DRAFT MINUTES

IUPAC DIVISION VII CHEMISTRY AND HUMAN HEALTH

SUBCOMMITTEE ON DRUG DISCOVERY AND DEVELOPMENT (SC-D3)

(Vienna, Austria, Hotel Rathauspark, Stefan Zweig Room)

Rathausstrasse 17, 1010 Vienna

Saturday, 26 August 2017, 10 AM - 5 PM

Participants: Sulejman Alihodžić (Croatia), David Alker (UK), Helmut Buschmann (Germany), Edmond Differding (Belgium), János Fischer (JF) (Chair), (Hungary), A. Ganesan (AG) (UK), Michael Liebman (USA), Gerd Schnorrenberg (GS)(Germany), Jörg Senn-Bilfinger (Germany)

Remote Participants: Balu Balasubramanian (USA), Paul Erhardt (USA), Jan Heeres (Belgium), Tom Perun (TP) (USA), John Proudfoot (USA), Mukund Chorghade (USA),

Excused: Vincenzo Abbate (IT), Sergey Bachurin (RU), Benny Bang-Andersen (DK), Jonathan Baell (AU), Eliezer Barreiro (BR), Henning Böttcher (G),Wayne E. Childers, Mukund Chorghade (USA), Rita Cornelis (BE), Flavio da Silva Emery (BR), Robin Ganellin (UK), William Greenlee (USA), Derek Maclean (USA), Henk Timmerman (NL), Toshi Kobayashi (JP) Mario Varasi (IT),

1. Introduction: opening remarks, minutes of the previous meeting in San Francisco

JF opens the meeting by welcoming all participants. The San Francisco meeting minutes are approved unanimously.

2. IUPAC News: General Assembly and Congress in Sao Paulo

Ganesan gives short summaries on the IUPAC General Assembly and the Division meetings in Sao Paulo, Brazil, mentioning that each Division and their subcommittees may be organized slightly differently. Each Division will in future have the possibility to manage their own content of the IUPAC website, in order to increase flexibility and visibility.

IUPAC will celebrate 100 years in 2019 holding the 47th IUPAC World Chemistry Congress and the 50th General Assembly at 'Palais des Congrès' in Paris, France. Each Division is invited to submit proposals for symposia.

Regarding the SC-D3, JF presents an update on the status of ongoing projects of the Subcommittee, and insists the objective should be to aim for two-year projects. Given the financial situation of IUPAC, the possibility is envisaged to renegotiate the royalties to be paid by Wiley to IUPAC for the book series 'Successful Drug Discovery' edited by JF.

3. IUPAC-Richter Prize 2018

JF presents the timelines and jury composition for the IUPAC-Richter Prize 2018. The call for nominations will be disseminated broadly as of September 30, 2017. Post-meeting information : the following societies and journals have been asked to publish the announcement of the 2018 IUPAC-Richter Prize :

IUPAC

EFMC (MedChemWatch and website)

ACS MEDI

The Chemical Society of Japan

Royal Australian Chemical Institute

ChemMedChem

J Med Chem

ACS Med Chem Letters

MedChemNet

EFMC Secretariat has also been asked to forward the announcement to the European National Med Chem Societies with a request to publish the announcement on their websites and send an information to their members by email.

December 15, 2017 will be the deadline for nominations. The Prize will be given at one the upcoming ACS Meetings, with the 36th ACS Medicinal Chemistry Meeting in Nashville (April 29- May 02, 2018).The second lecture is planned in Ljubljana at the EFMC-ISMC symposium (September 2-6, 2018). The announcement is the following:

2018 IUPAC-RICHTER Prize

in Medicinal Chemistry

Call for Nomination

The 2018 IUPAC-Richter Prize will be presented during the 36th National Medicinal Chemistry Symposium (April 29 - May 02, 2018) on Medicinal Chemistry in Nashville, Tennessee (USA), where the recipient will also give a plenary lecture on the subject of his/her research.

The prize is to be awarded to an internationally recognized scientist, preferably a medicinal chemist, whose activities or published accounts have made an outstanding contribution to the practice of medicinal chemistry or to an outstanding example of new drug discovery.

Prize USD 10 000

The Prize has been established by a generous gift from the **Chemical Works of Gedeon Richter, Plc.** (Budapest, Hungary) to acknowledge the key role that medicinal chemistry plays toward improving human health.

Applicants should be received by NOMINATION only, with just one person needing to serve in that capacity, although a total of five (5) individuals should be listed as referees overall. The package must be submitted electronically and should contain a complete resume, a professional autobiography of not more than two pages, and a one-page summary of what the individual considers to be his/her activities, accomplishments and/or publications that have had the most significant impact upon the field of Medicinal Chemistry. The material will be forwarded confidentially to an independent selection committee appointed by the IUPAC Subcommittee on Medicinal Chemistry and Drug Development.

For further information please contact Prof. Janos Fischer, Chairman of the IUPAC Sub-committee on Drug Discovery and Drug Development, by email at j.fischer@richter.hu

Nomination materials should be uploaded by 15 December 2017

to IUPAC Secretariat via the following form :

https://www.cognitoforms.com/IUPAC1/NominationFor2018IUPACRichterPrizeInMedicinalChemistry

4. Successful Drug Discovery-Vol-3 (Project 2016-027-1-700) (FJ)

The third volume is in layout phase. The proof-reading is in delay, nevertheless, the Publisher hopes to be ready with the e-book still at the end of this year.

This volume has a structural similarity to the first volume consisting of three parts : General Aspects, Drug Class Studies and Case Histories. The book series, supported by the International Union of Pure and Applied Chemistry (IUPAC), focuses on new drug discoveries. The third volume investigates recent drug discoveries , i.e. small molecule dugs and biologics approved between 2013-2016. The book therefore contains both medicinal chemistry and biological drug research with a concept to bring these two disciplines closer to each other.

The editors thank the advisory board members : Kazumo Kondo (Otsuka, Japan) and Barry V.L. Potter (Oxford University, UK) and the following reviewers who helped both the authors and the editors : Jim Barrow, Mark S. Cragg, Doriano Fabbro, Duke Fitch, Burkhard Fugmann, Jagath Reddy Junutula, Béla Kiss, Paul Leeson, John McCall, Carlo De Micheli, Jens-Uwe Peters, John Proudfoot, Chack Ramesha, Mathias Rask-Andersen, Jörg Senn-Bilfinger, Steve Staben, Ronald P. Taylor, Klaus T. Wanner, Scott Wolkenberg, Jay Wrobel and Takayuki Yoshino. Special thanks are due to Ron Weir for his reviewing work from the viewpoint of the IUPAC ICTNS (Interdivisional Committee on Terminology, Nomenclature and Symbols).

Part I : General Aspects

Gerd Schnorrenberg gives an overview in the introductory chapter „*New Trends in Drug Discovery*" on the changing status of new drug discoveries in which, beside small molecule drugs, an increasing role of biopharmaceutical drugs can be observed.

Ulrich Storz and coworkers summarize important information in their chapter „*Patenting Small and Large Pharmaceutical Molecules*" which will be useful for all drug discovery participants, both in academia and industry.

Part II : Drug Class Studies

Peng Wu and coworker review all approved *kinase inhibitor drugs*, whose number amounted to 38 when this article was prepared. This class represents one of the most prolific fields of drug discovery.

Arwed Clewe and coworker provide a account of how stepwise improvements in pharmacology, drug-like properties and selectivity improved the therapy of prostate cancer in their chapter „*Evolution of Non-sterodal Androgen Receptor Antagonists".*

Part III : Case Studies

1. Blinatumomab

Patrick A. Baeuerle describes the history, design and development of *blinatumomab* which is a new anti-CD19/CD3 bispecific antibody for the treatment of Philadelphia chromosome-negative adult patients with relapsed/refractory acute lymphoblastic leukemia.

2. Ceritinib

Pierre-Yves Michellys reports on the discovery and development of *ceritinib*, a new inibitor of anaplastic lymphoma kinase for the treatment of ALK-positive metastatic non-small cell lung cancer.

3. Daratumumab

Maarten L. Janmaat and co-workers contribute a chapter on the discovery and development of *daratumumab*, a new anti-CD38 monoclonal antibody for the treatment of multiple myeloma.

4. Obeticholic acid

Roberto Pellicciari and co-workers desribe how *obeticholic acid*, the first-in-class FXR agonist, was discovered to afford a new drug for the treatment of primary biliary cholangitis. The story provides a nice example of a successful cooperation between academia and indrustry in drug research.

5. Obinutuzumab

Christian Klein and coworkers contribute a chapter on the discovery and development of the Type II anti-CD20 monoclonal antibody *obinutuzumab*, which has been approved by FDA for the treatment of chronic lymphocytic leukemia and follicular Non-Hodgkin Lymphoma.

6. Omarigliptin

Tesfaye Biftu gives an overview of how the long-lasting DPP-4 inhibitor *omarigliptin* was discovered for the once-weekly treatment of type 2 diabetes.

7. Opicapone

László Kiss and coworkers describe the discovery and development of the very long acting catechol-*O*-methyltransferase (COMT) inhibitor *opicapone,* which is approved by EMA as an adjunctive therapy for Parkinson's disease.

8. Osimertinib

Michael J. Waring report on a third-generation EGFR inhibitor osimertinib for the treatment of advanced non-small-cell lung cancer.

9. Pitolisant

C. Robin Ganellin and co-workers describe the history of how they discovered and developed *pitolisant*, the first histamine H_3-receptor inverse agonist for the treatment of narcolepsy.

10. Safinamide

Mario Varasi and co-worker provide a chapter on safinamide, which was approved as an add-on therapy to L-dopa for the treatment of Parkinson's disease.

11. Trifluridine/tipiracil

Teiji Takechi and co-workers report on discovery and development of a new optimized antimetabolite combination drug, in which tipiracil prevents rapid metabolism of the nucleoside analogue trifluridine.

5. Successful Drug Discovery-Vol-4 (project proposal) (FJ)

The new volume will also consist of three parts.

Part I (General Aspects)

Two chapters are planned in Part I. J.P. Overington (UK) plans a chapter on targets of small and large molecule drugs. Still, we are waiting for his synopsis. In another chapter Andreas Ritzén and Laurent David (DK) will analyze the physic-chemical parameters of the FDA approved oral drugs in 2007-2016.

Part II (Drug Class Studies)

In this part three chapters are planned. Nicolas Joubert (F) writes an article on antibody drug conjugates. Wayne Childers (USA) and coworkers will give an overview on dopamine partial agonists. Finally Ayesha Sitlani (USA) will prepare a chapter on PCSK9 antagonists.

Part III (Case Studies)

FJ plans five case studies for SDD-Vol-4.

Etelcalcetide (Derek Maclean and *et al*) (USA)

Lenvatinib (Akhiko Tsuruoka and *et al*) (J)

Ocrelizumab (Andrew Chan and *et al*) (USA)

Rucaparib (Barnard T. Golding) (UK)

Venetoclax (Wayne J. Fairbrother *et al*) (USA)

An IUPAC project proposal and a contract with Wiley-VCH are in preparation.

6. Drug Discovery: Dealing with Reality of Co-Morbidities (project proposal)

ML reported on an update to his previous proposals of a project based on the examination of co-morbidities in real world patients and its potential impact on drug discovery. This proposal will now focus on the Incorporation of Real World Evidence into Drug Discovery and Development. A formal proposal will be completed and submitted.

A second project proposal was outlined that includes the development of a wiki-based glossary and database that focuses on details of safety and toxicology factors that negatively impact clinical trial development and success and will solicit/include data from contributing pharmaceutical companies. A formal proposal will be completed and submitted.

7. Aims and operational plan

Various points are discussed:

JF explains that given his tasks as editor of the book series 'Successful Drug Discovery' and as chairman of the IUPAC-Richter Prize Jury, he will finish his activities as subcommittee chair, and proposes GS as the new chairman, in order to focus on the book series Successful Drug Discovery and to chair the IUPAC-Richter Prize. After a lively and challenging discussion, GS is unanimously approved as new committee chair. BS will replace ED who is stepping down from his role as secretary.

The subcommittee members agree to have a broader discussion, with input from all, and led by the newly elected chair, on the strategic directions of the SC, including aims and potential broadening into areas beyond medicinal chemistry, clarification of guidelines and operational matters, including membership and election processes.

TP: IUPAC's newly elected Secretary General has asked all Divisions for operational plans, which TP has submitted. The remits of our Division's Subcommittees are unlikely to change much. One point under discussion is however the chairmanship of subcommittees, which might in future only be held by Titular Members of the Division.

8. Medicinal Chemistry Training (project proposal of Wayne Childers)

In Wayne Childers' absence, Paul Erhardt updated the committee on a previously presented proposal of a project to assess and report on the biomedical industry's vision of the academic training needed by medicinal chemists seeking to enter the industrial job market. The previously proposed strategy was to generate and circulate a survey among key hiring parties of companies from big pharma, biotech and the start-up sector, compile and analyze the responses and disseminate the results in a published white paper. This strategy has now been expanded to include the generation of a proposed didactic and experiential training paradigm that could be used by university chemistry and medicinal chemistry departments to better prepare their medicinal chemistry students for entry into the biomedical industry work force. A formal proposal will now be completed and submitted. PE requested that each of our members should forward the names of useful contacts for receipt of this project's survey to both him and to WEC by email message ASAP, and also do the same if anyone wants to join this project team.

9. Other Questions and Next Meeting

The next SC-D3 meeting will be held in the US at the 36th ACS Medicinal Chemistry Meeting in Nashville (Tennessee).