NOTICE

Dated: 28.07.2014

Subject: Stakeholders suggestions/comments on Clinical Trials conductance in India

During the briefing on CDSCO, Hon'ble Minister of Health & Family Welfare desired that there should be complete transparency and accountability in functioning of CDSCO.

Prof. Ranjit Roy Chaudhary Committee has also recommended that Information Technology should be used in all steps of a clinical trial to ensure transparency and faster dissemination of information among the stakeholders.

In pursuance to this, it has been decided that latest technology and modern tools are adopted by CDSCO in its regulatory functions including grant of approvals/ licences, enforcement etc.

In the first phase, CDSCO proposes to create an IT enabled system for online submission of various information on clinical trials to streamline the process of approval, maintaining comprehensive database and monitoring of clinical trials for ensuring the protection of rights, safety and well beings of trial subjects and authenticity of the data generated.

All concerned are requested for suggestions/comments within three weeks time to the Office of Drugs Controller General India through e-mail "dci@nic.in" or by fax 011-23236973 or by post to Central Drugs Standard Control Organization, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, FDA Bhavan, ITO, Kotla Road, New Delhi -110002

The details of the proposal is appended below:

CONTENT FOR COMMENTS

PROPOSAL FOR CREATION OF IT ENABLED SYSTEM FOR CLINICAL TRIALS

CDSCO proposes to create an IT enabled system for online submission of various information on clinical trials to streamline the process of approval, maintaining comprehensive database and monitoring of clinical trials for ensuring the protection of rights, safety and well beings of trial subjects and authenticity of the data generated. Looking at the current regulatory environment of clinical trial in India, it is important that all information related to 4 major domains of CT are captured through online in an organized manner. These domains are:

1. Sponsor/ CRO
2. Investigator
3. Ethics Committee (EC)
4. Patient

In order to capture exact information, all the sponsors/CROs, Investigators & Ethics Committees are required to put the information in a common repository related to a particular CT which is updated by the stakeholders on day to day basis.

It is proposed to have an IT enabled system where a Sponsor/applicant needs to submit the information related to clinical trial which pertains to full title of the trial, sponsor's protocol code number, name or abbreviated title of the trial where available. The additional information will include details for the identification of the Sponsor, local applicant identification, brief description of the investigational product, information on the use of placebo, information regarding the use of the comparator, site/ warehouse responsible for the release of the investigational medicinal product, brief summary of the protocol which includes the medical condition in which the trial is proposed, information regarding the disease prevalence in India, whether the disease is a rare disease, main objective of the trial, principal inclusion and exclusion criteria and the endpoint of the study. This information should also include the scope of the trial, whether the trial is diagnostic, prophylactic, therapeutic, safety, efficacy,

pharmacokinetic, pharmacodynamic, bioequivalence, dose response, pharmacogenomic, or other.

Applicant should also provide information regarding the trial design, which includes randomized, controlled which is open, single or double blind, parallel or cross over design.

The information regarding the investigational sites includes the complete details of the Investigators, correspondence addresses of the sites, contact details and email address of the Investigators. The detail regarding the team of the Investigator also needs to be disclosed on this system. If the trial is multi-country the details regarding the countries participating in the trial and number of sites and patients expected from those countries should also be disclosed.

The information should also include details of targeted patient population planned to be enrolled in the trial or whether any high risk or vulnerable patients are included in the trial. This includes infants, children, women of childbearing potential, lactating women, etc.

The complete details of the ECs responsible for the oversight of the trial should be given. The details should include, name and address of the EC, name of the Chairperson, and details of all members of the EC etc.. Details should also include the frequency of the meetings of the ECs. The ECs should also give the details on any duties or functions which are delegated.

Once this information regarding particular trial is put in the system,it would generate a Unique Identification Number (UIN) which is specific to a particular clinical trial. The CDSCO will keep track of all information in the system with the UIN. Once the UIN is granted to a Sponsor/applicant, they need to share the same with Investigators and the ECs, so that they can maintain the database on day to day basis.

The expectation is that whenever any patient is enrolled in a clinical trial, the Investigator or the site should disclose the details of enrolled patients including name, address, annual income, age, sex, qualification, name of nominee etc. of the trial subject, details of Serious Adverse Events (SAEs), if any, observed while the subject is on the trial and the outcome of the SAEs. In case clinical trial related SAEs, the details of the compensation paid/ claimed also needs to be captured.

Similarly the ECs should upload the minutes of every meeting conducted and any guidance/ instructions given to Sponsor/ Investigator.

The responsibility to update the information should be time-bound and a dedicated cell in CDSCO will monitor this activity. In case of any deviation, the regulatory authority may give instructions to put a hold on new recruitment in the trial and depending on the accountability, action against the Sponsor/ Investigator/ EC may also be taken.

As mentioned above, the concerned Sponsor/applicant, EC & Investigator will be required to upload detailed information as per **Annexure A** before initiating or making the clinical trial application to CDSCO. Once these informations are entered into the system, it will automatically generate an UIN for the applicant and they will be required to mention this UIN number at the time of filing the application to CDSCO.

Further it is proposed that once the trial is permitted by CDSCO, the concerned Sponsor/applicant, EC & Investigator will also be required to upload detailed information as per **Annexure B** in the proposed system during conduct of the trial on day to day basis. The stakeholders are also required to upload information as per **Annexure C** in the proposed system after completion of the trial and before making the application for Market Authorization.

The system should also have provisions to upgrade the software as and when required by addition or deletion of various elements entered into the system.

This system will be an exhaustive system and will capture all relevant information and will help in ensuring adequate accountability among various stakeholders. This should be considered as a step towards increasing the quality of the clinical trial in India and is in line with the objective of the CDSCO to bring transparency and to work towards patient safety.

Annexure A

Information to be uploaded before initiation of Clinical Trial and making application to CDSCO

A. **TRIAL IDENTIFICATION**

1 Reference number of Sponsor/applicant
2 Full title of the trial
3 Sponsor's protocol code number

B. **IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE TRIAL**

1 Sponsor Organization with complete address, town/city, country, contact no., e mail etc.
2 Legal representative of the Sponsor in India (In case of foreign Sponsor), person/organization, town/city, with full address, contact no., email etc.
3 Status of the Sponsor: commercial or non-commercial
4 Delegation of authority of the Sponsor to the legal representative in India(in case of foreign Sponsor) Y/N

C. **INVESTIGATIONAL PRODUCT (IP) INFORMATION ON EACH INVESTIGATIONAL PRODUCT BEING USED IN THE TRIAL EXCEPT FOR PLACEBOS (to be used either as test, comparator or both):–**

1 Has the IP a Marketing Authorization (MA) in the country?
2 If no to1, has the IP a MA in any other country?
3 In the protocol treatment is defined only by active substance Y/N
4 Has the IP been designated in this indication as an orphan product in any country?
5 If yes, give the details

D. **DESCRIPTION OF THE IP**

1 Product name and product code where applicable
2 Name of each active substance (INN or proposed INN, if available)
3 Other available name for each active substance (CAS, sponsor code, other descriptive name etc)
4 Pharmaceutical form (standard terms)
5 Route of administration (standard terms)
6 Concentration (all strengths to be used)
7 Does the IP contain an active substance:
of chemical origin?
of biological/ biotechnological origin?

8: Is this
1 a cell therapy medicinal product?
2 a gene therapy product?
3 a radiopharmaceutical product?
4 an immunological product (such as vaccine, allergen, immune serum)?
5 a herbal medicinal product?
6 a homeopathic medicinal product?
7 a medicinal product containing GMO(s)?
8 another medicinal product? – specify
9 Is placebo used yes/No

E. **AUTHORISED SITE RESPONSIBLE FOR THE RELEASE OF IP**

1 Who is responsible for the release of the finished IP?
   1.1 Manufacturer or importer or both (tick box)
   1.2 Organization, town/city, Country
   1.3 Identify the products released at this site

F. **GENERAL INFORMATION ON THE TRIAL**

1 Medical condition or disease under investigation
2 Specify the medical condition (free text)
3 is it a rare disease? In the opinion of the sponsor.
4 Scope of the trial (all yes/no)
   Indicate all which apply: diagnostic, prophylaxis, therapeutic, safety, efficacy, pharmacokinetic, pharmacodynamic, bioequivalence, dose response, pharmacogenomic, pharmacoeconomic, others(specify)
5 Trial type and phase:
   1 Human pharmacology (phase I)
   2 Exploratory (Phase II)
   3 Confirmatory (Phase III)
   4 Post Marketing trial (Phase IV)
   5 Is it a first administration to humans?
   6 Bioequivalence study
   7 Other (specify)
6 Design of trial:
   8.1 Randomised
   8.2 Controlled
   8.3 Placebo controlled
   8.4 whether standard care allowed
   8.5 Concomitant medication
9 Compensation policy to meet the requirements as per the Drugs & Cosmetics Rules.

G. **POPULATION OF TRIAL SUBJECTS (All Yes/No)**
1 Age limit
2 Are any patients under 18 included: Y/N, if Y specify:
3 In Utero
4 Preterm newborn infants (up to gestational age ≤37 weeks)
   4.1 Newborn (0-27 days)
   4.2 Infant and toddler (28 days - 23 months)
   4.3 Children (2-11 years)
   4.4 Adolescent (12-17 years)
5 Adult (18-65 years)
6 Elderly (> 65 years)
7 Gender
   7.1 Male
   7.2 Female
8 Population of trial subjects
   8.1 Healthy volunteers
   8.2 Patients
   8.3 Women of child-bearing potential
   8.4 Pregnant women
   8.5 Nursing Women
   8.6 Emergency situation– if yes specify
   8.7 Subjects incapable of giving consent personally (specify)
   8.8 Other (specify)
9 Planned number of subjects to be included in India:
10 In case of Global clinical trial:
   10.1 Names of participating countries

10.2 Names of countries where the trial protocol is already approved
10.3 Planned number of subjects in India
10.4 Planned no. of subjects globally

H. **ETHICS COMMITTEE**

1 Name and address, Registration no.
2 Name of members, chairman and their qualification/ experience
3 Whether any subject experts were included in the meetings
4 Whether any specific patient group was included in the committee
5 Type of research reviewed by the committee e.g. Pharmaceutical, device, herbals etc.
6 No. of meetings of the committee conducted in respect of the concerned trial
7 Date when the EC was last inspected by CDSCO
8 Opinion
8.1 Given opinion:
8.2.1 Date of opinion
8.2.2 Favourable or non-favourable and date

I. INVESTIGATOR (SITE WISE)

1. Name of investigator, complete address, contact no., email etc.
2. Registration no.
3. Whether GCP trained
4. Years of experience in relevant field and details of CTs conducted so far
5 Name and address of Pathology lab for testing and whether GLP certified
6 Undertaking of investigator as per appendix VII of schedule Y Y/N

J. INFORMED CONSENT DOCUMENT

1. Whether patient information sheet mentions all essential elements as per appendix V of schedule Y Y/N
2. If no, details thereof

Annexure B

Information to be uploaded during the conduct of Clinical Trial

A. DATE OF INITIATION OF TRIAL

B. **WHETHER ANY DSMB APPOINTED, IF YES, DETAILS THEREOF**

C. NAME OF MONITOR OF THE TRIAL, HIS ADDRESS, PHONE NO.

D. ETHICS COMMITTEE

1 Opinion
  1.1 Date of opinion
  1.2 Favourable or non-favourable
2 Competent Authority concerned:
3 Name, town/city, country
4 Clinical Trial approved/refused
5 Date of approval or rejected

E. **AMENDMENTS TO THE PROTOCOL OR THE REQUEST**

1 Substantial amendment to the protocol:
  1.1 Amendment code number
  1.2 Date of Amendment
2 Ethics committee opinion on substantial protocol amendment
  2.1 Date of opinion concerning the amendment
  2.2 Favourable or non-favourable
3 Regulatory approval of substantial protocol amendment
  3.1 Protocol Amendment approved/refused
  3.2 Date of approval or rejected
4 Substantial amendment to request:
  4.1 Amendment code number
  4.2 Date of Amendment
5 Regulatory approval of substantial amendment to request
  5.1 Amendment to request approved/refused
  5.2 Date of approval or rejected
6 Ethics committee opinion on substantial amendment to request
  6.1 Date of opinion
  6.2 Favourable or non-favourable

F. Details of Trial subjects (Site wise)

1 No. of subjects enrolled actually with address, Age, sex, annual income etc. :
2 No. of patients randomized:
3 Annual income of Patient
4 Nominee of the patient
5 If Minor, Name and address of Guardian
6 If illiterate, Name and address of impartial witness
7 Age limit
8 Are any patients under 18 included: Y/N, if Y specify the no. of subjects enrolled/randomized:
9 In Utero
10 Preterm newborn infants (up to gestational age ≤37 weeks)

10.1 Newborn (0-27 days)
10.2 Infant and toddler (28 days - 23 months)
10.3 Children (2-11 years)
10.4 Adolescent (12-17 years)

11 Adult (18-65 years)

12 Elderly (> 65 years)

13 Gender

13.1 Male
13.2 Female

14 Population of trial subjects

14.1 Healthy volunteers
14.2 Patients
14.3 Women of child-bearing potential
14.4 Pregnant women
14.5 Nursing Women
14.6 emergency situation– if yes specify
14.7 Subjects incapable of giving consent personally(specify)
14.8 Other (specify)

G. DETAILS OF SAEs REPORTED: PATIENT WISE

Name of the patient with address, DOB, Gender, socio-economic background with annual income

1 Nature of SAE: injury/ death
2 Nature of trial: Cardiology/ Oncology/Pulomonology…….?
2 In case of death, cause?
3 Date of event:
4 Name and address of EC
5 Opinion of Investigator
6 Opinion of EC
7 Opinion of Sponsor
8 Causality analysis: Related/not related/……
9 Date of reporting to EC and sponsor
10 Date of reporting to Licensing Authority
11 Details of compensation recommended
12 Details of compensation paid with date and mode of payment
13 Name of beneficiary

Annexure C

Information to be uploaded after completion of Trial

A. DECLARATION OF THE END OF THE CLINICAL TRIAL- site wise

1 Date of the end of the trial
2 Is it the completion of the trial
3 Is the trial terminated early? Yes/No specify reason(s)
  3.1 Safety
  3.2 Lack of Efficacy
  3.3 Not commenced
  3.4 Suspended
  3.5 Other
4 Is it a temporary halt?
5 Decision of CDSCO on temporary halt?
6 Details of the patients dropped and reasons

B. INSPECTION OF CLINICAL TRIAL SITES

Inspection reference number
1: Was the inspection?
  1.1 Trial specific –
    1.1.1 CDSCO number (repeat as needed for several trials)
    1.1.2 Sponsor protocol code number in case of third country inspection of protocols without a CDSCO number
  1.2 System or facility inspection (not clinical trial specific)
  1.2.1 Specify system or facility
2 Type of site (drop down list)
3 date of on-site inspection
4 Name and address of site
5 Inspection outcome

C. INSPECTION OF INVESTIGATIONAL PRODUCT MANUFACTURER/IMPORTER

Inspection reference number
1 date of inspection
2 Inspecting authority
3 Site inspections – name and address of site
4 Type of site manufacturer, importer, manufacturer/importer
5 Was the inspection part of the site authorisation process;
  5.1 Initial authorisation inspection
  5.2 Re-inspection
6 was the inspection part of the control of a particular product(s)?
  6.1 Specify product(s)
7 Was the inspection part of the control of a particular trial(s)?
  7.1 Specify the CDSCO number(s) or if there is no CDSCO number specify the sponsor protocol code number(s)
8 Inspection outcome

D. DETAILS OF SAEs REPORTED: PATIENT WISE

Name of the patient with address, DOB, Gender, socio-economic background with annual income
1 Nature of SAE: injury/ death

2 Nature of trial: Cardiology/ Oncology/Pulomonology…….?
2 In case of death, cause?
3 Date of event:
4 Name and address of EC
5 Opinion of Investigator
6 Opinion of EC
7 Opinion of Sponsor
8 Causality analysis: Related/not related/……
9 Date of reporting to EC and sponsor
10 Date of reporting to Licensing Authority
11 Details of compensation recommended
12 Details of compensation paid with date and mode of payment
13 Name of beneficiary