

IUPAC DIVISION VII CHEMISTRY AND HUMAN HEALTH
SUBCOMMITTEE ON DRUG DISCOVERY AND DEVELOPMENT
Brussels, Belgium
(The Royal Academies for Sciences and the Arts of Belgium)
Hertogsstraat 1- Rue Ducale
Wednesday 28 May 2014, 9 AM - 3.00 PM

The minutes have been prepared by Edmond Differding and János Fischer

Attendees: János Fischer (Chair), Sergey Bachurin, H. Buschmann, Edmond Differding, Robin Ganellin, Vladimir Gubala, Jan Heeres, M. Liebman, Tom Perun, Linda Johnston,
Invited: Robert Schoonheidt (Belgian National Chemistry Committee)

Excused: Alhodzic, David Alker, Balasubramanian, Barreiro, Bremner, Eli Breuer, Henning Böttcher, Derek Buckle, Mukund Chorghade, Paul Erhardt, Arun Ganesan, William Greenlee, Chris Hill, Reuben Hwu, Toshi Kobayashi, Yvonne Martin, Péter Mátyus, Serge Mignani, John Proudfoot, Rahatgaonkar, David Rotella, Joerg Senn-Bilfinger, Henk Timmerman, Ulander, Varasi, Patrick Woster, Vincenzo Abbate

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

JF opens the meeting with a short overview of the structure of IUPAC and recent activities of its Subcommittee on Drug Discovery and Development. JF accepted to take over the chairmanship of the subcommittee in 2014 after Tom Perun, its previous chair, became President of IUPAC Division VII.

The minutes of the Dallas meeting are accepted.

2. Matters arising from the Minutes.

2.1 2014 IUPAC-Richter Prize

JF summarizes the selection process by the jury, chaired by Robin Ganellin, that led, out of nine nominations, to this year's prize winner Helmut Buschmann, for his contribution to the discovery and development of Tapentadol at Grünenthal.

The extension of the agreement between IUPAC and Richter, with an initial commitment for 5 (biennial) editions from 2005-2015, is under discussion. RG proposes to include a clarification of the rules for the future editions, and will make a recommendation at the next subcommittee meeting.

2.2. IUPAC Emeritus Fellows

TP informs RG about the Div VII Committee's proposal to make him an IUPAC Emeritus Fellow in recognition of his outstanding contributions over many years. RG is delighted to accept and will receive a plaque from TP during the IUPAC-Richter Prize ceremony at ISMC 2014 in Lisbon. ED to coordinate this with the ISMC organizers.

3. Membership

3.1. Division VII Committee Membership for 2014-2015 and upcoming elections

The Committee has six new members for the 2014-15 term: Tom Perun, Rita Cornelis, Helle Moller Johannessen, Linda Johnston, Vladimir Gubala and Edmond Differding. The following current members will step down after the upcoming 2015 elections: JF, Paul Illing, and Wayne A. Temple,

The Nomination Committee will be chaired by Rita Cornelis, and will include M. Schenk, Paul Erhardt, Robin Ganellin, and Urban Forsum.

Nominations will be submitted by NAOs, but can also include recommendations by current committee members. The aim is to have two candidates per vacant position, spread across all three subcommittees, with a good diversity in terms of gender and geography.

3.2. Future modus operandi of the DDD Subcommittee

After the change from 'Subcommittee on Medicinal Chemistry and Drug Development' to 'Subcommittee on DD&D', it is agreed to use for future daily communications the 'easier' name 'Subcommittee on Drug Discovery'

Unfortunately most current subcommittee members had to decline the attendance of the Brussels meeting, be it for agenda or for budget reasons. Since IUPAC does not reimburse travel expenses to members without an accepted project, and since industry has become exceedingly reluctant to pay for their own members' expenses, JF will clarify with all current members who wants and can afford to participate at the subcommittee meetings as active members or as corresponding members.

It has become urgent to agree on how to pay for current expenses related to the organization of the subcommittee meetings. One possibility is to use the budgets of projects, as these require a well-functioning subcommittee to coordinate their projects. Future projects should include such expenses as a fraction of their running costs.

This leads to a discussion on how IUPAC in general can become again more attractive to potential members, and how to use web-based technologies and social networks to connect to the world's chemistry communities.

4. Projects

4.1. Nomenclature and terminology

- Glossary of Combinatorial Chemistry Terms. Project 2003-044-1 (A. Ganesan): The task group leader plans to complete the project by the end of 2014.

- Glossary of Drug Metabolism Terms. Project 2000-009-1-700 (P. Erhardt). The project will be completed by the end of 2014. No news since the last meeting in Dalls.

- Glossary of Terms in Pharmaceutical Process Chemistry. Project 2001-049-2-700 (M. Chorghade). Project highly unlikely to be finished, no progress for years.

- Glossary of Terms used in Computational Drug Design Project 2010-057-3-700 (Y. Martin): The glossary is completed and will be sent out for reviewing. The task group leader and seven members prepared the manuscript (35 pages) as the second part of these glossaries. 187 new and revised terms have been defined. After the reviewing phase it will be published in PAC.

A general discussion follows on new web-based publication tools which allows a regular update of the fields of interest. This is however likely to be in conflict with IUPAC's strict refereeing and publication rules.

4.2 Training and Development

- A Survey of Research into New Drugs for Neglected Tropical Diseases in Latin America. Project 2009-033-1-700 (R. Ganellin): has been published in *Chemistry International* (May-June 2013). RG to follow up with H. Cerecetto for a translation into Spanish for publication in Latin American journals. The project has been able to map close to 50 research groups in drug discovery, using a questionnaire, and aims at connecting these for future collaborations. It is proposed to schedule a workshop with participating groups. RG will contact HC regarding the possibility to hold this at Uruguay University, co-funded by IUPAC. RG will also aim at publishing a revised version in other journals, e.g. in *Annual Reports in Medicinal Chemistry*. ML proposes to connect the groups with the Neglected Diseases Center at the University of Texas Medical Branch in Galveston, TX, as well as to the Gates Foundation. It would be highly interesting to extend this survey to other countries such as South Africa and India. As ISMC 2014 in Lisbon will include a session on neglected diseases, it is proposed to invite the session chair, Prof. Kelly Chibale, Cape Town University, to the subcommittee meeting in Lisbon.

- Medicinal Chemistry India, Project 2012-032-2-700 (B. Balasubramanian). The short course "Medicinal Chemistry India 2013, held at Sri Ramachandra University, Chennai, India, during February 11-15, 2013 was a successful meeting. A detailed report has been published in *Chemistry International*, 36 (2), 2014.

4.3 New Technologies and Special Topics

- Human Drug Metabolism Database. Project 2011-018-1-700 (P. Erhardt).
No news since the last meeting in Dallas.

- Natural Products with Medicinal and Nutritional Value. Project 2001-050-2-700 (M. Chorghade).
The project has been completed according to the IUPAC homepage.

- Successful Drug Discovery. Project 2013-016-1-700 (J. Fischer):

Eleven manuscripts are ready after the reviewing phase. In case of two manuscripts (linaclotide and vilazodone) the approvals did not yet arrive from the company (Forest). Two manuscripts have been declined and in two cases the manuscripts could not be completed because of personal reasons of the authors.

These are the following manuscripts :

1. Janos Fischer and David P. Rotella :
Serendipity in Target-based Drug Discovery
2. David Swinney
Drug Discoveries and Mechanism of Action
3. Insulin Analogues Improving the Therapy of Diabetes
John M. Beals
4. Discovery of Avanafil for the Treatment of Eerectile Dysfunction
Kiichiro Yamada, Tosiaki Sakamoto, Kenju Omori and Kohei Kikkawa
5. Dapagliflozin, a Selective SGLT2 Inhibitor for the Treatment of Diabetes
William N. Washburn
6. Hisashi Shinkai
Elvitegravir, a New HIV-1 Integrase Inhibitor for Antiretroviral Therapy
7. Matthias Eckhardt, Thomas Klein, Herbert Nar and Sandra Thiemann
Discovery of Linagliptin fro the Treatment of Type 2 Diabetes Mellitus
8. Edward Taylor
The Discovery of Alimta (pemetexed)
9. Shigeki Hibi

Perampanel : a Novel, Non-competitive AMPA Receptor Antagonist for the Treatment of Epilepsy

10. Govinda Rao, Mark A. Murcko, Mark Tebbe and Ann D Kwong
Discovery and Development of Telaprevir, a Protease Inhibitor for the Treatment of Hepatitis C Infection
11. Sandhya Girish, Gail D. Lewis Phillips, Fredric S. Jacobson, Jagath R. Junutula and Ellie Guardino
Antibody-Drug Conjugate : Design and Development of Trasuzumab Emtansine (T-DM1)

All these manuscripts will be sent to Wiley-VCH for layout by June 30, 2014. The book will be published at the end of 2014.

There is a general discussion on the title, i.e. 'discoveries' versus 'discovery'. The latter one might be more convenient and broader, as it will allow chapters on technologies, strategies, etc... in addition to case studies.

4.4 New Projects

- Medicinal Chemistry India, Part II. Project 2014-011-2-700 (B. Balasubramanian):

The second course will include more lectures than the first one, and four speakers from India. Industrial people from USA will have their own funding. Speakers from academia will get their travel cost refunded. The meeting is scheduled on Feb 9-15, 2015 in Chennai.

- Highlights in Medicinal Chemistry, Rio de Janeiro, January 26-30, 2015 Project Proposal 2014-022-1(J. Fischer):

Within the framework of the XXI Summer School of the Federal University of Rio de Janeiro the SC on Drug Discovery and Development will teach a short course with 12 lectures to postgraduate students. The local expenses of the lecturers will be covered by the Summer School organizer, and in case of the approval of the project proposal, the travel expenses will be covered in part by IUPAC and ACS.

The following lectures are planned :

1. Abou-Gharbia, Magid (Temple University, Philadelphia, USA)
Medicinal Chemistry Approaches for the Innovative Therapeutics
2. Bernstein, Peter (PhaRmaB LLC, Rose Valley, USA)
Where Next in Anti-inflammatory Drug Discovery ?
3. Breuer, Eli (Hebrew University, Jerusalem, Israel)
Tumor Microenvironment as Target in Cancer Therapy
4. Buschmann, Helmut (PharmaConsulting, Aachen, Germany)
Pain Research Today: from Morphine to Tapentadol
5. Fischer, János (Richter Plc, Budapest, Hungary)
Serendipitous Target-based Drug Discovery
6. Fischer, János (Richter Plc., Budapest, Hungary)
Optimizing Drug Therapy by Analogues
7. Ganesan, Arun (University of East Anglia, Norwich, UK)
Physicochemical Properties in Drug Design
8. Heeres, Jan (retired from Janssen, Belgium)
The Discovery of Rilpivirine
9. Perun, Tom (IUPAC, Div.VII, Chemistry and Human Health)
IUPAC Role in Human Health

10. Senn-Bilfinger, Georg (University of Stuttgart)
The Role of Proton-Pump Inhibitors (PPIs) in the Treatment of Gastrointestinal Diseases
11. Wanner, Klaus (LMU University of Munich, Germany)
MS Binding Assays and their Application to the Development of New GABA Uptake Inhibitors
12. Woster, M. Patrick (MUSC, Medical University of South Carolina, USA)
Design of Epigenetic Modulators as Potential Therapeutic Agents

In August it is planned to finalize the program of the Short Course in Rio de Janeiro.

- Successful Drug Discovery, Vol. II (J. Fischer) The aim is to start a series on this topic, eventually with the help of section editors, who are experts in their domain. Several new topics are collected based on the new drug introductions of the last years. A new book project for the second volume of Successful Drug Discovery is in planning phase.

- Project proposal by Michael Liebman :

A proposal is being developed involving translational medicine and focusing on the issue of bringing real world patients into the early consideration for drug development to enhance potential success. Currently, most drug development proceeds as if the patient only presents with a single disease or condition and does not recognize the issues of co-morbidities, or the additional effect of other drugs that the patient may likely be taking that could interact with the drug under development. This is becoming a significantly more common occurrence as the population continues to age and it is documented that elderly patients typically have 4 or more co-morbid conditions. A further complexity of this is the difference in patients across age, gender, geographical and socio-economic situations.

This project would highlight the more common situations, both for co-morbidities and drug treatments, including the variation that may take place between US, Europe and Asia. It will not be an exhaustive review of all possible situations but rather try to show some of the relevant breadth of the situation as well as some very specific examples, e.g. for patients with hypertension and/or diabetes. The duration of this project should be accomplished in a reasonably short time period, 1-1.5 years, and become a basic approach that could and should be periodically extended/updated as a service to the industry.

It is also intended that that this project and its resulting database could serve as a prototype for moving away from the traditional published glossary format that tends to be quickly out of date. The project would establish a website that can be continually updated without requiring major effort as the published documents do now.

5. Other Business

- European Federation for Medicinal Chemistry (EFMC): ED to contact the ISMC 2014 organizers regarding a time slot at the IUPAC-Richter Prize ceremony for the IUPAC Emeritus Fellow plaque presentation by TP to RG.

Post-meeting information : The IUPAC-Richter Prize lecture will be on September 10.

- Asian Federation for Medicinal Chemistry (AFMC) (T. Kobayashi): AIMECS 2015 to be held in Korea on October 18-21, 2015.

- Next Meeting : 06 September 2014 (Lisbon)