International Federation of Clinical Chemistry

Scientific Division

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

Minutes of meeting, Dubrovnik March 9 – 11, 2001

Titular members present: Urban Forsum (UF) chairman of the C-NPU, Antonin Jabor (AJ) Gunnar Nordin (GN), René Dybkær (RD) and Wolf R. Külpmann (WRK).
Associate member present: Henrik Olesen, attended the meeting March 9 - 10.
Regrets: Pedro Soares de Araujo (PSA)

0.0 The chairman called the meeting to order at 0900 and welcomed all present TMs and AM.

0.1 The committee agreed on the following overall structure and agenda for the meeting based on the provisional agenda circulated by UF and suggestions made in pleno:

1) Secretary for the meeting
2) Prague meeting minutes
3) Preparation for the meeting with IFCC Scientific Division
4) Reports from the meeting with WHO in Geneva, knowledge on LOINC and the revision of ENV1614
5) Members reports, including review of ongoing projects
6) Project report: Transfusion Medicine
7) Project report: Renal Calculi
8) Project report: Tolerance tests
9) Project report: Molecular biology
10) Proposals for IUPAC projects to be superseding the present commission
11) Presentations at IFCC congress in Prague, (Posters, GN Lectures).
12) Poster at IUPAC General Assembly, Brisbane
13) Future projects for C-NPU

Ad 3. At Friday 9th 14.30 the C-NPU will meet with the Scientific Division, for presentation of the work of the group.

Ad 9. At Saturday 10th 11.15 C-NPU will meet prof. Christine Mannhalter, chair of the IFCC molecular biology technique in clinical chemistry group (C-MBT), for discussion on the molecular biology paper.

1. Secretary for the meeting

In the abscence of the C-NPU secretary, GN was charged to do the minutes for this meeting.

2. The minutes from the Prague meeting:

WRK asked for a clarification of the schedule for the Brisbane meeting: UF will send confirmation to the group as soon as possible, and also collect information on which of the members that are going to attend. There might be problem with low fare tickets, if reservation not already has been made. Still not clear if IUPAC will cover the expences for RD. UF to take action and raise the matter with IUPAC Division VII chair Anders Kallner.

3. Preparation for meeting with Scientific Division (SD):

The C-NPU wishes and expects promotion from IFCC for the use of the NPU coding scheme. The main arguments to be raised are the following:
IFCC, as a top global scientific body ought to promote a conceptually sound scientific system of nomenclature based on the SI system, that is NPU. The system is rather complete after the inclusion of transfusion and parts of molecular biology. Implementation and validation of the system has been made in Denmark and Sweden. It should be stressed that NPU also can handle "local dumps" in form of local adaptations of the system. The NPU coding scheme is therefore now ready for promotion by SD. Major countries, such as France and Germany, has to be recruited for the further development and promotion of the system.

The laboratory areas in the Electronic Patient Records belong naturally to IFCC. Soft ware developers suffer from large costs for Electronic health care records systems. A structured way to deal with the laboratory area is greatly needed. The NPU-coding scheme should be given status comparable with the ICD 10 system as a global nomenclature of core value for human health care.

There is now a need for maintenance of the NPU system, which is an important reason for the C-NPU to continue to exist as a high level scientific body charged with the task of keeping the NPU system coherent and updated. Maintenance of the NPU coding scheme structure and content involves several aspects of keeping a website running and staffed by professionals. These aspects of the NPU maintenance might have to be done in conjunction with other interested parties such as national health care systems, standardization bodies or the WHO.

The meeting between C-NPU and the scientific division (SD), headed by vice chairman John Ratcliffe, was arranged at Friday 9th. UF described shortly the work done by the committee and the expectation for support by SD. C-NPU expressed a hope that SD supports the use of NPU coding schemes in favour of other coding schemes. The C-NPU was recommended to identify the target for any activities from SD and to specify on what to improve.

4. WHO meeting.

UF reported from the meeting between him, TJ, Anders Kallner and representatives of the WHO among them Pierre Lewalle at WHO in Geneva December 18th 2000.: Pierre Lewalle expressed views sympathetic with the suggestion made by the C-NPU delegation that the NPU coding scheme ought to be of sufficient interest for human health care to be entrusted to an international consortium that would bring together self-funded interested parties operating with an international mandate under the coordinating authority of WHO. Considering the mandate of WHO a proposition of handling the NPU in a similar way as ICD 10 has to be approached from an governmental level, that is it have to be a political issue. UF, HO and Anders Kallner have acted to raise the question with Swedish authorities (Nina Renquist, National board of health), Danish aurthorities (Gunnar Schiøler, National board of health) and colleagues in France (Alain Carayon and Bernard Gouget) in order to seek governmental support. UF expressed optimism about having the NPU coding scheme brought up on the WHO GA agenda in april as a petition for action.

(cf Mathias Mullers opinion in letter to UF and Anders Kallner, december 2000:
"I am in favour of your initiative related to the IFCC/IUPAC nomenclature. I also agree that we must jointly make more efforts to make all the different documents (elephant, etc) more available to the membership and to the public (especially the metrology institutions). As you know I tried to get on-line the compendium from the Swedish site - which was rather troublesome. In Austria the metrology institute is just discussing it. My specific proposal to you and to other is as follows: 1) you should work on the WHO line further to accept the NPU nomenclature and the elephant. 2) The NPU documents should be made available for downloading with a low license fee. 3) The IFCC web site will be shifted to a professional provider within the next few weeks. At the new site there is the possibility of installing various databases; one could be related to NPU. The structure of the new site - as designed and approved - will be clearly structured. I can envisage that the NPU documents (like others) should be in the section of IFCC-SD products. Detailed information and professional support will be given by C. WEBSTER and A. WOOTTON CPD's web co-ordinators. The technical aspects of this web based NPU approach should be discussed with these two IFCC officers. 4) With the new IFCC web site (located in UK) the problem of a long lasting site for the NPU documents might be solved. 5) A public relations action could also be initiated after having installed the NPU documents at the IFCC web site: e.g. a joint email letter (IFCC/IUPAC, SD, CPD to our membership, to other international organisations (ISO, CEN, NCCLS, WHO, ...), to industry, to metrology institutes, IRMM. In this letter the appropriate use of the NPU documents to reach conformity should be stressed")

5. Members reports, including review of ongoing projects (UF last

modified 2001-03-01).

The need for new projects, such as eg forensic medicine, cytokines, surface proteins, were shortly discussed. Only projects for clinically relevant areas will be considered.

RD reported on accepted projects for the EU 5th Framework Programme on non SI- traceability and quality assurance of qualitative analysis, MEQUALAN.

RD is the IFCC representative, via C-NPU, to the Joint Committee for Guides in Metrology (JCGM) working group 2, VIM and working group 1, GUM. Reports to IFCC from this work are given through C-NPU. RD is also IFCC representative to the Consultative Committee on Amount of Substance (CCQM) and on Units (CCU) at BIPM. In this capacity RD reports directly to the IFCC SD.

HO raised the question on how the specification **"**procedure" is handled in HL7, and which consequences could be expected if TC251 and HL7 merge in the future. As far as the members of C-NPU knew, especially UF, there is no difference today between HL7 and TC251 in the ability to handle codes for properties (being LOINC or NPU) and to carry the additional information, such as information about ("specifications").

Revision of ENV1614: UF reported that the TC251 WG2 convenor Göran Holmberg has asked Anders Thurin to revise ENV1614. The objective is to transfer the ENV to an EN with only minor changes; e.g. the notation will be changed. Major changes, however has to wait for next VIM version.

6. Project report: Transfusion medicine

A draft 2001-02-20 prepared by HO was discussed. The work should be considered as a separate project. UF has made a proposal to ISBT working party for terminology for red cell surface antigens and it´s convenor Geoff Daniels; they have accepted to co-operate on the project.

The draft deals with erythrocyte surface antigens and corresponding antibodies. An example is:

Ercs(B)—Erythrocyte-surface antigen; taxon(AB0; Rh D) =

Some of the items discussed: Is "AB0" a specification to the component or to the k-o-p? If it is a definition of the scale then it is a specification to k-o-p. Regarding the two alternative notations, either O or 0 for the blood group substance (O)hne, the number 0 is used in this draft. According to some schools the AB0-antigens on erythrocyte surfaces are no true antigens, and should more correctly be denoted carbohydrate "substances" (the so called "natural" antibodies detected against A and B substances are in fact raised against other antigens than the absent erythrocyte substances).

For the non-AB0 antigens the proposed syntax was:

Ercs(B)—Erythrocyte-surface antigen; taxon(not AB0 or Rh D) = Ria; Cw

Items discussed: Is the terms "not AB0"/"AB0" proper? An alternative could be "uncommon" and "common" antigens. The transfusionists have to decide.

For the non-AB0 antibodies the following syntax was proposed:

P—Erythrocyte-surface antibody; taxon(not AB0 or Rh D; 37 ºC) = He-Ab; Mur-Ab

Items discussed: Is it necessary to add "antibody" to the component, as well as in the specification to the k-o-p and in the result line? As the set is defined by the procedure it might be enough to include "antibody" in the specification to k-o-p?

The general syntax of the cross-match investigation may be:

Plasma—Donorerythrocyte-surface-antigen antibody
arbitrary concentration(Donorbag ID; 37 ºC; agglutination, no agglutination;

procedure)

Items discussed: Should a dash be included in “Donor-erythrocyte”? Is “epitope” a more proper term than antigen? It may be more informative to add the scale 0 or 1, rather than “agglutination,.no agglutinationl” in the specification to k-o-p. The term “Compatibility” or “incompatibility” is preferably given as a comment to the result.

Is donor bag ID a specification to the component or to the k-o-p? If the specification to k-o-p is regarded as specification to the complete property, it seems suitable to place this specification after k-o-p.

A letter of invitation has been sent (by UF) to Dr. Jurgen Bux, who is convenor of a working party on platelet and neutrophil antigen. No reply so far.

UF will forward the deliberations of the C-NPU of the draft by HO to Geoff Daniels and invite his working party to join forces with C-NPU on the project.

7. Project report: Urinary calculi

Draft version 2001-02-18 discussed.

The use of kind-of-property in headers was again discussed (cf discussion below on functional examinations)
a) When the subsequent lines have the same kind of properties, the use of this k-o-p in the header is recommended
b) When the subsequent lines covers different k-o-p, no k-o-p, or a blank sign in the field is recommended
c) The use of the unspecific term “calculus” in headers is OK.

RD suggested the term “component” instead of “constituent” as a component.

“Number of entities” is the correct term to use for the k-o-p, according to the Silver book.

The paper has the Project number XVII/2000. It should be checked with PSA if the project already is registered, otherwise it should be registered as a new project for 2001.

After the discussions in Prague the new k-o-p “dimension” was suggested, and that the result should be given using the syntax “?mm; ?mm; ?mm”. Are these results regarded as three repeated values on a ratio scale that should be reported as three separte results, or is it a triplet of numbers reported as one result on a nominal scale (GN)?

8. Project report: Tolerance tests:

A new draft for NPU for tolerance tests has been prepared by AJ after the discussions at the Prague meeting. A general header with the following syntax was proposed:

Patient—Tolerance of something; kind-of-property

In contrast to earlier drafts the investigated function is now regarded as the component. This new approach was approved by the C-NPU. A suggestion was made that the term “Functional examination” should be used in favour of “tolerance test”.

Following earlier discussions a term “kind-of-property” is used as a placeholder when there is no real kind-of-property in the property. One of the reasons for this arrangement was that the structure of the NPU working database in Sweden required some k-o-p for all entries. The question was again raised if it should be necessary for a header to contain a kind of property (RD). The database structure in the Swedish database can probably be handled by using a blank sign as a dummy in the k-o-p field (GN). K-o-p in headers may still be used when all underlines contain the same k-o-p. The insufficiently clear structure of the header, as well as the link to the properties covered by the header, is probably due to a universal lack of definition? (Neither in the Silver Book nor in ENV1614).

The term “Glucose tolerance test” was not approved for the description of the well known

property of glucose metabolism. GTT may instead be covered in the header (RD), if the general structure of the header will allow it.

The tested organ should be identified as system. Gonads (Leydig cells) are preferred to Leydig cells.

Patient is the system when the examination covers several organs. When a specific organ is involved, that is the system. The plural form should be used when the tested organs are more than one; e.g. is kidneys, if the investigation does not deal specifically with left or right kidney.

Information on the stimulating substance is given as a specification to the kind-of-property. Even when "kind-of-property" is omitted in the property it should be able to use a specification. The parenthesis after "kind-of-property" may be used as a specification to the whole property, not only to the k-o-p (RD) e.g.

Kidneys—Solute concentration ability; (desmopressin)

Specific NPU codes should be raised for test procedures recognised by international organisations, i.e. GTT according to WHO tests.

AJ makes a new draft of the "Tolerance tests/Functional examinations" in accordance with the above discussions, and subsequently circulates it in the group.

9. Project report: Molecular Biology.

A new draft (version 5) of the manuscript has been distributed by mail from Pedro. The draft incorporates the suggestions from the Prague meeting, with the following general syntax:

DNA(Lkcs; B)—*BRCA2* gene (OMIM 600185); sequence(proc.) = IVS23-2A>G

HO, in pleno, suggested the following, slightly different, general syntax:

DNA(Lkcs, B)—CFTR-gene (OMIM602421); mutation =
IVS10, G—A-10(OMIN602421.008)

The main argument, according to HO, is that OMIM is already using this nomenclature.

The argument for the use of term mutation as k-o-p instead of sequence, as was suggested in Prague, is the difficulty to completely describe the sequence, because the result line might be expected to contain the whole sequence. Arguments were raised that Altered sequence or Sequence variation could be more proper than the sole term sequence. None of these alternatives, however, cover the concept of polymorphisms.

TJ raised the question on the use of OMIM codes inside NPU codes ("codes in codes") The OMIM codes should be used as eg ATCC codes in clinical microbiology, CAS codes in chemistry.

The problem with redundant information in the result field was further discussed, with the coagulation factor V gene in draft 5 as an example:

DNA(Lkcs; B)— Coagulation factor V gene (OMIM 227400); sequence(proc.) = ARG506GLN, 1691G-A

The reports of both amino acid changes and nucleotide changes is redundant, the nucleotide change seems, according to C-NPU, to be enough. In addition, a sequence of amino acids isimpossible as the result of an investigation of the system DNA.

The gene nomenclature uses *italics* to denote gene names. That is *CFTR* has the same meening as CFTR gene (n.b. no hyphen but two words). The C-NPU preferred the latter form for NPU.

A laboratory "procedure" is necessary in the report to describe what has actually been investigated. E.g. exactly what mutations have been investigated for.

How to deal with allelic variants was further discussed. An allelic variant could either be regarded as the component being investigated (result on ordinal scale) or as the k-o-p of the gene as a component?

Christine Mannhalter (CM), chair of the IFCC CMT, participated in the C-NPU meeting during 2001-03-09. RD gave a short description of the structure of the system and UF gave a summary of the NPU work on molecular biology. The question was raised on what other coding schemes exists?

CM gave an illustrative example of the importance of the necessity of stringent nomenclature in laboratory reports. A result from an investigation of FV Leiden, was misinterpreted because the requester mixed the amino acid sequence and the nucleotide sequence in the report.

A much used convention, favoured in the OMIM database, is to give the result as the amino acid sequence when the mutation result in a amino acid change, the nucleotide sequence when the mutation does not change the amino acid sequence. As 3 different mutations can give rise to the same amino acid sequence, this convention contains a risk for loss of information. For that reason CM suggested that the nucleotide sequence always should be added in the report.

The amino acid sequence may preferable be given as a comment to the result. RD suggested that the information on the meaning of the examination (e.g. a disease) should be given in a header.

Among the alternative terms for the k-o-p – mutation/sequence/sequence variation – was *sequence variation* to be preferred according to CM.

The problem with the nomenclature of allelic variation is that the “normal variant” also may be a mutation. As an example a specific IL6-mutation, rare in blacks but usual in caucasians was mentioned.

Normal sequence of OMIM = 0
heterozygous for an allelic variation = 1
homozygous for an allelic variation = 2

A problem: When the normal variant in the OMIM is regarded as 0, how to handle with cases with two alleles??

When a sequence analysis has detected only one allelic variant, it can not be concluded that the origin of this allele is from both chromosomes. A deletion of the gene on one of the chromosomes can not be excluded.

According to CM the nomenclature of translocations and rearrangements is fare more complicated, and OMIM is of minor help. Both minor and major breakpoints are described; but which breakpoints are defined? Currently no general nomenclature is accepted. NPU was suggested to use the most frequent nomenclature, for the time being.

A strategy to bring the molecular biology paper to a final stage was discussed. HO has still some suggestions to make. It was suggested that the HO suggestions as well as the suggestions discussed at this meeting were sent to PSA for incorporation in the material, and that some of the other authors on the paper, e.g Pedro Alia Ramos, were engaged more actively in the further work with this paper. UF will write a letter to Alia Ramons inviting him to actively take part in the C-NPU deliberations.

Suggestions for the continuation of the work: Short notes are made from the discussions in this meeting. The draft 5 may then be changed accordingly. The new draft will be sent to Christine Mannhalter and the Molecular Biology group.

10. Discussion on future project for IUPAC

Matters discussed were:

How to handle traeceability in the C.NPU coding scheme? RD suggested that traceability could be argued to be regarded as a mandatory item in the term of a property.

When traceability is included in the procedure description the coding schemes might be in better accordance with the revised VIM.

The NPU work is divided into three levels:
- Coding scheme structure
- Coding schemes
- Content of coding schemes

The following hierarchy of the coding schemes might be described:
NPU1 SI traceable properties
NPU2 WHO reference material traceable properties
NPU3 International reference material traceable properties (not WHO) or traceability to a reference examination procedure
NAT1 national traceable properties (national reference material or procedure)
LOC1 locally traceable properties (i.e. traceable to a procedure in the quality manual of the laboratory

For the continuation of the C-NPU we can see both
- Maintenance project
- New specific projects

The basic coding schemes have been done, and the schemes for the time being have to be filled and used. Therefore, updating and maintenance of the system should have priority. In addition guidelines on how to do the do local implementations should be done.

In case IFCC will be engaged in “The connectivity consortium”, the work in C-NPU has to be included. UF will approach either the EB or SD.

In the future EDIFACT (CEN) and HL7 are expected to fuse into a new ISO standard. The use of NPU should be encouraged, as the scientific valid way to classify measurements and observations,

Project suggestions:

- Maintenance of coding schemes (authorization) including the expansion of NPU codes.

A responsibility for WHO/IFCC and not for IUPAC??
- Implementation guidelines
- Presentation through website
- On the use of procedures in the system, and how to explicit traceability (cf EN/ISO17511).

Clarifying and generalising the concept of traceability in NPU. A special problem is to express traceability for the ordinal scale observations. (cf Paul de Bievre´s traceability project)
- Generalizing the concept for use in other fields for encyclopaedia reason (“candidate properties”)(AJ)
- Harmonization with other groups (that is other IUPAC/IFCC groups) i.e. environmental chemistry
- Projects 18/87/XVII and XVIII should be formally registered as new projects. The transfusion project has to be added to the list. + 4 to 5 additional unfinished projects (see below).

Outside expert referents for our projects are to be suggested by us to IUPAC. Some suggestions were made: Desmod Kenny, Elvar Theodorsson, Peter Lehmann (New Orleans), Sverre Sandberg.

11. Euromedlab meeting in Prague, May 2001

GN is invited to give a presentation in the symposium “Computers in Clinical Laboratory”. The presentation has been given the title *“Unambiguous identification of measured properties when interfacing LIS in clinical laboratories and clinical wards”* and gives us possibility to promote the NPU system. Abstracts will be presented in a conference CD, if available end of March. C-NPU agreed to give input to a synopsis for an abstract if mailed to the group within a few days. In addition a special handout ought to be prepared. The committee suggested the presentation to cover a) general structure b) the generic NPU database c) national implementations in Sweden and Denmark, eg with an example of streamlining of laboratory procedures in the Swedish

Health Care company Nova Medical.

12. Poster at Brisbane?

Between IUPAC General Assembly and IUPAC Congress a poster session is planned. A poster might be a good opportunity for C-NPU to promote some of our projects. The following title was suggested: Nomenclature for Properties and Units for every Chemist. UF sends an application to IUPAC and if the C-NPU gets a poster slot UF provides GN with some raw text, thereafter input expected from the members of C-NPU.

At Saturday 10th a meeting between C-NPU and IFCC Publishing Division, chaired by Bernard Gouget, was arranged. Possibilities for C-NPU to publish information on eJIFCC and the electronic info were discussed.

The main sessions for the IFCC general conference in Dubrovnik, especially the parts on the IFCC global strategy on diabetes, were followed by the C-NPU.

Closing. The meeting closed 2001-03-11 at 1445.

Uppsala April 22, 2001
Gunnar Nordin