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

Utrecht, The Netherlands, May 14th 2014, 9:00

Present: Gerard Moss (GPM, Chairman); Ron Caspi (RC, secretary); Kristian Axelsen (KA); Richard Cammack (DC); Ture Damhus (TD); Marcus Ennis (ME); Karl-Heinz Hellwich (KHH); Derek Horton (DH); Masaaki Kotera (MK); Andrew McDonald (AGM); Amelia Rauter (AR); Dietmar Schomburg (DS); Ida Schomburg (IS); Keith Tipton (KFT); Hans Vliegenthart (JFGV).

1) The chairman welcomed the participants.

2) The agenda was slightly modified and approved.

3) The minutes from the 2012 meeting in Hinxton were accepted in principle (see 4 below).

4) The minutes from the 2013 meeting in Dun Laoghaire were accepted (with one clarification by JFGV regarding the level of funding of the carbohydrate project).

   However, before the minutes become public (see below) there will be an additional short period of review allowing members to make sure they are comfortable with the information becoming public. All members are to notify RC by email whether they have an objection to any item becoming public.

   Once final confirmation is obtained from all members, GPM will publish the minutes online, and RC will provide the files to TD to be also published on the IUPAC website. The JCBN minutes will no longer be bound with the minutes of the Division VIII meetings.

   There was some discussion whether the minutes should be made public. KFT mentioned that this may prevent members from discussing topics of a private nature in the meetings. TD reminded that the minutes have been public for a number of years. It was decided that when there is a need to discuss a topic that requires privacy, it will be specifically excluded from the public minutes.

5) Matters arising. TD asked DS for the PowerPoint presentation he presented at the 2012 meeting. DS sent the file to JCBN shortly after.

6) Reports

   a) Chairman's Report (GPM)
   GPM reported that the enzyme task force continues to create about 300 new enzyme entries per year. He also acknowledged the progress made by AR with the flavonoid project and the progress being made on the carbohydrate project.

   b) Treasurer's Report (RC)
   With funding from IUBMB plus support for individual members through IUPAC projects, the committee was within budget in 2013. However, the IUBMB funding would end after this meeting, as the last funding decision was for the 2012-2014 years. Action items: RC and GPM to contact the IUBMB treasurer to start the process of allocating funds for the following years.

   GPM and KHH confirmed that JCBN meeting room costs would be split equally between the two organizations (IUBMB and IUPAC).

   c) IUPAC Report (KHH)

   The new Blue Book, Nomenclature of Organic Chemistry, IUPAC Recommendations and Preferred Names 2013, had been completed and has been available from the Royal Society of Chemistry (RSC) since Christmas 2013. The book contained a number of errors, a list of which is currently being compiled. The list of corrections is currently available online, and will probably be published at some stage. GPM asked members who have access to the book to report errors

they encounter. A PDF file of the book will be made available only 1-2 years after the book went into print.

Brief Guides: The Brief Guide to Polymer Nomenclature was very successful and has already been reprinted in some 12 Journals. A brief guide to the nomenclature of inorganic compounds should be published later this year, and a guide on organic-chemical nomenclature should be published soon thereafter.

International Chemical Identifier (InChI) project: Ongoing projects include "Implementation of InChI for chemically modified large biomolecules" to handle large biomolecules.

Another newly established project is "End-of-line hyphenation of systematic chemical names".

The 2014 meeting of Division VIII Committee is scheduled for August 3 – 4 2014 in Bangor, Wales.

René Deplanque, IUPAC Secretary General, as well as John Petersen, the Managing Director, have recently resigned. Colin Humphris has been elected the new Acting Secretary General until a new person is elected. Bryan Pearson, who was responsible for IT operations, also left, and that position needs to be filled as well.

The division's budget was reduced by 15 %. Reimbursements now require receipts.

Deficiencies of the website have been acknowledged by the president, who has decided to give a high priority to fixing the problems. The goal is to have a fully functional website by August next year.

The publishing house deGruyter has been contracted for publishing of the IUPAC journals Pure and Applied Chemistry and Chemistry International, starting as January 1st 2014.

Future IUPAC sponsored conferences shall be called IUPAC endorsed conferences.

TD: A new project regarding boron chemistry has been running for a year now.

GPM mentioned a project entitled "Nomenclature of transition states and their analogs for phosphoryl transfer reactions" conducted by Division III, which regards the 3-dimensional structure of phosphotransferases. The first meeting will be at the end of October 2014.

7) Enzyme Nomenclature and Classification

a) Report on enzymes classified during the past year (AGM)

The enzyme task force performs the tasks of assigning new EC-numbers and updating current entries. About 10 people are involved in the process.

About 300 new enzymes were entered in the last year. The EC list currently contains 6313 EC numbers. They comprise 5385 existing entries, 635 transferred entries, and 293 deleted entries.

The ExplorEnz website receives 2.2 million hits per year (including web crawlers). After filtering, the website processes 660,000 successful page requests by human users.

GPM had no current statistics about the use of his website, due to technical obstacles that limit his ability to access his website remotely.

When a new batch of enzymes has been approved by the enzyme task force, the JCBN is notified, so that they can look over the entries before they enter public review. The current deadline for response from the JCBN is two weeks from the time of notification.

b) Report from the Enzyme Taskforce meeting (KFT)

i) The electron transfer document published by NC-IUB recommends using the term "heme-thiolate" enzymes, but this term has not been accepted by the community. Thus, the enzyme task force has decided to stop using it. Instead, the EC list would start using the phrase "cytochrome P-450 (heme-thiolate)"

ii) The case of pyridoxal phosphate (PLP)-dependent deaminases: these enzymes are actually lyases, breaking a C-C, C-O, or C-S bond without the involvement of water. However, the products of the lyase reaction undergo tautomerization, followed by a spontaneous hydrolysis that releases ammonia. The enzyme task force debated whether they should be classified by the overall reaction (making them carbon-nitrogen lyases) or by the first, enzyme-catalysed reaction, making them carbon-carbon lyases, carbon-oxygen lyases, or carbon-sulfur lyases. It was decided to proceed with the former option, except for the carbon-sulfur lyases, which would remain classified as such.

iii) The term “decyclizing” would be replaced with “ring-opening”, which allows specifying which ring is being opened, where desirable.

iv) Regarding procedures of curation of the enzyme list, the enzyme task force will use the “blocking” feature of DraftEnz more frequently. When an entry is blocked, it cannot proceed to the next stage until the block has been lifted. This would ensure that entries would not proceed until comments and queries have been addressed.

v) Chemical compound names that appear in the accepted name but not in the reaction equation, and may be unfamiliar to a reader (such as “mimosine”), are to be defined in glossary entries.

vi) The abbreviation list, mentioned in the minutes of last year’s meeting, has been prepared and is available at the ExplorEnz website. It includes terms that can be used in the EC list without being defined within the entry.

vii) The number and variety of GPM’s diagrams continue to increase. They reside on GPM’s website, while relinked copies are hosted on ExplorEnz.

viii) The Wikipedia entry for the EC commission is inadequate and misleading. KFT and DC will prepare a new entry, and the other members of the enzyme task force would review it and help with updating the entry.

ix) The classification rules, available online, will be updated to reflect current curation guidelines.

x) The Brief Guide: the question arises whether IUPAC is the most appropriate agency for supporting this project, since the enzyme list is an IUBMB project. For the time being, KFT will circulate the guide he wrote among the enzyme task force members, but a decision about the exact publishing route need not be made at this time.

xi) The single existing entry in the enzyme list for the enzyme that attaches ubiquitin to polypeptides, which has been shown to be incorrect, is being replaced, through an initiative by IS, by a number of new entries.

xii) The enzyme task force would consider adding new sub-sub classes of EC 5 (isomerases) for conformational isomerases.

xiii) Newsletters, which used to be a means by which the Enzyme Commission and the IUB-NC communicated information to the public, will be replaced by News Items, published on the ExplorEnz website at http://www.enzyme-database.org/news.php (see also section 10 below). It is recommended that the JCBN web page at IUPAC will be updated to point to this URL.

xiv) For a small number of compounds the reaction equations use a formula instead of a name (e.g. CO_2). In some cases these formulas imply a specific charge (e.g. HCO_3^-), which is not desired. Such formulas should be replaced with names that do not imply a charge. HCO_3^- will be replaced with hydrogen carbonate.

KHH asked to discuss the Brief Guide again. He suggested that if a guide is prepared, it should be published in Pure and Applied Chemistry. The issue of copyrights was raised: DH read the guidelines, which state that in order for an item to be published in multiple journals, IUPAC requires acknowledgement of the IUPAC source (including the copyright symbol). However, since the enzyme list is an IUBMB project, IUBMB should most likely hold the rights. Another complication is

that publication would require that the guide is an IUPAC project. KHH suggested that the guide could potentially be published in Pure and Applied Chemistry after publication elsewhere.

8) IUPAC Project Reports

a) Nomenclature of Flavonoids (AR)

AR presented progress on the project. The document was reviewed by 23 reviewers, and the team members are now revising the document to address the reviewers' comments. The document has already been accepted, provided those comments are adequately addressed. Once a final version is prepared, it will be circulated among the JCBN members.

b) Revision of Carbohydrate Nomenclature

DH described the progress made during the carbohydrate group meeting. The team went over the 2-Carb document and identified required changes. Due to time constraints they were able to get only through part of the document (up to section 33), and will meet again to go over the rest of the document. The document would be updated to discuss glycoinformatics. DH emphasized that the iconic representation of complex oligosaccharides is catching on.

An expert has been identified to help with cyclodextrins and would be contacted.

JFGV discussed the topic of glycoinformatics, and why it is important to consolidate different approaches. Challenges include clarifying some fundamental concepts, such as the definition of a minimal recognizable carbohydrate building block, which is essential for the algorithms that identify carbohydrates in complex structures.

There was some discussion of carbohydrate databases. JFGV pointed to difficulty in obtaining funding for maintenance and growth of the databases.

Regarding the issue of naming very complex carbohydrates, GPM pointed to the problem of classifying natural products. When does a heavily modified glycine stop being an amino acid? He mentioned "general nomenclature" which provides non-ambiguous names that are not the preferred IUPAC names, but are acceptable. He suggested that a similar approach may help the carbohydrate field. KHH mentioned that in the chapter on natural products in the new Blue Book, preferred names are generally not given.

c) Glossary of Small Molecules of Biological interest (DC)

DC pointed out that the progress on the project has been slow. He was the only one working on it, and was busy with several other projects during the past year. The project currently covers about 200 compounds, and will eventually be published in Pure and Applied Chemistry. The compounds will be available online in a database form. AGM is responsible for the computerized portion of the project, which is to be made available online, initially through the ExplorEnz website. This will be distinct from the development version, currently hosted at Trinity College Dublin.

9) Database Progress Reports

a) MK described recent developments in KEGG. Among recent projects is the creation of a reaction module database (reaction modules are sets of reactions that involve different compounds but similar chemical modifications). The work is described in the following papers:
http://www.ncbi.nlm.nih.gov/pubmed/23384306
http://www.kegg.jp/kegg/reaction/rmodule.html

Recent development in the KEGG-related project GenomeNet (managed by Dr. Goto) includes updating of the E-zyme project (E-zyme2, http://www.genome.jp/tools/e-zyme2/) to incorporate suggestions for genes that may encode enzymes catalysing the transformation of a given reactant into a given product. The E-zyme project already enabled automated assignment of EC sub-subclasses for a specified chemical transformation.

b) Progress in the BRENDA database (DS)

BRENDA has secured funding at least until 2019. BRENDA contains about 75,000 experimentally characterized enzymes. In addition to curated data there are data imported from other databases (Uniprot, PDB etc) and calculated data. AMENDA is a much larger database

generated by automated text mining, but is of lower quality. DS demonstrated several features of BRENDA, such as searches (e.g. full text search), browsing ontologies, 3D structures, and more. DS also mentioned the BKM database which integrates reactions from BRENDA, KEGG and MetaCyc.

KFT described the STRENDA project, a project aimed at standardizing the reporting of enzyme-kinetic experimental data in publications. These guidelines have already been accepted by a number of relevant journals.

10) ExplorEnz:

It was discussed whether it is sufficient to publish news items (see section 7 b xiii above) on the website, or whether they should be distributed actively to recipients. After a short discussion it was decided that the former is sufficient.

a) Specific news items to be written:

- DC will write a news item describing the change from heme-thiolate to P-450 in enzyme list entries.
- DS will write a request for a nucleic acid enzyme expert to join the enzyme task force.

b) It was suggested to add publications of general interest to the publication section in ExplorEnz (http://www.enzyme-database.org/publications.php).

11) Update on Action Items from the Minutes of the 2013 Meeting: no items to discuss

12) Discussion of IUBMB funding for the next years

Since the IUBMB funding expires in 2014, GPM and RC will contact IUBMB to arrange funding for the next few years. They will send IUBMB the minutes from the 2013 and 2014 meetings, as well as a document listing the progress of the enzyme task force during the years 2012-2014. AGM should prepare a draft of the progress document that would also include a graph showing the increase in annual new enzyme entries, and will cite the recent publication by AGM and KFT, Fifty-five years of enzyme classification: advances and difficulties (www.ncbi.nlm.nih.gov/pubmed/24103004).

13) Membership of the committee

a) GPM will send a list of the recipients of the JCBN and enzyme task force mailing lists to the members of JCBN to ensure there are no errors or omissions in the lists.

b) RC will invite Bernard Henrissat to participate in the next meeting of the enzyme task force.

14) Any Other Business

KHH mentioned a revision of the phosphorus document that was started, but never finished, by the late Hal Dixon. It was decided to establish a panel consisting of KHH, GPM, TD and ME to examine potential ways to renew the project.

AR asked for help solving a nomenclature problem, typified by glucose-6-sulfate, where the oxygen is named twice. KHH pointed out that this is similar to the case of glucose-6-phosphate, and reminded that it is important that the two documents (the carbohydrate document and the phosphorus document) would be consistent.

GPM described a potential project of naming conjugates. The problem occurs most frequently with two drugs conjugated to each other via a linker unit. There is no action item associated with this potential project.

15) Date and Place of the 2015 Meeting

DS and IS invited the committee to meet in Braunschweig, Germany on May 11-13 2015 (Mon-Wed).

16) GPM thanked JFGV on behalf of the committee for his help in organizing the 2014 meeting.

The meeting was adjourned at 15:20.