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Indian Ministry of Health and Family Welfare Amends Informed Consent Rules



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On July 31, 2015, the Indian Ministry of Health and Family Welfare (the ''Ministry'') enacted a regulatory change that modifies the informed consent rules for clinical trial subjects. Most significantly, the amendment cuts back on the requirement that an audio-video recording of the informed consent process be obtained for all subjects in all trials. However, as discussed below, the extent of the cutback is unclear because the amendment leaves open important questions regarding scope. The amendment also requires that two specific statements on clinical trial effectiveness be included in the consent form; unlike the audio-video language, this requirement is straightforward, but will require those responsible for the informed consent process to review consent forms to ensure that these statements are included in future consents.

Audio-Video Recording of Informed Consent Process

In November 2013, the Ministry's Central Drugs Standard Control Organization (the ''CDSCO'') issued an order stating that ''in all clinical trials, in addition to the requirement of obtaining written informed consent, audio-[video] recording of the informed consent process of each trial subject . . . is required.''[1] The order emphasized that the audio-video recording requirement was ''applicable to the new subjects to be enrolled in *all* clinical trials including Global Clinical Trials.''[2] Upon issuing this broad mandate, India appears to have become the only country to mandate audio-video recording for all clinical trial subjects. By contrast, the U.S. Food and Drug Administration (''FDA'') *recommends*—for illiterate English-speaking patients only—a ''video tape recording of the consent interview.''[3]

The July 31, 2015, regulatory change takes the form of an amendment to the informed consent requirements (preceded by a proposed amendment in 2013, which was subject to public comment) in Schedule Y of the Drugs and Cosmetics Rule, 1945. Before the change, Schedule Y only set out that ''a freely given, informed, written consent is required to be obtained.''[4] The Ministry published the proposed amendment on June 7, 2013. The proposed amendment was consistent with the CD-

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[1] CDSCO, F. No. GCT/20/SC/Clin./2013 DCG1 at 1 (Nov. 19, 2013), *available at* http://www.cdsco.nic.in/writereaddata/Office%20Order%20dated%2019.11.2013.pdf. The CDSCO order uses the term ''audio-visual recording,'' whereas the proposed and final amendment use the term ''audio-video.'' There does not appear to be a meaningful distinction, and therefore for consistency we use the latter formation in all instances here.

[2] *Id.* (emphasis added).

[3] FDA, *A Guide to Informed Consent – Information Sheet* (last updated June 25, 2014), *available at* http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm.

[4] Drugs and Cosmetics Rules, 1945, Schedule Y (''Schedule Y''), § 2(4)(i).

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SCO order that was issued later in the same year, stating that Schedule Y would be amended to include an audio-video recording requirement for all subjects: ''An audio – video recording of the informed consent process of individual subject, including the procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record.''[5]

The final amendment, enacted July 31, 2015 (the ''Amendment''), cuts back on the universal nature of the audio-video recording requirement found in the draft amendment and CDSCO order.[6] Taking the form of a new subsection to Schedule Y, Section 4, the Amendment sets forth that an audio-video recording must be maintained by the investigator ''in case of vulnerable subjects in clinical trials of New Chemical Entity or New Molecular Entity.''[7] For anti-HIV and antileprosy drug-related trials, only an audio recording must be maintained.[8]

This revision to the audio-video recording requirement is a welcome change. It unmistakably cuts back, to some extent, on the universal nature of the requirement in the draft amendment and the CDSCO order and it will therefore, to some extent, reduce the burden and cost of obtaining consent in India. However, the magnitude of this cutback is not clear. Significantly, the Amendment does not explain which patients will be considered ''vulnerable'' and therefore trigger the audio-video recording requirement. There is some guidance in the existing language of Schedule Y, which mentions ''vulnerable subjects'' in the section on ''Responsibilities of the Ethics Committee''—which is located just after the section on ''Informed Consent''—and provides this illustrative list of such subjects:

> e.g., members of a group with hierarchical structure (e.g. prisoners, armed forces personnel, staff and students of medical, nursing and pharmacy academic institutions), patients with incurable diseases, u[n]employed or impoverished persons, patients in emergency situation[s], ethnic minority groups, homeless persons, nomads, refugees, minors or others incapable of personally given consent.[9]

Nonetheless, until the Ministry provides clarification, there will be uncertainty surrounding who is a ''vulnerable'' subject under the new provision in Schedule Y, and such uncertainty is likely to force investigators to proceed with universal recording until guidance is offered.

Additionally, on its face, the rule applies only to certain investigational products. The audio-video recording requirement is for ''vulnerable subjects in clinical trials of *New Chemical Entity* or *New Molecular Entity*.'' As the draft version of the amendment did not include the ''New Chemical Entity'' and ''New Molecular Entity'' qualifiers, this contrast between the draft and final rules suggests that the appearance of these qualifying terms in the final rule is not a drafting error, and that the recording requirement now applies only in the narrow range of trials of new chemical and molecular entities.

Additional Information in Informed Consent Form

The Amendment also adds two statements to the ''checklist of essential elements to be included in the study subject's informed consent document'' in Schedule Y to the Drugs and Cosmetics Rules, 1945, at Appendix V. The statements are as follows:

14. Statement that there is a possibility of failure of investigational product to provide intended therapeutic effect.

15. Statement that in the case of placebo controlled trial, the placebo administered to the subjects shall not have any therapeutic effect.[10]

Those responsible for drafting informed consent forms should carefully review whether this language exists (either in form or in substance) in the existing informed consent documentation for subjects in India, and incorporate statements 14 and 15 where they are not already part of the informed consent form. The amended language does not appear to be retroactive, and therefore there should be no need to revisit forms that have been executed.

Conclusion

In short, while the Amendment appears to reduce the scope of the audio-video recording requirement for clinical trials in India, the full impact of this new language remains to be seen. Most importantly, the Ministry will need to provide additional clarity about who is a ''vulnerable subject'' before those involved in administering the informed consent process can view the Amendment as a break away from the universal audio-video recording requirement. Additionally, those responsible for the informed consent process should ensure that the two additional statements about therapeutic effect discussed above are included in all informed consent forms for clinical trial subjects in India moving forward.

Clinical trial sponsors and investigators will need to monitor closely the developments related to clarification of these issues as well as any additional rules or modifications that may come into effect in the near future, as the Ministry continues to re-evaluate its existing clinical trial regulatory regime. Less than one month after the Amendment was enacted, the Ministry's Technical Committee, which assists the Secretary of the Ministry in supervising and monitoring the con-

[5] Ministry, *Notification: G.S.R. 364(E)* (June 7, 2013).
[6] Ministry, *Notification: G.S.R. 611(E)* (July 31, 2015).
[7] *Id.* ¶ 2.
[8] *Id.*
[9] Schedule Y, § 2(5)(i).
[10] Ministry, *Notification: G.S.R. 611(E)* at ¶ 2.

duct of clinical trials,[11] recommended waiving the three-trial-per-investigator rule that is currently in effect for all trials in India. This ruling came in a specific phase III trial then before the Technical Committee, which found that the trial should be ''allot[ed] a special status,'' thus allowing investigators in the trial to exceed the three-concurrent-trial limit per investigator.[12] This recommendation, which would lift the three-concurrent-trial limit now in effect, may well be adopted by the Ministry, but the legal status of a Technical Committee recommendation is less firm than that of an Office Order or other more authoritative regulatory issuances.

[11] The Technical Committee was created in 2013 as part of the Ministry's efforts to ''put into place a system of supervision of clinical trial of new chemical entities.'' *Minutes of the Meeting Held on 27-2-2013 Under Chairmanship of DGHS for Supervising Clinical Trials on New Chemical Entities in the Light of Directions of the Hon'ble Supreme Court of India on 03.01.2013* at 2, available at http://www.cdsco.nic.in/writereaddata/1st%20Minutes%20of%20meeting%20under%20DGHS%2027-02-2013.pdf. As part of this system, the Technical Committee ''meet[s] every month to oversee the conduct of clinical trials and give its recommendation to the [final approval authority] for taking further appropriate action.''

[12] *Minutes of 28th Meeting of the Technical Committee Held on 21.08.2015 Under the Chairmanship of DGHS for Supervising Clinical Trials on New Chemical Entities in the Light of Directions of the Hon'ble Supreme Court of India on 03.01.2013* at 4-5, *available at* http://www.cdsco.nic.in/writereaddata/Final-Minutes-of-28th-Techinical-Commitee-21-08-2015.pdf.