IUPAC DIVISION VII CHEMISTRY AND HUMAN HEALTH
SUBCOMMITTEE ON DRUG DISCOVERY AND DEVELOPMENT

Antwerp, Belgium, Radisson Blu Astrid Hotel, Koningin Astridplein 7
Sunday 13 September 2015, 9 AM - 4.00 PM

Attendees: Henning Boettcher, Helmut Buschmann, Edmond Differding, Janos Fischer (Chair), Robin Ganellin, Jan Heeres, Michael Liebman,

By teleconference (in part): Vincenzo Abbate

Excused: Sulejman Alihodzic, David Alker, Sergey Bachurin, Jonathan Baell, Balu Balasubramanian, Eliezer Barreiro, Eli Breuer, Mukund Chorghade, Flavio da Silva Emery, Paul W. Erhardt, A. Ganesan, William Greenlee, Reuben Hwu, Toshi Kobayashi, Per Lindberg, Derek Maclean, Yvonne Martin, Peter Matyus, Tom Perun, John Proudfoot, Anjali Rahatgaonkar, Jörg Senn-Bilfinger, Henk Timmerman, Johan Ulander, Mario Varasi, Patrick Woster, Zhu-Jun Yao

1. Introductions, Opening Remarks, and Minutes of the Previous Meeting in Rio de Janeiro.

JF opens the meeting by welcoming the participants, and by inviting Henning Boettcher to introduce himself to the other Committee members (and vice versa). This is followed by a short overview of the structure of IUPAC, the historical background and recent activities of its Subcommittee on Drug Discovery and Development.

The minutes of the Rio de Janeiro meeting are accepted after a minor amendment.

2. Membership

2.1. Division Committee membership

Following the recent elections of the Division Committees of IUPAC, the composition of "Chemistry and Human Health Division" (Division VII) Committee for 2016-2017 is as follows (vacant positions to be filled later, depending on ongoing discussions):

Name	Status	Term	NAO
Dr. Thomas J. Perun	TM – President	2016-2017	United States
Prof. Michael Schwenk	TM – Secretary	2014-2017	Germany
Dr. Rita Cornelis	TM - Vice-President	2016-2017	Belgium
Dr. Vincenzo Abbatte	TM	2016-2017	Italy
Dr. Helle Møller Johannessen	TM	2016-2017	Denmark
Dr. Linda Johnston	TM	2016-2017	Canada

Name	Status	Term	NAO
Dr. Edmond Differding	TM	2016-2017	Belgium
Dr. A. Ganesan	TM	2016-2017	United Kingdom
Dr. Vladimir Gubala	TM	2016-2017	Slovakia
TBD	TM		
Dr. Sulejman Alihodzic	AM	2016-2017	Croatia
Dr. Balu Balasubramanian	AM	2016-2017	United States
Dr. Urban Forsum	AM	2016-2017	Sweden
Prof. Geok Bee Teh	AM	2016-2017	Malaysia
Dr. Assunta Borzacchiello	AM	2016-2017	Italy
TBD	AM		
Prof. Jonathan Blackburn	NR	2016-2017	South Africa
Prof. Sergey Bachurin	NR	2016-2017	Russia
Prof. Bengt Erik Haug	NR	2016-2017	Norway
Prof. Reuben Jih-Ru Hwu	NR	2016-2017	Taiwan
Prof. Nestor Carballeira	NR	2016-2017	Puerto Rico
Prof. Mohammad Saeed Iqbal	NR	2016-2017	Pakistan
Prof. Chulbom Lee	NR	2016-2017	Korea
Prof. Mirja Kiilunen	NR	2016-2017	Finland
Prof. Pavlina Dolashka-Angelova	NR	2016-2017	Bulgaria
TBD	NR		
	10 TMs, 6 AMs, 10 NRs		

2.2. Subcommittee on Drug Design and Development

The SC D3 currently counts 21 active members and 14 corresponding members (for the detailed composition, refer to the Minutes of the Rio de Janeiro meeting, January 27, 2015). Serge Mignani resigned in July from his position as active member.

The chairman opens the discussion on the need for change, in particular for the future chairmanship of the committee. After exchanging their views, all members unanimously invite Janos Fischer to continue in his current role, with Edmond Differding acting as secretary. Both accept.

The committee expresses its concerns about the difficulties members experience to get the required travel budgets to attend the SC meetings. With the way IUPAC finances projects rather than meetings, and with the changes in the pharmaceutical industry over the past decade in particular, and stricter budget controls both in industry and academia, this is however not likely to change. It is therefore proposed to adapt our means of communication, such as through a more extensive use of videoconferencing tools (e.g. Skype) for the whole day, rather than for specific contributions. ML proposes his advice on for the upcoming meeting(s).

Other points that are discussed in relation to communication in general are:
- the long delays for publishing in Chemistry International and the journal's non-availability online (paid subscription only)
- the proposal to adapt the SC's mission statement in order to include related disciplines, in order to keep in touch with the industry which is rapidly evolving

3. Projects

3.1. Nomenclature and Terminology

3.1.1. Glossary of Combinatorial Chemistry Terms. Project 2003-044-1-700 (Ganesan)

The team members are currently reviewing exiting entries, each member taking care of ~1/5 of the glossary. Will review in October and then discuss addition of new entries.

3.1.2. Glossary of Terms used in Computational Drug Design. Project 2010-057-1-700 (Martin)

The glossary manuscript has been submitted online (16 August 2015) and will be reviewed for publication in Pure and Applied Chemistry (PAC) (message from Yvonne Martin, 09 September 2015)

Post-meeting information: The manuscript has been accepted for publication in Pure and Applied Chemistry.

The future need for glossary projects is discussed. Proposed new topics could include biomolecular drugs, or specific fields of medicinal chemistry, such as cancer, diabetes, viral infections, etc… With the rapid changes not only in the pharmaceutical industry, but also in the discipline of medicinal chemistry and in the terminologies used, any such glossary projects should be carefully evaluated in terms of the needs of potential users. It is however still felt that glossaries are very useful for patents and for teaching.

3.2. Training and Development

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

The project aims to identify chemistry researchers and testing laboratories, and their equipment and facilities, in Latin America who are currently working to discover new drugs to treat NTD's. An initial e-questionnaire to 47 scientists in Latin America was met with limited success, which might in part be due to language issues. Based on 6 positive replies, initial contacts were established by RG with Cerecetto and Gonzalez, who expressed their interest in organising a workshop together with a postgraduate programme in Montevideo in 2015. This has however not progressed further, and RG

expresses the need for additional contact people. ML proposes to explore contacts via the Center for Tropical Diseases at the University of Texas Medical Branch at Galveston, or the Gates Foundation.

3.2.2. Highlights in Medicinal Chemistry. Project 2014-022-1-700 (Fischer)

Ten years ago, in 2005 the Subcommittee held a Short Course "Highlights in Medicinal Chemistry" in Brazil. In 2015 the short course has been organized again as part of the 21st Summer School of the University of Rio de Janeiro (25-31 January, 2015).

Prof. Eliezer J. Barreiro (Federal University of Rio de Janeiro, UFRJ) and leader of LASSBio (Laboratory of Evaluation and Synthesis of Bioactive Substances), coordinated a very successful meeting with 125 participants (undergraduates, postgraduates and professionals) from 9 different Brazilian states, and from more than 15 different universities.

The program included 15 lectures spread over 5 sessions:
- Tom Perun, president of IUPAC Chemistry and Human Health Division) opened the meeting and gave an overview on IUPAC activities. Then Patrick M. Woster informed the audience on ACS Division of Medicinal Chemistry.
- General aspects of medicinal chemistry have been discussed in the following lectures: Serendipity in Target-based Drug Discovery (Janos Fischer) and Medicinal Chemistry Approaches (Magid Abou-Gharbia), Chemical Technology in Drug Discovery (Peter Bernstein), Optimizing Drug Therapy (Janos Fischer), Kinase Inhibitors (Wendy Young), Physicochemical Properties (A. Ganesan), MS Binding assays (Klaus Wanner).
- Some special topics and drug discoveries have also been discussed: Pain Research (Helmut Buschmann), Proton-Pump Inhibitors (Jörg Senn-Bilfinger), Discovery of Rilpivirine (Jan Heeres) and Anti-Inflammatory Drug Discovery (Peter Bernstein) and Epigenetic Modulators (Patrick M. Woster).

As a social activity, volumes of the book series Analogue-based Drug Discovery (Vol. I-III.) have been presented to the students.

3.2.3. Medicinal Chemistry India, II. Project 2014-011-0 (Balasubramanian, Greenlee)

The 2nd Medicinal Chemistry and Drug Discovery India (2015) residential program was held on February 8-12, and was co-sponsored by IUPAC, ACS MEDI Division, and ACS. The program was attended by 105 industrial an academic scientists from India, and covered topics beyond Medicinal Chemistry, with a focus on how other disciplines of drug discovery such as Biology, Pharmacology, DMPK, Toxicology, Clinical development, and formulation play critical roles for a Medicinal Chemist in designing medicines and improving the qualities of Medicine. Also included was an introduction to the concept of Biologics with an emphasis on fundamentals of Biologics Medicines with examples of monoclonal antibody drugs that are becoming the next generation medicines. Also introduced in this session was the targeted drug delivery with Antibody Drug Conjugates (ADC). The keynote speakers in the opening day included the American Chemical Society President Dr Diane G. Schmidt. There was

participation and encouragement from the ACS President office, ACS publication group and the ACS local India section. The feedback from the participants was very positive. There is lot of enthusiasm for this program to be continued in 2017. Based on the feedback, the project team considers changing the venue to another location under the same SRU-MCADDI 2017 banner, and is planning to keep the website open all year around so that it will be accessible to all interested and supporting groups.

Towards this end, BB is planning a visit to India during the first week in October, to meet with local industry and academic leaders in other major cities. Bill Greenlee and BB plan to attend the IUPAC meeting at the upcoming ACS National meeting scheduled for March 13-17, 2016 in San Diego, and submit a project proposal.

3.3. New Technologies and Special Topics

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

Volume 1 of "Successful Drug Discovery" has been published in March 2015 by Wiley-VCH.

Post-meeting information: Dr Tobias Gabriel (Novartis Pharma AG, Switzerland) published a review on the book in ChemMedChem (2015), 10, 1762. According to this review, the book "provides a diverse set of insights into successful drug discovery cases and concepts. It is highly valuable both to support teaching and as a motivating read for medicinal chemist in academia and industry".

3.3.2. The Emerging Problem of Novel Psychoactive Substances. Project 2014-019-1-700 (V. Abbate)

Previous/Ongoing Activities:
• Exchange among the task group members about the procedure, collection and exchange of scientific material (2014). This is still ongoing and it will continue for all the duration of the project.
• Development of a scaffold for the manuscript and definition of further milestones (short meeting of Abbate and Schwenk in London, Sept. 2014)

Future Milestones:
• Production of first draft of manuscript (planned for 12/2015): Abbate to assemble draft manuscript, circulate to members for peer-review and collect comments. Each member to draft the agreed chapter/section then circulate for internal review
• The next Division meeting is planned to be in Copenhagen, Denmark September 3- 4, 2016. A Task Group meeting in connection with the Division meeting has been proposed.
• Last draft (12/16): Abbate to collect and analyze final manuscript, and circulate to members for peer review.
• Submission to PAC (expected maximum 06/17), as Technical Report.

Draft Manuscript Structure:
Introduction (Abbate). For this and all the sections, main focus on cannabinoids and cathinones
Chemistry: Structures, classification and names of main NPs (Abbate) (focus on cannabinoids and cathinones).
Analysis of compounds in non-biological materials and analysis of parent molecules and their metabolites in biological materials. Presley will make document on synthetic cannabinoids; Uchiyama will make document on synthetic cathinones.
Pharmacology and Toxicology (PK/PD, etc): different receptors which are present in the brain, and ligand and synthetic ligands typical effects (Schwenk), effects observed in poison centres, clinical aspects, etc (Presley).
Legislation: Regulative aspects and current/future market situation (Uchiyama plus other members to assist); a brief introduction to the problem with some examples in countries such as Japan, New Zealand and UK.

Activities in Social Media
The project team currently have a Facebook and a Linkedin page

4. New Projects

4.1. Successful Drug Discovery, Vol. II. (Fischer) Project 2015-026-1-700 (Fischer)

János Fischer (editor) and Wayne E. Childers (coeditor), together with an editorial team of section editors, are supervising the preparation of 15 Chapters, with the current outline:

Anti-infective drugs (Section Editor : John Proudfoot)
1. Discovery of Delamanid for the treatment of multidrug-resistant pulmonary tuberculosis - Hidetsugu Tsubouchi (Otsuka Pharmaceutical Co., Japan)
2. Discovery of Sofosbuvir for the treatment of hepatitis C - Michael J. Sofia (OnCore Biopharma, USA)

Anticancer Drugs (Section Editor : A. Ganesan (University of East Anglia, Norwich, UK)
3. Abiraterone Acetate (ZytigaR) : An Inhibitor of CYP17 as a Treatment of Prostate Cancer - Gabriel M. Belfort, Boyd L. Harrison and Gabriel Martinez Botella (SAGE Therapeutics, Cambridge, USA)
4. Belinostat - Paul Finn (TopoTarget, UK)
5. Selectivity of New Class of HDAC Inhibitor Chidamide Dictates its Immunotherapeutic Activity against Cancers - Xian-Ping Lu (Shenzhen Chipscreen Biosciences, Shenzhen, China)
6. Discovery and Development of Panobinostat for Anticancer Therapy - Peter Atadja (Novartis Institutes for Biomedical Research, Shanghai, China)
7. The Discovery and Development of FK228 (Romidepsin, a natural product HDAC Inhibitor - A. Ganesan (University of East Anglia, Norwich, UK)
8. The Creation of SAHA, a pioneering anticancer medicine - Ronald Breslow (Columbia University, New York, USA)

Cross-Therapeutic Drug (Wayne Childers)

9. Successful Drug Discovery : Nintedanib - Gerald J. Roth (Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany)

Drugs for the treatment of Cardiovascular and MetabolicDiseases, (Section Editor: Henry Havel)
10. Patient-Centric Design and Development of Dulaglutide, a Once Weekly GLP-1 Receptor Agonists for the Treatment of Type 2 Diabetes - Rohn Millican (Lilly Corporate Center, Indianapolis, USA)
11. Development of Tridentate Chelator Deferasirox - Carsten Spanka (Novartis, Basel, Schwitzerland)

CNS Drug, (Section Editor: Helmut Buschmann, RWTH Aachen, Germany)
12. The Discovery and Development of the Multimodal Acting Antidepressant Vortioxetine - Benny Bang-Andersen (Lundbeck, Denmark)
13. Discovery of Cariprazine, a New Atypical Abtipsychotic (Bela Kiss, Gyorgy Domany and Istvan Laszlovszky (Richter, Hungary)

Gastrointestinal Drug, (Section Editor: Jörg Senn-Bilfinger, Konstanz, Germany)
14. Discovery of Vonoprazan as a highly potent, long-lasting, and novel class of potassium-competitive acid blocker (P-CAB) - Haruyuki Nishida (Takeda, Kanagawa, Japan)

Two topics are still being discussed:
- Linaclotide, a guanylate cyclase agonist (Forest) for gastrointestinal disorders
- The Discovery of Vilazodone - Henning Böttcher (Merck, Darmstadt, Germany)

4.2. Drug Discovery: Dealing with the Reality of Co-morbidities (Liebman)

Current drug development does not adequately consider the complexity of real world patients in either the design of new drugs or the design of clinical trials. This presents a risk that even with success in the specific population of the clinical trial, and regulatory approval, the drug may not be a commercial success. One critical consideration involves the likely pattern of co-morbidities that the targeted patient population may present in real world medicine. It is well documented that most patients will present with more than one disease, either being currently managed, previously managed or potentially undiagnosed, and this increases to an average of 4 or more in the elderly. In addition, these patterns vary across age, gender, geographical and socio-economic situations.

This project proposal (to be submitted) will highlight the more common instances of co-morbidities and resulting polypharmacy and consider variation between US, Europe and Asia. It is intended to provide additional proof-of-principle that this situation can needs to be incorporated into early drug development processes and maintained through clinical studies to help improve commercial success. It will build on an existing study in diabetes and hypertension and should be completed within a 1-1.5 year period. Publication of the results are intended to provide guidance across the drug development process (and healthcare as well), to improve the probability of achieving both commercial success and improving human health in real world situations

Task Force: M. Liebman (proposer), W. Greenlee, J. Proudfoot, H. Buschmann

5. Other business

5.1. European Conferences:

a. European Federation for Medicinal Chemistry:
EFMC - ISMC: Manchester, UK - August 28 - September 1, 2016

b. EuCheMS (European Association for Chemical and Molecular Sciences)

6th EuCheMS Chemistry Conference Seville, Spain - 11-15 September 2016

5.2. Asian Federation for Medicinal Chemistry

Update by Reuben Hwu:
- AFMC only has society members, and no individual memberships.
- AFMC has AIMECS (AFMC Int. Med. Chem. Symposium) every other year. In 2013 AIMECS13 received financial support from 25 companies.
- AFMC has 9 society members + 1 observer from Japan, China, Turkey, Australia, Taiwan, Korea, Indonesia and Singapore
- AIMECS15 will be held in Korea (chair: Prof Moon Woo Chun) - E-mail : mwchun@snu.ac.kr

5.3. IUPAC-Richter Prize

Post-meeting note: The agreement for the second period of the IUPAC-Richter Prize (2015-2024) has been signed.

5.4. Next SC meetings:

a. The upcoming SC-D3 meeting is scheduled for March 12, 2016 (San Diego), prior to the ACS meeting

b. The subsequent meeting will be held in:

Manchester, 27 August 2016 - EFMC-ISMC (Aug 28 - Sept 1, 2016)