No.12-01/14-DC Pt. 47/DFQC
Government of India
Ministry of Health & Family Welfare
Department of Health and Family Welfare
(DFQC Section)

Nirman Bhawan, New Delhi
Dated the 6th November, 2015

Office Memorandum

Subject: Presentation made before Secretary (HFW) on issues relating to conduct of clinical trials – forwarding of minutes – regarding.

The undersigned is directed to refer to the presentations made before Secretary (Health and Family Welfare) on 20.8.2015 and 6.10.2015 on the issues relating to conduct of clinical trials followed by deliberations on the said issue and to forward herewith a copy of the approved minutes of the said deliberations.

(R. G. Singh)
Under Secretary to the Government of India
Tele: 23063019

To

1. Secretary, D/o Health Research and Director General, ICMR, Ansari Nagar, New Delhi
2. Director General of Health Services, Dte.GHS, Ministry of Health and Family Welfare, New Delhi
3. Dr. Y. K. Gupta, Head, Department of Pharmacology, All India Institute of Medical Science, New Delhi
4. Drugs Controller General (India), CDSCO, FDA Bhawan, Kotla Road, New Delhi

Copy to: PS to Secretary (H&FW) / PPS to AS (KBA) / PS to DGHS / PPS to JS (KLS) / Director (D)

(R. G. Singh)
Under Secretary to the Government of India

Minutes of the meeting of meeting held on 06-10-2015 at 1600 hrs in Committee Room No. 155 A, Nirman Bhawan, New Delhi on Clinical Trials related issues

The following were present.

D/o Health and Family Welfare:

1. **SHRI BHANU PRATAP SHARMA**, Secretary, Ministry of Health and Family Welfare- in Chair
2. **SHRI K.B. AGGARWAL,** Additional Secretary, Ministry of Health and Family Welfare
3. **SHRI K.L. SHARMA**, Joint Secretary, Ministry of Health and Family Welfare
4. **DR. SHAILENDRA KUMAR**, Director, Ministry of Health and Family Welfare

D/o Health Research

5. DR. SOUMYA SWAMINATHAN, Secretary, DHR and DG, ICMR

DGHS

6. **DR. JAGDISH PRASAD**, Director General, Health Services

CDSCO

7. DR. G.N. SINGH, Drugs Controller General of India, CDSCO
8. DR. V.G. SOMANI, Joint Drugs Controller (I), CDSCO

Experts

9. **PROF. (DR.) RANJIT ROY CHOUDHARY**, Chairman of the Committee for framing policy for approval of new drugs, clinical trials and banning drugs
10. **DR. Y.K. GUPTA**, Professor & Head of Department of Pharmacology, AIIMS, New Delhi

Secretary, Department of Health & Family Welfare extended welcome to everyone to the meeting for discussing the remaining issues on clinical trial in continuation to the meeting dated 20-8-2015 [Minutes attached below].

2. A brief review of issues discussed on 20/8/2015 was undertaken. The decisions taken on that day were ratified with some further comments on the issue of clinical trial for academic/research purposes wherein it was reiterated that the permission of DCG (I) shall not be required in such trials provided that the trials were approved by Ethics Committee and are not for regulatory submission. DCGI however, would need to be informed and its no-objection, if any, should be awaited for 30 days. However, various examples of such cases shall be spelt out in the guidance document

3. Thereafter the remaining issues were discussed:

A. Non uniform working of various subject experts in the subject expert committee:

After detailed deliberations, it was agreed that SoPs will be prepared for subject experts to bring uniformity in their functioning and one request can be made to review the decision of Subject Expert Committee.

B. Sequential approval of clinical trial protocol requiring permission of DCGI after each phase of trial.

It was pointed out that after each phase of trial, prior permission of DCGI is required as per rules to proceed for next phase of trial (i.e phase I to phase II & phase III etc). This procedure delays the trial project especially, if it has to go through all three tiers. It was noted that there wass a need to review the results of each phase and by DCG(I) before proceeding to next phase and the current, therefore, practice may continue.

C. Issues regarding need for removing the practice of repetition of preclinical/toxicological studies if it is already done as required by the Hon'ble Minister of Govt. of India, Smt. Maneka Gandhi.

The Committee noted the recommendation of the IND committee and the DTAB that if a drug was already approved outside India after conducting pre-clinical and toxicological studies on animals, it shall not be required to be repeated while approving their proposal for import/ manufacture in India unless there were specific concerns. The concerns, however, needed to be recorded in writing.

D. Requirement of approval of RCGM (DBT) for r-DNA derived drugs like Insulin, Monoclonal antibody, etc.

Before submission of application to DCG (I) for clinical trials, prior clearance/permission of Review Committee for Genetic Manipulation (RCGM) is required for preclinical animal toxicity studies. Since the processing of clearance are serially, considerable time is lost during the process.

In order to cut delays, it was agreed that the applicant may submit parallel application to DCG (I) and RCGM. However, DCG (I) shall complete the scrutiny of application and issue permission.

E. GEAC clearance from Ministry of Environment and Forests (MOEF) before grant of marketing authorization of drug / vaccine containing live modified organism.

Before grant of market authorisation of any drugs/vaccines containing Living Modified Organisms (LMOs), clearance from Genetic Engineering Appraisal Committee (GEAC) of the Ministry of Environment, Forests and Climate Change required to be obtained.

The Office of the DCG (I) refers such cases to the Department of Animal Husbandry, Ministry of Agriculture (for veterinary products), who further refer such cases to GEAC.

The Department of Animal Husbandry thereafter does not evaluate proposals till clearance from GEAC is received.

Concerns have been raised that (GEAC) meetings are not being conducted regularly causing delay in grant of marketing authorization to such drugs/vaccines mainly for veterinary products.

After deliberations, it was noted that the Department of Animal Husbandry, Dairying and Fisheries may be requested to evaluate proposals parallely for safety and efficacy without waiting for prior approval of GEAC & forward their comments to the DCG (I) with the condition that their final decision may be taken only after the approval of GEAC was received. It was also decided that the Ministry of Environment and Forests may be requested to hold meetings of GEAC regularly.

4. The Meeting ended with thanks to and from the chair.

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Minutes of the meeting held on 20-08-2015 at 1500 hrs in Committee Room No. 155 A, Nirman Bhawan, New Delhi on Clinical Trials related issues

The following were present.

D/o Health and Family Welfare:

1. **Shri Bhanu Pratap Sharma**, Secretary, Ministry of Health and Family Welfare- in Chair
2. **Shri K.B. Aggarwal,** Additional Secretary, Ministry of Health and Family Welfare
3. **Shri K.L. Sharma**, Joint Secretary, Ministry of Health and Family Welfare
4. **Dr. Shailendra Kumar**, Director, Ministry of Health and Family Welfare

D/o Health Research

5. **Dr. Soumya Swaminathan**, Secretary, DHR and DG, ICMR
6. **Dr. Roli Mathur,** Scientist E, ICMR

DGHS

7. **Dr. Jagdish Prasad**, Director General, Health Services

CDSCO

8. **Dr. G.N. Singh**, Drugs Controller General of India, CDSCO
9. **Dr. S.E. Reddy**, Joint Drugs Controller (I), CDSCO
10. **Dr. V.G. Somani**, Joint Drugs Controller (I), CDSCO

Quality Council of India

11. **Dr. K.K. Kalra**, Director, NABH, QCI
12. **Dr. B.K. Rana**, Joint Director, QCI
13. **Dr. Deepti Mohan**, Additional Director, QCI

Experts

14. **Prof. (Dr.) Ranjit Roy Choudhary**, Chairman of the Committee for framing policy for approval of new drugs, clinical trials and banning drugs
15. **Dr. Y.K. Gupta**, Professor & Head of Department of Pharmacology, AIIMS, New Delhi
16. **Dr. Nilima Kshirsagar**, Professor, ICMR, Mumbai
17. **Dr. Shripad Banawali**, Professor oncology, Tata Memorial Hospital

Secretary, Department of Health and Family Welfare extended welcome to everyone to the meeting. On being asked by Secretary, HFW, Shri K.L. Sharma, Joint Secretary (R), informed that the agenda included two issues relating to clinical trials *viz.* (a) accreditation of Ethics Committees, Investigators and Clinical trial sites; and (b) Discussion on stakeholders concerns and the way forward relating to some issues on conduct of clinical trials in India. He briefly recapitulated the background and informed the current status of issues and steps taken by the Quality Council of India on the basis of a decision taken by the Department about accreditation. He also apprised that clinical trial related issues have been discussed at different *fora* earlier by the representatives of academic institutions and industry associations and the concerns covered in the presentation have been raised in those meetings and a number of representations have also been received in this regard. In response to a query from Secretary, DHR, he clarified that the objective of today's meeting was to (i) take decisions about the next steps in the accreditation process; and (ii) seek guidance about the manner in which the concerns expressed by stakeholders on some of the existing guidelines/ rules, etc. could be addressed.

2. Thereafter, with the permission of the Chair, Dr. Kalra, Director, NABH, QCI made a detailed presentation on the modalities for rolling out the accreditation process. After detailed presentation by the QCI, it was

felt that the accreditation process could commence in phases. It was opined that if the accreditation of all the three components *i.e.* Ethics Committees, Investigators and clinical trial sites is taken up simultaneously, the resurgent workload on OCI may become unmanageable and may adversely affect clinical trials. It was, therefore decided that though accreditation of all three would be desirable, the process could commence initially with the Accreditation of Ethics Committees (ECs). It was also felt that the ECs would need to be strengthened to ensure that the trial sites met all the requirements for proper conduct of trial and Investigators are competent to conduct clinical trials.

3. It was also felt that the fee to be charged for accreditation should be so structured that it did not act as a deterrent for smaller organizations/ institutions and thus become an impediment to Clinical Trials in India. It was decided that since only Ethics Committees were proposed to be accredited, fee could be suitably reduced. The fact that the QCI worked on self-sustaining model through revenue generation was duly noted. Taking into account all these factors, it was decided that the fee charged to meet the expenditure on issues such as assessment and accreditation, etc. would need to be rationalized and the QCI could come up with a revised proposal.

4. Keeping in view the need to empower the Ethics Committees, the development of standardized guidelines, procedure, and training material ensuring uniformity in its working was felt necessary. Professor Y. K. Gupta mentioned that the consortium approach needed to be adopted for this purpose. It was decided that guidelines/ procedure can be evolved by a Committee comprising DG, ICMR, CDSCO and Dr. Y.K. Gupta, HoD, Pharmacology, AIIMS. The Committee may also seek inputs from other experts /stakeholders as and when required. It was decided that once the ECs were empowered, depending upon the risk and complexity

involved in a clinical trial, these would be able to take appropriate decisions.

6. Thereafter Dr. Somani, JDCI made a detailed presentation on the concerns raised at different *fora* and possible solutions. These included:

(A) Restriction of conducting three clinical trials per investigator

I. After detailed discussion, it was decided that the restriction of three trials per investigator is not based on any scientific basis and had been fixed arbitrarily keeping in view the situation prevalent at that point of time. During the discussion, the need to strengthen the Ethics Committees was underlined so that these could take decisions about the number of trials that can be allowed to be taken up by an investigator keeping in view the risk and complexity involved in the trials being conducted/ proposed to be undertaken. It was also decided that a guidance document will be prepared for the purpose by a small Committee to be chaired by Dr. Y.K. Gupta, Professor and HoD, Pharmacology, AIIMS, and a few other experts. The document so prepared may also be shown to DG, ICMR and Secretary DHR for inputs/ concurrence before finalisation.

II. It was also decided that in no case, an Ethics Committee should be headed by the Head of the Institution as it gives rise to conflict of interest and suitable clarification for the purpose be issued.

III. Since the decision to have not more than three clinical trials per investigator had been placed before the Supreme Court earlier, it was decided that any change in the policy would be first placed before the Supreme Court.

(B) Requirement of 50 bedded site for clinical trial

I. The concerns and possible solutions were presented. After detailed discussions, it was considered that the number of beds may not always be the deciding criteria for choosing a Clinical Trial site. It was noted that such a requirement, may not be applicable in case of OPD based trials. It was noted at the same time that the trial site, where 'in-patient' based Clinical Trials are conducted, needed to have emergency rescue and care arrangements along with all other necessary facilities required for that particular Clinical Trial which must be clearly brought out in the Clinical Trial protocol. It was noted that management of the maximum possible adverse events associated with such trials should be possible within the trial site. As regard the suitability of any particular site. It was decided that the Ethics Committee would be the most appropriate forum to take a call looking at the requirements as well as the available factors. Appropriate guidelines for this needed to be evolved. It was decided that subject to suitable guidelines being developed, the restriction on the number of beds need not be there. However, if this had been placed before the Supreme Court earlier, it was decided that the change in policy would have to be first placed before the Apex Court.

(C) Audio-visual recording for informed consent.

It was noted that new rules had already been framed and this issue had already been addressed and no further action was considered necessary at this stage. Secretary, D/o Health and Family Welfare directed that Hon'ble Supreme Court may be suitably apprised.

(D) NOC from DCGI for addition of new clinical trial site or investigator.

After detailed deliberations, it was decided that the Ethics Committee after due diligence can approve proposals for addition of site(s) and investigator(s) and no NOC from DCGI in the normal course, should be necessary. A view was also expressed that DCGI would needs to be kept in picture regarding the addition of new sites because otherwise they may not be able to exercise adequate supervision. In the light of the above, it was decided that the DCGI would be informed about any such addition/ deletion and thereafter if no objection was received, it would be deemed to have the concurrence of CDSCO.

(E) Permission for conduct of clinical trials for academic/ research purposes that are Non Regulatory in nature.

It was noted that the clinical trial for academic/research purpose did not require permission of DCGI. However, it was also noted that at times there were some overlapping issues where prior clearance was necessary. It was decided that the Ethics Committee of the respective Institution may be permitted to take a view. They should inform the DCGI about the cases where permission of DCGI was not required. In case, if no objection was received from DCGI within 30 days, the clearance of DCGI may be presumed.

(F) Waiver of Local Clinical Trial requirement for new drugs already approved in other countries.

After detailed discussions, it was decided that the matter needed further deliberation and it was decided that an Expert Committee may prepare the list of serious/ Life threatening diseases and diseases of special relevance to India along with the principles on the basis of which the waiver for bridging clinical trials in India can be given to the Drugs already approved in other countries. Till such time, the principles are approved, the waiver may continue to be

considered in accordance with the criteria already specified with the recommendations/ approval of the Technical and Apex Committees.

7. Owing to paucity of time, other items included in the presentation could not be taken up for consideration and it was decided that one more meeting be convened to address these issues. Copies of the presentations made by QCI and CDSCO are at Annex I and II, respectively. The meeting ended with thanks to and from the chair.

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