

Report of the 1st meeting of the JCTLM Executive Committee

1 March 2004, BIPM Sèvres

List of participants:

Prof J. Thijssen (JCTLM Chairman, IFCC)
Dr R I Wielgosz (JCTLM Secretariat, BIPM)
Prof J-C. Forest (IFCC)
Dr R. Kaarls (BIPM)
Dr W.E. May (JCTLM WG1 Chair)
Prof M.Muller (IFCC)
Dr L. Penberthy (ILAC)
Dr H. Schimmel (JCTLM WG1 Chair)
Prof L. Siekmann (JCTLM WG 2 Chair)
Mr A. Squirrell (ILAC)
Prof L. Thienpont (JCTLM WG 2 Chair)
Prof A. Wallard (BIPM)

Report of meeting:

1. JCTLM Framework and Declaration of Cooperation [JCTLM-EXEC-04-01]

Prof Thijssen opened the meeting and reported that the Declaration of Cooperation establishing the Joint Committee for Traceability in Laboratory Medicine (JCTLM) had been signed by the IFCC, ILAC and the BIPM, thus formally establishing the JCTLM.

1.1 JCTLM membership [JCTLM-EXEC-04-02,03,04,05,06]

Dr Wielgosz pointed out that the Declaration of Cooperation document contained an Appendix 1, in which organizations which had been granted member status of the JCTLM (in accordance with Appendix IV: Participation of Organizations in the JCTLM) would be listed. He stated that letters inviting organizations, which had already expressed interest in the JCTLM, to apply for membership would be sent out in the next few weeks.

Prof Muller confirmed that it was important that other professionals' organizations participated and were members of the JCTLM. He agreed that IFCC would provide the Secretariat with a list of the appropriate organizations and people, to whom letters for application for membership should be sent.

Mr Squirrell pointed out that there were some discrepancies in the lists of members of the JCTLM working groups and that, for example, Dr Penberthy's name was missing from the WG1 members' list.

Dr Kaarls reported that together with Prof Wallard and Dr Wielgosz he had recently visited WHO and met with Dr Steffen Groth (Director, Department of Essential Health Technologies) who had recently taken over the WHO department dealing with Biological Standards. The WHO was not currently a member of the JCTLM, but had provided input into its meetings. Dr Groth was interested in finding out more about possible further interactions.

ACTIONS:

- (A1) Prof Muller/IFCC to provide JCTLM Secretariat with contact names and details of professionals' organizations to be invited to apply for membership of the JCTLM (29 March)**
- (A2) JCTLM Secretariat to send out 'invitation to apply' letters (14 April)**
- (A3) JCTLM WG Chairpersons to provide the Secretariat with up to date lists of their members (14 April)**

2. JCTLM WG1 report – current status [JCTLM-EXEC-04-16]

2.1 Approval of reference materials and reference methods for publication [JCTLM-EXEC-04-15]

Dr May presented an overview of the work of JCTLM Working Group 1 to date, and particularly its activities in collating and reviewing nominated reference methods and materials against the criteria set out in ISO 17511, 15193 and 15194, by selected review teams made up of experts. Only pure materials and materials with blood or urine matrices and corresponding methods were considered in this round of the review process. This review had focused on a selected number of key types of measurand. The types of measurand considered would be extended in the next review round. He summarized that the methods and materials submitted for review had been classed as either: fully compliant with the review criteria (α); provisionally acceptable, although not fully compliant (β); or not meeting requirements (γ).

Only those materials and methods that had been classed as either α or β were now presented for approval by the Executive Committee.

Materials and methods were presented for approval in the following lists:

- Category I Reference Methods;
- Category I Reference Materials;
- Category II a, Reference Materials;
- Category II b, Reference Materials.

Category I and II had been used following the metrological traceability system outlined in ISO 17511. WG 1 defined Categories I and II as:

Category I. Certified reference materials and reference measurement procedures for well-defined chemical entities with determined values traceable to SI units, and internationally recognized reference procedure-defined measurands; e.g., enzymes are placed in Category I.

Category II. International conventional reference materials where the measurand(s) is/are not metrologically traceable to the SI but which by international agreement are used as reference values for a defined quantity; e.g., WHO reference materials are placed in Category II.

Dr Thijssen replied that the Executive Committee had not had sufficient time to look at the lists currently presented to it in detail, and that it should be given the opportunity to do so. Nevertheless, he asked the Executive to consider each of the lists for approval for publication.

Dr May suggested the Executive should start by considering Category I Reference Methods.

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Prof Muller asked why the list of higher order reference methods contained methods that were considered as routine methods?

Prof Siekmann noted that for certain analytes a primary and a secondary measurement procedure were given for the same measurand, but that there was no link between these procedures. He suggested that this situation could be remedied if the uncertainty associated with measurements using the secondary method was increased so that it covered any bias in relation to the primary procedure.

Prof Thijssen asked why for a particular measurand two methods were listed that were known to give different measurement results?

Dr May answered that the list was one of higher order methods and not highest order methods. He concluded that much of the previous discussion was prompted by the inclusion of the Abell–Kendall method for cholesterol in the list in addition to the IDMS based procedure. He reminded the Executive Committee that the Abell-Kendall method was used throughout the US, and US industry was required to bench-mark its cholesterol measurements relative to this method. It was possible to determine the average bias of the Abell-Kendall method relative to the IDMS procedure, and this was of the order of about 2 %.

Prof Siekmann noted that the comparability of different methods would be demonstrated once the results of the JCTLM WG 2 ring trials (comparisons) were published. He also pointed out that IUPAC conventions for the names of particular analytes were not being used consistently in the lists.

Mr Squirrell insisted that the preamble to a publication should clearly state that a thorough technical peer review of the lists had been performed, and that the list was not simply the result of self-declaration.

Prof Thijssen summarized that it would be reasonable to approve the list as it was, but that the preamble relating to the list would need to clearly state the criteria for the inclusion of all approved methods within the list. He stated that the Category I Reference Materials list was also approved, provided that the preamble was modified accordingly.

Dr May went on to present the reference materials that had been placed in lists Category IIa and Category IIb. He explained that Category II materials were International Conventional Reference Materials, where the measurand is not clearly defined and/or no internationally recognized reference measurement procedure is available. Coagulation factors and nucleic acids had been put into Category IIa, whereas proteins were listed as Category IIb. Category IIa and IIb contained a number of WHO International Standard Preparations. He pointed out that consensus had not been reached by the WG 1 team reviewing proteins, and that all materials that had been submitted remained listed for publication (Category IIb).

Dr. Schimmel pointed out that the review teams did not find objective scientific/technical criteria for exclusion of particular materials. All materials listed had been produced according to stated procedures and, hence, are largely in compliance with the relevant ISO standards. However, a reference material may not be suitable for the calibration of a particular method whereas it would be for another and *vice versa*. To obtain the objective

technical criteria would, in most cases, require major research efforts. Such efforts therefore need to be prioritized. Dr. Schimmel suggested addressing the advantages and disadvantages of the different approaches used for certification of materials in the category II list in the preamble and to point out that the mere existence of a reference material of higher order without properly designed reference methods and/or commutability of the reference material, may have only a limited effect on the comparability of measurements.

Dr May stated that WHO International Standards, provided by definition an internationally recognized measurement standard. Dr Schimmel pointed out that other materials within the lists were also fit-for-purpose and should remain listed, and that the list should not be limited to WHO preparations. He pointed out that for a number of materials, the values assigned were relative to a WHO International Standard, and asked what the status of such materials would be when the WHO standard was replaced by a subsequent WHO preparation? Dr May replied that the lack of reference methods for notionally the same measurand made it difficult to compare reference materials in this category.

Dr Thijssen summarized that a number of issues that needed to be clarified in relation to Category II materials and WHO International Standard Preparations, and that the WHO should be informed of these issues. He asked WG1 to carefully reconsider the materials for publication under Category II and to draft a preamble that clearly stated the criteria for the inclusion of all approved materials within the list

Actions:

- (A4) WG 1 Chairs to redraft preamble for Category I Reference Materials and Methods to arrive at a statement that provides an explanation covering the inclusion of all published materials/methods. To be submitted to the JCTLM Executive for comment, prior to the publication of Category I lists. (submitted 15 March)**
- (A5) WG 1 Chairs and review teams for Category II reference materials to redraft a preamble for Category II Reference Materials that provides an explanation covering the inclusion of all approved reference materials. Preamble and recommended Category II list to be submitted to JCTLM Executive for approval before December 2004.**
- (A6) Prof J. Thijssen to draft letter to WHO on issues of concern related to biological standards for IVDs. (3 May 2004)**

2.2 Review of JCTLM WG1 quality manual [JCTLM-EXEC-04-18]

Dr May presented the draft quality manual for WG1, which had been prepared under the Chairmanship of C. Jackson, with contributions from R. Miller, D.L. Duewer and R.I. Wielgosz. He thanked the group for their hard work in preparing the draft document in a short period of time. He noted that the document had only been distributed during the meeting and that detailed discussion should be delayed until the Executive had been given sufficient time to study the document.

Dr Thijssen stressed that this was an important document that needed to be published to demonstrate the transparency of the process being undertaken within the JCTLM. The

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Executive agreed to provide comments on the document by the end of April, so that a revised quality manual could be presented to it by August.

Dr Wielgosz asked where the checklists for the review of each material were currently being archived. Dr May replied that the review team leaders currently maintained this information. Prof Thijssen noted that in order to maintain the transparency of the process and ensure accessibility to these documents in the case of dispute or query, that a completed check list for each material together with the review team's recommendation should be registered with the JCTLM Secretariat.

Actions:

- (A7) JCTLM Executive to provide comments on draft quality manual to Dr W.May by April 30**
- (A8) JCTLM WG1 (Dr May) to submit revised quality manual to the JCTLM Executive (by 1 August, 2004)**
- (A9) Quality manual to require JCTLM WG1/JCTLM review team leaders to provide JCTLM secretariat with completed review forms for each reviewed material / method for archiving (1 August 2004).**

2.3 Development of the JCTLM website(s)

Dr Wielgosz reported that the approved JCTLM lists would initially be published in Excel format on both the BIPM and IFCC websites. The development of a searchable database for reference materials and methods was being planned, with the database to be developed on the BIPM website with appropriate links made to the IFCC website. The database would not be ready until the end of the year.

2.4 Second call for reference materials and methods

Dr May reported that a second call for nominations of higher order reference materials and methods would go out in the next few weeks.

Actions:

- (A10) Dr May to draft and circulate letter for a second call for the nomination of reference materials and methods. (circulated 16 March)**

3. JCTLM WG 2 report – current status [JCTLM-EXEC-04-18]

3.1 Planned IFCC EQAS rounds

Prof Siekmann gave an update of the activities of WG 2. Approximately 70 laboratories had nominated themselves as being able to perform measurements as a Reference Measurement Laboratory (RML). Information on these laboratories had been sent to the review teams of WG1. Prof Siekmann had already initiated the first IFCC EQAS round, and had invited these laboratories to participate. 45 measurands were proposed in the study, with laboratories given the choice as to which measurements they would perform. Twenty eight of the seventy nominated laboratories participated in the ring trial, and results were still expected from a number of laboratories. Dr Siekmann gave examples of the results of the study without disclosing the identity of the participating laboratories.

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Prof Siekmann reviewed the information which had been requested from laboratories to assess if they could meet the requirements to act as a Reference Measurement Laboratory as described in ISO 15195. He remarked that the IFCC EQAS rounds would provide a means for laboratories to demonstrate their measurement capabilities for particular measurands.

Mr Squirrell stated that ILAC would not support a system where laboratories could be designated as competent Reference Measurement Laboratories based on the results of ring trials alone.

Prof Wallard, referring to the 'declaration of cooperation' establishing the JCTLM, noted that ILAC, IFCC and BIPM had already agreed that 'the technical competence of the laboratories shall be demonstrated by their performance in international comparisons, and their operation of an appropriate quality system. International recognition of the implementation of the quality system is achieved via accreditation or equivalent documented peer review'.

Dr Wielgosz asked what the future plans were for the ring trials, how they should be referred to, where they would be published and whether a quality manual would be prepared describing the process?

Dr Siekmann answered that these ring trails should be referred to as IFCC EQAS, and that the IFCC was developing written protocols describing how the comparisons were to be performed, and how the data would be treated. The current round had been free of charge, but laboratories would need to pay a fee for participation in future rounds, which he anticipated would be organized on a six monthly basis. The protocol of the current ring trial stated that the identity of individual laboratories would not be revealed. However, in future rounds laboratories would be identified, and informed of this prior to their participation in the ring trial. For the present round, the IFCC was considering only publishing the results of those laboratories that agreed to be identified against their measurement result. Publication of the results of the ring trials was currently foreseen either on the DGKC website or the IFCC website, but Prof Siekmann indicated that these published results should eventually be available within a JCTLM database on the BIPM website. The data should then underpin statements on the technical competence of laboratories as RMLs.

Dr Penberthy suggested that PT scheme providers could also provide material for the IFCC EQAS schemes, and that this would be an efficient way of linking the reference values of PT schemes to higher order reference methods. Prof Siekmann replied that he hoped that PT scheme providers would adopt the use of reference values provide by Reference Measurement Laboratories. He pointed out, however, that the provision of reference values for PT scheme materials would be a service offered by RMLs, and this should not be confused with the role of the IFCC EQAS, which should allow RMLs to demonstrate their measurement competence.

Mr Squirrel and Dr May noted that laboratories that had calibration and measurement capabilities (CMCs) within the BIPM key comparison database for relevant clinical measurands should be considered technically competent as RMLs for these measurands

since the criteria for the publication of these CMCs were equivalent to those required to provide a statement on the technical competence of a laboratory as a RML.

Actions:

- (A11) JCTLM WG2 chairs to ensure that data within the BIPM key comparison database and CMC claims for clinical measurands are checked in assessing the list of nominated Reference Measurement Laboratories.**
- (A12) IFCC advisory group to formulate a quality manual / procedures for IFCC EQAS within six months (to be presented to the JCTLM Executive).**

4. Liaison with the EC

4.1 Report of visit with representatives of DG Enterprise

Dr Wielgosz presented a short report on his recent visit to DG Enterprise, summarizing the following key points:

- Experts from the competent authorities and notified bodies in member states are not overly familiar with the issues of traceability or the work of the JCTLM;
- Awareness of the issues of traceability is higher amongst industry;
- It would be appropriate for a presentation on the activities of the JCTLM to be made to the next meeting of experts from the competent authorities of the member states. DG Enterprise will be organizing the next meeting in June/July. This group of experts was responsible for drawing up the Common Technical Specifications (CTS) related to Annex II list A and B materials, where measurement standards have been specified for particular measurands. DG Enterprise will invite representative(s) of the JCTLM to the next meeting of experts. A report of the expert meeting will be tabled at the subsequent meeting of competent authorities of member states.
- DG Enterprise suggested that an effective way to promote the work of the JCTLM to the member states would be through their links to the competent authorities.
- DG Enterprise is not able to provide financial support to initiatives such as the JCTLM.
- Medical devices have not been a high priority item within the EU research programmes. DG Research should be approached for further information on funding possibilities within the 6th Framework Programme.
- The JCTLM should prepare a document on their activities, which DG Enterprise will circulate to experts from member states prior to their next meeting.
- Representatives of DG Enterprise intend to continue to participate in JCTLM meetings.

Actions:

- (A13) JCTLM Secretariat with Working Group Chairmen to produce document on JCTLM activities for EC-DG-Enterprise (May 2004).**
- (A14) DG Enterprise to inform JCTLM Secretariat of next meeting of the expert group from the Member States.**
- (A15) JCTLM secretariat to keep DG Enterprise informed of future JCTLM activities.**

4.2 Formal contact with the EC-DG Enterprise

The JCTLM Secretariat will maintain contact with EC-DG Enterprise.

5. Liaison with ISO TC 212

Dr Siekmann reported that relevant standards developed by Working Group 2 of ISO TC 212 had been voted upon and accepted, and that no further written standards were being prepared.

6. Liaison with the WHO

6.1 WHO-ECBS [JCTLM-EXEC-04-07]

Dr Thijssen stated that it was important to have liaison with the WHO-ECBS on issues of standards and traceability for IVDs. He expressed the opinion that WHO-ECBS should increase the level of its activities in relation to IVDs, and ensure that sufficient resources at the WHO were allocated to this area, and that it would be useful if WHO-ECBS organized a subsection that dealt specifically with biological standards for IVDs. He proposed to write a letter to the WHO on behalf of JCTLM (IFCC, BIPM and ILAC) on this issue.

Actions:

See (A6)

6.2 ISO 17511 and related standards and biological reference materials [JCTLM-EXEC-04-08, 09]

Dr Wielgosz briefly presented documents recently produced by the WHO on biological standards, where statements on traceability and uncertainty were inconsistent with the approach outlined in ISO 17511. He asked how progress could be made in this area?

Dr Schimmel suggested that the JCTLM should collect information on cases where shifts in the value of measurement results had been observed due to a change of the WHO International Standard Preparation.

Dr Thijssen summarized that there had been many discussions on this topic over the last few years, but many issues were still unresolved. He suggested that for progress to be made the JCTLM should organize a scientific workshop in liaison with the WHO on 'Reference measurement systems and traceability for biologicals', with clear examples given on how a traceable system of measurements is applied in the field of biologicals.

Actions:

(A16) Prof Thijssen and JCTLM Secretariat to organize a workshop on 'Reference measurement systems and traceability for biologicals' (December 2004)

6.3 Reference materials for infectious diseases [JCTLM-EXEC-04-10,11,12]

Prof Thijssen outlined the papers which had been submitted to the Executive describing some concerns regarding reference materials for infectious diseases.

7. Publicity for the JCTLM

Prof Thijssen asked what publicity was planned for the activities of the JCTLM.

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Prof Muller stressed that this was an important topic, and that those active in the field of IVDs should be made aware of JCTLM activities.

Several suggestions were made by the Executive: provision of web cards and information leaflets; a letter to regulatory authorities describing the activities; an event at the AACC meeting (July 2004); an article to ISO for the ISO Focus publication.

Actions:

- (A17) JCTLM WG Chairs to organize event at the AACC meeting (edutrak and manufacturer's update) (July 2004)**

8. Future meetings of the JCTLM

8.1 Full meeting of the JCTLM and Symposium

It was agreed that the next meeting of the JCTLM working groups would be held during the AACC meeting (July 2004). The meetings of the working groups would only be open to working group members. A meeting for all stakeholders in JCTLM (JCTLM full meeting) will also be organized during the same AACC meeting in Los Angeles.

Actions:

- (A18) Dr May to inform JCTLM Executive/Secretariat of exact dates of the JCTLM WG meetings to be held at the AACC meeting.**

8.2 JCTLM Executive meeting

It was agreed that the next meeting of the Executive would be organized at the BIPM in conjunction with the JCTLM workshop on biological standardization, planned for the last quarter of 2004.

Actions:

- (A19) JCTLM Secretariat to confirm date of next JCTLM Executive meeting.**

9. Any other business

Dr Thijssen asked if there was any other business.

Dr Wielgosz noted that the current version of the WG1 quality manual stated that the BIPM would coordinate reference material comparability studies. Prof Wallard replied that the BIPM would undertake this coordination role if it had sufficient resources to do so.

Dr Schimmel noted that the term comparability was not used consistently within the WG1 quality manual. Dr Wielgosz replied that within the CIPM-MRA the term 'degree of equivalence' was used to describe the level of comparability of measurement standards, and urged that this accepted terminology be used within the quality manual.

Dr Thijssen thanked the participants for their input, and closed the meeting.

R.I. Wielgosz (BIPM)
17 March 2004
Revised 28 April 2004

Annex 1: Summary List of Actions

- (A1) Prof Muller/IFCC to provide JCTLM Secretariat with contact names and details of professionals' organizations to be invited to apply for membership of the JCTLM (29 March)**
- (A2) JCTLM Secretariat to send out 'invitation to apply' letters (14 April)**
- (A3) JCTLM WG Chairpersons to provide the Secretariat with up to date lists of their members (14 April)**
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- (A7) JCTLM Executive to provide comments on draft quality manual to Dr W.May by April 30**
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- (A15) JCTLM secretariat to keep DG Enterprise informed of future JCTLM activities.**
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- (A18) Dr May to inform JCTLM Executive/Secretariat of exact dates of the JCTLM WG meetings to be held during the AACC meeting.**
- (A19) JCTLM Secretariat to confirm date of next JCTLM Executive meeting.**

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