

Nomenclature Committee of IUBMB (NC-IUBMB) and IUPAC-IUBMB Joint Commission on Biochemical Nomenclature (JCBN)

Minutes for the Annual NC-IUBMB and JCBN Nomenclature Meeting

Mariner Room, Royal Marine Hotel, Dun Laoghaire

May 15th 2013, 09.00

Present: Gerard Moss (GPM, Chairman); Richard Cammack (DC, Secretary); Kristian Axelsen (KA); Ron Caspi (RC); Ture Damhus (TD); Karl-Heinz Hellwich (KHH); Derek Horton (DH); Masaaki Kotera (MK); Andrew McDonald (AGM); Ida Schomburg (IS); Keith Tipton (KFT); Hans Vliegthart (JFGV).

Observers: Amélia Rauter (AR)

Apologies: Marcus Ennis; Sameer Velankar; Dietmar Schomburg

- 1) The chairman welcomed the participants.
- 2) The agenda was approved.
- 3) After some changes and corrections suggested by KHH, the minutes from the 2012 meeting in Hinxtton were accepted¹.
- 4) There were no matters arising.
- 5) Reports

- a) Chairman's Report (GPM)

GPM summarized the recent activities of the committee and of the Enzyme Taskforce, most of which are covered in the items below.

Enzyme list statistics: the number of views of the database of enzymes classified had increased in 2011, and then dropped somewhat in 2012. It was assumed that users were obtaining the information from other bioinformatics databases. KFT pointed out that the information on enzymes listed elsewhere was not always consistent with that published by the Nomenclature Committee.

A new document on nomenclature of Flavonoids had been agreed at the recent meeting of the Flavonoids group.

- b) Treasurer's Report (DC)

Francesco Bonomi is the new IUBMB treasurer. A budget for the 2012-2014 years of \$6000 per year had been set by IUBMB for funding of NC-IUBMB activities. This was to cover attendance of titular members of NC-IUBMB and joint NC-IUBMB/JCBN members. IUPAC would continue to fund the Secretary and one other JCBN member at meetings, in addition to approved Projects.

- c) IUBMB Report

The new IUBMB Executive Member for Publications, Prof. Avadhesh Surolia, was in India, and not expected to attend. Action: Secretary to send JCBN minutes and reports of our recent activities to Prof Surolia.

¹ Following the 2013 meeting several members pointed out some inaccuracies in the 2012 minutes that required correction, and as a result, the minutes would have to be approved again during the 2014 meeting.

6) Enzyme Nomenclature and Classification

a) Report on enzymes classified (AGM)

New enzymes submitted by researchers are entered on online forms, assigned to a member of the Enzyme Taskforce, and transferred to the DraftEnz website (which has curatorial tools) by that member. Following private review by the taskforce (on average 1 month) they are transferred to the publicly accessible CurEnz Website for public review.

AGM agreed to prepare a document on procedures for the taskforce, to be circulated (Action AGM). KFT commented that enzymes of relevance to other groups, e.g. carbohydrates, should be circulated to those groups.

A total of 324 enzymes were classified in 2012; statistics are available on the ExplorEnz website. The total in the list was currently over 5000. The rate of growth had increased significantly with the expansion of the Enzyme Taskforce.

About 2000 enzymes were illustrated with diagrams of compound structures and mechanisms, drawn by GPM.

The current EC list is accessible via the ExplorEnz database, which is MySQL-based and is maintained by AGM at Trinity College Dublin (www.enzyme-database.org). Data from ExplorEnz is used to update the html-based website maintained by GPM at Queen Mary, University of London (www.chem.qmul.ac.uk/iubmb/enzyme). ExplorEnz has a search facility, while the list at QMUL is searchable by Google. The ExplorEnz site served over 1 million successful page requests in the past year.

b) Report from the Enzyme Taskforce meeting (KFT)

The current taskforce comprises KA, DC, RC, IS, AGM, GPM, DS, and KFT. Its major work was in creating and curating entries in the EC list. In addition, it dealt with answering questions from the public and providing requested information about the list.

The DraftEnz database was working well, and procedures were continually refined during the curation process.

KFT emphasized that ExplorEnz is not a reaction database, but a database of enzymes classified based on the reactions they catalyse. Two other fields in the database were discussed:

- i. Accepted name: the name used in the literature (often for a long time). The accepted name is unique, and cannot be shared by two entries in the list. In order to distinguish entries it was sometimes necessary to add short qualifying terms in parentheses.
- ii. Reactions: reactants in reactions should be listed by their biochemical names. When appropriate, common or alternative names are provided in a glossary section. Some commonly used abbreviated terms can be used without definitions within the specific enzyme entry, as they are defined in the glossary (www.enzyme-database.org/glossary.php).

TD asked about rules that are used to construct enzyme names. GPM stated that some of these names had been in use for over 50 years, during which time IUPAC recommendations had changed, and may have not been updated. KA had been revising names in earlier entries in order to improve consistency, although no comprehensive effort has been done yet.

Small ("trivial") errors are corrected without a formal process. This speeds up the curation process, though occasionally it could lead to consequential changes in other entries.

Reaction direction: The "Reaction" field is intended purely to balance the reaction, so the direction shown is not to be taken as the direction in which the reaction is catalysed *in vivo*. In some cases the reaction direction can be deduced from the enzyme's name. For example, if an enzyme is named "x-reductase", it indicates that the enzyme catalyses the reaction in the direction of reduction of x. Reaction direction is indicated in the diagrams drawn by GPM.

Cytochrome P450 enzymes: the recommended name at present is “heme-thiolate enzymes” (see Nomenclature of electron-transfer proteins, IUBMB recommendations 1989), but this term is unfamiliar to many biochemists. This might form the basis of a Newsletter item (Action: DC).

Peptidases: these are named inconsistently in the list at present, and the listing of new peptidases is a problem. According to the EC rules, we would classify them according to the reaction catalysed, i.e. sites of cleavage of a polypeptide chain. However names used in the literature use various other criteria to distinguish them, such as the type of enzyme active site (serine, aspartyl etc.) and the source of the peptidase (see the MEROPS database, <http://merops.sanger.ac.uk>). Some historical enzymes, such as trypsin and pepsin, have EC numbers that do not adhere to the enzyme classification rules. This problem was noted, but with no obvious means of resolution. It has been decided that until a solution is at hand, the taskforce would only classify new peptidases if a specific request is made.

Engineered enzymes: it had been suggested in 2012 that engineered enzymes could be classified in the enzyme list for a payment. However because patent disputes might lead to expensive litigation, this suggestion had not been adopted. Instead, it was decided to not list engineered enzymes. If any are already present in the list, they would not be deleted.

Bifunctional enzymes. Bifunctional enzymes have two active sites catalysing different reactions, sometimes of different types. Such enzymes are dealt with in an inconsistent manner. In some cases there is an entry for the overall reaction (e.g. EC 1.2.1.25, 2-oxoisovalerate dehydrogenase (acylating)), and in other cases there are separate entries for the individual active sites (e.g. EC 2.3.1.12, dihydrolipoyllysine-residue acetyltransferase). This is often due to the fact that the enzyme may exist as several separate entities in some species. This problem was deferred to a later meeting of the Taskforce.

Publication of a printed version of the EC list: The previous IUBMB Member for Publications, Prof Willy Stalmans, had been in correspondence with Elsevier, to whom the committee had provided some details. However there was insufficient interest from publishers to print what would be a very large book (over 2000 pages), which would soon become out of date.

Prof Stalmans had also suggested some years ago that the IUBMB take over the operation of the enzyme list website. However the present IUBMB website uses a content management system that would prevent the access that the enzyme taskforce requires for active curation.

Enzymes.me.uk This website listed all the EC list entries, and claimed copyright on everything. The owner of this site, which was offering advertising space, appeared to be in Kazakhstan. DS had sent a letter to the website owners, and the site appears to have removed some of the content. Enzyme names and EC numbers are still listed, but the rest of the information from the enzyme list is not included. It was decided that the site no longer poses a problem.

Definition of a Cofactor Paul Engel had written to ask for an official definition. There appeared to be several versions. Action: KFT to consult and prepare a response

Enzymes that use A or B face of NAD(P). There are six pairs of entries of the list for enzymes that differ in this manner. Since few enzymologists are carrying out the necessary tests, for most organisms it is not known which EC number applies. It has been decided to keep the existing entries, but create a new entry for cases when this information is not available. New entries would not be based on this distinction, even if there is information available about the specificity. However, the information should be described in the comments. In addition, there has been a change in the recommended nomenclature: A = *Re*, B = *Si* face.

Action: GPM to provide a diagram to explain the stereochemistry: A = *Re*, B = *Si* face.

Prior to the next meeting, the finalized taskforce minutes should be sent to the JCBN secretary, who would forward them to IUPAC division VIII as well as to the IUBMB (Action: KA).

7) Project on flavonoid nomenclature (Rauter)

The project group had met in Dun Laoghaire to finalize the document prior to submission to IUPAC. The document comprised definitions of different classes of flavonoids, including flavonoids, isoflavonoids, neoflavonoids, chalcones, anthocyanins and flavonoid oligomers. The project group had identified a list of potential referees.

8) Carbohydrate document (JFGV)

Carbohydrates are an important area; Pubchem comprises more than 120,000 carbohydrate-containing molecules. DH reported that they had many new monosaccharides to consider. Cyclodextrins have expanded enormously.

A project to update the current recommendations had been funded at 50% of the level applied for. The group had met in Dun Laoghaire to revise and consolidate the previous documents on carbohydrates, glycolipids, and also glycoproteins, glycopeptides and peptidoglycans.

DH reported that the 1996 document, Recommendations for the Nomenclature of Carbohydrates (abbreviated *2-Carb*) on the QMUL website was to be updated as *3-Carb*, incorporating the latest nomenclature. It would incorporate nomenclature from the glycoprotein and glycolipid documents. The project group had divided into sub-task groups on different types of carbohydrates and glycoinformatics.

A proposal submitted to the committee on *abbreviations for aldonic acids* had also been considered.

Inositols are a related area in need of revision. They are difficult to name because of symmetry. KHH stated that they need a new document, which could form the basis of another project.

9) Small molecules Glossary project (DC)

This was to be a glossary of small molecules ($M_r < 1500$) of central importance in biochemistry that were not adequately described in current IUPAC nomenclature. Many of them were found as substrates and inhibitors of enzymes. About 200 compounds had been selected for the glossary so far, on the basis of highly cited publications in biochemistry and molecular biology.

The list included some compounds that presented particular problems of nomenclature, for example free radicals and organometallic complexes. A list was being circulated and checked by the project group, for nomenclature and atom numbering.

10) Update on Action Items from the Minutes of the 2012 Meeting

- a) IUPAC has been working to produce 'brief guides' to various areas of chemical nomenclature. A polymer nomenclature document has been prepared, and KHH promised to send it to all participants of the meeting. It has been suggested that similar documents could be prepared on biochemical nomenclature of the following topics:

- i) flavonoids (AR)
- ii) carbohydrates (DH)
- iii) Enzyme nomenclature (from ExplorEnz website)

11) Other nomenclature topics

- a) New Blue book, on Nomenclature of Organic Chemistry, was close to publication; and was expected to be published by early 2014.
- b) A document was being prepared on the Kappa convention, which aims to provide a precise description of coordination of metals to ligands, e.g. to polypeptides.
- c) Development of InChI
InChI was an ongoing project. There was to be a report in Istanbul on the stage the project had reached.

12) Membership of the committee

- a) Election of Chairman

GPM had been elected chairman in 2012, seconded by KFT. This was approved unanimously.

- b) Election of Secretary

Following the 2012 meeting RC had been invited to act as secretary starting after the 2013 meeting and has accepted the invitation. His name was proposed by GPM, seconded by KFT, and approved unanimously. The post is funded by IUPAC. **Action:** RC to inform IUPAC Secretariat of the situation.

- c) DC agreed to continue on the committee *pro tem* as an IUBMB titular member.
- d) AR was nominated a new Associate Member of JCBN and the nomination was accepted unanimously.

13) Any Other Business

a) IUPAC website

The committee had experienced difficulties during the year with the IUPAC website, which had not been updated. The website was in an unsatisfactory state, having been taken over by a commercial publisher which had taken ownership of the web software.

b) IUBMB website

The information about the nomenclature committee was out of date. Action: GPM to write Prof Surolia and the Chairman of the Information Transfer Committee/Website Manager (Prof. Peter Ott) to remind them of the current status.

14) Date and Place of Meeting in 2014

Proposed dates were 5-7 May or 12-14 of May; the meeting to be organised in Utrecht by JFGV.