EUFEPS

NEWS Letter

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LEADING ARTICLE

"Changing of the Guard" – EUFEPS' New President and Past President Share Views

In this contribution the EUFEPS Past-President, Christian R. Noe, and the new President, Daan J.A. Crommelin, look over their shoulder into the past and then forward into the future. What has been achieved? What are the challenges that EUFEPS faces? What are the targets for new activities? What forces can be mobilised to fulfil the mission, alone or with allies in Europe and outside this region?

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On the Organisation

Science is not "up in the sky". Science should not be kept in an "ivory tower". Science is the systematic application of logical thinking and logical action for the benefit of humankind. At the same time, as a kind of art, it is an intrinsic element of human culture. Scientific organisations should provide a bridge between their member scientists and society. Therefore, such organisations are subject to an obligation far beyond the activities of cultural and social clubs.

At the time of its foundation, EUFEPS was very aware of this obligation. The best pharmaceutical scientists of Europe joined forces to tackle **the European challenge**, to generate a strong and committed pharmaceutical scientific community in Europe. Amazingly (or not) nowadays and after a series of Presidents, this first challenge is still high on the agenda of EUFEPS. A lot has been achieved. Many of the national organisations in European countries are members and a high percentage of European pharmaceutical scientists are connected to EUFEPS through their national organisations. The EUFEPS initiated PharmSciFair is the first pan-European meeting point for scientific organisations of many countries and pharmaceutical disciplines. The voice of the scientists has reached Brussels through EUFEPS. Important initiatives like the "New Safe Medicines Faster" and the "Innovative Medicines Initiative" would not be there without EUFEPS.

More than one year ago, the Presidents of 10 European scientific organisations dealing with drug research had their first meeting in Vienna to discuss the formation of a **"European Pharma Sciences Leadership Forum"**. At that meeting, which had been organised by EUFEPS, about 200,000 pharmaceutical scientists were – through the Presidents of the organisations – virtually present at the table. In follow-up meetings, the enthusiastic atmosphere of the first meeting suffered somewhat from the attitude of some trying to "stake their claims" and "divide the cake", instead of implementing joint initiatives and planning for a coherent community of pharmaceutical scientists in Europe. Nevertheless, common ground is recognised and there is commitment to proceed. Without doubt, EUFEPS will actively contribute >>>

to further development of the Forum, fully aware that complex situations are not unusual in human society and that sorting complexity out requires patience. EUFEPS does not want to devour or suppress any other organisation, but it feels obliged to continue the initiative to bring together pharmaceutical scientific organisations in Europe and to shape the pharmaceutical scientific community of this region.

While the meetings with Presidents of European sister organisations has the long term goal of broadening the community of our science as a whole, the meetings of the Presidents of our **Member Societies** have been installed to optimise cooperation of EUFEPS with its members and between its members. An increasing number of conferences, jointly organised by Member Societies with and without participation of EUFEPS, indicates progress in this area. Nevertheless, there is still a strong demand by members of our Federation, including the **Individual Members**, who ask for more joint action. EUFEPS is committed to address these demands. Actions include;

- use of the EUFEPS Online (website) for announcing events
- a EUFEPS database for education and training courses
- EUFEPS-coordinated "*in silico*" learning programmes, as well as strengthened and harmonised national websites
- increased membership of national organisations and EUFEPS
- inspiration of pharmacy students, young pharmacists and those with a Masters Degree in pharmaceutical sciences, to be interested in the science underlying their discipline from the beginning of their professional careers
- a widened European network to improve chances for successfully receiving research grants and participating in debates on 'hot' topics in the pharmaceutical sciences.

The fact that the competence of our members in such areas ranges from very high to non-existent is a further indicator of the importance of such pan-European cooperation.

For the last year, there has also been a new membership category within EUFEPS – **Member Institutions**. This category is open to universities and research institutions and/or clusters of them. As will be discussed below, actions have started to address common needs among academic institutions, producing science and scientists useful for the discovery, development and use of medicines. Furthermore, it was recently, suggested that EUFEPS look into how to provide useful support to Small and Medium Size Enterprises (SMEs).

EUFEPS does not only look around within Europe to collaborate with sister and member societies. EUFEPS has also operated and will operate on **the global scene**. Of course, "EUFEPS and the world" means above all close and loyal co-operation with the FIP Board of Pharmaceutical Sciences. Such a co-operation that will benefit from the fact that the current EUFEPS President is also Chair of the FIP Board of Pharmaceutical Sciences. Since EUFEPS is, probably, the most efficiently organised regional pharmaceutical scientific organisation in the world, it can be an efficient partner on the global scene elsewhere. Bilateral regional work (e.g. with AAPS, DUPHAT and the newly established Asian Federation for Pharmaceutical Sciences) will be continued and further co-operation may be initiated. The fundamental ethical commitment of our science does not allow us to ignore needs in other parts of the world.

On Science and Scientists

Pharmaceutical R&D is certainly a huge endeavour. It is a billion dollar undertaking to bring a new active compound to the market. After discovery, the development work of a specific new drug candidate may take eight years or more before the product reaches the market. The disciplines involved range from molecular biology and genetics to economics and even ethics. Certainly, the variety of different scientific languages spoken by the involved scientists has contributed to the long lasting decline in the number of new drugs (NCEs) reaching the market. The complexity of huge pharmaceutical research projects renders overall competence a desirable but very rare skill. The impossibility of solving the problems of scientific language and complexity just by interdisciplinary work is certainly one of the reasons for the massive reorientation, which nowadays takes place in all fields of sciences. Classical disciplines are more and more reduced to areas of "general scientific competence" and technical skills. Areas of importance (e.g. nutrition, health, environment, materials) connecting scientific progress directly to societal requirements are taking precedence over the classical scientific disciplines of the "academic ivory tower". This situation offers a unique chance for the **pharmaceutical sciences to develop into a core field of the natural sciences**, instead of remaining a loose conglomerate of cooperating scientists from different disciplines. The goal is clear: pharmaceutical research and development is moving to cover all scientific activities aimed at curing and preventing diseases through medicines.

On Credibility and Competence

Credibility and competence are closely connected to each other. It is easy to claim a leading role in a science, which has huge future importance. But there is no credibility of such claims without competence. Of course, over time, EUFEPS has built up significant and structured competence in its Executive, Steering and Advisory Committees. This competence is truly proven; it is credible and has been the basis of both the general line of development of EUFEPS and of its specific actions, like conferences, workshops and courses. The ambitious goal to lead the European pharmaceutical sciences to as much excellence as achievable has fostered the decision to set up, in addition to the existing instruments, a body of European top experts, covering all areas of competence of pharmaceutical science. This body will be named the **EUFEPS Senate** and will give advice to the Executive Committee, primarily, in strategic scientific planning Hopefully, the Senate will become a think-tank to help EUFEPS reach a highly recognised position in the European scientific arena.

On Relevance and Excellence

However, excellence should not only be a feature limited to a few selected people, the elite, but it should be the goal that each pharmaceutical scientist should aim for. Nowadays, funding of sciences is a real problem in the academic world. It is obvious that, in times of shortage, funds will be assigned according to a number of rules, such as the relevance of the topic, and the excellence of the project, which frequently goes hand in hand with the excellence of the scientists involved. There is no doubt about the **relevance of pharmaceutical research** itself. It is so important that it is even frequently abused as an "ivy leaf" for research, which, in reality, has – at least in the medium term – little to do with medicines. Sometimes otherwise excellent scientists, in particular molecular biologists, seem to use this "ivy leaf" approach in their fund-raising. A significant portion of public research money, earmarked for pharmaceutical research, has been channelled into projects, which may be important for other reasons, but which are of little pharmaceutical relevance. Hopefully, the EU "Innovative Medicines Initiative" will primarily support projects which are clearly oriented to develop "new safe and effective medicines faster". >>>

Achieving professional excellence is a challenge for every scientist, in particular for those responsible for academic education. The regular activities of EUFEPS with cutting-edge conferences, workshops and courses help those pursuing excellence. To further promote the inter-institutional dialogue, EUFEPS has created the category of Institutional Members, which already includes several prestigious academic pharmaceutical research centres. However, support for educational and co-operational approaches will not be enough. Of course, the question of assessing quality of research is a critical one. Regular evaluation of research institutions, and ranking of papers and scientists, comprises a significant element of competition for funding and thus for performing research. Parameters for fair evaluation of work are required. The different national **peer reviewing systems** are an important element of this quality-driven approach. The debate on 'best practices' in institutional peer reviewing is high on the EUFEPS agenda.

On Contents and Challenges

Leadership is a prerequisite to make progress, but it is even more important to know, where to go. It is a particular ambition of EUFEPS to be a **leading institution in generating new ideas and taking up new lines of thinking in the drug discovery and development process**, long before they become part of the mainstream 'routine'. The EUFEPS New Safe Medicines Faster Initiative (NSMF) was a very successful "translational science" activity at a time when this term was not even coined. EUFEPS can now watch, in full confidence, the development of its "baby", the Innovative Medicines Initiative (IMI), without being concerned that it might not be sufficiently recognised and rewarded for being one of the early initiators. EUFEPS has taken important steps towards a comprehensive implementation of "systems biology in pharmaceutical sciences". This is at a time when the scientific community has just started to be fully aware of this paradigm shift in life sciences. Consequently, during the 2007 EUFEPS Basel Conference, a next step was taken as "biosimulation" and "modelling" research were discussed in the light of systems biology. "Biomarkers" and "PAT science" describe other topics, which were brought up and handled by EUFEPS as a pioneer. EUFEPS has proven, from the very beginning, that it has a good feeling where pharmaceutical sciences are going. It is competence, based on knowledge. Certainly, this feeling for future trends will enable EUFEPS to retain this leadership role in the future.

What will be the major scientific challenges for EUFEPS, in the years to come, both within its traditional field of competence and beyond? Certainly, the **translational science** aspect will continue to play a significant role, because 'monodisciplinary' and 'silo' thinking is perceived as a cause of the existing inefficiency in the drug discovery and development process. Translational approaches in the pharmaceutical science – 'translational pharmaceutical science' – are meant to make drug discovery and development more successful by stimulating direct interactions between the different tasks and disciplines forming the building blocks of the full process. Such science aims facilitate the translation of ideas, findings and concepts into products. Specifically, it addresses phases and steps in the drug discovery and development processes, such as the discovery-development transition or the preclinical-clinical transition. Clearly, emerging paradigms such as individualised medicines and therapies will specifically ask for translational approaches to ensure rapid introduction in the health care system.

A further major task will certainly be to contribute to a **harmonised integration of biotech pharma** into pharmaceutical sciences. It is amazing to observe the general lack of the notion in the biotech field that a biotech product will have to be developed according to similar scientific and regulatory criteria as small molecules. On the biotech side, one can observe an insufficient knowledge of the rules and relevance of drug development, while many of the "conventional" pharmaceutical scientists forget that they must embrace new scientific fields – like molecular biology and genetics – to be able to claim full scientific competence in their own area.

Concerning systems biology, it has not been too difficult for EUFEPS to generate awareness of the importance of systems approaches in a science that is intrinsically based on interference with biological systems. However, beyond this "**general systems biology**" awareness, "**specific pharmaceutical systems biology**" is a rapidly growing field of research, where genomic, proteomic and metabolomic data are correlated by the use of biomathematics, bioinformatics and other "*in silico*" methods. "Metabolomic networks based drug discovery" – together with "biosimulation" and "rational drug design" – will significantly change approaches and efficiency in drug discovery. In fact, **the "*in silico*" world** has grown up over the years not only to complement almost every area of experimental pharmaceutical research, but also to provide us a tremendous wealth of scientific information via the Internet and other sources. Bearing this important development in mind, EUFEPS will strengthen its efforts to promote the use of the full scope of "*in silico*" methods and applications in pharmaceutical sciences both for experts and for those scientists for whom these methods will be complementary elements in their research.

On the Mission to be Completed

At this moment of change in Presidency, both the President and the Past President are convinced that EUFEPS is right on track to fulfil its mission. It has embarked on a spectrum of initiatives with active participation of colleagues from academia, industry and regulatory bodies to further shape the future of the pharmaceutical sciences in Europe.

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Conference on

The Future of Medicines

"Harvesting the molecular biology revolution", has been the working title for a new EUFEPS Conference that should provide additional food for thought on how to make even better use of the knowledge base available:

- What came forth?
- What is real progress?
- What lessons to be learned?
- What to make additional use of?
- How to fund relevant initiatives?

The date and location was, recently, set to December 1-3, 2008 in Vienna, Austria. So, make a note of it, and watch out for information to be circulated, including on the EUFEPS Online at: www.eufeps.org

Attractive conference topic - room packed from the beginning to the end of the Conference.

EUFEPS & COST B25 Conference on Bioavailability (BA) and Bioequivalence (BE):

Focus on Physiological Factors and Variability

This Conference, jointly organised by EUFEPS and COST B25 in Athens, Greece, on October 1-2, 2007, was attended by some 170 participants from pharmaceutical industry and from academia as well as by delegates from regulatory authorities of various European countries and the United States. The objective of the Conference was to provide better understanding of the factors causing variability in oral bioavailability and to discuss the current thinking on the design, analysis and regulatory expectations for BE studies with highly variable drugs and drug products. Each of the sessions was followed by a 30-minute discussion moderated by the session leaders, allowing time for interaction between the conference participants and the presenters. Developers of software for physiologically-based predictions of drug absorption and bioavailability were given the opportunity to demonstrate their packages as well as to give a brief oral presentation in the main Conference room. Furthermore, there were 27 interesting posters showing *in vitro* and *in vivo* results in the area of BA and BE.

Daan Crommelin, EUFEPS President, and Panos Macheras, University of Athen, COST B25 Co-chair, opened the Conference. Both emphasised the great opportunity to have experts from industry, academia and regulatory authorities together in the Conference allowing discussion and exchange of thoughts on current practices, unresolved issues and possible future regulatory policies. The conference had four sessions entitled: "Physiological factors affecting drug absorption", "Role of pre-systemic effects on bioavailability", "Impact of variability in BE studies" and a final discussion session on "Unresolved issues in BA/BE regulations".

In the first session, Clive Wilson (Strathclyde Institute, UK) highlighted the complexity of the gastro-intestinal physiology contributing to variability in drug exposure. For example, the impact of pulses of gastric emptying from changing posture or after food were shown. Investigational tools, including triggered capsules and imaging, may assist in mapping the absorption of a drug and the disintegration of formulations, and can assist in the development of appropriate *in vitro-in vivo* relationships. The use of various tools to investigate regional or site-dependent drug absorption *in vivo* were further shown by Thomas Gramatté (SocraTec, DE). Perfusions within the intestinal lumen allow the simultaneous measurement of the disappearance of the drug from the intestinal lumen and the drug appearance in the systemic circulation. Several examples demonstrated how great the absorption can vary tens of centimeters beyond your teeth for drugs with a different physicochemistry. Impressive images were shown by Werner Weitschies (University of Greifswald, DE) illustrating the different position of extended-release tablets in the stomach after intake of the formulation before a meal, with a first bite, and after a meal. The tablet taken after a meal stayed in the proximal part of the stomach on top of the food leading to elongated residence in the stomach, delayed absorption and possibly late high peak plasma drug concentrations. Sigrid Stockbroeckx (Johnson & Johnson, BE) indicated the trend that drug candidates are becoming less soluble, more lipophilic and of higher molecular weight requiring sophisticated drug formulation technologies to solubilise the compounds.

The role of pre-systemic effects on the oral drug BA was discussed in the second session. Amin Rostami-Hodjegan and Geoff Tucker (both from University of Sheffield, UK) presented the value, the achieved progress but also the current limitations of integrated gastro-intestinal physiological and pharmacokinetic mechanistic models. Knowledge of the variability of the biological systems is cru- >>>

A number of 27 posters contributed as well to the success of the Conference.

cial to develop useful models. For example, a reliable prediction of the extent of intestinal first-pass drug metabolism from *in vitro* data is still challenging as the current models do not yet fully accommodate the additional complexities from gradients of enzymes and drug transporters in the gut. Despite these challenges, there is continuous progress in the field of *in-silico* predictions of oral absorption and bioavailability as demonstrated by the software developers (Simulations Plus Inc, Bayer HealthCare AG, Simcyp Ltd). Henning Blume (SocraTec, DE) indicated that the current global regulatory requirements to measure metabolites in bioavailability and bioequivalence studies are not uniform. While metabolites should generally be measured in BA studies, regulations are not as explicit for BE studies, where the measurement of metabolites is recommended if they are meaningfully contributing to the efficacy and/or safety. Les Benet (UCSF, USA) questioned whether we are using the right model, and he therefore stressed the value of having simple drug classification approaches such as the Biopharmaceutical Classification System (BCS) and the more recent Biopharmaceutical Drug Disposition Classification System (BDDS). Whereas BCS may help decisions to obtain regulatory waivers for bioequivalence studies, BDDS was developed to predict clinically significant effects e.g. on the direction and importance of food effects. Benet showed that high and low permeability closely correlates with the extent of metabolism of a compound, which provides easily available additional information to support decisions on a waiver for bioequivalence studies. The BDDS seems a very nice and simple approach to categorise compounds according to their pharmacokinetic characteristics, which is very useful to guide drug development and drug therapy.

The third session, on the second day of the Conference, focused on variability in bioequivalence studies. Kamal Midha (University of Saskatchewan, Canada) was the first speaker and defined "within-subject variability" as the variability in response measured when the same subjects take two doses of a drug in solution on two different occasions. Estimation of the within-subject variability following a solution is the most pure measure of variability and helps to understand whether the drug or the formulation is highly variable. Midha also demonstrated the value of assessing the AUCE, which is the partial AUC truncated to the median Tmax of the reference product. AUCE is particularly valuable for the comparison of the variability in drug exposure during the absorption phase, as demonstrated in an example where the reference innovator product was more variable than the generic formulation. The degree of within-subject variability for each of the formulations can only be properly assessed through study designs with replicates of each drug formulation. In the context of suitable study designs for highly variable drugs and drug products, Achiel Van Peer (Johnson & Johnson, BE) showed that examination of the trough concentrations or a repeated measurement of the AUC in a multiple-dose BE study provides useful information on the within-subject variability of each formulation. Furthermore, the within-subject variability at steady-state was lower than following single doses. Although diminished variability at steady-state is favorable to reduce the number of study subjects, regulators in both Europe and at FDA do not support the use of multiple dose BE studies as they hide differences in absorption profiles between formulations. Panos Macheras (University of Athens, Greece) reviewed the historical evolution of the statistical analysis methods for bioequivalence studies, and strongly recommended to go away from the current position of having a within-subject variability of 30% as cut-off point for considering a drug or drug product highly variable. Having a single-point discontinuity at 30% is a very major drawback. Macheras proposed to resolve the problem by having BE acceptance limits gradually widening with the within-subject variability and having constraints on the geometric mean ratio of the formulations.

The formal presentations were closed by Tomas Salmonson (Sweden) and Barbara Davit (US) on the current regulatory thinking of EMEA and FDA, respectively, on the bioequivalence of highly variable drugs. Salmonson shared his personal view on the topic as EMEA has not yet come to a formal position from the 27 EU member states. One of the points of debate is how to justify wider acceptance limits based upon clinical data. It is expected that widening of Cmax, based upon demonstration of high within-subject variability and a clinical justification, will be taken up in the coming update of the EU BE guidance. Barbara Davit discussed the issues

From the left: Professors Amin Rostami-Hodjegan (Sheffield UK), Leslie Z Benet (San Francisco CA USA), Constantin Mircioiu (Bucharest RO), Achiel van Peer (Beerse BE), and Henning H. Blume (Oberursel DE), contributors to session on "Role of pre-systemic effects on bioavailability".

within the BE submissions for new generic drug products. About 20% of the drugs with acceptable *in vivo* BE studies reviewed by the Office of Generic Drugs during 2003-2005 were consistently highly variable. On average, the acceptable BE studies of highly variable drugs enrolled 50% more subjects than studies of less variable drugs. Simulations at FDA showed that it is possible to reduce the number of study subjects needed for acceptable BE for highly variable drugs when BE limits are adjusted by scaling to the within-subject variability of the reference product and by assessing that variability in a partially replicated crossover study with the test product administered once and the reference product administered twice. In addition, the traditional two-way crossover BE studies with high sample sizes remain acceptable.

The Conference was concluded by a 2-hour session allowing a series of short presentations on a variety of BE issues, often unresolved so far. Besides interaction with the conference participants, a panel of three delegates from three European regulatory offices (George Aislaitner, Alfredo Garcia-Arieta, and Jan Welink) addressed questions or provided their opinion.

In his concluding and closing remarks, Panos Macheras briefly went through the conference programme and emphasised the major progress made over the years. Factors causing variability in oral drug absorption and bioavailability are now better understood. With respect to the assessment of bioequivalence of drugs and drug products with high within-subject variability, the issues on study designs and analysis are recognised by the regulatory authorities, and it is expected that recommendations will be released in the near future.

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Safety Sciences: Now and Tomorrow

The current state

Steadily increasing investments and fantastic numbers of screened molecules, as well as higher and higher numbers of selected compounds for development, have not yet reversed the steady decline in the number of drugs reaching the market during the past years. Shareholders are losing interest and trust in our business. The low hanging fruits in pharmaceutical R&D have been harvested! The complexity of our business makes a rapid turn-around in drug development unlikely. The growing number of new and unexplored drug targets is accompanied by an increasing need for knowledge of the safety aspects of potential medicines.

Our industry cannot afford any longer to start with safety evaluation only after the candidate molecules are selected, knowing that many of them will fail rather quickly due to safety issues. Many of these compound deficiencies could have been discovered prior to candidate selection if enough API (Active Pharmaceutical Ingredient) had been available for a basic set of experiments looking at more than just acute toxicity, genotoxicity and QT-interval prolongation. Examples include: photo-toxicity, phospholipidosis, a reasonably short *in vivo* study in a suitable rodent or small non-rodent, as well as the use of gene-expression and of metabonomics data. Further pro-active data gathering that is tailored to the needs of candidate selection and to the development path of the future drug should take into account the indication and the target patient population with possible specific hazards, etc.

Most importantly, experienced multi-disciplinary safety experts will have to be an integral and creative part of the project teams during the pre-candidate selection phase. However, this type of scientist is not easy to find and there is no clear career path at the university level for interested students. The solution will be to use our grey matter before we test the white powder in order to come to a tailor-made safety strategy for every new molecule! This solution asks for more well trained multi-disciplinary Safety Scientists than currently available.

The future

The profile of a pre-clinical safety scientist has to go significantly beyond the one of a traditional toxicologist. The future safety scientist has to integrate knowledge accumulated in all safety-relevant disciplines (primary & secondary pharmacology, functional genomics, safety pharmacology, ADME, physico-chemistry, clinical and toxicology with all its special branches) to excel in modern risk assessment and risk management. In order to succeed in this ambitious endeavour, there is an urgent need for improved, enhanced and adapted academic training in safety sciences, aiming at closing the gap perceived in industry and regulatory sciences. Several university courses such as veterinary medicine, pharmaceutical sciences, medicine and biology should provide their students from the beginning with a transparent avenue towards a future career in multi-disciplinary 'Safety Sciences'. The Safety Sciences must become a visible and attractive area of specialisation.

How to proceed

To enhance training in the mid-term, we sought input from the interested parties (Academia, Industry and Regulatory Agencies), during a second EUFEPS Workshop (July 2 - 3, 2007 in Vienna, Austria) focussing on training needs in our university education system.

Workshop objectives

With the present safety needs and concerns in mind, the workshop was given the overall aim of arriving at a clear road map for the way forward. This should be achieved through the following four objectives.

1. To develop a European under- and post-graduate curriculum for safety science courses, making sure that safety sciences as a discipline is taught appropriately throughout all involved faculties and countries. In this way the undergraduate students should get a broad picture of this interesting scientific career and post-graduate students should achieve an internationally recognised accreditation.
2. To identify academic research topics linked to safety science education and training.
3. To build a European Network to educate and train future safety scientists.
4. To find ways to fund and organise the (new) European activities.

Outcome and actions

- The outline of a European curriculum for pharmaceutical safety science was created.
- A list of postgraduate courses needed at the European level for obtaining excellence in safety science was discussed.
- A list of safety science research topics suited for academic research was proposed
- The reinforced Network has the task to lay the foundation for mapping of the existing European undergraduate and postgraduate education at the national level in toxicology/safety science.
- The EUFEPS Network cooperates closely with the respective IMI/FP7 project on Education & Training for Safety Scientists, in order to avoid redundant approaches.

It is expected that the analysis of existing post-graduate education and training facilities will be finished in early 2008. Thereafter, it will be necessary to bring those institutions that will participate in education and training of Safety Scientists for a European accreditation to a comparable level of teaching.

Dr Helmut Sterz
EUFEPS Safety Sciences Network

The Revolution in Quality Thinking

This article has been taken from a presentation given on November 30, 2007, at the symposium "Advances in the Field of Pharmaceutics: From Pharmacy Education to Drug Research and from Drug Research to Science Based Drug Regulation", held in honor of the retirement of Professor A. Atilla Hincal from his position as Head of the Department of Pharmaceutical Technology, Hacettepe University, Turkey.

Unlike most other industries developing products with high added values for their customers, the pharmaceutical industry has not yet taken full advantage of progress in manufacturing science. Current process capability is approximately 2 – 3 sigma.

Manufacturing is expensive

In order to assure high quality products for distribution to patients, all manufactured product batches are subjected to extensive end product release testing. After a lot of expensive testing, a quality level of 5 – 6 sigma is reached. In order to reach and maintain the highest levels of quality assurance, authorities have created more and more directives, regulations and guidelines for developing APIs and finished products. Compliance to these became the first survival strategy for the pharmaceutical industry. Once marketing authorisation had been obtained, the manufacturing process and the analytical procedures were "frozen" and subjected to a rigorous change control regimen. Only recently, it was recognised that manufacturing costs the pharmaceutical industry more than its entire R&D programme.

Revolutionary thinking

In an environment of increasing costs and decreasing profits, the FDA's "GMPs for the 21st Century" initiative was welcomed by industry. It was followed by a guideline on Process Analytical Technology (PAT), and later by the ICH guidelines Q8 (Pharmaceutical Development), Q9 (Quality Risk Management) and Q10 (Pharmaceutical Quality Systems). There is a true revolution in Quality Thinking, and a paradigm change from "Quality by Testing" to "Quality by Design".

For industry it became rewarding to "flow with the QbD wave" because the science- and risk- based approach towards developing new medicines of high quality not only promises more efficient manufacturing processes, but also a degree of regulatory flexibility previously not permitted by the health authorities. Key in evaluating the quality attributes of the drug product and the process parameters is the application of Quality Risk Management. In exchange for enhanced documented knowledge of product and process, authorities consider giving more "space to move" within the agreed (section of the) "Design Space".

Implementation difficult

However, the implementation of the new Quality Thinking is a difficult task, with major challenges both for industry and health authorities, including assessors and inspectors. New working processes and quality management systems have to be adopted, and existing regulatory documentation and assessment procedures have to be adapted. In fact, all those involved including technologists, regulators, and inspectors have to be re-trained.

The challenge is so enormous that companies and health authorities are re-engineering their businesses. Companies now refocus on knowledge development, rather than on data generation. The US FDA has installed its Office of New Drug Quality Assessment, and universities are initiating new courses in areas like Regulatory Science.

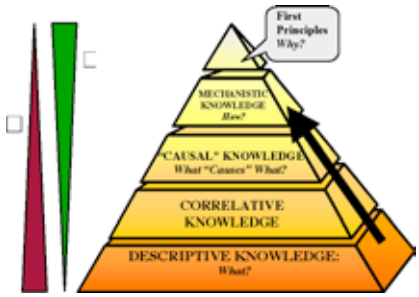
Academic challenge as well

Since the paradigm now is to develop science-based products and processes, it has become a major challenge for all academic departments of Pharmaceutical Technology and Pharmaceutical Engineering to teach their students Quality by Design and PAT tools, and to imprint the new Quality Thinking in the students' minds. In Europe, EUFEPS should play a major role in driving the academic institutions' courses in this direction. Not taking up this challenge will lead to a major misfit between the capabilities of industrial pharmacy students and today's needs of the pharmaceutical industry and the health authorities. In this respect we can paraphrase quality guru W. Edward Deming by stating "Change *of the Industrial Pharmacy curriculum* is not Mandatory, neither is Survival *of these academic departments*". Pharmaceutical sciences should drive the "desired state" of more product knowledge and enhanced process understanding.

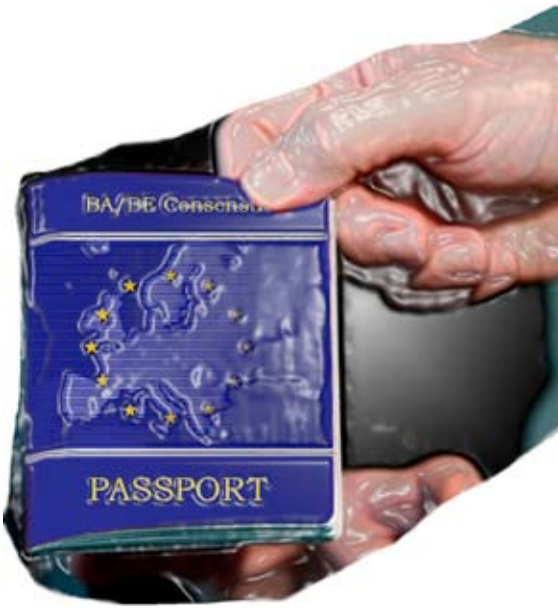
The new paradigm on quality – better science, better processes, better products! Let's go for it!

Tom Sam, PhD, MBM, FFIP
Global Regulatory CMC
Organon, a part of Schering-Plough Corporation
tom.sam@organon.com
The Netherlands

	Sigma	ppm Defects	Yield	Cost of Quality
Current Mfg	2σ	308,537	69.2%	25-35%
	3σ	66,807	93.3%	20-25%
	4σ	6,210	99.4%	12-18%
Quality provided to patients	5σ	233	99.98%	4-8%
	6σ	3.4	99.99966%	1-3%



Birth of the EUFEPS BABP Network



Most of the BABP Network Steering Committee in October 2007, at the Socratec Headquarters, Oberursel, Germany. The Steering Group include: Gerald Beurle, Henning Blume (Chair), Erich Brendel, Andrzej Dzierbicki, Hilda Köszegi-Szalai, Hans H. Linden, Henrike Potthast, Tomas Salmonson and Clive G Wilson.

The initiation of a EUFEPS Network on Bioavailability and Biopharmaceutics (BABP) appears to be a natural progression of the EUFEPS vision as biopharmaceutics forms the bedrock of many of the activities of the contributing societies. It is also an important opportunity to assist legislature in defining a harmonised approach across Europe

The proposed changes in European Guidelines for Bioavailability/Bioequivalence (BA/BE) have prompted the scientific community to engage in a more comprehensive communication with regulatory scientists and to stimulate exchange between both groups. In particular, efforts should focus on scientific questions, which arise from poorly resolved areas and on provision of a framework from which best practice can be developed.

Why a BABP network?

Biopharmaceutics is an encompassing discipline of pharmacology, material sciences, analysis and toxicology. Each year, many of the member organisations within EUFEPS host workshops and conference sessions to hear key opinion leaders talk about their research and viewpoints. It is a broad church; with so many disciplines represented, there will be a growth of knowledge and disparate standpoints, which do not always mesh smoothly. Naturally, this activity provides the basis of new thoughts and debate, but being geographically dispersed, there is no tendency to self-propel towards consensus statements, and clear messages may not emanate. Regulators want to follow best practice but if different viewpoints cannot be heard and reconciled, progress towards uniformity will be painfully slow. This was appreciated by both the regulators and the scientific communities across pharmaceutics. A core group, consisting of Professor Dr Henning Blume, Dr Gerald Beurle and Dr Erich Brendel, prompted by industry and the regulators took on the task of addressing these issues. They resolved to generate a focus group or network representing regulatory, generic and traditional strongly research-based industry assisted by academics from different countries. The outcome is a regionally-balanced network and steering group, which meets regularly to progress activities, including conferences and workshops within a EUFEPS-based Bioavailability and Biopharmaceutics Network.

What will the BABP Network provide?

The purpose of any EUFEPS network is to join scientists together. A mission of the BABP will be to provide an opportunity for EUFEPS members to get to know each other, to explore important issues in bioavailability, bioequivalence and biopharmaceutics through conferences and workshops and ultimately to propagate learnings through various published media. The effect of these activities will be to help Europe to lead debate rather than work in a reactive mode, confident that resolutions are well-rehearsed and strongly scientifically justified.

The starting point is communication and it is hoped that the BABP Website (www.babp-network.org) will develop into the common information platform. An additional early activity will be a two-day conference on science and regulation planned for June 2008. Topics will include BCS-based waiver beyond Class 1, considering transporter-excipient interplay and the interpretation of data from acidic BCS Class II and Class III substances, for the first day. The second day will consider the design of steady state studies and ideas for testing novel drug delivery systems including orally dispersible forms.

It is intended that the conference topics will provide a stimulus for debate and resolution, providing an opportunity for airing issues and looking for avenues which will facilitate consensus. A further conference is planned on publication of the guidelines at an appropriate point in the future.

Henning Blume, Professor, Frankfurt DE
Clive Wilson, Professor, Glasgow UK

Recent Awards in Pharmaceutical Sciences

Mathias Uhlén

The Scheele Prize

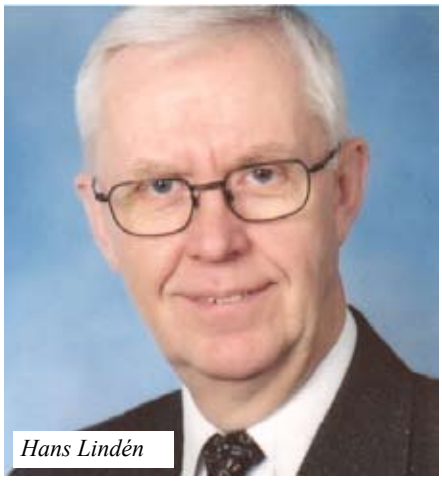
During the Scheele Symposium, on October 24, 2007, at the Annual Swedish Pharmaceutical Congress, Mathias Uhlen (Royal Institute of Technology, Stockholm, Sweden) was awarded the 2007 Scheele Prize, always presented to a particularly prominent and internationally renowned scientist in the field of drug research or related disciplines. Mathias Uhlen is the first scientist in Sweden to receive the annual Scheele Prize, and is now the latest in a series of outstanding scientists since 1961. He is leading the Human Protein Atlas (HPA) Programme, with the aim to systematically map the human proteome.

The 2007 New Safe Medicines Faster Award was presented by Profs. Christian R. Noe and Ole J. Bjerrum, Past-Presidents of EUFEPS, at the EUFEPS Optimising Drug Discovery and Development Conference, on December 5-7, 2007, in Basel, Switzerland.
From the left: Christian R. Noe, Peter York, Hans Leuenberger, Staffan Folestad, Jouko Yliruusi and Ole J. Bjerrum

The New Safe Medicines Faster Award

In the Opening Session of the EUFEPS Conference on Optimising Drug Discovery and Development, on December 5, 2007, in Basel, Switzerland, Staffan Folestad (AstraZeneca Mölndal, Sweden), Hans Leuenberger (University of Basel, Switzerland), Jouko Yliruusi (University of Helsinki, Finland), and Peter York, University of Bradford, United Kingdom) received the 2007 New Safe Medicines Faster Award, sponsored by Sanofi-Aventis – for outstanding contributions in advancing new methods and new technology which significantly shorten the drug development process, by pioneering PAT (Process Analytical Technology) Science.

Hans Leuenberger, Staffan Folestad, Jouko Yliruusi and Peter York



Hans Lindén

The Hermann Thoms Medal

On October 12, 2007, Hans H. Lindén was awarded the Hermann-Thoms-Medal ("pro pharmacia") by the German Pharmaceutical Society (DPhG), at its 2007 meeting in Erlangen, to recognise his outstanding contributions to the pharmaceutical sciences. Hans Lindén joined the EUFEPS Secretariat (part-time) in 1994, three years after its inauguration. Since 2002, he has been full-time Executive Director of EUFEPS.

Pieter J. Swart and Mirjam E. Kuipers

Christian R. Noe, Pieter J. Swart and Mirjam E. Kuipers

The Best Paper Award

Also in the Opening Session of the EUFEPS Conference on Optimising Drug Discovery and Development, on December 5, 2007, in Basel, Switzerland, Johannes H. Proost, Leonie Beljaars, Peter Olinga, Pieter J. Swart, Mirjam E. Kuipers, Catharina Reker-Smit, Geny M.M. Groothius, and Dirk K.F. Meijer (University of Groningen, The Netherlands), were awarded the Best Paper Award from papers published in the European Journal of Pharmaceutical Sciences during 2006, sponsored by Elsevier, for the paper on "Prediction of the pharmacokinetics of succinylated human serum albumin in man from in vivo disposition data in animals and *in vitro* liver slice incubations" – European Journal of Pharmaceutical Sciences 27 (2006) 123-132.

The Control of Infectious Diseases: Virulence, Antibiotics and Bacterial Infection
January 30, 2008, London, UK

Stability Testing of Pharmaceuticals
February 18-20, 2008, Cambridge, UK

Cannabinoid Medicines
March 10, 2008, London, UK

13th Arden House European Conference: Driving innovation, control and performance improvement on the critical path – the pivotal role of particle and powder technologies in dosage form manufacture
March 31-April 2, 2008, London, UK
Contact: Science Programme Manager
Royal Pharmaceutical Society of Great Britain
1 Lambeth High Street, London SE1 7JN, UK
Fax +44 20 7572 2506, Email science@rpsgb.org

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International Pharmaceutical Excipients Council Europe (IPEC Europe) Seminar and Annual General Meeting
January 31-February 1, 2008, Cannes, France
Contact: IPEC Europe Secretariat c/o Carole Capitaine, Avenue des Gaulois, 9 B1040 Brussels, Belgium, Tel +32 27 36 5354, Fax +32 27 32 3427, Email info@ipec-europe.org

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7th International Conference and Workshop on Biological Barriers and Nanomedicine – Advanced Drug Delivery and Predictive non vivo Testing Technologies "Cellcourse 2008"
February 20-29, 2008, Saarbruecken, Germany
Contact: Claus-Michael Lehr, Biopharmaceutics & Pharm.Technology, Saarland University
Campus A4 1, DE-6612 Saarbruecken, Germany
Fax +49 681 3024677
Email cellcourse2008@mx.uni-saarland.de

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Development of Safe Protein Therapeutics; Preclinical, Clinical and Regulatory Issues
March 10-11, 2008, Munich, Germany
Organised by EUFEPS and DPhG
Full details available under the Current Meetings link of EUFEPS Online, www.eufeps.org

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DUPHAT 2008 – Dubai International Pharmaceuticals and Technologies Conference and Exhibition
March 10-12, 2008, Dubai, UAE
Co-sponsored by EUFEPS
Full details at www.duphat.ae

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Faster and smarter analysis
April 3-4, 2008, London, UK

Biologically-Active Compounds in Foods and Drinks
May 1, 2008, London, UK

Combating counterfeit medicines – the challenge for the analyst
June 12, 2008, London, UK
Contact: Julie Churchill, Royal Pharmaceutical Society of Great Britain, 1 Lambeth High Street
London SE1 7JN, UK, Fax +44 20 7572 2506
Email science@rpsgb.org

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ISPE Conference on Innovation
April 7-11, 2008, Copenhagen, Denmark
Contact: ISPE Europe, Avenue de Tervueren 300, BE-1150 Brussels, Belgium
Fax +32 2 7431550
Email ispe@associationhq.com

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EDQM: Symposium on Alternatives to Animal Testing: New Approaches in the Development and Control of Biologicals
April 23-24, 2008, Dubrovnik, Croatia
Contact: Email franchine.baumgarthen@edqm.eu
www.edqm.eu/site/Alternatives-to-Animal-Testing-Dubrovnik-Croatia-259.html

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When Variability Becomes an Issue: How to Understand, Predict and Manage It in Drug Development
May 12-13, 2008, Verona, Italy
Full details will be available under the Current Meetings link of EUFEPS Online
www.eufeps.org

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15th Intermediate Workshop on Pharmacokinetic/Pharmacodynamic Data Analysis – A Hands-on Course Using WinNonlin
May 18-22, 2008, Cambridge, UK
Contact: Erik Ahlsén, Swedish Academy of Pharmaceutical Sciences, PO Box 1136 SE-111 81 Stockholm, Sweden
Email erik.ahlzenakemedelsakademin.se
or Science Programme Manager, Julie Churchill at science@rpsgb.org

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7th Training Course on High-throughput (HT) Drug Metabolism/Disposition (DMD)
May 26 - 30 • 2008 • Amsterdam The Netherlands
Full details will be available under the Current Meetings link of EUFEPS Online
www.eufeps.org

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2nd Monoclonal Antibodies Workshop: Cutting-edge Science for New Medicines
June 3-5, 2008, Heidelberg, Germany (Preliminary)
Full details will be available under the Current Meetings link of EUFEPS Online
www.eufeps.org

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19th International Symposium on Pharmaceutical and Biomedical Analysis
June 8-12, 2008, Gdansk, Poland
Contact: Department of Biopharmaceutics & Pharmacodynamics, Medical University of Gdansk, Gen. J. Hallera 107 Street
80-416 Gdansk, Poland, Fax. +48 58 3493262
Email pba2008@amg.gda.pl, www.pba2008.com

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9th Eilat Conference on New Antiepileptic Drugs (Eilat IX)
June 15-19, 2008, Sitges, Spain
Contact: The Secretariat, Eilat IX
P.O. Box 29041, Tel Aviv 61290, Israel
Fax +972 3 5175155
Email eilatix@targetconf.com
www.Eilat-aeds.com

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3rd International Symposium on Integrated Biomarkers in Cardiovascular Diseases
July 9 – 11, Seattle, Washington, USA
Contact: Biomarkers 2008, Giovanni Lorenzini Medical Foundation, 6535 Fannin
MS A-601 – Suite 754A, Houston, TX 77030
USA, Tel +1 713 7970401, Fax +1 713 7968853
Email biomarkers@bcm.tmc.edu

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11th Belgian Organic Synthesis Symposium (BOSS XI)
July 13-18, 2008, Ghent, Belgium
Contact: Symposium Secretariat, Dept. of Organic Chemistry, Ghent University, Belgium
All information on Symposium website
www.boss11.org
Deadline for abstract submission and early registration, May 1, 2008

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British Pharmaceutical Conference 2008
September 8-10, 2008, Manchester, UK
Contact: Julie Churchill, Royal Pharmaceutical Society of Great Britain, 1 Lambeth High Street
London SE1 7JN, UK, Fax +44 20 7572 2506
Email science@rpsgb.org

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Workshop on Vaccine Delivery
September 15-17, 2008, Geneva, Switzerland
Full details will be available under the Current Meetings link of EUFEPS Online
www.eufeps.org

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7th Central European Symposium on Pharmaceutical Technology and Biodelivery Systems
September 18-20, 2008, Ljubljana, Slovenia
Cosponsored by EUFEPS
Full details from www.cespt2008.org

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ESF-UB Conference on Pharmacogenetics and Pharmacogenomics
September 21-24, 2008, Santorini, Greece
Contact: Conference secretariat, Brigitte Hiegel
Université Henri Poincaré, 30 rue Lionnois, 5400 Nancy, France, Tel +33 3 83 68 21 71
Fax +33 3 83 32 13 22
Email Brigitte.Hiegel@cclm.uhp-nancy.fr

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2009 2nd PHARMSCIFAIR
Pharmaceutical Sciences Fair & Exhibition
June 8-12 • 2009 • Nice-Acropolis • Nice • France

2nd PharmSciFair
June 8-12, 2009, Nice, France
Contact: EUFEPS Meetings and Events
P O Box 1136, SE-111 81 Stockholm, Sweden
Fax +46 8 4113217
Email conferences@eufeps.org

To announce your conference, workshop and course, send brief information to the EUFEPS Secretariat.
For full address, see front page.

Season´s Greetings!