Minutes

IUPAC DIVISION VII CHEMISTRY AND HUMAN HEALTH
SUBCOMMITTEE ON DRUG DISCOVERY AND DEVELOPMENT
Lisbon, Portugal - Hotel Vilá Galé Ópera, Room "Metropolitan"
Saturday, 6 September 2014, 9 AM - 5.00 PM

(Minutes by Edmond Differding and János Fischer)

Attendees: Sergey Bachurin, Jonathan Baell, Helmut Buschmann, Edmond Differding, János Fischer (Chair), Robin Ganellin, Reuben Hwu, Tom Perun and Mario Varasi

Remote participation in part (Skype) : Balu Balasubramanian, Michael Liebman and Per Lindberg

Apologies : Vincenzo Abbate, Sulejman Alihodzic, Eliezer Barreiro, Eli Breuer, Mukund Chorghade, Paul W. Erhardt, A. Ganesan, William Greenlee, Jan Heeres, Toshi Kobayashi, Yvonne Martin, Péter Mátyus, Serge Mignani, Anjali Rahatgaonkar, Jörg Senn-Bilfinger, Johan Ulander and Patrick Woster

1. Introductions, Opening Remarks, and Minutes of the Previous Meeting in Brussels

After the introduction of the participants, JF gave an overview of SC activities between 2000-2014 with date and place of the subcommittee meetings, and their participants.

Then the minutes of the Brussels meeting were discussed.

TP recommends showing explicitly the dates of ACS and EFMC meetings when planning upcoming subcommittee meetings, given the difficulties to get funding to attend. RG suggests to add and publish who wrote the minutes, and to use rigorously the same numbering as in the agenda.

Taking into consideration these comments, the minutes of the SC meeting in Brussels were accepted unanimously.

2. Matters arising from the Minutes of the Brussels meeting

2.1. IUPAC-Richter Prize

Five IUPAC-Richter Prizes have been given between since 2006-2014. A new agreement is planned between IUPAC and Richter to continue this successful activity.

A short analysis of the awardees in years 2006-2014 shows a reasonable geographic diversity, but unfortunately no gender diversity with all recipients being male. It is recommended to highlight the need to have female nominees for the upcoming editions.

2.2. IUPAC Emeritus Fellow

The list of IUPAC Emeritus Fellows is reviewed (Lester A. Mitscher, John G. Topliss, Camille G. Wermuth, Naofumi Koga and C. Robin Ganellin). RG, the upcoming Emeritus Fellow, will receive a plaque from IUPAC during the opening ceremony of the IUPAC-Richter prize session at EFMC-ISMC in Lisbon.

3. Membership

JF summarizes his efforts to get feedback from subcommittee members to update the composition on the website.

3.1. Mission statement

It is agreed to accept the following mission statement of the subcommittee, as proposed by RG:

The IUPAC Subcommittee on Drug Discovery and Development has the goal to facilitate the use, understanding, public awareness, and application of medicinal chemistry and aspects of drug discovery and development worldwide.

RG reports on his manuscript in preparation an article for *Chemistry International* under the title "Medicinal Chemistry in IUPAC. Accomplishments During the Decade 2002-2012". Highlights are : four books : three volume of Analogue-based Drug Discovery (Editors : János Fischer and C. Robin Ganellin), and "Practical Studies for Medicinal Chemistry - An Integrating Approach for Developing Countries" (Editors: A. Monge and C.R. Ganellin), several glossaries, which are published in Pure and Applied Chemistry (PAC), and short courses for medicinal chemists in Latin America and India. IUPAC-Richter Prize will be summarized in the article.

Post meeting informations: Fabienne Meyers plans to publish the article in March or May issue of CI. She also proposed to review and improve the subscription of SC webpage on the homepage of IUPAC.

3.2. Future modus operandi of the DDD Subcommittee

General comment: it becomes urgent to stress the need for gender diversity in the subcommittee, and to encourage female nominations and applications.

Lack of financial resources: it is difficult for the majority of committee members to attend meetings in person. Therefore, the meetings will be organized before or after important medicinal chemistry meetings in Europe and America to minimize the travel expenses. JF stresses his time consuming efforts to get a reply from some members. Several options are discussed:

- open to web-based conferences (Skype?) – as done for some discussions and project presentations today (see below)

- repeat regularly by mail the questionnaire: choose 'active member' vs. 'corresponding member', and also consider the possibility to remove automatically members who have not been active for a longer time (2 years)

- importance of being well connected to National Adhering Organisations (NAOs), and in particular their Medicinal Chemistry Divisions.

It is expected that an *active member* attends a SC meeting at least once per year either in person or with the help of an electronic communication form (eg. Skype).

In case of a *corresponding member* it is not expected that the member participates in person in the SC meetings, however, a corresponding member also participates in SC activities, discussions and projects.

3.3. Membership, Chair and Secretary

The membership term as Subcommittee member follows the Division VII term, i.e. two years (current term: 2014-2015).

JF is unanimously confirmed in his role as Subcommittee Chair

ED is elected unanimously Secretary of the Subcommittee

The SC DDD has the following membership :

Active members : Vincenzo Abbate (UK), Sergey Bachurin (Russia), Jonathan Baell (Australia), Balu Balasubramanian (USA), Eli Breuer (Israel), Helmut Buschmann (Germany), Mukund Chorghade (USA), Flavio Emery (Brazil), Paul W. Erhardt (USA), János Fischer (Hungary), Edmond Differding (Belgium), Robin Ganellin (UK), A. Ganesan (UK), William Greenlee (USA), Per Lindberg (Sweden), Michael Liebman (USA), Derek Maclean (USA), Yvonne Martin (USA), Serge Mignani (France), Tom Perun (USA), Jörg Senn-Bilfinger (Germany) and Patrick Woster (USA).

Corresponding members : Sulejman Alihodzic (Croatia), David Alker (UK), Eliezer Barreiro (Brazil), Henning Boettcher (Germany), Jan Heeres (The Netherlands), Reuben Hwu (Taiwan), Toshi Kobayashi (Japan), Péter Mátyus (Hungary), John Proudfoot (USA), Anjali Rahatgaonkar (India), Henk Timmerman (The Netherlands), Johan Ulander (Sweden), Mario Varasi (Italy) and Zhu-Jun Yao (China).

4. Projects/Working Parties

4.1. Nomenclature and Terminology

4.1.1. **Glossary of Terms used in Computational Drug Design** Project 2010-057-3-700 (Yvonne Martin): The glossary project is in its final reviewing phase.

4.1.2. **Glossary of Drug Metabolism Terms**. Project 2000-009-700 (Paul Erhardt): The task group plans to prepare a draft of ca. 100 terms according to the revised deadline at the end of 2014.

4.1.3. **Human Drug Metabolism Database**. Project 2011-018-1-700 (Paul Erhardt): the task group chair plans to prepare an article to PAC or CI by the end of 2015.

4.2. Training and Development

4.2.1. A Survey of Research into New Drugs for Neglected Diseases in Latin America. Project 2009-033-1-700 (Robin Ganellin)

RG sent out an e-questionnaire to 47 scientists in Latin America asking whether they would attend a workshop on their research on NTD's. Received 9 enthusiastic replies, and 5 returns as undeliverable. Also contacted Drs Hugo Cerecetto and Mercedes Gonzalez several times for their help but received no replies from them.

Post meeting note: RG tried again to Cerecetto and Gonzalez and this time received a response (October 9) indicating their interest in organising a workshop in Montevideo in March-April 2015.

4.2.2. Medicinal Chemistry India, Part II. Project 2014-011-1 (Balu Balasubramanian)

BB joins the meeting by Skype conference. The short course in 2013 was well received. The second short course is organized by BB and William Greenlee, and includes Indian case studies.

South-East Asian institutes have been contacted (Taiwan, Singapore), but so far without success.

Fees for academics are one third of industrial fees.

4.2.3. Highlights in Medicinal Chemistry, Rio de Janeiro. Project 2014-022-1, (Eliezer Barreiro and János Fischer)

Professor Eliezer Barreiro, the local organizer of the Short Course "Highlights in Medicinal Chemistry" could not participate, therefore, Janos Fischer reported on the project status.

Eleven delegates of IUPAC and ACS will give 14 lectures :

Magid Abou-Gharbia (USA), Peter Bernstein (USA), Helmut Buschmann (Germany), János Fischer (Hungary), A. Ganesan (UK), Jan Heeres (Belgium), Tom Perun (USA), Joerg Senn-Bilfinger (Germany), Klaus Wanner (Germany) and Patrick Woster (USA), Wendy Young (USA).

The lecture titles were given in the Brussels minutes. Three further lectures are planned as follows:

Bernstein, Peter (USA) : The Evolving Role of Chemical Technology in Drug Discovery"

Ganesan, Arun (UK) : Physicochemical Properties in Drug Design

Young, Wendy (USA): Discovery of Kinase Inhibitors Across Multiple Therapeutics Indications

The lectures will be given in the XXI. Summer School in Medicinal Chemistry in Rio de Janeiro between January 26-30, 2015.

4.3. New Technologies and Special Topics

4.3.1. Successful Drug Discovery, Vol. I. Project 2013-016-1-700 (János Fischer)

It is the first volume of a new book series "Successful Drug Discovery". The fist volume is edited by János Fischer and David Rotella.

Seventeen authors were invited, but at the end eleven chapters will appear in the book. The major part of the invitations were successful. It is a good ratio if we consider the difficulties to publish new drug discoveries.

The book will be published by Wiley-VCH at the beginning of 2015.

4.3.2. The Emerging Problem of Novel Psychoactive Substances. Project 2014-019-1 (Vincenzo Abbate)

RG will propose a relevant Advisory Committee in the UK.

4.4. New Project Proposals

TP stresses the fact that the budgets have been reduced by 12-15% as a consequence pressure on IUPAC funds. 26,200 US$ of a total of 38,400 US$ (68%) have already been allocated to projects for the years 2014-15.

TP gives an update on new project proposals.

4.4.1. Successful Drug Discovery, Vol. II. (János Fischer)

The second volume is still in planning phase. Section editors of therapeutic fields should help with the editorial work.

4.4.2. Drug discovery: Dealing with the reality of co-morbidities (Michael Liebman)

Skype teleconference :

A task group is under organization. The project would produce a freely available, but limited prototype, followed by a full-fledged commercial version. TP stresses the fact that IUPAC funded projects are not allowed to make a profit, and therefore asks ML to submit a detailed project proposal and go through the formal approval process before deciding on next steps.

Further questions raised are:

- should this not be in the realm of clinical pharmacology, and do we know what tools have already been developed (RG)?

- is this type of approach not likely to be superceded by personal genetic profiling over the coming decade (MV)?

Post-meeting comments (Michael Liebman)

Ideally clinical pharmacology should address this but rarely, if ever, does....please see the following definition of clinical pharmacology from PhRMA:

"The intent of the program is to encourage multidisciplinary training designed to bring the perspective of molecular, cell and systems biology to bear on research in pharmacology in intact organisms. The scope of these programs includes basic studies of drug action, detection of cellular responses to drugs at the gene level that create opportunities to optimize individualized drug therapy, and the corresponding evaluation of pharmaceuticals in human and clinical populations."

The reality, however, is that this focuses on molecular processes, etc and their potential impact on human populations at a very general level and not the reverse which would incorporate real world patients to understand what they actually represent, especially in terms of co-morbidities, etc, and also how medicine is actually practiced, which more frequently than not does not follow established guidelines. Even ignoring the second element, the issue of patient complexity and its impact on diagnosis, treatment and response of patients to medications directed at specific targets is an issue that may not show up in clinical trials where inclusion/exclusion criteria are optimized to produce results leading to regulatory approval, and leaving a large gap that can impact the commercial viability of a drug because real world patients do not look like clinical trial patients. By way of confirmation of the importance of this issue, I am now working with 3 pharmaceutical companies, one biotech and two disease foundations with an emphasis on bringing "real world evidence" into the drug development process...with the goal of providing better and earlier decision making about product development, clinical trial populations, labeling an commercialization. I also chair the Translational Medicine and Therapeutics section of PhRMA and sit on its scientific advisory board and have on my committee the Assoc Direc of Drug Safety in the Clinical Pharmacology Office of the FDA who heads Clinical Pharmacology for PhRMA and who has indicated that this is not within their area of focus but is critical to their mission of drug safety and efficacy this study presents the basis for why this is relevant in real world populations)

4.4.3. The Role of Phenotypic Research in Drug Discovery (Per Lindberg)

PL joins by Skype teleconference, and explains the industry's need for a paradigm shift. A journal article is mentioned under the same title: Kalle Lötberg "Drug research needs a paradigm shift" in *Kemiväriden Biotech med Kemisk Tidskrift*. Nr. 3 March (2014), pp 27-28.

PL plans to prepare a project proposal on this topic to prepare a review article.

Future plans:

a.) It would be good to update the book "Pharmaceutical Salts (2002, Wiley-VCH)

b.) In order to broaden the chemical audience, by publishing outside of IUPAC journals, e.g. in Chemical & Engineering News, or Annual Reports in Medicinal Chemistry (ACS), Chemistry World (RSC), or Angewandte Chemie International Edition (GDCh),….

5. Other Business

5.1. European Federation for Medicinal Chemistry (EFMC)

JF and ED are the committee's interface with EFMC.

5.2. Asian Federation for Medicinal Chemistry (AFMC)

RH reports on AIMECS 2013, held in Taiwan, sponsored by IUPAC, and with speakers from ACS (TP) and EFMC (Uli Stilz). It has been attended by 554 participants from over 20 countries, of which 54% were foreigners. The book of abstracts has been published by ChemMedChem.

AFMC includes currently 8 associations, to which will be added Indonesia, with ongoing discussions with Singapore and Pakistan.

So far no Indian association is represented, which could be due to cost reasons. The Indian Society of Chemists and Biologists should be approached (ED).

5.3. Next meeting

Rio de Janeiro - January 2015 (7 committee members will be present)

Further options:

- South Korea, August 9-14, 2015 in Busan (General Assembly)

- Boston: ACS National Meeting, August 16-20, 2015

Post-meeting note: Antwerp (Belgium) - connected to 'Frontiers in Medicinal Chemistry' meeting, September 14-16, 2015