

**DRAFT Minutes**

**IUPAC DIVISION VII CHEMISTRY AND HUMAN HEALTH  
SUBCOMMITTEE ON DRUG DISCOVERY AND DEVELOPMENT (SC D3)**

**Rio de Janeiro, Brazil**

**(Lancelot Hall, Merlin Copacabana Hotel, Av. Princesa Isabel, 392)**

**Tuesday, 27 January 2015, 2 - 6 PM**

(Minutes by Helmut Buschmann and János Fischer)

**Attendees:** Peter BERNSTEIN (University of Delaware, USA), Helmut BUSCHMANN (RWTH, Aachen, Germany), Elizabeth Igne FERREIRA (University of Sao Paulo, Brazil), János FISCHER (Richter Plc, Hungary), A. GANESAN (UEA, Norwich, UK), Jan HEERES (University of Antwerp, Belgium), Thomas J. PERUN (IUPAC Division VII, USA), Joerg SENN-BILFINGER (University of Stuttgart, Germany), Klaus WANNER (LMU, Munich, Germany), Patrick WOSTER (Medical University, of South Carolina, Charleston, USA), and guest : Harold Hilarison FOKOUE (PhD student of the University of Rio de Janeiro).

**Remote participation in part (Skype) :** Balu BALASUBRAMANIAN (Pharma Innovation Sourcing Center, LLC, USA)

**Apologies :** Vincenzo Abbate, Sulejman Alihodzic, David Alker, Jonathan Baell, Eliezer Barreiro, Eli Breuer, Mukund Chorghade, Edmond Differding, Paul W. Erhardt, , Robin Ganellin, William Greenlee, Reuben Hwu, Toshi Kobayashi, Yvonne Martin, Péter Mátyus, Serge Mignani, John Proudfoot, Anjali Rahatgaonkar Henk Timmerman and Johan Ulander .

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

After the introduction of the participants, JF gave an overview of SC activities between 2000-2015 with date and place of the subcommittee meetings, and their participants with a specific focus on the meeting in Rio de Janeiro in 2005 and remembering the IUPAC participation in the XI Summer School in Pharmaceutical and Medicinal Chemistry in Rio de Janeiro 10 years ago.

The minutes of 8<sup>th</sup> January 2015 of the Lisbon meeting ( 6 September 2014) were accepted without any further changes.

**2. Membership**

**2.1 Division Committee membership for 2014-2015, nominations for 2016-2017.**

**Membership, Chair and Secretary of IUPAC Chemistry and Human Health Division (Div VII):**

**President:** Perun, Thomas

**Vice president:** Cornelis, Rita

**Secretary:** Schwenk, Michael

**Membership (2014-2015):** Differding, Edmond; Fischer, János; Gubala, Vladimir; Illing, H. Paul; Johnston, Linda; Møller Johannessen, Helle; Temple, Wayne

**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 has received a plaque from IUPAC during the opening ceremony of the IUPAC-Richter prize session at EFMC-ISMC in Lisbon.

**Nominations :** For the membership period 2016-2017 three of the current members are no longer eligible for the next period. Nominations are underway. The election will take place during the next IUPAC General Assembly in Busan (South Korea).

## 2.2 SC D3 website

### ***Mission Statement***

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.

Mission Statement (according to Robin Ganellin, Medicinal Chemistry in IUPAC, *Chemistry International*, (2002), 24, (5)) is as follows:

1. Subcommittee (SC) on Drug Discovery and Development provides a forum for the exchange of knowledge and views among medicinal chemists from different countries;
2. The SC meets twice yearly and also keeps contact with the volunteer members between the meetings;
3. For the industrially advanced countries these meetings provide useful information sources and improving understanding ;
4. For the less industrialized countries helps further the establishment of medicinal chemistry in their respective societies;
5. Creating and helping projects;
6. Output : books, glossaries, training of medicinal chemists .

### ***IUPAC-Richter Prize:***

Five IUPAC-Richter Prizes have been given between since 2006-2014:

- 2006 Malcolm Stevens (University of Nottingham)
- 2008 Jan Heeres (Johnson & Johnson)
- 2010 Arun K. Ghosh (Purdue University)
- 2012 Stephen Hanessian (University of Montreal)
- 2014 Helmut Buschmann (RWTH Aachen)

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.

### **SC D3 membership**

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

The SC DDD has the following membership:

**Subcommittee Chair:** János Fischer

**Secretary of the Subcommittee:** Edmond Differding

**Active members:** (21 by 29<sup>th</sup> July 2014): 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:** (14 by 29<sup>th</sup> July 2014: 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).

#### ***Membership term:***

1. The current SC membership is due for the period of 2014 and 2015;
2. The membership can be continued after 2015, however, a confirmation is required for the subsequent period;
3. Active member : it is expected that an active member attends a SC meeting at least per year either in person or with the help of an electronic communication form (eg. Skype);
3. Corresponding member : it is not necessary that a corresponding member participates at SC meetings, however, a corresponding member should *participate in the SC activities, in discussion and/or projects*;
4. Chair and Secretary (2014/2015).

### **3. Projects**

#### **3.1 Nomenclature and Terminology**

##### **3.1.1 Glossary of Combinatorial Chemistry Terms. Project 2003-044-1-700 (Ganesan)** Ganesan updated the current activities :

Ganesan summarized the current status as follows :

- The existing entries are reviewed according to actual use in the field of combinatorial chemistry ; Elimination of terms which are no longer in use.
- Identification of new terms to be added;
- 5 additional experts are reviewing the actual list of terms (e.g. Stephan Bräse, University of Karlsruhe)
- The glossary should be ready at the end of 2015.

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

The glossary project is in its final reviewing phase. Most of the suggested corrections and changes from the last reviewers' comments have been included. However, a final rework seems necessary to align all terms and to eliminate potential contradictions between the terms. Tom Perun suggested that Yvonne Martin should make the final corrections and decisions about the final corrections.

#### Proposals for new glossary projects

The following new glossary projects were discussed :

1. Biomolecular drugs
2. Special fields of medicinal chemistry, eg. Cancer, diabetes, viral infections, etc.

#### **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)**

In Latin America and the Caribbean regions at least 210 million people live below the poverty line. This is approximately 40% of the population. These impoverished and marginalized populations are heavily burdened with neglected tropical diseases (NTD's). Based on their prevalence and healthy life years lost from disability, hookworm infection, other soil-transmitted helminth infections, and

Chagas disease are the most important NTD's in Latin America and the Caribbean, followed by dengue, schistosomiasis, leishmaniasis, trachoma, leprosy, and lymphatic filariasis.

The solutions to this situation do not just depend on having appropriate drugs but are complex and involve public health, disease control, education and the political will. Even so, having appropriate drugs would be very helpful. 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.

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. RG contacted successfully Cerecetto and Gonzalez (October 9) indicating their interest in organising a workshop in Montevideo in 2015.

The next stage will be to stimulate other medicinal chemists in Latin America to also conduct research in this area, and to make contacts between them and the testing laboratories.

#### **Summary of presentation of Professor Elizabeth Igne FERREIRA (University of Sao Paulo, Brazil)**

LAPEN, the Laboratory of Drug Design and Synthesis on Chemotherapeutic Agents is active in research of drugs for treatment of neglected diseases. IF is responsible for teaching undergraduate, Master and Doctor students, besides postdoctors and research on drug design and synthesis on Chagas disease, leishmaniasis, malaria and tuberculosis, using prodrug design, other processes of molecular modification and also rational drug design, through SBDD and LBDD. From 2006 on dendrimers are used as carriers, which provide bioavailability and efficacy improvement of the drug/bioactive compounds employed. The research work includes new and specific molecular targets for the rational approach, specially in the areas of tuberculosis. One of the compounds, a hydroxymethylnitrofurazone, is promising and is used as a lead compound in the development of drug candidates mainly for Chagas disease. The institute has many national and international collaborators mainly for biological purposes.

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

Short Course of the 21<sup>st</sup> Summer School of the University of Rio was taking place on January 25-31, 2015 organized by Eliezer Barreiro and János Fischer. 15 lectures were given for postgraduate students during the summer school.

For further information please refer to the web page of the summer school:

[http://www.evqfm.com.br/xxi\\_evqfm/](http://www.evqfm.com.br/xxi_evqfm/)

#### **Session 1 (26 January 2015)**

1. Perun, Tom (IUPAC, Chemistry and Human Health Division): Introductory lecture on the IUPAC Role in Human Health

2. Woster, M. Patrick (MUSC, Medical University of South Carolina, USA): Activities of Division of Medicinal Chemistry of ACS
3. Fischer, János (Richter Plc., Budapest, Hungary): Serendipitous Target-based Drug Discoveries
4. Abou-Gharbia, Magid (Temple University, Philadelphia, USA): Medicinal Chemistry Approaches for the Discovery of Innovative Therapeutics

#### **Session 2 (27 January 2015)**

1. Woster, M. Patrick (MUSC, Medical University of South Carolina, USA): Design of Epigenetic Modulators as Potential Therapeutic Agents
2. Bernstein, Peter (PhaRmaB LLC, Rose Valley, USA); The Evolving Role of Chemical Technology in Drug Discovery
3. Buschmann, Helmut (PharmaConsulting, Aachen, Germany): Highlights in Medicinal Chemistry of Pain Research (plenary lecture);

#### **Session 3 (28 January 2015)**

1. Senn-Bilfinger, Jörg (University of Stuttgart, Germany): The Role of Proton-Pump-Inhibitors (PPIs) in the Treatment of Gastrointestinal Diseases
2. Fischer, János (Richter Plc, Budapest, Hungary): Optimizing Drug Therapy by Analogues
3. Heeres, Jan (University of Antwerp, Belgium): The Discovery of Rilpivirine (plenary lecture)

#### **Session 4 (29 January 2015)**

1. Ganesan, A. (University of East Anglia, Norwich, UK): Case Drug Discovery
2. Young, Wendy (Genentech, USA): Discovery of Kinase Inhibitors Across Multiple Therapeutics Indications
3. Bernstein, Peter (PhaRmaB LLC, Rose Valley, USA): Where Next in Anti-inflammatory Drug Discovery ?

#### **Session 5 (29 January 2015)**

1. Wanner, Klaus (LMU University of Munich, Germany): MS Binding Assays and Their Application;
2. Ganesan, A. (University of East Anglia, Norwich, UK): Physicochemical Properties in Drug Design.

### **3.3 New Technologies and Special Topics**

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

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

Advisory Board members :

- Klaus P. Bøgesø (Lundbeck, Denmark)
- Kazumi Kondo (Otsuka, Papan)
- John A. Lowe III (JL3Pharma LLC)
- Barry VL Potter (Uni of Bath, UK)

25 authors from Germany, Hungary, Japan, UK and USA are contributing as authors of eleven book chapters. The book will be published by Wiley-VCH in March 2015.

### I. General aspects

#### 1. Serendipities in Target-based Drug Discoveries

János Fischer (Richter) and David Rotella (Montclair Uni.)

#### 2. Drug Discoveries & Mechanism of Action

David Swinney (Inst. for Rare and Neglected Diseases, USA)

### II. Drug Class Study

#### 1. Insulin Analogues

John M. Beals (Lilly, USA)

### III. Case Histories

1. **Avanafil** Koichiro Yamada (Tanabe-Mitsubishi, Japan)
2. **Dapagliflozin** William Washburn (BMS, USA)
3. **Elvitegravir** Hisashi Shinkai (JT, Japan)
4. **Linagliptin** Matthias Eckhardt (Boehringer Ingelheim, G)
5. **Pemetrexed** Edward Taylor (Princeton University, USA)
6. **Perampanel** Shigeki Hibi (Eisai, Japan)
7. **Telaprevir** Govinda Rao (Vertex, USA)
8. **Trastuzumab emtansine** Sandhya Girish (USA)

#### **3.3.2** Emerging Problem of Novel Psychoactive Substances. Project 2014-019-1-700

(Abbate)

**Outline of the project:** In the past few years, the world has experienced a large increase in the number of compounds appearing on the illicit drug market. Such substances are designed to circumvent governmental regulations as the manufacturers routinely take a known psychoactive compound reported in the scientific literature and alter it chemically in order to produce compounds

that will mimic its pharmacological activity but not have an identical structure to the parent molecule.

Many of these substances are commonly sold via the internet or in “head shops” as products “not to be used for human consumption” to avoid legal regulation and prosecution. In particular, products known as “bath salts” usually contain mixtures of cathinone-derived compounds with effects such as increase of the synaptic concentrations of biogenic amines (norepinephrine, dopamine, and serotonin).

Another class of potentially dangerous products are sold as “spice” or “herbal incense” and usually contain mixtures of compounds termed “synthetic cannabinoids” (CB receptor ligands) sprayed onto botanical material. The number of new drugs of abuse appearing on the market is rapidly increasing, making it very difficult for government agencies to control them. Users are attracted by the low cost of these substances as opposed to conventional recreational drugs (i.e. MDMA, cocaine), which poses additional risk with respect to the potential ease of overdosing. Use and abuse of these products has often been linked to a series of side effects including psychosis, seizures and other psychotropic effects, and in certain cases suicide or death.

The objective of this project is to critically review the present status of NPS, with special regards to structure-activity relationships, synthetic and analytical aspects, and their potential biological effects. The results of this project will aid in educating scientific, social and governmental bodies with respect to this ever-growing phenomenon and the challenges it poses.

During the discussion the importance of such a project was confirmed by the participants. However, it was concluded to compile all relevant information with the the focus on analytical identification and characterization of these compounds without giving any detail of synthetic procedures to avoid a misuse as a handbook of preparation of psychoactive drugs.

#### **4. New Projects**

##### **4.1. Successful Drug Discovery, Vol. II. (Fischer)**

The second volume is under concrete planning. Section editors of therapeutic fields are identified and contacted to support the editorial work.

The goal of the book series has the goal to help the participants of the drug research community with a reference book series and to support teaching in medicinal chemistry with case histories and review articles of new drugs.

The case histories and drug class studies are described by their key inventors. Review articles on already existing drugs of the last decade are welcome.

**Advisory Board Members:** Abou-Gharbia, Magid (Temple University, USA); Graven Sams, Anette (Lundbeck, DK); Kondo, Kazumi (Otsuka, Japan); Lowe, John A. (JL3Pharma LLC, Stonington, USA); Potter, Barry (University of Oxford, UK).

**Editors:** Fischer, Janos (Richter Plc, Hungary); Childers, Wayne E. (Temple University, USA)

Editorial team of section editors will be completed in the next weeks



#### 4.2 Medicinal Chemistry India, II. Project 2014-011-1 (Balasubramanian and Greenlee)

Skype teleconference:

The second Residential course MCADDI 2015 is scheduled to be held at Sri Ramachandra University (Medical School) Chennai, India from Feb. 9 to Feb.13, 2015.

The inaugural course held in 2013 was supported by IUPAC, ACS MEDI Division, ACS, Department of Science and Technology (India) was a real success. Many of the Indian Pharma/biotch/CRO and academic scientists participated and the feedback was very positive.

The 2015 program is also supported by IUPAC, ACS MEDI division. Further funding support will be sought from Indian local Govt.

Due to the overwhelming feedback from the participating companies and academic institutions in India, the 2015 program is expanded its teaching curriculum to Medicinal Chemistry, Biology/Pharmacology, Preclinical Toxicology, Pharmaceuticals and Early Clinical Development.

Local faculty participation in 2015 was increased. Additionally, local Pharma R &D leaders were invited to be part of the organizing committee.

##### **Course Outline:**

1. Basic Principals of Medicinal Chemistry - 1 (Prof. Thomas E Prisinzano, University of Kansas )
2. Basic Principals of Medicinal Chemistry - 2 (Prof. Thomas E Prisinzano, University of Kansas )
3. Target Identification and validation (Dr. Manjunath Ramarao, BMS-Biocon Research Center)
4. Receptors, Enzymes and Ion Channels, (Dr. Manjunath Ramarao, BMS-Biocon Research Center)
5. Phenotypic Screening (Dr. Dr Indranil Mukhopadhyay, Glenmark)
6. Hit-to-Lead Process (Prof. Craig Lindsley, Vanderbilt University)
7. Lead Optimization (Prof. Craig Lindsley, Vanderbilt University)
8. Drug-Like Properties in Drug Discovery (Dr. Swamy Yeleswaram, Incyte)
9. Bioisosteres - 1 (Dr. Nick Meanwell, Bristol-Myers Squibb)
10. Bioisosteres - 2 (Dr. Nick Meanwell, Bristol-Myers Squibb)
11. G-Protein Coupled Receptors (Prof. Craig Lindsley, Vanderbilt University)
12. Structure-Based Drug Design (Dr. Vincent Stoll, AbbVie)
13. Molecular Modeling (Dr. Vincent Stoll, AbbVie)
14. Protein Binding (Dr. Swamy Yeleswaram, Incyte)
15. Drug Metabolism and Pharmacokinetics (Dr. Swamy Yeleswaram, Incyte)
16. Toxic Pharmacophores (Dr. Nick Meanwell, Bristol-Myers Squibb)
17. Pharmaceuticals and Developability Characteristics (Dr. Nancy Barbour, Bristol-Myers Squibb )
18. Preclinical Toxicity Evaluation - 1 (Dr. Bruce Car, BMS-Biocon Research Center)
19. Preclinical Toxicity Evaluation - 2 (Dr. Bruce Car, BMS-Biocon Research Center)
20. Clinical Development ( Dr. Reddy's Laboratories)
21. Case History Presentation 1, Ruxolitinib, JAK2 Inhibitor (Dr. Swamy Yeleswaram, Incyte)
22. Case History Presentation 2, Saroglitazar, PPAR $\alpha$ /g Agonist (Dr. Mukul Jain, Zydus)
23. Case History Presentation 4, Title TBD (Dr. Neelima Joshi, Glenmark)
24. Case History Presentation 3, Title TBD (speaker TBD)
25. Keynote Lecture (Wednesday evening banquet) – Dr. Joel Barrish, Bristol-Myers Squibb

### **4.3 Drug Discovery : Dealing with the Reality of Co-morbidities (Liebman)**

The project proposal was postponed by Michael Liebman via email to Tom Perun prior to the meeting in Rio de Janeiro. It is planned to be discussed in the subsequent SC meeting.

## **5. Other Business**

### **5.1 European Federation for Medicinal Chemistry (Edmond Differding)**

#### ***EFMC International Symposia on Medicinal Chemistry:***

Frontiers in Medicinal Chemistry with ACS MEDI : Sept. 14-16, Antwerp

EFMC-YMCS is the EFMC Young Medicinal Chemist Meeting. The first edition took place in Lisbon, and the second one is scheduled to take place in Antwerp, after the Frontiers Meeting.

EFMC - APMC : Tel Aviv, Israel - Nov. 15 - 18, 2015

EFMC - ISMC : Manchester, UK - Aug. 28 - Sept. 1, 2016

#### ***EFMC Short Courses on Medicinal Chemistry:***

Protein-protein interactions - April 2015, The Netherlands

Engineering of Biopharmaceuticals - Oct. 2015, The Netherlands

### **5.2 Asian Federation for Medicinal Chemistry (Reuben Hwu)**

AFMC only has society members. 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 Cun, E-mail :

mwchun@snu.ac.kr)

### **5.3 Teleconferences**

*Post meeting note : Information about Arkadin was provided by Ly Differding (EFMC) :*

For the next meeting in Antwerp (Belgium), connected to 'Frontiers in Medicinal Chemistry' meeting, September 14-16, 2015, it is suggested to use Skype as a technological platform to allow any member to participate via internet. The advantage of Skype is that it is for free, or even if a professional

subscription is taken in order to connect more than 3 people to a webconference, the fees are very reasonable. The EFMC uses the services of Arkadin (<http://www.arkadin.com/select-country>). EFMC has always had only one Council meeting per year and since 2013 they started to add a TC every 3 months in order to favour interaction between all members. As there are always up to 40 participants in these TCs, they have always been organised with a web conference, allowing participants to share files and presentations, so that everybody sees the same document on his screen. For Arkadin, depending on the length of the call and the countries from where participants are calling, the costs are more substantial. For Arkadin, with about 30 participants for a call of 2 hours, you have to count on approximately 850 €. In order to have a good result from a TC / web conference, you need to be well prepared and ask all those who have a presentation, to send their slides in advance, in order to have one person uploading the presentations. The experience of EFMC is quite positive.

#### **5.4 Next meeting :**

Antwerp, Belgium - 13 September 2015 prior to the conference „Frontiers in Medicinal Chemistry” between September 14-16, 2015