

GLOBAL HARMONISATION TASK FORCE

STUDY GROUP 5 – CLINICAL EVIDENCE

Minutes of Meeting Wednesday 14 September and Thursday 15 September 2005

Hilton Hotel, Gaithersburg, Maryland, USA

The third meeting of the Global Harmonisation Task Force (GHTF) Study Group 5 was held at the Hilton Hotel in Gaithersburg, Maryland, U.S.A. on 14 and 15 September 2005.

Apologies were received from Dr. Graeme Harris, Chair of the Group, as well as Susanne Ludgate, Wolfgang Ecker, Maria Teresa de Martin, Klaus-Dieter Willamowski and Mary Anne Hinkson who were unable to attend this meeting. Dr. Eric Mann, Food and Drug Administration, USA, served as the Acting Chair. Other attendees at the meeting were:

Johan Brinch, MIAA, AUSTRALIA
Kazuhiro Sase, Juntendo University Medical School, JAPAN
Yoshihiro Noda, JFMDA, JAPAN
Peter Rattke, COCIR, AUSTRIA
Alain Prat, AFSSAPS, France (September 14th only)
Christophe Bailleul, EUCOMED, BELGIUM
Kimber Richter, Food and Drug Administration, USA
Gregory Campbell, Food and Drug Administration, USA
Joanne Less, Food and Drug Administration, USA
Mitchell Krucoff, Duke University Medical Centre, USA
Patricia Garvey, AdvaMed, USA
Keith Butler, Health Canada, CANADA
Greg LeBlanc, MEDEC, CANADA

Mr. Atsushi Tamura, Coordination Director, Office of Medical Devices, Pharmaceuticals and Medical Devices Agency Japan also attended the meeting as an observer.

Item 1 Welcome and introductions

The Acting Chair welcomed members to the third meeting of Study Group 5. Members of the group were invited to introduce themselves for the benefit of new attendees.

Item 2 Adoption of agenda

There were no changes to the draft agenda circulated in advance of the meeting. It was noted that Yoshihiro Noda asked for a discussion of the role of risk management which was tabled until a future meeting. Thus, the following agenda was adopted:

1. Welcome, introductions and housekeeping information
2. Adoption of agenda
3. Minutes from previous meeting

4. Harmonisation of definitions
- Revision of SG5/N1R2
5. Guidance for clinical evaluation
- Consideration of SG5/N2R1
6. Standards relating to clinical investigation
- Report from ISO/TC 194 WG4 members
7. Consideration of SG1's Conformity Assessment document
8. Appointment of a Vice Chair for SG5
9. Other business
10. Next meeting

Item 3 Minutes of previous meeting

Members were thanked for their feedback on the draft minutes from the May 2005 meeting. One minor wording change resulted from the feedback in relation to item 5: the request was for a definition of "investigation site" rather than "institution" as originally drafted. After incorporating this change, the minutes were sent to the GHTF Secretariat for posting on the website on 22 June 2005. The highlights of the London meeting were briefly reviewed with the group as a basis for the current meeting's agenda.

Item 4 Harmonisation of definitions--revision of SG5/N1R2

The group reviewed this document and proposed edits. The definition of "clinical performance" that was developed at the previous meeting was added as well as definitions for "monitor" and "investigation site". The figures were discussed. Figure 2 was deleted due to concerns that it had not been formally endorsed by any group within GHTF and may not accurately represent certain aspects of the developmental/regulatory pathway for medical devices (e.g. the depiction of risk analysis/management within the model).

A revised version of Figure 1 was also developed. The output of clinical data should be shown by an arrow as feeding into the process of clinical evaluation. It was noted that clinical evaluation should be represented as a continuous process. It was also suggested that a more linear chart using standardized symbols for processes, outputs, decisions, etc., would be easier to comprehend and use. Johan Brinch drafted an alternative figure using these symbols which will be circulated among the group for consideration. It was noted that the document does not include all the definitions used in the Clinical Evaluation document. The group thought this document should be made comprehensive, but did not make the changes. It was also noted that section 2.2 is similar in this document and the clinical evaluation document and should be updated if necessary based on latest thinking about the clinical evaluation process. Perhaps there should be a footnote referencing the other document as well.

The group was optimistic that with final review and editing the document will be ready for the Steering Committee before or shortly after the next SG 5 meeting. Dr. Mann will send the latest version to Dr. Harris who will circulate it to the group.

The group also discussed the question of how best to incorporate guidance on *in vitro*

diagnostic devices (IVDs) into the definitions and clinical evaluation documents. It was also a topic of discussion at the joint meeting with SG 1. Study Group 1 described their experience addressing IVD issues in several documents. They have had some difficulties and find that it may be cleaner to prepare parallel but separate documents for use by this specialized industry group. It was also noted that there might not be sufficient IVD clinical research expertise amongst current SG 5 members. The consensus of the joint meeting was that SG 5 might best proceed with IVD's by establishing a subgroup and writing separate but parallel documents, especially for the clinical evaluation process. This was tabled for further discussion at the next meeting.

Item 5 Guidance on clinical evaluation

Members reviewed the draft guidance on clinical evaluation. The group addressed some basic organizational issues as well as specific edits. The decision was made to split out at least three sources of information for the clinical evaluation – scientific literature, clinical use, and clinical investigation - and to describe the process for evaluating them in separate sections. This general breakdown of information sources corresponds well with the sources of clinical data as depicted in Figure 1 of the N1 draft document. The scientific literature section will now include only published literature. Unpublished clinical experience was discussed separately under a new section on clinical experience. The group began to work on this section, but was unable to complete a draft of the section before the end of the meeting. The last section on clinical investigation was not discussed.

There was significant discussion about whether pre-clinical information should be part of the clinical evaluation process. In some diagrams it has been shown feeding into the STED and conformity assessment process separately, in other diagrams it appears to be a factor in clinical evaluation. If it is part of the clinical evaluation process, then a fourth source of information that includes bench testing, laboratory work and animal testing might need to be added to the document.

There was discussion about whether all devices require a clinical evaluation to demonstrate conformity with essential principles. The group was in general agreement that the depth of the evaluation should be flexible so that well known and low risk devices do not require unduly burdensome documentation. However, no final consensus or decision was reached on whether a clinical evaluation should always be required for all devices.

The group briefly discussed the relationship of this document to the STED and conformity assessment documents of Study Group 1. It was discussed further during the joint SG 1 and SG 5 meeting. Some language may need to be added to the clinical evaluation document to clarify the integration of these concepts and documents. No final decision or wording was decided.

Item 6 Update on ISO TC 194 WG 4 Meeting

The members received copies of a summary of the recent ISO TC 194 WG 4 meeting in advance. Kimber Richter led discussion of the key points. The group felt that GHTF could provide some standardized guidance on the labelling of investigational product, and this should be discussed by SG 5 and SG 1. It was also suggested that ISO 14155 include brief wording on this topic.

The ISO Working Group had suggested that SG 5 write a guidance on the harmonized regulation of ethics committees and informed consent for medical device investigations, along with related issues. (Wording was provided by ISO that might serve as the basis of such a guidance document.) SG 5 determined that this work would be challenging, and was not on the initial priority list. There was some interest in considering it as a future work item for a subcommittee within the group.

ISO TC 194 WG4 has agreed to keep the lead on the format and content of final reports for clinical investigations, with SG 5 reviewing the draft language.

Item 7 Consideration of SG1's Conformity Assessment Document

The group discussed SG1's Conformity Assessment Document (SG1(PD)/N040/R15) in order to provide feedback during the combined SG1/SG5 meeting later in the afternoon on 15 September. In general, the group commented that the document was well written and ready for wider circulation and public comment. With respect to having a summary of clinical requirements for conformity assessment, the group thought it would be more appropriate to cross-reference the Clinical Evaluation (N2) guidance within the SG1 document. The group stressed the need to harmonize definitions for "Clinical Evaluation" and "Clinical Investigation" in Essential Principles SG1/N041 and SG5 documents and expressed a desire to discuss with SG1 how the Clinical Evaluation (N2) guidance should work with SG1's STED, the Conformity Assessment Document, and Classification Document. Additionally, SG5 recognized the importance of post market in the continuous and ongoing Clinical Evaluation process as part of Quality Systems (as emphasized in the Conformity Assessment document). Additional areas of discussion with SG1 were identified:

- Relative to the progress of Conformity in device classification, should SG5 begin to consider device class specific recommendations for Clinical Evaluation?
- Roles of the Study Groups, contents of deliverables, stages of work or trajectories of work (i.e., coordination of work plans between the two groups where there are areas of overlap).

Item 8 Appointing a Vice Chair for SG 5

The group discussed the request from the Steering Committee that a Vice Chair be appointed, preferably from industry. Greg LeBlanc offered to serve in this role, and the group agreed. His name will be forwarded by Dr. Mann to the Chair. If Dr. Harris agrees he will forward the recommendation to the Steering Committee.

Item 9 Other

The group discussed plans for the next meeting. It was agreed that a third day should be scheduled. The meeting will now tentatively be planned for January 16, 17 (and likely) the 18th of January, 2006 in Sydney, Australia.

Members revised and agreed to a statement that would be used by the Chair if approached by the media.

Members noted correspondence from EUROM VI TC Medical Technology Technical Committee. It was noted that Peter Rattke is a member of that group, and he was asked to be a liaison point between the two groups.

Item 10 Next meetings

- Gaithersburg: Combined Meeting with SG1 on afternoon of 15 September and combined SG Meeting on 16 September 2005
- Sydney: SG5 Meeting 16 - 18 January 2006
- Lubeck, Germany: SG5 Meeting 26 and 27 June 2006; GHTF Conference 28-30 June 2006

Addendum:

Combined Meeting with SG1 on 15 September 2005

A brief presentation of SG5's activities was given by Dr. Kimber Richter during this afternoon session. There were few comments on the draft definitions (N1) document. However, SG1 members expressed strong interest in reviewing the clinical evaluation guidance when it is ready for circulation. SG1 members recommended that IVDs be considered separately and early on in SG5's work plan and work products by individuals with expertise in this area. In general, SG1 appeared to favour referencing SG5's clinical evaluation guidance in the STED document rather than incorporating it into the STED.

Dr. Ginette Michaud, SG1 Chair, presented an overview of SG1's activities and opened the floor for discussion of the Conformity Assessment Document. Dr. Mann conveyed the SG5's comments as summarized in Item 7 in the above meeting minutes.

Combined SG Meeting on 16 September 2005

Dr. Kimber Richter presented an overview of SG5's terms of reference, work plan, and accomplishments to date which was well received by the combined SGs.