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# The 9<sup>th</sup> Solvias Science Day

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**ABSTRACT:** The 9<sup>th</sup> "Solvias Science Day" took place at the Congress Centre in Basel, Switzerland, on October 25<sup>th</sup>, 2010. Solvias Science Days have become in the last years a fixed annual date for experts in chemical development and catalysis.

This edition of the Science Day attracted around 280 specialists from academia and industrial research from Switzerland and Europe who followed in three parallel sessions a series of seminars in the areas of Chemical Development and Catalysis, Solid-State Development and Pharmaceutical and Biopharmaceutical Analysis.

In addition to that, the winner of the "Solvias Ligand Contest", a prize established in 2002, presented its project within the Science Day.

The contest challenges university professors, researchers, students, academic groups and industrial scientists worldwide to submit new and improved applications of Solvias ligands and catalysts.

The winner is selected on the basis of the novelty, scientific rigor and originality of the work submitted, as well as its practical applicability in organic synthesis.

### THE 9<sup>TH</sup> SOLVIAS SCIENCE DAY

The 2010 *Solvias Science Day* covered in three very dense parallel sessions the areas of Chemical Development and Catalysis, Solid-State Development and Pharmaceutical and Biopharmaceutical Analysis, three fields also corresponding to the core competencies of Solvias.

As a novelty, this year, a session on solid-state development, including polymorphism and crystallization studies, was included for the first time into the program.

The event, far from being a marketing event, saw highly qualified speakers from industry and academia providing speeches on the latest development in their research areas.

### GENERAL OPENING LECTURE

The Day was inaugurated by a joint general lecture held by Dr. Rene Imwinkelried, Global Head Small Molecules Technical Development at Roche, entitled *What Really Matters in Drug Substance Process Development*. The lecture based on the assumption that R&D productivity in healthcare industry has been moving in the wrong direction for a long time, with consequent unsustainably high attrition rates. The talk focused on the fact that the most important task is to deliver a safe and effective drug to the patient.

Delivering a drug substance with the right physical attributes in a predictable and consistent way is the most important goal of drug substance R&D.

### THE WINNER OF THE SOLVIAS LIGAND CONTEST

The award of the 8<sup>th</sup> "Solvias Ligand Contest" was won by Prof. Jaesook Yun, Department of Chemistry of the Sungkyunkwan University, Korea, "for her manifold contributions in the development of stereoselective catalytic reactions based on chiral complexes of inexpensive metals". The motivation of the prize states that: "the enantioselective boron conjugate addition to cyclic or acyclic unsaturated carbonyl compounds as well as the asymmetric synthesis of nitriles with a stereogenic centre bearing two different aryl groups have an interesting synthetic potential".

Both reactions use Cu catalysts and significantly extend the scope of the Solvias ligand portfolio. The award ceremony and the speech of Prof. Yun were held within the *Chemical Development and Catalysis* session.

### LECTURES OF THE CHEMICAL DEVELOPMENT AND CATALYSIS SESSION

The session consisted of five speeches. Dr. Ioannis Houpis, Janssen Pharmaceutica, Belgium, presented a speech entitled "Selective, tunable cross coupling reactions directed by the carboxylate ion".



The presentation focused on the selective, Pd-catalyzed, cross coupling reactions (Kumada, Suzuki, Amination) of electronically equivalent halides and its advantages in benefits in medicinal and synthetic chemistry. Prof. Steven V. Ley, Department of Chemistry, University of Cambridge, United Kingdom, held a speech entitled "New tools for molecule makers: enabling technologies".

Prof. Ley described the application of continuous flow reaction systems, along with advanced scavenging agents and catch-and-release techniques, to optimize multi-step reaction paths for the rapid and flexible production of pharmaceutical molecules at various scales.

He concluded his speech pointing out that future vision of the emerging field of flow chemistry applications, replacing batch technologies, could well cause a paradigm shift in the way chemical synthesis is conducted.

The Solvias AG scientist Dr. Christian Mössner held a talk entitled "Process development for TV-7130 – a candidate for treatment of sepsis and disseminated intravascular coagulation (DIC)". During his speech he presented the development of a pseudo-tripeptide sulfate salt - candidate for treatment of sepsis/DIC at TEVA Pharmaceuticals.

"Organotrifluoroborates: organoboron reagents for the 21st century" was the title of the talk held by Prof. Gary Molander, University of Pennsylvania, USA.

The speech focused on the latest developments of the organoboron reagents employed in the Suzuki coupling reaction: boronic acids, commonly used for Suzuki-Miyaura coupling, are far from ideal. The use more robust organotrifluoroborate reagents able to expand the range of retrosynthetic pathways using Suzuki coupling reactions was discussed in the talk. Last, but not least, Prof. Jaesook Yun - the winner of the "Solvias Ligand Contest". Prof. Yun presented in her talk the two types of copper-catalyzed conjugate addition reactions developed in her laboratory: the conjugate reduction of  $\alpha,\beta$ -unsaturated nitriles and the conjugate addition of diboron to  $\alpha,\beta$ -unsaturated carbonyl compounds.

#### LECTURES OF THE SOLID-STATE DEVELOPMENT SESSION

The session consisted of five speeches. "Perspective on the crystal/amorphous duality of pharmaceuticals" was the title of the speech held by Prof. Marc Descamps, University of Lille, France. The speech described the features and problems associated to the state variations of drug compounds during processing. About 80 percent of the drugs are formulated in the solid state, which can be crystalline or amorphous. Solid state modifications during processing, like grinding and dehydration can have a strong impact on the bioavailability chemical stability and reactivity of compounds.

Dr. Christoph Saal, Merck, Germany, made a presentation entitled "Successfully screening and selecting salts - salt selection and bioavailability". Salt selection represents an efficient way of optimizing physical-chemical parameters of pharmaceutical research compounds.

The presentation provided an introduction into salt selection techniques and in addition gave an overview on the trends in pharmaceutical salt selection together with the reasons behind these trends, depicting examples and specific aspects which gained importance over the last years. Dr. Wolfgang Beckmann, Bayer Technology Services, Germany presented a talk entitled *Control strategies for crystallization processes - from process research to production*.

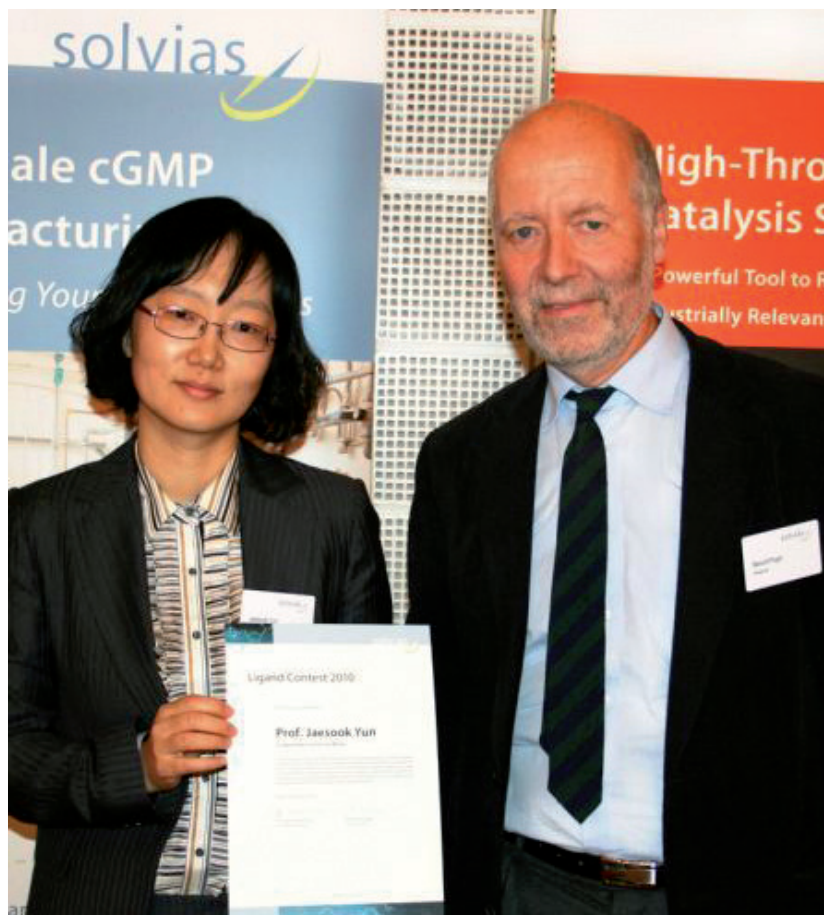
The talk described process research apt to uncover all relevant solid state forms, which comprises searching for polymorphs, solvates and the search into salt formation and other compounds with the new chemical entity to optimize production flows and yield.

*Nature and practical aspects of drug hydrates* was the title

of the presentation made by Prof. Ulrich Griesser, University of Innsbruck, Austria the general and special features of hydrates and some of the implications in drug formulation were discussed on the basis of a series of selected examples. The formation of such water adducts is a critical issue for many basic pharmaceutical operations.

The last talk of the session was held by Prof. Marco Mazzotti, ETH Zurich, Switzerland, and was entitled *The potential of modeling of crystallization processes*.

Crystallization and precipitation from solution include several fundamental mechanisms, i.e. nucleation, growth,



Prof. Jaesook Yun, Sungkyunkwan University, Korea and Dr. Benoit Pugin, Solvias AG.

agglomeration and breakage, which determine the particle size distribution (PSD) and shape of the precipitated product. If the particles formed are metastable, e.g. amorphous, they can undergo a solvent mediated transformation to the stable form, i.e. to the stable crystals. The ability to measure the kinetics of all these mechanisms is required to develop accurate and reliable crystallization models, which are of crucial importance for process design, development and scale-up.

#### LECTURES OF THE PHARMACEUTICAL AND BIOPHARMACEUTICAL ANALYSIS SESSION

Also this session consisted of five speeches. *The history and development of hybrid silica based HPLC columns (Xterra) and instruments operating at elevated pressure (UPLC)* was the title of the speech held by Prof. Bruce Jon Compton, Northeastern University, Barnett Institute, Centre for

Advanced Regulatory Analysis, USA. The talk focused on the technological difficulties as well as organizational and customer perceptions which need to be overcome to make HPLC hybrid silica based stationary phases (Xterra) and HPLC instruments operating at elevated pressures (UPLC) a solid commercial reality and success.

Another speech was held by the Solvias AG scientist Dr. Guido Sonsmann and was entitled *Peptide map - a versatile tool from proteomics to quality control*. The talk focused on the current and future applications of peptide mapping based on HPLC-MS in quality control environment. Peptide mapping has become an important routine tool for proteins and explorative tool for Protein Drug Conjugates.

Dr. Imre Molnar, Molnar Institute, Germany, held a further presentation entitled *Aspects of quality by design in HPLC method development*.

The presentation described a 3-dimensional critical resolution cube, which allows exact column comparisons and can predict experiments in a multifactorial space with reasonable precision.

Dr. David McCalley, School of Life Sciences, University of the West of England, UK made a talk entitled *A consideration of the potential impact of two emerging techniques in HPLC: a) fused core particles and b) hydrophilic interaction chromatography*. The talk analysed the claims associated to fused core columns containing sub-3 micron particles, i.e. that such columns have an efficiency that approaches that of sub-2 micron particles, and yet require only about half of the operating pressure, allowing the use on conventional instruments. In addition, the talk also analysed advantages and limitations of hydrophilic interaction chromatography (HILIC), a technique which has been used since the very earliest days of liquid chromatography and that recently has received renewed interest.

The last talk of the session was held by Prof. Gerhardus de Jong, University of Utrecht, The Netherlands, and was titled *CE-MS: new possibilities for the characterization of biopharmaceuticals*. The characterization of these biopharmaceuticals is mandatory and also very challenging as protein pharmaceuticals and their formulations represent samples of high complexity.

The talk described the use of Capillary Electrophoresis associated to Mass Spectrometry (CE-MS) methods for the characterization and the stability monitoring of biopharmaceuticals.

## **SOLVIAS AG**

In 2009, Solvias celebrated its 10<sup>th</sup> birthday. In 1999 the scientific "competence centre" of the Novartis company, generated by the merger of Ciba-Geigy with Sandoz, was acquired by its management bringing to life Solvias AG, which started business as an independent private company on October 1<sup>st</sup> 1999. Much of Solvias success can be attributed to a systematic development from a specialist for analytical services and technology provider in chemical catalysis to an integrated pharmaceutical service provider for analytical and chemical development including GMP manufacturing up to Phase II.

## **REFERENCES AND NOTES**

- More information on Solvias AG and on the event can be found on the homepage of Solvias AG ([www.solvias.com](http://www.solvias.com))
- F. Weighardt, *Chimica Oggi/Chemistry today*, **27(5)**, pp. 56-57 (2010).