensation provided in case of study related injuries or deaths. In case of no compensation has been paid, reason for the same should be obtained and documented from both the Sponsors and Ethics Committee.

DATA COLLECTION AND HANDLING

- Study tabulations: List of all studies for marketing Authorization
- Data Tabulations: Number of subjects. Verify if number in CT application same as marketing Authorization application(compare to CRFs submitted)
- If any subjects not included in the marketing Authorization application? Why not included?
- Review of SOPS to verify compliance to assure the integrity of safety and efficacy data collected from clinical investigators
- Verify that the SOPs were followed and document any deviations
- Deviations/Data queries resolutions
- Statistical processes
- Primary endpoints Compare the tabulations with CRFs and source documents
- Record retention

ELECTRONIC RECORD AND CLINICAL DATABASE:

- Person responsible for designing and developing data base
- Can it be modified, or has it been modified? If so, by whom?
- If the clinical investigator can modify it, how would the sponsor be aware of any changes?
- Validation :Person responsible, Process, Documentation of process
- Error logs maintained for errors in software and systems?
- Do error logs identify corrections made?

DATA COLLECTION

Following aspects may be verified:

- Responsibilities : Authorization to access the system, to enter data and to change data
- Use of electronic data capture or data transcription from paper CRFs into an electronic record
- Audit trail: to record Changes to electronic records, Person Responsible for the change and Time of the change
- Process of data transmission from the clinical investigator to sponsor or CRO

COMPUTERIZED SYSTEM SECURITY

Following aspects may be verified:

- Management of system access e.g. access privileges, authorization/de-authorization procedures, physical access controls
- Records of authorized personnel , Names, Titles. Description of their access privileges

- Access methods e.g., identification code/password combinations, tokens, biometric signature, electronic signatures, digital signatures
- Data security in case of disasters, e.g., power failure
- Contingency plans and backup files
- Controls in place to prevent data from being altered, browsed, queried, or reported via external software applications that do not enter through the protective system software

INVESTIGATIONAL PRODUCT(IP)

Following aspects may be verified:

- Transferred data from central lab to sponsor
- Integrity Procedures to ensure integrity of IP from manufacturing to receipt by the clinical investigator.
- If IP met required release specifications by review of the Certificate of Analysis?
- Storage of IP and the conditions of storage
- Process of verification of IP integrity during shipment to investigator.
- IP label
- If the test article was recalled, withdrawn, or returned?

ACCOUNTABILITY

Following aspects may be verified:

- Names and addresses of clinical investigators receiving IP Shipment, date (s), quantity, batch number.
- Final disposition of the test article.
- Detailed audit if serious violations are suspected.
- Sufficient records to reconcile IP usage (compare the amount shipped to the investigators to the amount used and returned or disposed of).
- Check whether all unused or reusable supplies of IP returned to the sponsor when either the investigator(S)

discontinued or completed participation in the clinical investigation, or the investigation was terminated. If the test article was not returned to the sponsor, describe the method of disposition and determine if adequate records were maintained.

REPORTING OF INSPECTION

The Inspection should be documented in writing in both during and after inspection. After the inspection a narrative report containing details of inspection finding should be prepared and submitted to CDSCO (HQ).

INSPECTION OF BIO EQUIVALENCE STUDIES

Inspection of the facilities carrying out BA/BE study should be carried out as per the inspection format given below: -

BIOANALYTICAL AND STATISTICAL PART

Name and address of the Site

Date: **Inspectors:**

VISIT OF THE ALB AND GENERAL ORGANIZATION

1. General organization of the site

Activity

Ask for the presentation of the laboratory and its general activities. Try to determine in particular.
Does the test facility management ensure that principles of GLP are complied with in its facility?

Personnel

Ask for an organization chart of the laboratory and note the following points:
Number and categories of people employed

- Description of the qualifications, training and experience (CVs) and job responsibilities of the personnel.
- The review of these points should be more through for the personnel who worked on the trial, especially the experience of the people in charge of the method validation and analysis of the samples for the trail.

Quality Assurance

Ask for a description of the quality assurance system set up at the laboratory.
Check the existence, availability, accessibility and validity of the SOP's (ask for the list of the operating procedures used for the study)

Quality Assurance System	YES	NO	NC/NA
Does a Quality Assurance system exist in the test facility to ensure that studies performed are in compliance with the Principles of Good Laboratory Practice?			
Are records of qualifications, training, experience and job description for each professional and technical individual maintained.			

2. Visit of Facilities

	YES	NO	NC/NA
General			
Is the test facility of suitable size, construction and locations to meet the requirements of the study and to minimize disturbance that would interfere with the validity of the study?			
Does the design of the test facility provide an adequate degree of separation of the different activities to assure the proper conduct of the study?			
Facilities for Handling Test and Reference Items			
To prevent contamination or mix-ups, are there separate rooms or areas for receipt and storage of the test and reference items.			
Archive Facilities			
Are archive facilities provided for the secure storage and retrieval of study plans, raw data, final reports and samples of test items?			
Does the archives design and conditions protect the contents from untimely deterioration?			
Waste Disposal			
Is the handling and disposal of wastes carried out in such a way that the integrity of studies is not jeopardized? (This includes provision for appropriate collection, storage and disposal facilities, and decontamination and transportation procedures).			

3. Apparatus, Materials and Reagents

	YES	NO	NC/NA
Is the apparatus (including validated computerized systems) used for the generation, storage, and retrieval of data, and for controlling environmental factors relevant to			

the study, suitably located and of appropriate design and adequate capacity?			
Is the apparatus used in a study periodically inspected, cleaned, maintained and calibrated according to SOP's?			
Are records of these activities maintained?			
Is calibration, where appropriate, traceable to national or international standards of measurement?			
Does the apparatus and materials used in a study interfere adversely with the test systems?			
Are chemicals, reagents and solutions labelled to indicate identity (with concentration if appropriate), expiry date and specific storage instructions?			
Is information concerning source, preparation date and stability available? (The expiry date may be extended on the basis of documented evaluation or analysis?			

4. Test and Reference Items

	YES	NO	NC/NA
Are records maintained for test item and reference item characterization, date of receipt, expiry date, and quantities received and used in studies?			
Are handling, sampling and storage procedures identified in order that the homogencity and stability are assured to the degree possible and contamination or mix-up are precluded?			
Does storage container(s) carry identification information, expiry date, and specific storage instructions?			

5. Standard Operating Procedures

	YES	NO	NC/NA
Does the test facility have approved written			

SOP's intended to ensure the quality and integrity of the data generated by that test facility?			
Are revisions to SOPs approved by the test facility management?			
Does each separate test facility unit or area have current SOP's relevant to the activities being performed therein available immediately? (Published text books, analytical methods, articles and manuals may be used as supplements to these SOPs).			

STUDY SPECIFIC INSPECTION

1. Organization and Quality assurance

	YES	NO	NC/NA
Was the quality assurance in place at the time of the study?			
Were all the raw data of the study, logbooks, chromatograms, etc available?			
Were the qualification, background and experience of the study director appropriate?			
Were the personnel involved in the study trained on GLP?			
Was a pre study meeting organized where adequate information was given to all staff involved in the trial?			
Were monitor and audit reports available?			
Was the washout period compatible with the half life of the analyte?			
Note: The wash out period should ideally be equal to or more than five half life's of the moieties to be measured.			

2. Apparatus, Materials and Reagent

	YES	NO	NC/NA
Identify individual items of apparatus or special equipment used in the study, and examine the calibration, maintenance and service records for these items.			

Review the records relating to the stability of the test substances, analyses of test substance and formulations.			
Was the certificate analysis (COA) of teh reference standard available?			
Was the purity of the reference standard mentioned on the COA used in the calculations?			
Was the duration of the storage of the solution supported by the stability study data?			
Were the number of Quality Control and number of calibration samples prepared, consistent with the number of results reported?			

3. Method Validation

	YES	NO	NC/NA
Was the bioanalytical method used to determine drug/metabolite well characterized, standardized, fully validated and documented to yield reliable results that can be satisfactorily interpreted?			
Note: The validation of the analytical method can be envisaged to consist of two distinct phases. ***The prestudy*** involves the validation of the method on biological matrix human plasma samples and spiked plasma samples. ***The study phase*** in which the validated bioanalytical method is applied to actual analysis of samples to confirm the stability, accuracy and precision.			
Pre Study: Does following characteristics of the bioanalytical method evaluated and documented to ensure the acceptability of the performance and reliability of analytical results.			
1) Stability: a) Does the stability of the drug and/or active metabolites in the biological matrix under the conditions of the experiment (including any period ofr which samples are stored before analyses) established.			

b) Was the freezing and thawing cycles repeated at least three times? c) Does the absence of absorption by sampling containers and stoppers established?			
2) <u>Specificity / Selectivity:</u> It is the ability of an analytical method to differentiate and quantify the analyte in the presence of other components in the sample.			
Was the data generated to demonstrate that assay does not suffer from interference by endogenous compounds, degradation products, other drug likely to be present in study samples, and metabolites of the drug (s) under study?			
3) <u>Sensitivity:</u> is the capacity of the test procedure to record small variations in concentration.			
a) Was the chosen analytical method capable of assaying the drug/metabolites over the expected concentration range?			
b) Was sensitivity ensured at the lower limit of quantification?			
4) <u>Precision and Accuracy:</u> Precision is the degree of reproducibility of individual assays and Accuracy is the degree to which the "true" value of the concentration of drug is estimated by the assay.			
a) Were replicate analyses of samples containing known amounts of the analyte done for the determination of accuracy and precision?			
b) Were a minimum of three concentrations in the range of expected concentrations found used as recommended (low, medium, high) for the determination of accuracy and precision?			

Note: Where low is the vicinity of the lowest concentration to measured, high is a value in the vicinity of Cmax and medium is a suitable intermediate value.			
c) Was the intra assay precision determined at each concentration level around the mean not above 15% coefficient of variation (CV) except for the LLOQ, where it should not exceed 20% CV?			
d) Was the inter assay precision determined at each concentration level around the mean not above 20% CV?			
e) For accuracy, was the mean value within 15% of the theoretical value.			
5) <u>Recovery:</u> Is there a documentation of extraction recovery at high, medium and low concentrations.			
6) <u>Range of Linearity:</u> Does the quantitative relationship between concentration and response adequately characterized over the entire range of expected sample concentrations.			
<u>Note:</u> For linear relationships, a standard curve should be defined by at least five concentrations. If the concentration response function is non-linear, additional points would be necessary to define the non-linear portions of the curve. Extrapolation beyond the standard curve is not acceptable.			
7) <u>Analytical system stability:</u> Does the reproducibility of the standard curve monitored to assure that analytical system remains stable over the time course of the assay.			
<u>Note:</u> A minimal design would be to run analytical standards at the beginning and at end of the analytical run.			
<u>Study Phase:</u> In general, with acceptable variability as defined by validation data, the			

analysis of biological sample can be done by single determination without a need for a duplicate or replicate analysis. The need for duplicate analysis should be assessed on a case-by-case basis. A procedure should be developed that documents the reason for re-analysis.			
Was the standard curve generated for each analytical run for each analyte?			
Quality control samples:			
Was the quality control sample prepared and stored as recommended.			
Repeat analysis:			
a) Was the reason for repeat analysis stated.			
b) Was the criteria for repeat analysis determined prior to running the study and recorded in the protocol/Lab SOP.			
Were the source documents (chromatograms, validation data of analytical methods used and calibration status of the instruments) identified, dated and signed?			

STATISTICS

	YES	NO	NC/NA
Does appropriate statistical methods used for data analysis			
Does sample size adequate for the study			
Does statistical procedures specified in the protocol (The protocol should specify methods for handling drop outs and for identifying biologically implausible outliers)			
Does this procedure lead to a decision scheme which is symmetrical with respect to the two formulations			
Does calculated 90% confidence interval for AUC and Cmax fall with in the range of 80-			

125%			
Does non parametric 90% confidence interval for Tmax lie within a clinically acceptable range			

FINAL REPORT

	YES	NO	NC/NA
General:			
Is the final report of the study prepared			
Is the final report signed and dated by study director and scientist involved in the study to indicate the acceptance of responsibility for the validity of the data			
Does the corrections and additions to final report in the form of amendments			
Does the amendment specify the reason for corrections or additions			
Does these amendments signed and dated by the study director			
Content of the Final Report:			
Does final report include (as a minimum) the following sections,			
A descriptive title			
Table of contents			
Name and address of the sponsor			
Name and address of any test facilities and test sites involved			
Name, credential and address of the responsible investigators and their signatures			
Experimental starting and completion dates.			
Description of study design			
Identification of test and reference item			
Report of protocol deviations			
Demography data of subjects			
Details of dropout and withdrawal			
Results			
An evaluation o and discussion of the results and where appropriate conclusions			
Archival of data			

INSPECTION
OF
BIOEQUIVALENCE STUDIES

CLINICAL PART

Name and address of the site

Date: Inspectors:

INSPECTION PROCEDURE CLINICAL PART

1. **General organization of the site**

Ask for an organization chart of the company and note the following points:

- Number of staff including Doctors (Physician fulltime/On call), (Pharmacist and Nurse, Nursing assistant and Lab. Tech
- Description of the qualifications, training and experience of the personnel (CVs)
- Training program and records.

Check the existence, availability, accessibility and validity of the standard operating procedures. Ask for a list of the standard operating procedures used for the trial.

2. **Quality Assurance**

Ask for a organization chart of the organization and note the following points:

- Number and categories of people employed.
- Description of the qualifications, training and experience of the personnel (CVs)
- Training program and records.

Quality Assurance System	YES	NO	NO/NA
Is a quality assurance system established?			
Are records of training and assessment of knowledge of GCP maintained?			
Is there a list of sample signatures of authorized personnel?			

Visit of the Facility

Facility	YES	NO	NO/NA
Facility			
Is DCGI operating license available?			
Was adequate space and facility available to house at least 16 volunteers			
Was adequate are available for dining			
Was adequate are available for recreation			
Was adequate are available for sleeping			
Any hospital attached in case of emergency?			
Additional space and facility should be provided for the following			
Office and administrative function			
Sample collection and storage			
Instrumental Laboratory			
Documentation archival room			
Facility for cleaning, washing and toilets			
Adequate resources			
Potential for recruiting the required number of suitable subjects within the agreed recruitment period?			
Adequate number of qualified staff for the foreseen duration of the trial to conduct the trial properly and safely			
Were qualification, readiness to use and maintenance of blood pressure measure device, X-ray devices and ECG			

recorder satisfactory?			
Was the space and number of beds suitable for the studies conducted?			
Was the blood sampling area designed and equipped to avoid mix ups and confusion between subjects and samples.			
Were the different watches synchronized?			
Intensive Care Unit			
Were the storage conditions appropriate and the drugs within their expiry dates?			
Was the readiness to use and maintenance of oxygen supply device appropriate?			
Was the readiness to use and maintenance of defibrillators and electronic monitoring system adequate?			
Clinical Laboratory			
Was qualification, readiness to use and maintenance of the equipment used adequate?			
Were expiry dates of reagents monitored			
Was the use and frequency of quality control adequate?			
Were the final results signed by qualified persons (not a technician			
Blood processing area			
Was the system set up to avoid any confusion between samples (preparation and labelling of sampling tubes, distribution and handling the tubes)			

Was the qualification, readiness to use and maintenance of the centrifuges appropriate?			
Was the qualification, readiness to use and maintenance of deep freezers appropriate?			
Was there an alarm in case of failure and SOP on intervention in case of alarm?			
Were records of temperatures available?			
Pharmacy			
Were premises, storage conditions (segregation of products, temperature and humidity) adequate?			
Were records of shipments, delivery, receipt storage, retain, destruction and possibly returns kept and available?			
Archiving			
Was access to archive storage areas controlled, restricted and recorded?			
Were the records kept under conditions that will prevent deterioration including protection from fire?			
Are the records are maintained for at least 2 year after the expiration date of the batch			
Documentation of file movements			
Did quality systems exist?			
Are the standard operating procedures available?			

3. **Study specific inspection**

	YES	NO	NO/NA
Responsibilities			

Did the contract describe any transfer of responsibility?			
Up-to-date curriculum vitae of investigators /staff			
A list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties?			
Were the responsibilities in all areas described or allocated prior to initiation of study			
Was there any insurance cover for the study?			
Protocol			
Was the version number of protocol used in the study versus the version number of the approved protocol identical?			
Protection of trial subjects			
Was the independence of Ethic Committee satisfactory?			
Was the time taken for the review of the study protocol and related documentation sufficient?			
Consent form			
Were informed consent forms signed by all subjects ?			
Was the language and level of complexity adequate for the volunteers?			
Was the information on compensation and insurance in case injury provided and understandable ?			
Was the information on quality of blood taken and sampling method (multi-puncture or canula) given?			
Responsibilities of the investigator			
Was a CV of principal investigator available and up to date?			

Was given to all staff involved in the trial?			
Were the signatures of the staff involved in the study recorded?			

	YES	NO	NO/NA
Responsibilities of sponsor and monitor			
Was the study monitored?			
Was the monitor present at least 3 times during the study (site assessment prior to study, staff education, during study and end of study)?			
Was the monitor independent from the Quality Assurance department?			
Were the monitoring reports and audit reports available and documented before release of the final study report?			
Record keeping and Handling of Data	**YES**	**NO**	**NO/NA**
Were case report forms used?			
Was each page of the case report identified for the subject and study?			
Were the lab results, ECG, vital signs before and after administration (temperature, Blood pressure, X-rays, consistent and coherent?			
Was the data reported on the CRF derived from source documents are consistent with the source documents?			
Were all corrections to CRFs and to raw data made in a way which does not obscure the original entry (with reason if not obvious and initials of investigator)?			
Was the selection of the subjects based on the inclusion			

and exclusion criteria documented?			
When deviations occurred, were they explained in accordance with the protocol?			
Was the dosing procedure described in an SOP?			
Were records of dosing (Administration) including mouth check and the date and time of dosing for each subject available as per SOP?			
Did the documentation of dosing confirm that each subject received the product dispensed for that subject and that for each product received the identity was checked?			
Was, after check of the records, the dosing done according to the randomization code?			

Were standardized meals, snacks and drinks planned and provided to study subjects in accordance with the clinical trial protocol?			
Was the clinical report prepared?			
Was the data reported in the clinical report derived from source documents?			
Biological Samples Handling and Accountability	**YES**	**NO**	**NO/NA**
Were there documented procedures for the collection, preparation, transport and storage of samples?			
Was the labelling of collected samples clear to ensure correct identification and traceability of each sample?			
Was the equipment used for taking the samples sterile, within its shelf-life and for single use?			
Were the people in charge of blood sampling appropriately			

qualified and experienced?			
Were the actual time of sampling documented?			
Was the following details are explained in the protocol, Anticoagulant Centrifugation: speed, duration, temperature			
Was there a record of the storage and retrieval of the samples			
Was the storage and retrieval procedure defined in an SOP?			
Were the packages, boxes or containers adequately identified?			
Were the storage conditions (temperature, etc.) monitored and recorded?			
Were the refrigerators and freezers equipped with a temperature recording system?			

Pharmaceutical Products Handling and Accountability	**YES**	**NO**	**NO/NA**
Were all study medication kept in a securely locked area accessible only to authorized persons?			
Were records of the products used available as dosage form, strength, batch number, expiry date, certificate of analysis, other coding that identifies the specific characteristic of the product tested?			
Was the shipping letter of the test and reference products from the sponsor to the investigator available?			
Were the records of delivery and receipt of the test and comparator products available?			

Was the investigational product stored properly?			
Were the investigational products labelled for clinical research purpose only?			
Was the dispensing done according to the randomization code			
Archive facilities	**YES**	**NO**	**NO/NA**
Was access to archive storage areas controlled, restricted and recorded?			
Were the records kept under conditions that will prevent deterioration including protection from fire?			
Documentation of file movements			
Inspection preliminary conclusion based on the number of findings	**Total of findings**		
Critical finding (s)			
Major finding (s)			
Other finding (s)			
Conclusion			
Are additional information requested as a follow up of the inspection to reach a conclusion?			
Area additional information requested as a follow up of the assessment to reach a conclusion?			
The study was found done at an acceptable level of compliance with GCP?			