

IUPAC Division VII Chemistry and Human Health  
Drug Discovery and Development Sub-committee

Dallas, Texas, Omni Hotel (USA)

19 and 20 March 2014

MINUTES

**Members present:** Balu Balasubramanian (teleconference), Mukund Chorhade, János Fischer (Chair), William Greenlee, Michael Liebman, Sanjay Malhotra (observer) and Tom Perun

**Apologies from:** David Alker, Sergey Bachurin, Eli Breuer, Derek Buckle, Edmond Differding, Paul Erhardt, Robin Ganellin, Arun Ganesan, Yvonne Martin, Péter Mátyus, John Proudfoot, David Rotella, Georg Senn-Bilfinger and Henk Timmerman

**Minutes of the last meeting:** The minutes of the last meeting held in Istanbul (11. August 2013) were accepted without change. They were sent to the secretariat for posting on the IUPAC homepage.

**Matters arising from the Minutes:**

*2014-IUPAC-Richter Prize*

Robin Ganellin summarized as follows :

There were 9 candidates nominated, one of whom had been previously nominated three times and so was no longer eligible to be included.

As before, they represented an outstanding group of candidates. However, I had to remind the Selection Committee that the prize is not really meant to be awarded as a “life-time” achievement in chemical pharmacology, but really we are seeking an outstanding contribution to the practice of medicinal chemistry or to an important new drug discovery.

We, again, used a system whereby each member of the committee voted with 4 points for the first choice, then 3 points, 2 points and 1 point for 4<sup>th</sup> choice. As before, I as chairman, did not vote.

Actually we had several drug discoverers, but two of them stood out from the others and, in the event, Dr. Helmut Buschmann won by a small margin (receiving 20 points out of a possible 28) for his work in the discovery of the centrally active analgesic drug tapentadol (Nucynta™, Palexia™, Tapal™). This drug has a dual mode of action; it is a  $\mu$ -opioid receptor agonist and a norepinephrine (noradrenaline) reuptake inhibitor. It was marketed in the USA in 2008. The research was done at Grünenthal GmbH, Aachen, Germany. It is particularly good to have awarded the prize to Dr. Buschmann since he has so far received very little public recognition.

It is interesting and rather good to see that we have had a good representation of countries by the 5 prize winners, namely (in order) UK, Netherlands/Belgium, USA (India), Canada and now Germany.

## **Membership**

Janos Fischer will chair the SC between 2014-2015.

The SC name has been discussed.

The written opinions from Robin Ganellin, Arun Ganesan, John Proudfoot and Mukund Chorghade have been summarized : RG, AG and JP would preserve “Medicinal Chemistry” in the of SC name. JP also proposes “Chemistry of Drug Discovery and Development”. Tom Perun would accept this modification. MC supports the present name of the SC of Drug Discovery and Development.

## **Glossary Projects:**

*Glossary of Combinatorial Chemistry Terms. Project 2003-044-1 (A. Ganesan).*

Previous project (D. Maclean) under the same title has been completed and published in 2000. The present project has a goal to update the terms. The task group leader plans to complete the glossary by the end of 2014.

*Glossary of Drug Metabolism Terms. Project 2000-009-1-700 (P. Erhardt).*

“This project will be completed by the year’s-end. The draft glossary will be prepared before the end of second quarter and forwarded to the Subcommittee for e-comment/feedback. Then a publication will be prepared to PAC.

*Glossary of Terms in Pharmaceutical Process Chemistry. Project 2001-049-2-700 (M. Chorghade).*

Mukund Chorghade will prepare the manuscript and submit to PAC by April 30, 2014.

*Glossary of Terms in Computational Drug Design. Project 2010-057-3-700 (Y. Martin).* The glossary is completed and will be sent out for review. Yvonne Martin (chair) and seven task group members prepared the manuscript (35 pages) as the second part of these glossaries. Task group members were : R. Abagyan, G.G. Ferenczy, V.J. Gillet, T.Y. Oprea, J. Clander, D. Winkler and N.S. Zefirov. Altogether 187 new and revised terms have been defined. After the reviewing phase it will be published in PAC.

## **Training and Development Projects:**

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

Robin Ganellin discussed with Antonio about having a semi-replacement for him and he recommended Prof Hugo Cerecetto of the Universidad de la Republica, Montevideo, Uruguay and said that he would write to him. However, the focus of this project is not so much about publication, but is really for co-ordination, to get the various interested scientists in Latin America to interact with each other and collaborate so that they do not feel so isolated. Then, for example, academic chemists can work with academic biologists in a productive manner. The idea had been to provide information so that scientists

could access the facilities elsewhere that they themselves lacked.

post-meeting note :

Prof. Hugo Cerecetto is very positive about continuing the work that Antonio began and is clearly keen to contribute.

*Medicinal Chemistry in India. Project 2012-032-2-700 (B. Balasubramanian).*

The Medicinal Chemistry India 2013, a pilot study aimed at improving the educational aspects of Medicinal chemistry as applied to Drug Discovery, held at Sri Ramachandra University, Chennai, India during Feb. 11-15, 2013 was a resounding success. A total of 112 students from industry and academia attended this short course. Industry and academic experts from US participated in the interactive teaching sessions and discussions. The key organizing and supporting teams include Dr. Balu N. Balasubramanian (previously at Bristol-Myers Squibb, now at Pharma Innovation Sourcing Center, LLC), Dr. William Greenlee (previously at Merck, now at Medchem Discovery LLC) and Dr. Tom Perun from IUPAC (President, Chemistry and Human Health Division). The Division of Medicinal chemistry was officially represented by Dr. Joel Barrish (2013 MEDI Chair), Professor Craig Lindsley (MEDI Long-Range Planning Committee, Editor-in-Chief of ACS Chemical Neuroscience), Dr. Nick Meanwell (MEDI Long-Range Planning Committee) and Dr. William Greenlee (MEDI Councilor), all of whom made presentations for the Course. The faculty also included Professor Phil Bowen (Mercer University), who currently teaches an ACS Short Course on medicinal chemistry, and several other members of the MEDI Division. A range of topics from fundamentals of Medicinal Chemistry to understanding the importance of chemical structures modifications as applied to a) interactions with biological targets, including receptors and enzymes, to elicit desired pharmacological response; b) improve the drugability characteristics such as minimizing any associated toxicology, drug metabolism and pharmacokinetic profile, solubility and stability requirements were covered. Industry experts also presented case histories of projects to illustrate the nuances involved in the discovery and fine tuning of lead optimization process towards successful clinical and commercial medicines. The four day course also offered ample opportunities for the participants from diverse research and academic institutions to interact in a very productive manner. Each attendee received a certificate of completion signed by representatives of the organizing team, University and the ACS MEDI Division and IUPAC Division. In addition, a set of local experts from industry and academia were also present at select sessions with the aim to becoming future lecturers at these sessions. The program was sponsored by grants from IUPAC, ACS Medicinal Chemistry Division, ACS Innovative Grants, Department Science and Technology, India as well as Indian pharmaceutical companies and Contract Research Organizations. Positive feedback from the attendees and their organizations not only warrants the continuation of this program but also highlights the importance of expansion of this program to other Asian and African countries.

### **Projects for New Technologies and Special Topics:**

*Human Drug Metabolism Database. Project 2011-018-1-700 (P. Erhardt).*

A modified completion date of December 2015 has been requested by Paul Erhardt in an email to Fabienne Meyers on February 14, 2014. Recognizing that the original intent of the project is not

feasible with current funding, the project will now consist of a summary article which discusses the progress made, and describes what needs to be accomplished to achieve the goal.

*Natural Products with Medicinal and Nutritional Value. Project 2001-050-2-700 (M. Chorghade).*

Mukund Chorghade plans to submit a manuscript and submit to PAC by 30 April, 2014.

### New Projects:

*Successful Drug Discoveries (János Fischer)Project 2013-016-1-700*

János Fischer summarized the status of the book project. This short status report will be published in the May/June issue of Chemistry International :

The new project “Successful Drug Discoveries” (project : 2013-016-1-700) is an extension of the completed project “Analogue-based Drug Discovery” affording three books published in 2006 (project: 2002-051-1-700), 2010 (project : 2008-013-1-700)and 2013 (project : 2011-011-1-700) by Wiley-VCH. The book series focused on drug analogues. The plan of the new project is to present novel drugs that have been approved for use. This will include both pioneer drugs (first in class drugs) and drug analogues (follow on drugs) and both small molecule and biological drug discoveries in a range of therapeutic areas. The new project has a broader scope, nevertheless, we want to preserve the structure of the completed book series.

The book is written by 30 authors from Germany, Hungary, Japan, UK and USA.

The editorial work of Janos Fischer (Richter Plc, Hungary) is helped by co-editor David P. Rotella (Montclair University, USA)and and the advisory board members : Klaus P. Bøgesø (Lundbeck, Denmark), Roy Jefferis (University of Birmingham, UK) Kazumi Kondo (Otsuka, Japan), John A. Lowe III (JL3Pharma LLC, USA) and Barry VL Potter (Uni. of Bath, UK).

The following table shows the book chapters and the names of their authors. The book will be published at the end of 2014.

Chapter	Authors
1. Small molecules-peptides- Biomolecules	James Samanen (USA) (Samanen Consulting)
2. Serendipities in target-based drug Discoveries	János Fischer (Hungary) Richter Plc.
3. Drug discoveries and mechanism of action	David Swinney (Inst. for Rare and Neglected Diseases, USA)
4. Insulin analogues	John M. Beals (Lilly, USA)
5. Abiraterone acetate for the treatment of prostate cancer	Gerry Potter (UK) Leicester (UK)
6. Discovery of avanafil, a novel PDE5 inhibitor	Koichiro Yamada, Toshiaki Sakamoto, Kenji Omori and Kohei Kikkawa (Tanabe-Mitsubishi, Japan)
7. Dapagliflozin, a SGLT2 inhibitor for the treatment of type 2 diabetes	William Washburn (BMS, USA)

8. Elvitegravir, a new HIV-1 integrase inhibitor for antiretroviral therapy	Hisashi Shinkai Central Pharmaceutical Research Inst., JT Inc., Japan
9. Ibrutinib, a covalent BTK inhibitor in B cell malignancies	Betty Y. Chang and David J. Loury (Pharmacyclics, USA)
10. Linaclotide, a new drug for the treatment of functional gastrointestinal disorders	Angelika Fretzen, Caroline B. Kurtz and Inmaculada Silos-Santiago (Ironwood, USA)
11. Discovery of linagliptin for the treatment of type 2 diabetes	Matthias Eckhardt, Thomas Klein, Herbert Nar and Sandra Thiemann (Boehringer Ingelheim, Germany)
12. Lorcaserin, a selective 5-HT <sub>2C</sub> agonist antiobesity drug	Brian M. Smith, (Arena, USA)
13. Discovery of pemetrexed antitumor agent	Edward Taylor (Princeton University, USA)
14. Perampanel, a non-competitive AMPA antagonist for the treatment of epilepsy	Shigeki Hibi (Eisai, Japan)
15. Telaprevir, a protease inhibitor to treat hepatitis C	Govinda Rao, Mark A. Murcko, Mark Tebbe and Ann D. Kwong (InnovaTID, USA),
16. Vilazodone, new antidepressant with 5-HT <sub>1A</sub> stimulation and 5-HT reuptake inhibition	Henning Böttcher Darmstadt (Germany)
17. Antibody-Drug Conjugates: Design and Development of Trastuzumab Emtansine (T-DM1)	Sandhya Girish, Gail D. Lewis Phillips, Fredric S. Jacobson, Jagath R Junutula, and Ellie Guardino (USA)

There are problems with some of the planned chapters. In two cases the companies have withdrawn the chapters (ibrutinib and linaclotide), and the status of the chapter of vilazodone is not yet clear because of the same reason. In two cases the authors are inhibited to prepare their chapters because of health reason (abiraterone and lorcaserin).

All the other chapters are ready or will be ready very soon.

The first volume of “Successful Drug Discoveries” is planned with 12 chapters.

A continuation of the book project has been discussed. It would be helpful to establish a team of section editors.

*Medicinal Chemistry India Part II Project 2012-2-700 (B. Balasubramanian)*

The tentative date for this course is Feb. 2015. For this upcoming session, the team is considering expanded curriculum to include the key areas for drug discovery such as target selection/identification/validation, screening platforms including phenotypical and virtual, fragment-based, structure-based, formulation and biomarkers and early clinical processes that emphasize regulatory elements.

### *Translational medicine and new drug discovery (M. Liebman)*

Most of drug development proceeds as if the patient only presents with a single condition and does not recognize the issues of co-morbidities, and the additional effect of other drugs that the patient may be taking that could interact with the drug under development. 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. Such a project could be accomplished in a reasonably short time period, 1-1.5 years.

### **Other Business:**

#### *Next meetings :*

The next meeting will be organized in Brussels on May 28, 2014 following the meeting of Division “Chemistry and Human Health”. Then a meeting is planned in Lisbon, on September 06, 2014 before the EFMC-ISMC symposium.