International Federation of Clinical Chemistry

Scientific Division

Committee on Nomenclature, Properties and Units (C-NPU)

Minutes of meeting, Hannover 2002-11-09--11

1) Opening of the meeting – The meeting opened at 09:00 PM, November 09, 2002.

2) Participants and apologies – Present for the opening of the meeting were the following titular members for the C-NPU (TM): Urban Forsum (UF) chairman of the C-NPU, René Dybkaer (RD), Wolf R. Külpmann (WRK) and Gunnar Nordin (GN) and Huib Storm (HS). Due to different reasons Pedro Soares de Araujo (PSA) secretary of the C-NPU and Antonin Jabor (AJ) could not participate.

3) Secretary for the meeting – in the absence of the committee secretary GN was appointed secretary of the meeting.

4) Approval of provisional agenda – The provisional agenda prepared by UF was discussed and approved, as well as a **general meeting schedule.**

5) Minutes from Copenhagen – The minutes prepared by PSA was appreciated. The spelling for Kim Varming was corrected, and the hyphen indicating interval between two dates were corrected

Project reports

6) Properties and units for Transfusion Medicine and Immunohaematology (UF)

Recently the suggested coauthors from ISBT (International Society for Blood Transfusion) have declined further participation in the preparation of the manuscript. The revised manuscript of 021010 was carefully scrutinized, with the starting point “who is the intended reader?”. A decision was taken that the numbering of elements of entry should stick strictly to the original paper 1995/4. UF will forward the suggestions to the author group.

Detailed comments (not intended for the minutes):

a) Page 2. The general introduction is inadequate to introduce the general reader into the subject and the purpose of the work.

b) Page 3. RD pointed out that the equation “**Property = Results**” may be regarded as a paraphrase of Maxwells “Quantity = Value * Unit”, and added that according to modern views the result also shall cover uncertainty. VIM: 1993 differentiates between a “result” and a “full result”!). For that reason a better frasing might be “Property and result combined by an operator”. The numbering of equations in the manuscript seems not necessary, as only one is given.

c) Page 4. The numbering of elements of entry should stick strictly to the original paper 1995/4.

d) The understanding of “Compatibility” either as a System [**Blood—Compatibility, electronic; time(expiry date and hour)]** and a kind-of-property **[Plasma—B-lymphocyte antibody; compatibility(donationID; 0 1)]** is not easily understood. The use of compatibility as a kind-of-property was recommended.

e) What is meant by the results 0 and 1 for the property **[Plasma—B-lymphocyte antibody; compatibility(donationID; 0 1)]**? Can 0 be interpreted as the presence of antibodies, however not reactive with a specific donation? The correct interpretation should be elaborated in the prologue of the paper.

f) Could compatibility be expressed on an ordinal scale, as 0/1? The presumption is needed that it is more being compatible than being incompatible! It may be more proper to express the results on a nominal scale:.
[Blood (recipient)—B-Lymphocyte; compatibility = outcome (compatible/incompatible)]

g) The meaning of entitic in [**Ercs(B)—Complement+Immunoglobulin; arb.entitic num.(proc.) = ? arb.unit]** is not evident for the ordinary reader.

h) The used abbreviations of systems should be listed.

i) Note that Coombs is a name (used as an explanation as an “Other name”). The note was followed by a general discussion about the use of popular terms in the database. No decisions were taken.

j) Temperatures are normally specified in the procedure, eg the enzymes. The inclusion of temperatures in properties such as [**P—Erythrocyte `N' antibody; arb.subst.c.(20 °C; proc.)= ? arb.unit/l]** has to be explained.

k) What is the meaning of `N’ in [**P—Erythrocyte `N' antibody; arb.c.(37 °C; proc.)= ?].** A general discussion followed regarding handling of superscripts. For sensible solutions see Schadow, G., C. McDonald, et al. (1999). "Units of Measure in Clinical Information Systems." Journal of American Medical Informatic Association **6**(2): 151-162.

l) The use of number ratio as kind-of-property on several entries on page 85 was questioned e.g. [**Lymcs(B)—Stimulation, allogene cells induced; number ratio(actual/norm)= ?**]. A number ratio is the ratio between two components in the same system, compared to a relative number ratio, that is the ratio between the same component in different systems.

m) The use of Stimulation e.g. [**Lymcs(B)—Stimulation, allogene cells induced; number ratio(actual/norm)= ?**] was questioned.

7) Properties and units in Medical Molecular Biology (PSA)

The current version of the manuscript (02-11-06) was analyzed and some suggestions to improvement were given:

The synopsis should be expanded in order to present the subject to the common reader.

In lack of a hitherto published definition of the concept taxon, an intentional definition should be given in the text. The following phrasing was suggested: “k-o-p indicating the position of a component within a system for classification of components”

The use of “sequence variation” as k-o-p was discussed: An extensional definition is given by den Dunnen & Antonorakis (Hum Genet 109(1): 121-124). The use of “Sequence variation” as a k-o-p was accepted by C-NPU. An intensional definition should be added in the molecular biology manuscript. The following phrasing of an intensional definition was

suggested: “change in the structure of one or more given genes defined by a stated reference to the human genome as shown in the DNA, RNA, or proteome.”

Some detailed comments (not intended for the minutes):

a) All agreed symbols and names should be explained explicitly.

b) A question raised during the discussions was if the genome formally includes RNA? Have investigations on RNA level to be handled separately? Note also that eg BCR-ABL1 is not in the HUGO database.

c) In a note it is recommended that sequence variation should include such changes as substitution deletion, insertion, fusion, duplication etc. Which type is relevant in a given case should be indicated in the result.

d) If no sequence variation is found the result should be 0, or alternatively a full description of the outcome.

8) Properties and units for Urinary calculi (AJ)

(The discussions postponed to next meeting)

9) Properties and units for Function examinations (AJ)

(The discussions postponed to next meeting)

10) Global use of C-NPU concept system for properties in Toxicology (WRK)

WRK reported from the first meeting in August 2002 with a working group consisting of WRK, John Duffus, Rita Cornelis, René Dybkaer. Next meeting is planned to December 5^{th} –6^{th} in Brussels. The funding of the project from IUPAC is exhausted with the Brussels meeting (3 000 US$).

The continuation of funding for the project was discussed. A possibility is to ask IFCC to transfer the remaining funds for IFCC projects for 2002 to 2003 (remaining IFCC funds due to the fact that AJ and PSA have been prevented to participate in the IFCC projects as planned).

11) Requests and reports in laboratory medicine (UF)

UF reported on ongoing work, however no manuscript yet to be presented.

12) C-NPU concepts and traceability of measurements (GN).

The project is currently on hold, awaiting a description of the distinctions from the intradivisional IUPAC project headed by Paul de Bievre on traceability in clinical chemistry.

The description of the project was discussed. The project has been described as a specification to property according to the view that the specification to a property could include necessary information not only of the procedure as such but also on traceability of

the result. It may be more proper to describe traceability as a specification to the result instead of a specification to the property.

An example of a traceability chain, as stated in the procedure, might be “Enzyme activity determined by a procedure traceable through IFCC reference measurement procedure to the katal”.

Notes outside the minutes: Several examples were discussed in which questions arise on traceability of results.

a) Results from glucose primarily measured in plasma are converted by conventionally algorithms to the expected concentration in whole blood. The procedure of converting the results leads to specific questions on how to describe traceability.

b) May traceabilities be of different types, number of steps etc?

c) Procedure using either dye binding methods and immunochemical methods for the determination of albumin

d) Haematology: automated and manual

e) Enzymes: Measured at different temperatures (eg 20 and 37%) and converted to the other temperature).

In all we should be reluctant to new NPU-codes, and only create new codes when necessary. The group agreed that the mechanisms exist to describe traceability in the system and several examples can be given. The traceability project should therefore be rephrased.

It was decided that GN returns with a rephrased description of the project. Next meeting with the Scientific Division will be in December.

13) Report from IUPAC Division Meeting

UF reported from the meeting held Boston in June 2002. The ownership of the database was discussed. It was decided that IUPAC and IFCC should be mutual owners.

14) Update on Names-Lab.

In the recent paper (Ann Biol Clin 2002, 60:173-81) the Names-Lab system is claimed to be implemented in 50 hospitals. The NPU-system is on the whole not mentioned. UF has tried to contact all the four authors by e-mail, without success.

One of the authors (S. Cormont) will be invited in conjunction with the IUPAC Scientific Division meeting at Brussels in December 2003. A meeting between UF, Anders Kallner and Rita Cornelis will be arranged December 6th in Brussels.

15) Funding of databases for nomenclature

A general discussion on existing possibilities for funding. Several questions raised.

Notes ouside the minutes: US: To what extent is the LOINC system funded through the incorporation in the HL7? UK: What is the situation for Reed Codes? Germany: LOINC seems to be the only known system in Germany. French: What is the funding of Names-lab?

On HL7: When using NPU codes in the HL7 the units have to be contained in a specific field. UF will write to Gunnar Klein and Clement McDonald/Stanley Huff to elaborate this further.

16) Letter from IFCC on availability of NPU database

UF has been approached from IFCC through a letter from Emanuela Maffioli at the IFCC Office about the current availability of the generic NPU database. UF responds.

17) IFCC meeting Euromedlab in Barcelona June 1st – 5th 2003.

It was decided that a C-NPU meeting should be held in connection with the meeting. UF will suggest a proper date.

18) Promotion of NPU

Promotion of the work by C-NPU should be made on three levels: a) a strategic level, including IFCC and IUPAC. b) scientific level, through publications in e.g. European Clinical Lab Medicine, eIFCC journal. At the Euromedlab meeting in Barcelona material ought to be presented orally as well as through posters. c) national societies in various ways. Translation to local languages is important when material is ready.

19) European Laboratory Medicine.

UF informed about measures to get information about European Laboratory Medicine (ELM, former ECLM).

Note outside the minutes: UF has received the minutes. Should we suggest an invitation for C-NPU to present our work. Chairman is Rainer Echel. Note that Blaton is a member, but president of FESCC.

20) Substance versus mass concentrations.

The C-NPU view on proper metrology and usefulness of the NPU codes implies that use of substance concentration as the k-o-p when the molecular mass for a substance is well defined.
The implementation of the coding system in Denmark and Sweden has revealed practical problems with proteins and drugs, where mass concentrations as k-o-p are in practical use. C-NPU decided to allow for mass concentration with the numerator litre (L) for substances other than electrolytes in the database.

Note outside the minutes: ppm is not accepted for mass fraction or mass concentration.

21) Units and katal

The enzyme unit U/L is not coherent with SI, which is the argument hitherto for not accepting the unit U/L as stated by IUB, in the NPU data base. If, however, the minute is allowed as unit for time by SI (check with the SI brochure or www.bipm.org.) then there will be no formal hindrance for C-NPU to accept the unit U/L as an exception to the katal. On the assumption that SI accepts the minute, C-NPU decided to define the 20 - 30 most common properties for enzymes into properties expressed as U. The denominator shall be Litre.

Note outside the minutes: The prefix milli is accepted, but probably not micro (RD ask Terry Quin).

22) Principles for size of values:

The numerical value of the measurement result should preferable be in the range 0.1-999 with at most with 3 significant figures. Exceptions will exists for properties with a large span of values, e.g. the substance concentration of metothrexate in plasma, and the mass concentration of choriogonadotropic hormone in urine.

23) Long term host for the generic NPU data base.

The database is currently hosted on a server at the University of Linköping, Sweden. A migration to a server at EQUALIS, Uppsala, Sweden is planned. Anders Kallner (IUPAC), Howard Morris (IFCC) and UF (C-NPU) will take further actions.

24) Revision of the IUPAC Gold Book.

Dr Jenkins circulate (through Anders Kallner) information that a revision of the manuscript for the 3rd edition is under way. The C-NPU will be further informed.

25) The concept of pauciscale

The pauciscale seems to have been introduced in the NPU database without formal definition and thorough discussion in C-NPU. Pauciscale is used to specify a ratio scale with very limited number of results. GN now raised the question if there, in addition to a pauciscale also was a need to define “richiscale”, for properties measured with e.g. extraordinary exactness or with very low level of detection. No decisions were taken.

26) Nomenclature of Carbohydrate Deficient Transferrin

The term “Carbohydrate Deficient Transferrin” (MeSHC056759, as used e.g. in the entry NPU10000) is indistinct as it does not denot which of the different carbohydrate deficient transferrin forms is measured. In Sweden it has been agreed that the component measured and reported from HPLC should be exclusively the form disialo-transferrin. C-NPU decided upon creation of a specific entry in C-NPU for disalo-transferrin in addition to the existing property.

As IFCC will raise a working group for standardization of Carbohydrate Deficient Transferrin, C-NPU ought to make a suggestion for nomenclature.

27) The unit One

Unit One, used for counting things, in fractions and relative quantities, is a derived unit in the SI, with the symbol 1. Earlier suggestions for symbols have been “I” and “uno” with the symbol “U”. The symbol 1 cannot be used with a prefix name or prefix symbol, only with a numerical factor. Solutions to the problem have been discussed for many years in CIPM and CCU, in which RD currently is the IFCC representative. A group of Mills (Reading),

Kose (PTB), and RD is now actively working on a suggestion, after the problem again was brought up at the latest CCU meeting (RD). RD produces a first version of a manuscript.

28) 'The Arbitrary Matter'

The letters from Robert Zender (200-01-05-07) and Christopher Riggs were again discussed.

On the one hand any unit is arbitrary in the strict sense, also the SI units. On the other hand do we need a terminology in order to differentiate scientifically agreed units and locally defined, or arbitrary, units.

It was concluded that Zender has a point but no solution, and that 'arbitrary' might be wrong, but still useful. RD will ponder on a reply.

29) HL7 and CEN TC251

HL7 and CEN TC251 both deals with health care informatics. UF will try to contact key persons in both HL7 and CEN, in order to emphasize the importance of the NPU system.

30) Possible new projects

The need for new projects for C-NPU was discussed. The major missing areas for the moment are calculi, function examinations, pharmacogenetics, "nuclear medicine" (in the sense of use of isoptopes for imaging), clinical immunology (outside transfusion medicine and allergology), inflammation markers, tumor markers, inborn errors of metabolism, mycology, parasitology and forensic medicine.

In addition there may soon also be a need for revision of older projects in C-NPU.

Administrative items

31) A presentation of the NPU-system should be arranged at the Barcelona meeting.

32) Chairman and members of C-NPU. UF is wiling to continue as chairman. GN candidates for a new term. Associate member (1998-2001) Eugeny V. Yurtov has been searched by UF without success. HS is suggested as a new member, TJ will be asked to continue for a new term.
Members of C-NPU is thus suggested to be UF, WRK, TJ, PSA, GN, and HS. RD continuously consultant.

33) Information about the new IFCC project manager: Howard Morris will be liason from January 2003.

33) Discussion about the **formal relation between IFCC and IUPAC branches** of the work with NPU as the common denominator. It was concluded that C-NPU (IFCC) should be responsible for the sc-NPU (IUPAC) projects.

34) Finances of the C-NPU/SC-NPU: IUPAC project leaders receive, in coordination with IFCC, 4 000 SF 2002 from IFCC. Also for the next year 4 000 SF is expected.

35) The annual report from C-NPU should be presented to the IFCC Office/Scientific Division and Executive Board. UF will prepare the report.

Reports

36) Minutes from the meeting with IFCC executive board meeting Vienna shortly reviewed

37) The paper by Xavier Fuentes-Arderiu on uncertainty of measurement in clinical microbiology (eJIFCC vol 13, 4) was shortly reviewed by UF.

38) Document D2 from Organisation International de metrologie legal (OIML) was shortly commented by RD.

39) RD reported from Joint Committee on Traceability in Laboratory Medicine (JCTLM): IFCC, CIPM in the shape of CCQM, WHO and ILAC have initiated the committee. The committee met at BIPM where also NIST, IRMM, ILAC, EU, industry and others presented their views. Two working groups, WG1 and WG2, were formed. WG1 will be double chaired by NIST and IRMM, and produce a list of available reference materials and reference measurement procedures. A first version of a list has already been drafted by Rudy Lequin. A specific problem dealt with by WG1 will be the uncertainty statement of WHO calibrators. WG2 will be chaired by Lothar Siegmann/Linda Thienpoint and the work focused on the creation of networks of reference measurement laboratories (HbA1c, Cholesterol, Enzymes etc).

40) RD reported from JCGM. Two working groups are active; one on GUM and one on VIM. Items under current discussion in the GUM group is how the industry should work with GUM, the use of Bayes theorem, and the possibilities to use Monte Carlo simulations supplemental to GUM in the evaluation of uncertainty. The VIM group is also active and has an advanced draft (more information on the BIPM webside).

41) Miscellany. No items to be discussed.

42) The next meeting with the C-NPU planned in connection with the IFCC-FESCC Barcelona meeting May 2003.

43) The meeting was closed at noon Monday 11th.