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PRESENTATION OF THE INSTITUTE

A. Organisation

The Institute of Pharmaceutical Technology (Head: H.Leuenberger) is part of the Department of Pharmacy of the University of Basel. The Department of Pharmacy of the University of Basel [Uni BS] forms together with the Institute of Pharmaceutics of the Federal Institute of Technology Zürich [ETHZ] the Centre of Pharmaceutical Sciences of Uni BS and ETHZ. (See the different organizational charts in the attachment). The Centre of Pharmaceutical Sciences Basel-Zürich fits well into the concept to establish and strengthen the cooperation between Swiss Universities (see H.Leuenberger "Geist und Geld" für einen gemeinsamen Aufbruch in Lehre und Forschung, NZZ, 24.7.01; Attachment).

B. Location

Basel and its neighbourhood is the home of the world famous pharmaceutical companies Novartis Pharma, Roche and of pharmaceutical small and medium sized enterprises as well as of the equipment manufacturer Glatt. Thus Basel provides an excellent environment for research and teaching in pharmaceutical sciences. Recently an increasing number of start-up and spin-off companies have been founded and a special platform "BioValley" was formed to stimulate the cooperation and foundation of companies in the area of biotechnology.

The Institute of Pharmaceutical Technology is located on the second and partially on the third floor of the Pharmacentre of the University of Basel. A special research and teaching laboratory for Powder and New Process Technology is within walking distance at the Mühlhauserstrasse 49/51.

C. Mission

The mission of the Institute of Pharmaceutical Technology is defined as follows:

Excellent Teaching and Research in Pharmaceutical Technology which shall permit the student to follow a career in academia or in pharmaceutical industry or in related fields such as hospital pharmacy, retail pharmacy or governmental health offices, based on a Basel University Diploma in Pharmaceutical Sciences and/or a Federal Diploma as a Pharmacist (mandatory for retail, hospital pharmacy) and/or a PhD in Pharmaceutical Sciences (generally suggested for a career in academia, industry).

MAXIM: "Science fascinates us as the Key for Technologies changing the world" (freely adapted from I.Asimov)

D. Teaching

D. 1. Undergraduate Teaching (Diploma students)

For the preparation of the diploma work (21 weeks) the following courses, including practical laboratory training work, are offered:

- Liquid-sterile Dosage Forms
- Semi-solid Dosage Forms
- Solid Dosage Forms

Quality assurance and GMP topics are included in the Seminar „Pharmaceutical Technology” which complements the contents of the courses mentioned. In addition, the seminar is designed for the training of the presentation skills.

Within the following two years, it is planned to update the courses taking into account new learning technologies and to have the theoretical courses available in German, English and Russian language (see D. 3).

The Institute of Pharmaceutical Technology is a member of GPEN [Global Pharmaceutical Education Network] <http://www.hbc.ukans.edu/phch/gpen.htm>

D. 2. Postgraduate Teaching

D.2.1 CEIP-Courses, Head: PD Dr.G.Imanidis

CEIP [Continuing Education in Industrial Pharmacy] are offered for PhD Students as part of post-graduate education and for participants from the pharmaceutical industry. The concept of CEIP-program is reviewed each year and includes in general specialists from the pharmaceutical industry in the teaching staff. In 2001 a course for hospital pharmacists was organised:

- Hospital Pharmacy. Course and Workshop between August 30 and November 16, 2001, sponsored in part by CEIP-Continuing Education in Industrial Pharmacy. Total duration 12 full days.

D.2.2 Postgraduate education in cooperation with the Federal Institute of Technology (ETH) Zürich

In 2001 Dr. Verena Renggli, pharmacist, was hired by the ETHZ in the succession of Dr. Ruth Mosimann to organize the postgraduate courses. According to the agreement between the University of Basel and the ETZ Zürich the organization of postgraduate courses by the Centre of Pharmaceuticals Sciences Basel-Zürich plays a key role in the implementation of the function of the Centre.

Since 1996, Dr.G.Imanidis and Dr.S.Marrer have organised together with Dr.A.Beck-Sickinger (since 1999 Professor at the University of Leipzig) special postgraduate courses in Quality Assurance.

- A.Beck-Sickinger, S.Marrer and G.Imanidis. Quality Assurance in the Development, Production, Control and Registration of Peptides and Proteins (Editorial). *Pharm.Acta Helv.* **71**:381 (1996).
 - A.Beck-Sickinger, G.Imanidis and S.Marrer. Quality Assurance in Computer Validation Systems (Editorial). *Pharm.Acta Helv.* **72**:315 (1998).
 - A.Beck-Sickinger, G.Imanidis and S.Marrer. Externe und interne Inspektionen von Qualitätssicherungssystemen (Editorial). *Pharm.Ind.* **61**:1075 (1999).
- Under the umbrella of the centre of Pharmaceutical Sciences Basel-Zürich the following event was organised:
- Research Meeting of the Ph.D. students of the Centre for Pharmaceutical Sciences Basel-Zurich, October 24, 2001. Sponsored by F. Hoffmann-La Roche Ltd., Basel.

D.2.3 Co-operation with the TTC (Technology Training Centre), Binzen

The Glatt Group has established a special Technology Training Centre [TTC] at the Binzen Facility, Germany. Binzen is located close to Lörrach and can be reached easily with the highway from Basel in ca. 20 minutes. The Institute of Pharmaceutical Technology has a close co-operation with Klaus Eichler, head of the TTC.

The program of TTC is available at the following Web Site: <http://www.glatt.de/ttc/index-d.htm>.

In case, that the courses are not overbooked a limited number of PhD students can participate at the individual courses. The participation at these courses is counted as part of postgraduate education of PhD students in Pharmaceutical Technology.

D. 3. New Learning and Teaching Technologies **Co-operation with MUCTR, Moscow, Russia/Development of Curriculum**

In connection with the Swiss National Science Foundation a co-operation with the Cybernetic Department Computational Science Project of MUCTR (Mendeleev's University of Chemical Technology of Russia) has been established. MUCTR wants to extend its teaching and research focus in the direction of pharmaceutical Technology, developing a corresponding curriculum. This Co-operation is supported by the grant (7IP 062613) given by the Swiss National Science Foundation for the time period 1.10.2000 until 1.10.2002.

E. Research

The research work is mainly conducted by PhD (ca. 20) and diploma students (ca 10 per year) in the laboratories of the Institute of Pharmaceutical Technology or the Pharmaceutical Industry (Novartis Pharma, Roche or small and medium sized enterprises, including start-up companies) or in the labs of the Glatt Group (Manufacturer of Pharma Process Technology Equipment).

Research work is supervised by the Faculty of the Institute of Pharmaceutical Technology and is in general supported by the National Science Foundation of Switzerland, by private grants or by grants offered by the industry.

The research, which is conducted outside the Pharmacentre in privately owned laboratories, is usually supervised by a specialist on site, who keeps close contacts with the Faculty of the Institute of Pharm. Technology. The PhD-students in the Pharmacentre have part-time the function as teaching assistants. Diploma thesis work can be done in connection with a research project at the Pharmacentre, in the industry or in affiliated labs (see G Research and Co-operation Network).

More than 95% of PhD students, who have completed their studies at the Institute of Pharmaceutical technology, work later in the industry.

E. 1. Research Areas

E.1.1 Main Areas

Research in Powder Technology Dry and Moist Agglomeration of Powder, i.e. Granulation, Tableting

- Control and Scale-up of the Moist Agglomeration Process
- Computer assisted Design of Solid Dosage Forms
- Preformulation and Formulation Research

New Process Technologies

- Vacuum Fluidised Bed System.
- Spray Freeze Drying at Atmospheric Pressure.
- Scale-up in the 4th Dimension (Moist Agglom. and Drying Process).
- Supercritical CO₂ and Liposomes
- High Temperature Short Time Sterilization

Basic Research Activities (SNF, Industry)

- Application of Percolation Theory and Fractal Geometry:
- Formulation Research: Robustness and Percolation Thresholds (Critical Concentrations).
- Multicomponent Formulations: Fractals and Order in a Chaotic System!
- Solubility, Structure of Water, Hydrophilic Solutions.

Drug Absorption; (PD Dr. G. Imanidis)

- Interface Dosage Form/Body of Patient.
- Drug Transport: Intestine/Systemic Circ.
- Transmucosal, Transepithelial Transport.
- Problem of Bioavailability of topical dosage forms.
- Problem of Drugs with a Poor Water Solubility.

Specifically, research related to Drug Absorption is subdivided into two focus areas:

1. Dermal (topical) and transdermal (systemic) delivery of drugs including low molecular weight organics and peptide analogues employing formulation design and iontophoresis as a means to modulate and enhance delivery rate.

Fundamental *in vitro* studies of the effect of phase structure in multi-phasic systems and of

parameters involved in iontophoresis (pH micro-environment, electroosmotic flow, fraction of aqueous channel pathway) are undertaken, modelling processes based on physicochemical principles to allow quantitative assessment of the influencing factors. Simultaneous transport and metabolism in the skin is considered, drug concentration within cutaneous tissue is estimated and pharmacological concentration/response relationships established *in vivo* using site of action concentration as a measure of skin bioavailability.

2. Intestinal drug absorption using the Caco-2 cell line and phospholipid vesicles as model to simulate the absorption epithelium. A mechanistic approach is taken to identify the routes that are relevant for transepithelial transport of drugs and to establish possible relationships between the fluidity of the plasma membrane of the cells and the phospholipid bilayer of the vesicles and the permeation rate. Steady state and real time fluorescence depolarisation measurements are used to obtain a measure of membrane fluidity and the effect of adjuvants such as surfactants and lipids contained in drug formulations on the membrane is evaluated. The interrelation between membrane properties and the function of efflux mechanisms such as those related to P-glycoprotein is studied and cellular pharmacokinetics considering transport and metabolism established.

E. 2. Research Policy

- Problem oriented, derived from needs. (Applied and Basic Research).
- Themes, Projects are interrelated. Identification of interesting Niche Topics.
- Optimisation of Return on Investment.
- Close Cooperation with the Industry (Pharma, Equipment Manufacturer).

E. 3. Important Research Papers

E.3.1 Application of Percolation Theory and Fractal Geometry

- Percolation Theory, Fractal Geometry and Dosage Form Design, H.Leuenberger, L.Holman, M.Usteri and S.Winzap, *Pharm.Acta Helvetiae* **64**:34-39 (1989).
- The application of percolation theory in powder technology (Invited review), Hans Leuenberger, *Advanced Powder Technology* **10**:323-353 (1999)

E.3.2 New Process Technologies

- Granulation and Drying in Vacuum Fluidised Bed Systems, B.Luy, B.Hirschfeld and H.Leuenberger, *Drugs made in Germany* **32**:3-8 (1989).
- Atmospheric Spray Freeze Drying: a suitable alternative in freeze drying technology, M.Mummenthaler and H.Leuenberger, *Inst.Journal of Pharm.* **72**:97-110 (1991)
- Development of a new plant for quasi-continuous granulation and multiple chambered fluid-bed drying of pharmaceutical granules, B.Dörr and H.Leuenberger. Pre-prints of the 1st European Symposium: Process Technology in Pharmaceutical and Nutritional Sciences (Editor: H.Leuenberger, Basel), ISBN 3-921590-55-8, PARTEC 98, Nürnberg, March 10-12, 1998, p. 247-256.

E.3.3 Experimental Design; Surface Response Methodology

Artificial Neural Networks; Expert Systems

- A Factorial Design for Compatibility Studies in Preformulation Work, H.Leuenberger and W.Becher, *Pharm.Acta Helv.* **50**:88-91 (1975).
- Mathematische Modellierung und Optimierung pharmazeutisch-technologischer Qualitätsmerkmale fester Arzneiformen, H.Leuenberger, P.Guitard und H.Sucker, *Pharmazie in unserer Zeit* **5**:65-76 (1976).
- Basic Concepts of Artificial Neural Networks (ANN) Modelling in the Application to Pharmaceutical Development, J.Bourquin, H.Schmidlin, P.vanHoogevest and H.Leuenberger, *Pharm.Development and Technology* **2**:95-109 (1997).

E.3.4 Drug Delivery through Biological and Artificial Membranes

- G.Imanidis, K.C.Hartner and N.A.Mazer. Intestinal Permeation and Metabolism of a Model Peptide (Leuprolide) and Mechanisms of Permeation Enhancement by Non-Ionic Surfactants. *Int.J.Pharm.* **120**:41-50 (1995).
- G.Imanidis, C.Waldner, C.Mettler and H.Leuenberger. An Improved Diffusion Cell Design for Determining Drug Transport Parameters across Cultured Cell Monolayers. *J.Pharm.Sci.* **85**:1196-1203 (1996).
- G.Imanidis, S.Helbing-Strausak, R.Imboden and H.Leuenberger. Vehicle-dependent *In Situ* Modification of Membrane-controlled Drug Release. *J.Control.Release* **51**:23-34 (1998).
- R.Imboden and G.Imanidis. Effect of the Amphoteric Properties of Salbutamol on its Release Rate through a Polypropylene Control Membrane. *Eur.J.Pharm.Biopharm.* **47**:161-167 (1999).

E. 4. Suggested Further Reading

E.4.1 Application of Percolation Theory and Fractal Geometry

- Fractal Dimension of Porous Solid Dosage Forms, M.Usteri, J.D.Bonny and H.Leuenberger *Pharm.Acta Helv.* **65**:Nr. 2 (1990): 55-61.
- Formation of a Tablet: A Site-Bond Percolation Phenomenon, H.Leuenberger and R.Leu *J.Pharm.Sci.* **81**:Nr. 10 (1992): 976-982.
- Matrix-Type Controlled Release Systems: I. Effect of Percolation on Drug Dissolution Kinetics, J.D.Bonny and H.Leuenberger *Pharm.Acta Helv.* **68**:(1993): 25-33.
- Percolation Effects in Matrix-Type Controlled Drug Release Systems, H.Leuenberger, J.D.Bonny, M.Kolb *Int.J.of Pharm.* **115**:(1995): 217-224.
- Use of Percolation Theory to Interpret Water Uptake, Disintegration Time and Intrinsic Dissolution Rate of Tablets Consisting of Binary Mixtures, R.Luginbühl and H.Leuenberger *Pharm.Acta Helv.* **69**:(1994): 127-134.
- Percolation Theory and Robust Formulations in Powder Technology, H. Leuenberger in Proceedings '96 China-Japan Symposium on Particology edited by Yong Jin, Mooson Kwauk, Genji Jimbo and Yasuo Konseka, Tsinghua University Beijing May 24-25, 1996.

E.4.2 Process Technology/Solid Dosage Form Design

- Theory of the Granulating Liquid Requirement in the Conventional Granulation Process, H.Leuenberger, H.P.Bier and H.Sucker *Pharm.Techn.Intern.* **3**:(1979): 60-67.
- Scale-up of Granulation Processes with -Reference to Process Monitoring, Acta Pharm.Techn. **2**:(1983): 274-280.
- Monitoring Mass Transfer Processes in order to control moist agglomeration, H.Leuenberger and G.Imanidis *Pharm.Techn.* **10**:(1986): 56 - 73
- Monitoring the Granulation Process: Granulate Growth, Fractal Dimensionality and Percolation Threshold, H.Leuenberger, M.Usteri, G.Imanidis and S.Winzap *Boll. Chim. Pharm.* **128**:(1989): 54-61.
- Agglomeration of Binary Mixtures in a High-Speed Mixer, M.Usteri and H.Leuenberger *Int.J.of Pharm.* **55**:(1989): 135-141.
- Design and Modification of Powders - A Must in Pharm. Technology, H.Leuenberger *Proceed. 2nd World Congress Particle Technology*, Sept. 19-22, 1990, Kyoto, Japan Vol. III. p. 317-328, The Society of Powder Technology, Japan.
- Design and Optimisation Approaches in the Field of Granulation, Drying and Coating, H.Leuenberger *Pharmacy World Congress '93, Tokyo*, *Proceed. of the 53rd Int. Congress of Pharm. Sciences 1993*, D.J.S.Crommelin, K.K.Midha, T.Nagai editors, Medpharm. Scientific Publishers, Stuttgart 1994, p. 493-511.

E.4.3 New Process Technologies

- Prozess Monitoring bei der Emulsionsherstellung Drehmomentenmessung als In Prozess Kontrolle bei der Emulsionsherstellung, R.Randegger, G.Imanidis, R.D.Juch, G.Birrenbach, H.Leuenberger *Pharm.Ind.* **56**:(1994): 648-654
- Wet spherical agglomeration of proteins as a new method to prepare parenteral fast soluble dosage forms, A.Bausch and H.Leuenberger *Int.J.of Pharm.* **101**:(1994): 63-70
- List of Preparation of Liposomes Encapsulating Water Soluble Compounds Using Supercritical Carbon Dioxide, L.Frederiksen, K.Anton, P.vanHooegevest, H.R.Keller and H.Leuenberger *J.Pharm.Sci.* **86**:(1997): 921 -928 xxxxx
- Thermal Sterilization of Heat Sensitive Products using High-Temperature Short-Time Sterilization, A.Mann, M.Kiefer and H.Leuenberger, *J.Pharm.Sc*, **90**:(3), 275-287 (2001).

E.4.4 Drug Delivery through Biological and Artificial Membranes

- P.Lütolf, G.Imanidis and H.Leuenberger. Transdermal Iontophoresis of an Amphoteric Compound: Effect of Charge and Interaction with Human Skin, In: P.Couvreur, D.Duchéne, P.Green and H.E.Junginger (Eds.), *Transdermal Administration, A Case Study, Iontophoresis*, Editions de Santé, Paris, 1997, pp. 360-364.
- G.Imanidis and R.Imboden. Utilizing Vehicle Imbibition by a Microporous Membrane and Vehicle Viscosity to Control Release Rate of Salbutamol, *Eur. J. Pharm. Biopharm.* **47**:283-287 (1999).
- F.P.Schwarb, G.Imanidis, E.W.Smith, J.M.Haigh and C.Surber. Effect of Concentration and Degree of Saturation of Topical Fluocinonide Formulations on *In Vitro* Membrane Transport and *In Vivo* Bioavailability on Human Skin. *Pharm. Res.* **16**:909-915 (1999).

E. 5. Publications: Institute of Pharmaceutical Technology 1996-2000

1996

Albumin Nanospheres as Carriers for Passive Drug Targeting: An Optimized Manufacturing Technique. Publication, in english. Bernhard G. Müller, Hans Leuenberger, Thomas Kissel, *Pharm.Res.* 13 (1), 1996, 32-37. ISSN 0724-8741.

An Improved Diffusion Cell Design for Determining Drug Transport Parameters across Cultured Cell Monolayers. Publication, in english. Georgios Imanidis, Christoph Waldner, Christoph Mettler, Hans Leuenberger, *J.Pharm.Sci.* 85 (11), 1996, 1196-1203. ISSN 0022-3549.

Dissolution properties of praziquantel- β -cyclodextrin systems. Publication, in english. Silvia Kocova, Hans Leuenberger, *Pharm.Dev.Technol.* 1 (3), 1996, 307-315. ISSN 1083-7450.

Percolation Theory and Robust Formulations in Powder Technology. Proceedings, in english. Hans Leuenberger, *Proc.CJP'96* 1996, 37-41. 96 China-Japanese Symposium on Particuology; Beijing 24.05.96 - 25.05.96.

Quality assurance in the development, production, control and registration of peptides and proteins. Publication, in english. Annette Beck-Sickinger, Georgios Imanidis, Stephan Marrer, *Pharm.Acta Helv.* 71 1996, 381-381. ISSN 0031-6865.

Study of percolation thresholds in ternary tablets. Publication, in english. Isidoro Caraballo, M. Fernandes, Monica Millán, Antonio M. Rabasco, Hans Leuenberger, *Int.J.Pharm.* 139 (1.2), 1996, 177-186. ISSN 0378-5173.

The Application of Percolation Theory in the Field of Powder Technology. Proceedings, in english. Hans Leuenberger, *Proc.2nd Part.Techn.Forum Paper No.95d* 1996. 2nd International Particle Technology Forum; San Diego 14.07.96 - 18.07.96. In conjunction with 5th World congress of chemical engineering

Zero-order release periods in inert matrices. Influence of the distance to the percolation threshold. Publication, in english. Isidoro Caraballo, Monica Millán, Antonio M. Rabasco, Hans Leuenberger, *Pharm.Acta Helv.* 71 (5), 1996, 335-339. ISSN 0031-6865.

1997

An extended model based on the modified Nernst-Planck equation to describe transdermal iontophoresis of amphoteric compounds. Proceedings, in english. Georgios Imanidis, Peter Lütolf, Hans Leuenberger, ISSN 1022-0178. *Proc.24th Int.Symp.Controlled Release Bioact.Mater.* 1997, 29-30. 24th International Symposium on Controlled Release of Bioactive Materials; Stockholm 15.06.97 - 19.06.97.

Analysis of drug/plasma protein interactions by means of asymmetrical flow field-flow fractionation. Publication, in english. Maja Madörin, Peter van Hoogevest, Rolf Hilfiker, Birgit Langwost, G.M. Kresbach, M. Ehrat, Hans Leuenberger, *Pharm.Res.* 14 (12), 1997, 1706-1712. ISSN 0724-8741.

Application of Artificial Neural Networks (ANN) in the Development of Solid Dosage Forms. Publication, in english. Jacques Bourquin, Heinz Schmidli, Peter van Hoogevest, Hans Leuenberger, *Pharm.Dev.Technol.* 2 (2), 1997, 111-121. ISSN 1083-7450.

Application of Percolation Theory to Characterize the Release Behaviour of Carteolol Matrix Systems. Publication, in english. Isidoro Caraballo, M.A. Holgado, M. Fernandes, Monica Millán, Antonio M. Rabasco, *Drug Dev.Ind.Pharm* 23 (1), 1997, 1-8. ISSN 0363-9045.

Basic Concepts of Artificial Neural Networks (ANN) Modeling in the Application to Pharmaceutical Development. Publication, in english. Jacques Bourquin, Heinz Schmidli, Peter van Hoogevest, Hans Leuenberger, *Pharm.Dev.Technol.* 2 (2), 1997, 95-109. ISSN 1083-7450.

Percolation theory and physics of compression. Publication, in english. Hans Leuenberger, Lotti Ineichen, *Eur.J.Pharm.Biopharm.* 44 (3), 1997, 269-272. ISSN 0939-6411.

Permeation of a probe molecule (mannitol) through phospholipid bilayer membranes: correlation with membrane microviscosity. Proceedings, in english. Georgios Imanidis, Fabienne Rosa, Hans Leuenberger, ISSN 1022-0178. *Proc.24th Int.Symp.Controlled Release Bioact.Mater.* 1997, 429-430. 24th International Symposium on Controlled Release of Bioactive Materials; Stockholm 15.06.97 - 19.06.97.

Pharmaceutical technology and quality assurance: the impact of novel concepts in the production of granules and tablets. Publication, in english. Hans Leuenberger, *S.T.P.Pharma Sci.* 7 (1), 1997, 19-25. ISSN 1157-1489.

Preparation of Liposomes Encapsulating Water-Soluble Compounds Using Supercritical Carbon Dioxide. Publication, in english. Lene Frederiksen, Klaus Anton, Peter van Hoogevest, Hans Rudolf Keller, Hans Leuenberger, *J.Pharm.Sci.* 86 (8), 1997, 921-928. ISSN 0022-3549.

Research in solid dosage forms - an obsolete topic?. Publication - Editorial, in english. Hans Leuenberger, *Pharm.Dev.Technol.* 2 (3), 1997, VII-VIII. ISSN 1083-7450.

Transdermal Iontophoresis of an Amphoteric Compound: Effect of Charge and Interaction with Human Skin. Proceedings, in english. Peter Lütolf, Georgios Imanidis, Hans Leuenberger, *Transdermal Administration* 1997, 360-364. ISBN 2-86411-110-1. Editor(s) Duchêne Dominique, Couvreur P., Green P., Junginger H.; 1997 European Symposium; Transdermal administration, a case study, Iontophoresis; Paris 03.03.97 - 04.03.97.

1998

Advantages of Artificial Neural Networks (ANNs) as alternative modeling technique for data sets showing non-linear relationships using data from a galenical study on a solid dosage form.. Publication, in english. Jacques Bourquin, Heinz Schmidli, Peter van Hoogevest, Hans Leuenberger, *Eur.J.Pharm.Sci.* 7 (1), 1998, 5-16. ISSN 0928-0987.

Comparison of artificial neural networks (ANN) with classical modeling techniques using different experimental designs and data from a galenical study on a solid dosage form. Publication, in english. Jacques Bourquin, Heinz Schmidli, Peter van Hoogevest, Hans Leuenberger, *Eur.J.Pharm.Sci.* 6 (4), 1998, 287-301. ISSN 0928-0987.

Development of a quasi-continuous production line for granules – a concept to avoid scale-up problems. Preprint, in english. Benno Dörr, Hans Leuenberger, *Preprint,1st Europ.Symp.Process Technology in Pharmac.and Nutrit.Sciences* 1998, 247-256. ISBN 3-921-590-55-8. Editor(s) Leuenberger Hans. 1st European Symposium; Process Technology in Pharmaceutical and Nutritional Sciences; Nürnberg 10.03.98 - 12.03.98. combined with 4th International Congress for Particle Technology

Dissolution Properties of Praziquantel - PVP Systems. Publication, in english. Silvia Kocova, Hans Leuenberger, *Pharm.Acta Helv.* 73 (2), 1998, 89-94. ISSN 0031-6865.

Effects of Formulation and Process Variables on the Aggregation of Freeze-Dried Interleukin-6 (IL-6) After Lyophilization and on Storage. Publication, in english. Barbara Lückel, Bernhard Helk, David Bodmer, Hans Leuenberger, *Pharm.Dev.Technol.* 3 (3), 1998, 337-346. ISSN 1083-7450.

Formulations of Sugars with Amino Acids or Mannitol - Influence of Concentration Ratio on the Properties of the Freeze-Concentrate and the Lyophilizate. Publication, in english. Barbara Lückel, David Bodmer, Bernhard Helk, Hans Leuenberger, *Pharm.Dev.Technol.* 3 (3), 1998, 325-336. ISSN 1083-7450.

Granulation - Novel Concepts. Publication/Abstract, in japanese. Hans Leuenberger, *AchemAsia '98*, 1998, 168-169. 4th International Meeting on Chemical Engineering and Biotechnology; Beijing 11.05.98 - 16.05.98.

How to Monitor and Control the Moist Agglomeration Process. Bookchapter, in english. Hans Leuenberger, *Data Acquisition and Measurement Techniques* 1998, 141-157. ISBN 1-57491-037-X. Editor(s) Vromans Herman, Munoz-Ruiz Angel

Modified Young's Modulus of Microcrystalline Cellulose Tablets and the Directed Continuum Percolation Model. Publication, in english. Martin Kuentz, Hans Leuenberger, *Pharm.Dev.Technol.* 3 (1), 1998, 13-19. ISSN 1083-7450.

Orden en sistemas farmacéuticos complejos formados por medios desordenados. Inaugural Lecture, in spanish. Hans Leuenberger, *Inaugural Lecture*, 1998. 1998 Inauguration at the Royal Academy of Pharmacy of Spain; Madrid 05.03.98 - 05.03.98.

Order in Complex Pharmaceutical Systems of Disordered Media. English Version of: Orden en sistemas farmacéuticos complejos formados por medios desordenados. Inaugural Lecture, in english. Hans Leuenberger, *Inaugural Lecture*, 1998. 1998 Inauguration at the Royal Academy of Pharmacy of Spain; Madrid 05.03.98 - 05.03.98.

Pitfalls of artificial neural networks (ANN) modeling technique for data sets containing outlier measurements using a study on mixture properties of a direct compressed dosage form.. Patent Specification, in english. Jacques Bourquin, Heinz Schmidli, Peter van Hoogevest, Hans Leuenberger, *Eur.J.Pharm.Sci.* 7 (1), 1998, 17-28. ISSN 0928-0987.

Preparation of Liposomes Encapsulating Water-Soluble Compounds Using Supercritical Carbon Dioxide. Proceedings, in Lene Frederiksen, Klaus Anton, Peter van Hoogevest, Hans Rudolf Keller, Hans Leuenberger, ISSN 1022-0178. *Proc.25th Int.Symp.Controlled Release Bioact.Mater.* 1998, 46-47. 25th International Symposium on Controlled Release of Bioactive Materials; Las Vegas 21.06.98 - 26.06.98.

Quality Assurance in Computer Validation Systems. Publication/Editorial, in english. Annette Beck-Sickinger, Georgios Imanidis, Stephan Marrer, *Pharm.Acta Helv.* 72 1998, 315-315. ISSN 0031-6865.

Relationship between fine Particle Fraction and Percentage of Drug Retained after Air Jet Sieving of Model Carrier-Based Salbutamol Dry Powders for Inhalation. Proceedings, in english. Lise-Marie Fueg, Kotaro Iida, Hans Leuenberger, Rudi Müller-Walz, *Drug delivery to the lungs IX* 1998, 64-67. IX Drug Delivery to the Lungs; London 14.12.98 - 15.12.98.

Solubility Properties of Racemic Praziquantel and its Enantiomers. Publication, in english. Silvia Kocova, Daniëlle Giron, Hans Leuenberger, *Pharm.Dev.Technol.* 3 (4), 1998, 557-564. ISSN 1083-7450.

Vehicle-dependent in situ modification of membrane-controlled drug release. Publication, in english. Georgios Imanidis, S. Helbing-Strausak, Roger Imboden, Hans Leuenberger, *J.Control.Release* 51 (1), 1998, 23-34. ISSN 0168-3659.

Validation of a Fully Automated Inspection Machine for the 100% Inlaine Control of Prefilled Syringes. Proceedings, in english. Jutta Peters, G. Paulini, Isabelle Conrot Bouley, G. Wolany, Hans Leuenberger. Proc.16th PDA Int.Congr., 1998. 16th PDA International Congress; Basel 23.02.98 - 25.02.98.

Validation of a Fully Automated Inspection Machine of Prefilled Syringes. Proceedings, in english. Jutta Peters, G. Paulini, Isabelle Conrot Bouley, G. Wolany, Hans Leuenberger. Proc.ISPE-Seminar, 1998. 1998 ISPE-Seminar; Manchester 20.05.98 - 21.05.98.

1999

Effect of Concentration and Degree of Saturation of Topical Fluocinonide Formulations on In Vitro Membrane Transport and In Vivo Bioavailability on Human Skin. Publication, in english. Fabian Schwarb, Georgios Imanidis, E.W. Smith, J.M. Haigh, Christian Surber, Pharm.Res. 16, 1999, 909-915. ISSN 0724-8741.

Effect of Separation Characteristics between Salbutamol sulfate (SS) Particles and Model Carrier Excipients on Dry Powder for Inhalation. Publication, in japanese. Kotaro Iida, Hans Leuenberger, Lise-Marie Fueg, Rudi Müller-Walz, Kazumi Danjo, YaZa 119 (10), 1999, 752-762. ISSN 0031-6903.

Effect of the Amphoteric Properties of Salbutamol on its Release Rate through a Polypropylene Control Membrane. Publication, in english. Roger Imboden, Georgios Imanidis, Eur.J.Pharm.Biopharm. 47, 1999, 161-167. ISSN 0939-6411.

Elasticity of polymer tablets considered as a network of contacts. Publication, in english. Martin Kuentz, Hans Leuenberger, Max Kolb, S.T.P.Pharma Sci. 9 (6), 1999, 531-538. ISSN 1157-1489.

Externe und interne Inspektionen von Qualitätssicherungssystemen. Publication/Editorial, in german. Annette Beck-Sickinger, Georgios Imanidis, Stephan Marrer, Pharm.Ind. 61, 1999, 1075-1075. ISSN 0031-711x.

Flow-cytometric investigation of cellular metabolism during oxidative stress and the effect of tocopherol. Publication, in english. Susanne Amann, Claudia Reinke, G. Valet, U. Moser, Hans Leuenberger, Int.J.Vitam.Nutr.Res. 69 (5), 1999, 356-361. ISSN 0300-9831.

Fracture in disordered media and tensile strength of microcrystalline cellulose tablets at low relative densities. Publication, in english. Martin Kuentz, Hans Leuenberger, Max Kolb, Int.J.Pharm. 182 (2), 1999, 243-255. ISSN 0378-5173.

Percolation theory, conductivity and dissolution of hydrophilic suppository bases (PEG systems). Publication, in english. Christian Siegmund, Hans Leuenberger, Int.J.Pharm. 189 (2), 1999, 187-196. ISSN 0378-5173.

Press-susceptibility of polymer tablets as a critical property: A modified Heckel equation. Publication, in english. Martin Kuentz, Hans Leuenberger, J.Pharm.Sci. 88 (2), 1999, 174-179. ISSN 0022-3549.

The application of percolation theory in powder technology. Publication - Invited review Hans Leuenberger, Advanced Powder Technol. 10 (4), 1999, 323-352. ISSN 0921-8831.

Utilizing Vehicle Imbibition by a Microporous Membrane and Vehicle Viscosity to Control Release Rate of Salbutamol. Publication, in english. Georgios Imanidis, Roger Imboden, Eur.J.Pharm.Biopharm. 47, 1999, 283-287. ISSN 0939-6411.

2000

A new model for the hardness of a compacted particle system, applied to tablets of pharmaceutical polymers . Publication, in english. Martin Kuentz, Hans Leuenberger, Powder Technol. 111 (1.2), 2000, 145-153. ISSN 0032-5910.

A new theoretical approach to tablet strength of a binary mixture consisting of a well and a poorly compactable substance. Publication - Thesis, in english. Hans Leuenberger, Martin Kuentz, Eur.J.Pharm.Biopharm. 49 (2), 2000, 151-159. ISSN 0939-6411.

Device with rotating blades for fluidized-bed treatment and agglomeration of particles.. Patent Specification, in german. Hans Leuenberger, Patentschrift (Switz.), 2000.

Effect of mixing of fine carrier particles on dry powder inhalation property of salbutamol sulfate (SS). Publication, in japanese. Kotaro Iida, Hans Leuenberger, Lise-Marie Fueg, Rudi Müller-Walz, Hirokazu Okamoto, Kazumi Danjo, YaZa 120 (1), 2000, 113-119. ISSN 0031-6903.

Focus on research in nanoscience and nanotechnology in Switzerland. Publication, in english. Hans Leuenberger, J.Nanop.Res. 2 (4), 2000, 391-392. ISSN 1388-0764.

Solubilization Systems - The Impact of Percolation Theory and Fractal Geometry. Bookchapter, in english. Hans Leuenberger, Silvia Kocova, Water-Insoluble Drug Form. 2000, 569-607. ISBN 1-57491-105-8.Editor(s) Liu Rong.

The Use of Fluorescence Resonance Energy Transfer to Study the Disintegration Kinetics of Liposomes Containing Lysolecithin and Oleic Acid in Rat Plasma. Publication, in english. Maja Madörin, Peter van Hoogevest, Rolf Hilfiker, Hans Leuenberger, Pharm.Res. 17 (9), 2000, 1118-1123. ISSN 0724-8741.

E. 6. Contribution by External Docents (see also attachment)

- Prof. Theodor Güntert, PhD, having important responsibilities in his job at Roche Basel is lecturing Biopharmaceutical and Pharmacokinetic topics and is supervising a tutorial with practical applications of Pharmacokinetic data. The list of his publications in 2001 can be found in the attachment.
- PD Daniëlle Giron, PhD, is expert and head of the Thermoanalytic laboratory at Novartis Pharma Ltd. Her contribution teaching thermoanalytical topics is highly appreciated. Her publications are listed in the attachment.
- PD Peter van Hoogevest, PhD, is an expert in the formulation and the manufacture of liposomes. He recently became CEO of Phares Drug Development Ltd., Muttentz, a company specialised in liposomal technologies and applications. He is teaching liposomal related topics (including practical training) at the Institute of Pharmaceutical Technology.

- PD Stephan Marrer, PhD, responsible for the production of solid dosage forms at Roche, is teaching Quality Assurance topics and is tutor in the seminar for Pharmaceutical Technology. He has submitted his scientific oeuvre at the Faculty of Natural Sciences to become Private Docent (PD) at the University of Basel.
- Ottheinrich Eichhorst, PhD, Dr. has completed his study as a Pharmacist in 1999 and started to collaborate in 2000 with the Institute of Pharmaceutical Technology.
- Klaus Eichler is head of the Technology Training Centre at Glatt GmbH in Binzen, BRD. He is an excellent organiser and moderator of Meetings, Workshops and Symposia world-wide. The Institute of Pharm. Technology is proud of working with him for years.
- Claudia Reinke, PhD, has a degree in biology (PhD) and pharmacy (diploma). She owns the company MedSciences, Basel.
- PD Michel Ulmschneider, PhD, is private docent at the Université de Haute Alsace, Mulhouse and is responsible for the PhD thesis of Lars Sukowski at Roche.
- Bernd Herzog, PhD, is head of several R+D application labs at Ciba Specialty Chemicals, Grenzach-Wylen within the segment of home and personal care (main focus on sun screens for skin protection).

F. Curriculum Vitae

F. 1. G. Imanidis

	BORN
Georgios Imanidis, June 8, in Serres, Greece	1958
EDUCATION	
High school (gymnasium) education with emphasis on sciences in Serres, Greece	1973 – 1976
University admission examination	1976 June
Pharmacy studies at the Aristotelion University of Thessaloniki, Thessaloniki, Greece	1976 – 1980
Graduation with the Pharmacy degree	1980 Nov.
Post-graduate studies in Pharmaceutical Technology and Industrial Pharmacy at the „Pharmazeutisches Institut“ of the University of Basel, Basel, Switzerland	1980 – 1982
Advanced diploma in Pharmaceutical Technology,	1982 Dec.
Ph.D. thesis in Pharmaceutical Technology under the supervision of Prof. H. Leuenberger at the „Pharmazeutisches Institut“ of the University of Basel, Basel, Switzerland	1983 – 1986
Doctor of Philosophy degree	1986 Feb.
PROFESSIONAL APPOINTMENTS	
Part-time (50%) teaching assistant in Pharmaceutical Technology at the „Pharmazeutisches Institut“ of the University of Basel, Basel, Switzerland	1983 – 1986
Post-doctoral fellow in Drug Delivery Research under Prof. W.I. Higuchi in the Department of Pharmaceutics, University of Utah, Salt Lake City, UT, U.S.A.	1986 – 1988
Senior research scientist in the Department for Drug Absorption Studies, TheraTech, Inc., Salt Lake City, UT, U.S.A.	1988 – 1990
Adjunct staff scientist in the Department of Pharmaceutics, University of Utah, Salt Lake City, UT, U.S.A.	1988 – 1990
Recipient of a scholarship from the Roche Research Foundation to study drug absorption using cell cultures as an alternative to animal experiments at the „Pharmazeutisches Institut“ of the University of Basel, Switzerland	1991 – 1992
Scientific staff member, „habilitand“, and head teaching assistant at the „Pharmazeutisches Institut“ of the University of Basel, Department of Pharmaceutical Technology, Basel, Switzerland	1992 – 1999
Awarded the title of a docent „PD“ by the Faculty of Natural Sciences of the University of Basel through the process of „Habilitation“.	2000
Faculty member (full time) at the Institute of Pharmaceutical Technology, University of Basel, Switzerland	since 2000

F. 2. H. Leuenberger

EDUCATION	
Diploma in Experimental Physics (University of Basel)	1967
PhD-Thesis in Nuclear Physics (University of Basel)	1971
INDUSTRIAL CAREER	
Head of R+D Laboratory (Preformulation work) Analytical R+D Department, Sandoz Ltd., Basel	1971-1973
Research Group Leader, Pharmaceutical R+D, Sandoz Ltd., Basel	1973-1982
SABBATICALS AND EXPERIENCES ABROAD	
University of Hamburg (Prof. Dr. H. Sucker) Germany	1973
University of Michigan, Ann Arbor (Prof. Dr. W.I. Higuchi, Prof. Dr. N.F. Ho, Dr. E.W. Hiestand), U.S.A.	1979
Head Pharma R+D, Sandoz España, Barcelona ad interim (Spain).	1980
CAREER IN ACADEMIA	
Part Time Lecturer at the University of Basel as Private Docent (PD) in Pharmaceutical Technology	1980
Full-Time Ordinary Professor of Pharmaceutical Technology and Head of the Institute of Pharmacy at the University of Basel, Totengässlein 3, CH-4051 Basel (Historical Site close to the Museum)	1982
Planning of a new building for the Institute of Pharmacy	1982-2000
Member of the Export Group 12 (Pharmaceutical Technology) of the European Pharmaceutical Commission, Strasbourg, France	1988-1993
Dean of the Faculty of Natural Science at the University of Basel, Founder of the Faculty Committee of Department Heads	1994/95
President of the Scientific Council [SC] of the Swiss Academy of Engineering Science [SATW] and founder of the Lateral Think Tank of the SC	1992-96
Vice President of the Swiss Academy of Engineering Science (for further nominations and awards see chapter F)	Since 1993
Member of Editorial Advisory Board (such as J.Pharm.Sci. 1990/92), Referee for different journals, Member of peer review committees: ETHZ (1993), University of Groningen and Utrecht (1997), Publications: more than 180, Patents: more than ten.	
SWISS MILITARY SERVICE RECORD	
Expert Officer (Nuclear Physics) as A-Specialist, Chief Physicist and AC-Laboratory Chief (retired since 1993), President of AC-Specialists-Study Group (AGAS) 1978-1982.	
HOBBIES	
Research in Genealogy, President of the Basel Society of Genealogy and Heraldics 1973-1982, Tennis	
At the new Building and address: Pharmacentre, Klingelbergstrasse 50; 4056 Basel	Since 2000

F. 3. Research Awards, Medals, Nominations (Membership Awards)

H. Leuenberger, on behalf of the Institute of Pharmaceutical Technology:

- ❖ Member of Swiss Academy of Engineering Sciences since 1987.
- ❖ University of Helsinki Medal 1989.
- ❖ Fellow of the American Association of Pharmaceutical Scientists [AAPS] since 1990.
- ❖ AAPS Research Award in Pharmaceutical Technologies 1993.
- ❖ Innovation Award for New Process Technologies of the Governments Basel-City and Basel-Country 1994.
- ❖ Honorary Member of the Swiss Society of Industrial Pharmacists [GSIA] since 1994.
- ❖ Jörg Bider Medal of the Swiss Society of Pharmacists [SAV] 1997.
- ❖ Corresponding Member of the Royal Academy of Pharmacy of Spain since 1998.
- ❖ Foreign Member of the Russian Academy of Engineering Sciences since 1998.
- ❖ IPS Medal 2000 [Industrial Pharmacy Section] of FIP [Fédération Internationale Pharmaceutique]. 2000.
- ❖ Member of the Scientific Advisory Board of the Grand École des Mines, Albi, France, since 2001.
- ❖ Award of Particulate Preparations and Design of the Society of Powder Technology of Japan, Kyoto, Japan, 2001

G. Research and Co-operation Network

G. 1. Academia

China Pharmaceutical University, Nanjing, P.R. China*

Federal Institute of Technology [ETH] Zürich*

École des Mines, Albi, France*

Gifu Pharmaceutical University, Gifu Japan*

Institute of Hospital Pharmacy, Basel

Institute of Informatics, University of Basel

Mahidol University, Bangkok, Thailand*

* Based on formal agreements.

Mendeleev University of Chemical Technology of Russia [MUCTR], Moscow*

Spitalapotheke, Kantonsspital Aarau

University of Kansas, Lawrence, Kansas, USA*

University of Seville, Seville, Spain*

G. 2. Industrial Partners

ADD, Advanced Drug Delivery Technologies, Muttenz

Asulab AG, Neuchâtel

Bachem AG, Bubendorf

Capsugel Ltd., Arlesheim

Ciba Specialty Chemicals, - Grenzach D

Drossapharm AG, Arlesheim

Glatt AG, Pratteln

Glatt GmbH, Binzen, BRD

Glatt, System Techniques, Dresden, BRD

Mepha AG, Aesch

Novartis Animal Health Ltd, Basel

Novartis Pharma Ltd., Basel

Pentapharm AG, Aesch

Pfizer GmbH, Arzneimittelwerk Gödecke, Freiburg i.Br.

Phares Ltd., Muttenz

Roche Ltd., Basel

Roche Ltd., Grenzach, BRD

Skye Pharma, Muttenz

Spirig AG, Egerkingen

* Based on formal agreements.

H. Progress Report 2001

H. 1. Special Events 2001

H.1.1 Promotion of Stephan Marrer, PhD, Private Docent

Dr. Marrer received in 2001 the VENIA LEGENDI of the University of Basel and has been promoted to become PD [Private Docent]. Dr. Marrer (external docent), Roche, has been involved in teaching since several years at the centre of pharmaceutical sciences in Basel and Zürich taking care of the area of Quality Assurance especially GMP and Validation issues.

H.1.2 Promotion of PD Dr. D. Giron (external Docent)

Dr. Giron, Private Docent at the University of Basel was promoted by Novartis Pharma Ltd. and received the title "leading scientist" (award). We congratulate!

H.1.3 H.Leuenberger, Recipient of the Kyoto Award

"Particulate Preparations and Design", Japan

The Society of Powder Technology of Japan decided to dedicate the Kyoto Award of Particulate Preparations and Design to Prof. Dr. Hans Leuenberger for his research work in the field of Powder Technology. The recipient did regret that he does not speak Japanese to thank after the award ceremony, which took place in Toyohashi, Japan, on Oct. 24, 2001. According to the vision of the recipient the science of powder technology, *i.e.* the so called "particuology" is rapidly evolving especially in Japan that a rigorous scientific framework can be developed which should lead to the creation of the discipline of "Physical Particuology". Such a development could be compared with the creation of "Physical Chemistry" as part of chemistry in the history of science.

H. 2. Home page of the Institute of Pharmaceutical Technology, IT-Support

The IT-Support for the computer network is playing an increasing role. The work of T.Kuny, A.Stengele and M.Sutter, PhD-students and responsible for IT-support, respectively for the home page is specially acknowledged. In 2001 the home page of the Institute of Pharm. Technology could be successfully established by T.Kuny.

H. 3. Research and Teaching Laboratory for Powder and New Process Technology at the Mühlhauserstrasse 49/51, Basel.

In 2001 the infrastructure of the external station at the Mühlhauserstrasse 49/51, Basel could be substantially improved with the implementation of the research lab of Dr.G.Betz. The research labs are installed in the rooms of a former bakery. The investments made in 2001 should allow that two Postdocs and three PhD-students can work permanently in this external station. The research work in this external station shall complement the work done in the labs of the Pharma Centre, especially in the area of powder and novel process technology including the development of expert systems for the formulation of capsules and tablets. For this purpose the lab received in 2001 a Bosch Capsule Filling Machine and will receive the so called Presster TM equipment which will allow to check the quality of a tablet formulation with a small amount of material to be run later on a high-speed tableting machine. This project is supported by PFIZER GmbH, Arzneimittelwerk Gödecke, Freiburg i.Br. which is specially acknowledged. The Presster equipment will be delivered in March 2002.

Within the topic of new process technologies the filling process of sterile solutions containing living cells will be investigated. This project and the appropriate equipment is sponsored by the company Alphacos SA, CH-2822 Courroux, which is specially acknowledged.

H. 4. Teaching

H.4.1 New Learning Technologies

The CD-ROM "Physical Pharmacy" which has been developed by Michael Lanz is now successfully used by the students of the 4th and 5th study years. This CD-ROM will be part of the new edition of the textbook: Martin et al., "Physikalische Pharmazie" (editor: H.Leuenberger; in cooperation with O.Eichhorst and M.Lanz) to be published in 2002 (Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart). In 2001 the teaching courses of H.Leuenberger have been upgraded and are now as a Learning and Teaching power point presentation available. Ms. Claudia Hersche prepared the Pharm.Tech. Course 'Feste Arzneiformen' and Ms. Marijke Walter the Pharm.Tech. Course 'Halbfeste Arzneiformen'. Both diploma theses have been supervised by Michael Lanz, O. Eichhorst and H. Leuenberger.

H.4.2 New Curriculum/Overlap

Due to the overlap of the old and the new curriculum the number of students for the winter-semester 2001/2002 did rise to 85, which needed a new organisation of the three practical training courses accommodating each 28/29 students. The enormous effort of the PhD-students supervising the different training courses, of Sonja Reutlinger, Stephan Winzap and Georgios Imanidis is specially acknowledged.

The new structure of the practical training courses already takes care of the new curriculum and of the future introduction of the bachelor/master degree in pharmaceutical sciences. For this purpose the three practical courses for 1) liquid sterile- 2) semi-solid- and 3) solid dosage forms have been coordinated with three courses of Molecular Pharmacy (I-III) during the third study year. These courses are compulsory for the students.

H.4.3 Diploma Studies

In the year 2001 eight students have completed this diploma work in the area of Pharmaceutical Technology. Diploma studies were performed in the Pharmacentre as well as in laboratories of partner institutions (see H.4.4., List of diploma thesis students, topics and location).

H.4.4 List of Diploma Students

with diploma thesis topics in Pharmaceutical Technology 2001

Bucher Christian	Transport von Amentoflavon durch CaCo-II Zellen	Pharmazentrum
Fiechter Tamara	Liposomen als Modellmembranen	Pharmazentrum
Herrsche Claudia	Pharm Tech Kurs Feste Arzneiformen	Pharmazentrum
Mäder Stefanie	Bioverfügbarkeit von Sonnenschutzfiltern in der Haut	Institut für Spitalpharmazie, Kantonsspital Basel
Sautter Caroline	In-situ bindende Implantate in der Veterinärpharmazie	Novartis Animal Health
Unternährer Jessica	Herstellung von Procain-HCl 50 mg/ml Vial à 500 mg als stabiles Parenteralia-Lyophilisat für den Spitalbedarf zur Verwendung als Lokalanästhetikum bei Patienten mit Allergie auf Präparate vom Amidtyp	Spitalapotheke Kantonsspital Aarau
Walter Marjike	Pharm Tech Kurs Halbfeste Arzneiformen	Pharmazentrum
Zimmermann Christine	Simultane Iontophorese eines Peptids und eines Markers	Pharmazentrum

H. 5. New Learning and Teaching Technologies **Co-operation with MUCTR, Moscow, Russia /** **Development of Curriculum / Computational Science Project**

The co-operation with the Cybernetic Department of MUCTR (Mendeleev's University of Chemical Technology of Russia) and the Institute of Pharm. Technology at the University of Basel is supported by the grant (7IP 062613) given by the Swiss National Science Foundation for the time period 1.10.2000 until 1.10.2002.

H.5.1 Development of Curriculum

Recently, a new Department of Technology of Chemical-Pharmaceutical and Cosmetic Products at MUCTR was founded. The co-operation Basel-Moscow has the aim to exchange expertise and to step towards the creation of a Faculty of Pharmacy at MUCTR. The program has as a goal to give Russian specialists the opportunity to strengthen the knowledge in Pharmaceutical Technology:

H.5.2 Phys Pharm

The CD-Rom Physpharm with mathematical model equation, designed by Michael Lanz (Supervisors: O. Eichhorst and H. Leuenberger) of the Institute of Pharmaceutical Technology, University of Basel, in cooperation with H. Burkhardt of the Institute of Informatics, University of Basel, is successfully translated into Russian by Maxim Poutchkov, D.I. Mendeleev University of Chemical Technology of Russia (MUCTR).

The CD-ROM Physpharm is part of the student education at MUCTR and at the University of Basel.

H.5.3 Teaching Presentation: Glatt equipment

The company Glatt, Binzen, Germany is a global leader in process equipment for life sciences. The equipment and the technologies, such as fluid bed, granulating, coating, drying etc. are presented in a power point presentation and translated into Russian by Denis Shishulin, MUCTR.

The teaching presentation is part of the student education in the field of modern technological equipment of pharmaceutical plants at MUCTR.

H.5.4 Multimedia Teaching Courses

The course Pharmaceutical Technology, Prof. Dr. H. Leuenberger, Institute of Pharmaceutical Technology, Basel consists of three parts:

- Liquid-sterile Dosage Forms
- Semi-solid Dosage Forms
- Solid Dosage Forms

The theoretical courses, Semi-solid Dosage Forms and Solid Dosage Forms are already in use as PowerPoint presentations at Institute of Pharmaceutical Technology in Basel taking into account new learning technologies and are currently translated into Russian at MUCTR.

The course Liquid-sterile Dosage Forms will be designed as PowerPoint presentation in summer semester 2002 at Institute of Pharmaceutical Technology, Basel and afterwards translated into Russian at MUCTR.

The teaching course will be part of the student education at MUCTR; the first course will begin in spring 2002 (Prof. N. Menshutina).

H.5.5 Development of an Expert System for Capsules, Tablets and Dragées

The primary goal of this expert system is to create a pharmaceutical formulation database for the manufacturing of solid dosage forms (Julia Mishina, MUCTR). In addition statistical experimental design studies and the application of artificial neuronal networks [ANN] are used for the optimisation of Pharmaceutical Dosage Forms.

H.5.6 Computational Science Project: Atmospheric-Freeze-Drying Project

Mathematical modelling (Denis Shishulin, MUCTR) with existing data of the Ph.D. thesis of Marco Mumenthaler: "Sprüh-Gefriertrocknung bei Atmosphärendruck: Möglichkeiten und Grenzen in der Pharmazeutischen Technologie und in der Lebensmitteltechnologie" and in a later stage verifying the theoretical models with further experiments at Institute of Pharmaceutical Technology, University of Basel, with the planned new "Spray Freeze Drying Equipment" equipment to be manufactured by Glatt, Binzen.

H. 6. Research

H.6.1 General Remarks

The research focus and the interest of the scientific community is reflected by the topics of the invited talks (see H.6.3). There is a special interest in topics related to Powder and Process Technology:

- the control of the production of pharmaceutical granules and new process technologies to shorten the time to market
- to provide a physical technique for optimising the water solubility of the active substance (freeze drying process).

The problem of drug permeation through a biological membrane is a research topic with increasing importance since the discovery that the efflux-transport effect of the p-glyco-protein in the membrane can be blocked by other drugs but also by certain excipients and/or natural products such as grapefruit juice. Actual research work is concerned with dermal, transdermal and transdermal-iontophoretic, and gastrointestinal and cellular drug delivery and absorption. Emphasis is placed on delivery and transport

mechanisms of drugs including peptides, peptide-analogues and model drug entities and drug carriers across biological, phospholipid bilayer and artificial membranes under special consideration of membrane properties, formulation design and time-dependent controlled drug delivery.

H.6.2 Publications 2001

A novel approach to the characterization of polar liquids Part 1: Pure liquids. Publication, in english. Andrea Stengele, Stephanie Rey, Hans Leuenberger, *Int.J.Pharm.* 225 (1.2), 2001, 123-134. ISSN 0378-5173.

Atmospheric Spray Freeze Drying - The Process of Choice for low water soluble Drugs?. Proceedings, in english. Hans Leuenberger, *Proc.Int.Sci.Sem.* 2001, 16-22. ISBN 5-7237-0302-1. Editor(s) Menshutina Nathalia V., Goncharova S.V., Shishulin D.V., 2001 International Scientific Seminar; Moscow 10.09.01 - 11.09.01.

Evaluation of flow properties of dry powder inhalation of salbutamol sulfate with lactose carrier.. Publication, in english. Kotaro Iida, Youhei Hayakawa, Hirokazu Okamoto, Kazumi Danjo, Hans Leuenberger, *Chem.Pharm.Bull.* 49 (10), 2001, 1326-1330. ISSN 0009-2363.

Heparin penetration into and permeation through human skin from aqueous and liposomal formulations in vitro. Publication, in english. Gabriele Betz, Reinhard Nowak, Roger Imboden, Georgios Imanidis, *Int.J.Pharm.* 228 (1.2), 2001, 147-159. ISSN 0378-5173.

How to Avoid Scale-up Problems in Manufacturing Pharmaceutical Granules: The Glatt Multicell Concept. Publication, in english. Hans Leuenberger, *Pharm.Technol.Jpn* 17 (10), 2001, 1563-1569. ISSN 0910-4739.

Interaction of liposome formulations with human skin in vitro. Publication, in english. Gabriele Betz, Dieter Imboden, Georgios Imanidis, *Int.J.Pharm.* 229 (1.2), 2001, 117-129. ISSN 0378-5173.

Method for producing particulate goods. Patent Specification, in german. Hans Leuenberger, Armin K.T. Prash, Bernhard Luy, *PCT Int. Appl.* 2001, 1-54.

New Trends in the Production of Pharmaceutical Granules: Batch versus Continuous Processing. Publication, in english. Hans Leuenberger, *Eur.J.Pharm.Biopharm.* 52 (3), 2001, 289-296. ISSN 0939-6411.

New Trends in the Production of Pharmaceutical Granules: The classical batch concept and the problem of scale-up. Publication, in english. Hans Leuenberger, *Eur.J.Pharm.Biopharm.* 52 (3), 2001, 279-288. ISSN 0939-6411.

Powder - the fourth state of matter?. Proceedings, in english. Hans Leuenberger, *Proc.18th Symp.Part.Prep.Design* 2001, 154-165. 18th Symposium on Particulate Preparations and Design; Toyohashi 24.10.01 - 25.10.01.

Scale-up in the field of Granulation and Drying. Chapter 6. Bookchapter, in english. Hans Leuenberger, *Drugs and the Pharmaceutical Sciences, Volume 118*, ISSN 0360-2583. *Pharmaceutical Process Scale-Up* 118 2001, 151-170. ISBN 0-8247-0625-0. Editor(s) Levin Michael.

Scale-up in the 4th dimension in the field of granulation and drying. Preprint, in english. Hans Leuenberger, *Preprints 7th Intern.Symp.Aggl.* 2001, 375-384. 7th International Symposium on Agglomeration; Albi CT Cedex 29.05.01 - 31.05.01.

Thermal Sterilization of Heat Sensitive Products using High-Temperature Short-Time Sterilization. Proposal, in english. Angelika Mann, Markus Kiefer, Hans Leuenberger, *J.Pharm.Sci.* 90 (3), 2001, 275-287. ISSN 0022-3549.

H.6.3 List of Presentations as an Invited Speaker in the year 2001

Year 2001		Title
January 22. H. Leuenberger	AAPS 36th Annual, Pharmaceutical Technologies Conference at Arden House, NY, USA	FASTER TIME TO MARKET: Scale-up in the 4th Dimension
January 24 H. Leuenberger	AAPS 36th Annual, Pharmaceutical Technologies Conference at Arden House, NY, USA	Granulation Endpoint Detection and Robust Dosage Form Design
February 7 H. Leuenberger	TTC, Technology Trainig Center, Glatt GmbH, Binzen Workshop "High Shear Processing"	Granulation Endpoint Determinaton and Robust Dosage Form Design
February 21 H. Leuenberger	PDA, International Congress, Courses and Exhibition, Kyoto, Japan 2001. Bridging the Healthcare and Pharmaceutical Worlds in the New Millennium	New Technologies for the Manufacture of Nanostructured Drug Carriers
March 15 H. Leuenberger	Atelier Pharmacie, Interchimie 2001, Paris, France	Scale-up in the 4th Dimension in the Field of Granulation and Drying
May 19 G.Betz	Pharmaceutical Lecture Series Prof. G. Avramenko, MUCTR , Moscow	The estimation of bioaccessibility of condensed dispersal systems in dermatological investigations
May, 29.-31.	7th International Symposium on Agglomeration In Honour of the late Professor Genji Jimbo, Ecole des Mines, Albi, France	Scale-up in the 4th dimension in the field of granulation and drying or how to avoid classical scale-up
June, 12-15 A.Stengele	Formation CPIC (Centre de Perfectionnement des Industries Chimiques) Mise en forme des solides divisés, Albi, France	Instrumentation des Procédés de granulation humide Transfert d'échelle (Scale-up)
July 9 H. Leuenberger	Verfahrenstechnisches Seminar, TU München, Institut für Verfahrenstechnik (Prof.W.Peukert), München-Garching	Sprühgefriertrocknung bei Atmosphärendruck – die Methode der Wahl für die Verarbeitung von schlecht wasserlöslichen Wirkstoffen?
September 4 H. Leuenberger	Peking Medical University, School of Pharmacy, Beijing	Atmospheric Spray Freeze Drying - The Process of Choice for low water soluble Drugs?

September 10 H. Leuenberger	International Conference “Modelling of biomaterials thermal treatment” MUCTR , Moscow, Russia	Atmospheric Spray Freeze Drying - The Process of Choice for low water soluble Drugs?
September 27 H. Leuenberger	University of Queensland, Department of Medicine, Brisbane,	Atmospheric Spray Freeze Drying - The Process of Choice for low water soluble Drugs?
October 8 H. Leuenberger	Université Paul Sabatier, Toulouse III, CNRS-IPBS, (Centre National de la Recherche Scientifique - Institut de Pharmacologie et Biologie Structurale)	Atmospheric Spray Freeze Drying -The Process of Choice for low water soluble Drugs?
October 11 H. Leuenberger	4th International Rencontres in Pharmaceutical Engineering, Ecoles des Mines, Albi, France	Research at the Institute of Pharm. Technology, Pharmacentre of the University of Basel
October 22 H. Leuenberger	University of Gifu, Institute of Pharmaceutical Technology, Gifu, Japan	Genomics, high through-put screening – what next? The industrialization of the pharmaceutical research activities
October 23 H. Leuenberger G.Betz	AAPS, Annual Meeting, Denver, Colorado, USA	New Trends in the Production of Pharmaceutical Granules: Batch. Continuous Processing
October 24 H. Leuenberger	Toyohashi, 441-8061, Japan Symposium on Particulate Preparations and Design. The Society of Powder Technology of Japan	Powder - the forth state of matter? Invited Award Presentation
October 25 H. Leuenberger	(morning) Takeda Chemical Industries, Ltd., Osaka	Scale-up in the 4 th dimension: How to avoid classical Scal-up in th Field of Granulation
	(afternoon) Shionogi Co. & Ltd., Osaka, Japan	Research at the Institute of Pham.Technology, Pharmacentre of University of Basel
November 6-7 H. Leuenberger	ECA – Modern Solid Dosage Forms Facilities, Darmstadt, Course organised by Concept-Heidelberg	Novel Technologies for a „Fast-To-Market“-Concept: New trends in the production of pharmaceutical granules

H.6.4 Participation in Symposia, Workshops, Project/coordination Meetings, Organisation of workshops etc.

Year 2001		Title
February 7	GSIA (Gesellschaft der Schweizerischen Industrie-Apotheker)	Presentation of the Department of Pharmacy at the Pharmacentre
March 16 H. Leuenberger	GVC-Fachausschuss Agglomeration, Freiburg i. Br.	Function: Session Chairman
May 9-11 Hans Leuenberger G. Betz	Institute of Pharm.Techn.. Basel, Project Coordination, Moscow (MUCTR) -BS	New Learning Technologies Physpharm, M. Poutchkov, Dr.V.Tsoukanov
May 19 G. Betz	Coordination Project MUCTR -BS, Meeting in Moscow Prof.G.Avramenko Prof.S.Goncharova V.Kim, Prof.L.Kovalenko	Implementation of practical courses: Liquid-sterile dosage forms, semi-solid dosage forms (with demonstrations) Lecture of G.Betz: see invited speakers
May 19-24 M. Sutter, V. Milojkovic, F. Rosa and G. Imanidis	Poster at the European Research Conference on Microdomains, Lipid Rafts and Caveolae, San Feliu de Guixols, Spain	Membrane Properties of Phospholipid Vesicles Affecting Drug Permeation
June 18-20 D. Hummel and G. Imanidis	Poster at the EUFEPS World Conference on Drug Absorption and Drug Delivery, Copenhagen, Denmark	Structure of Multi-phasic Dermal Formulations and the Influence of the Structure and of Vehicle Evaporation on Transdermal Permeation
July 6 H. Leuenberger	10th company anniversary of Glatt Systemtechnik GmbH Dresden	Function: Symposium Chairman
September 12-14 C. Kochhar and G. Imanidis	Oral presentation at the Startum Corneum III Conference, Basel, Switzerland	Transdermal Iontophoresis of Leuprolide In Vitro under Constant Voltage and Constant Current Conditions: Physicochemicla Modeling and the Effect of Adjuvants
September 12-14 D. Hummel and G. Imanidis	Oral presentation at the Startum Corneum III Conference, Basel, Switzerland	Structure of Multi-phasic Dermal Formulations and the Influence of the Structure and of Vehicle Evaporation on Transdermal Permeation
September 12-14 T. Schmidt, N. Widler, F. Gafner and G. Imanidis	Poster at the Startum Corneum III Conference, Basel, Switzerland	Stratum Corneum Lipid Composition as a Predictive Tool for Permeability?

September 12-14 T. Tassopoulos, S. Maeder, G. Imanidis, V. Figueiredo, E.W. Smith and C. Surber	Poster at the Startum Corneum III Conference, Basel, Switzerland	Evaluation of a Spectrophotometric In Situ Determination as a Stand-Alone Method for Percutaneous Bioavailability Studies
September 25 Hans Leuenberger	6th World Congress of Chemical Engineering, Melbourne 2001	Scale-up in the 4th Dimension: How to Avoid Classical Scale-up in the Field of Granulation and Drying
Oct. 24 G.Betz, G.Imanidis	PhD-Meeting of the Center of Pharm.Sci, Basel-Zürich, in Basel at F. Hoffmann - La Roche AG	PhDs present their research topics, event sponsored by F. Hoffmann-La Roche Ltd.
Dec. 3-7 H.Leuenberger G.Betz	Coordination Project MUCTR -BS, Meeting: Basel	Prof.S.Goncharova Anton Vetrov ; Project Progress Evaluation
Dec. 3-7 K.Eichler, TTC	TTC-Course on pelletisation, Binzen, Germany	Participation of Prof.Goncharova and Anton Vetrov, MUCTR

H.6.5 List of PhD-Theses in Pharmaceutical Technology completed in 2001

(Supported by)

Herrn Hummel Daniel

January 2001

Die Struktur topischer Formulierungen und der Einfluss strukturbedingter physikochemischer Parameter und Evaporation auf – die perkutane Resorption. (Spirig AG)

Frau Operschall Elisabeth Marie

Mai 2001

DNA Vaccines Encoding Viral Proteins and Strategies to Improve Immune Responses. (In Zusammenarbeit mit dem Institut für Medizin.Virologie der Universität Zürich)

Frau Kochhar Charu

July 2001

Untersuchungen zur Iontophoretischen Applikation von Peptiden. (Asulab/Bachem/Institut)

Frau Romann Claudine*

27.9.2001

Rezeptsammlung der Apotheke Brunner in Diessenhofen, Thurgau. Ein Beitrag zu Inhalt und Entstehungsgeschichte sowie zur Praxis der Arzneimitteltherapie in der 2.H.19.Jh.

Frau Rahlwes Isabel*

July 2001

Zur Behandlung der Krätze im 19.Jahrhundert.

Frau Rosset-Burkhalter Catherine

November 2001

Le pharmacien comme partenaire en reseau de santé dans le traitement de l'asthme

*) Doktorat in der Geschichte der Naturwissenschaften.

I. Outlook 2002

I. 1. On-Going Research Activities

I.1.1 PhD-Students, Topics (working title), Supported by

Altenbach	Melanie	Transdermale Iontophorese von geladenen und ungeladenen Verbindungen: Einfluss der Molekülladung und der Moleküllipophilie auf den Transport durch die menschliche Epidermis	Institute of Pharmaceutical Technology, University of Basel.
Bongartz	Christian	Modifying Surface Properties of Crystalline Drug Substances by Addition of Surface Active Substances During the Final Crystallization	F. Hoffmann - La Roche AG
Bausch	Ursula	Steriles Abfüllen von Lösungen mit Zellen	Alphacos SA, CH-2822 Courroux
Fueg	Lise-Marie	Einblick in die Entwicklung von Pulvern zur Inhalation mit dem SkyePharma multidose Dry Powder Inhaler (mDPI)	Skye Pharma AG
Guntermann	Anja	Scale-up of tablet formulations using the Presster TM equipment	Pfizer GmbH, Arzneimittelwerk Gödecke, Freiburg i.Br.
Hernandez	Engracia Maria	Dielectric Spectroscopy of hydrophilic solutions	Institute of Pharmaceutical Technology, University of Basel, (3 rd money)
Ketani	Damla	Ein Beitrag zur Theorie von hydrophilen Lösungen	Institute of Pharmaceutical Technology, University of Basel.
Krabichler	Michaela	The preventive effect of α -tocopherol on UVA/B-induced p53-gene photodamage in human skin fibroblasts	F. Hoffmann - La Roche AG
Kuny	Tanja	Untersuchungen zur Trockenagglomeration von pharmazeutischen Wirk- und Hilfsstoffen	Institute of Pharmaceutical Technology, University of Basel.
Lanz	Michael	The behaviour of disordered particulate systems in case of dry and moist agglomeration processes	SNF, Bern

Lenz	Corinna	Suche nach kritischen Konzentrationen bei der Herstellung von Pellets in der Rotorwirbelschicht	Spirig AG, Egerkingen
N.	N.	The production of Nanocomposites using the spray-freeze-drying technique	NCCR (National Center of Competence in Research) Nano-Center, Basel
Matschke	Christian	Slow release of veterinary formulations	Novartis Animal Health, Basel
Reitbauer	Susanne	Absorption paths of drugs through Caco-2 cells	Institute of Pharmaceutical Technology, University of Basel.
Sathayé	Bhaskar	Innovative Salbentechnologie	F. Hoffmann - La Roche AG, Grenzach
Sautter	Caroline	Slow release of veterinary formulations	Novartis, Novartis Animal Health, Basel
Schiffmann	Axel	CIP-Systeme bei der Wirbelschicht Granulierung	Glatt GmbH, Binzen, D
Schmidt	Timo	In vitro Permeabilität von β -Blockern für eine transdermale Applikation	Mepha, Aesch
Stengele	Andrea	Ein Beitrag zur Charakterisierung von binären, wässrigen Lösungsmittelmischungen mittels Dielektrischer Spektroskopie	Institute of Pharmaceutical Technology, University of Basel.
Sukowski	Lars	Online Near-Infrared Spectroscopy: Noninvasive Determination of Residual Moisture in Entire Batches of Lyophilized Pharmaceutical Products	F. Hoffmann - La Roche AG
Sutter	Marc	The Influence of phospholipid Bilayer Properties on Transmembrane Permeability	Institute of Pharmaceutical Technology, University of Basel.
Walter-de Rooy	Marijke	Konzeption, Entwicklung und Realisierung eines vernetzten e-Lehr- und-Lernprogrammes der Pharm. Technologie	Institute of Pharmaceutical Technology, University of Basel. (3 rd money).

I.1.2 Postdoctoral Positions

Dr.Betz	Gabriele	Implementation of Research and Teaching at the Powder Technology and New Process Technology Lab Mühlhauserstrasse 49/50	Institute of Pharmaceutical Technology, University of Basel.
Tanaka	Hiroshi	Project work (2002) at the New Powder and Process Technology	On sabbatical leave from Shionogi Co. & Ltd., Osaka, Japan

I.1.3 Topics of Diploma Theses in Pharmaceutical Technology planned for the year 2002

Allemann	Sabin	In-vitro Modell für topische Arzneiformen	S.Wieland-Berghausen, Novartis Animal Health
Amacker	Sonja	Entwicklung und Herstellung von Lactase Pellets	T.Kuny Institute of Pharmaceutical Technology, University of Basel
Blaser	David	Wirkstoffabsorption in Caco-2 Zellen	S.Reitbauer G.Imanidis Institute of Pharmaceutical Technology, University of Basel
Heigold	Barbara	Einflussnahme von Hilfsstoffen resp. Formulierungskomponenten auf die Verteilung von Wirkstoffen im Blut	B.Galli O.Kretz Novartis Pharma
Hilfiker	Marc	Neue Lerntechnologie, PharmTechKursFlüssigSterileArzneiformen	M.Walter H.Leuenberger Institute of Pharmaceutical Technology, University of Basel
Hofer	Renate	Einfluss von Komposition und Prozentparametern auf die Freisetzung von Proteinen aus Mikropartikeln	J.D.Bonny O.Lambert Novartis Pharma
Hofmann	Sandra	Applikationssysteme für die Lokalisierung von Mikrosphären am Wirkort	V.Luginbühl, ETH Zürich

Mathis	Katrin	Einflüsse der Tablettenformulierung auf die Feuchtagglomeration	G.Betz Institute of Pharmaceutical Technology, University of Basel
Pellanda	Carolina	Bioverfügbarkeit von Triamcinolonacetonid in der Haut	C.Surber V.Figuereido G.Imanidis Spitalapotheke Basel Institute of Pharmaceutical Technology, University of Basel
Saravia	Chantal	Thema noch offen	M.Schmid F. Hoffmann-La Roche Ltd., Basel
Schlatter	Philipp	Gezielte Kristallisation pharmazeutischer Wirkstoffe: Kontrolle von Partikelgrösse, Habitus und polymorpher Form	R.Hilfiker B.Siebenhaar, Solvias, Basel
Voelker	Eva	Anwendung eines neuen Modelles der Pulverkompression	M.Lanz Institute of Pharmaceutical Technology, University of Basel
Vuong	Hoa	Bioverfügbarkeit von Sonnenschutzfiltern in der Haut	T. Tassopoulos V.Figuereido C.Surber Institute of Pharmaceutical Technology, University of Basel
Zurbriggen	Fabienne	Einfluss der Membran-Fluidität von Caco2-Zellen auf den Wirkstofftransport	S.Reitbauer G.Imanidis Institute of Pharmaceutical Technology, University of Basel

I. 2. Grants (2001 and 2002)

I.2.1 National Science Foundation

	Grant Number / Title	
2001	2000-058941 The behaviour of disordered particulate systems in case of dry and moist agglomeration processes	30'000.-
2002	2000-058941 The behaviour of disordered particulate systems in case of dry and moist agglomeration processes	30'000.-
2001	7IP 062613 Development of new courses and scientific work in the field of pharmaceutical education	16'400.-
2002	7IP 062613 Development of new courses and scientific work in the field of pharmaceutical education	15'200.-

I.2.2 Private and Industrial Funds

2001	12 x 30'000.-	360'000.-
2002	12 x 30'000.-	360'000.-

I.2.3 PhD-Studies supported by the University of Basel

2001	6 x 50% positions à 30'000.-	180'000.-
2002	6 x 50% positions à 30'000.-	180'000.-

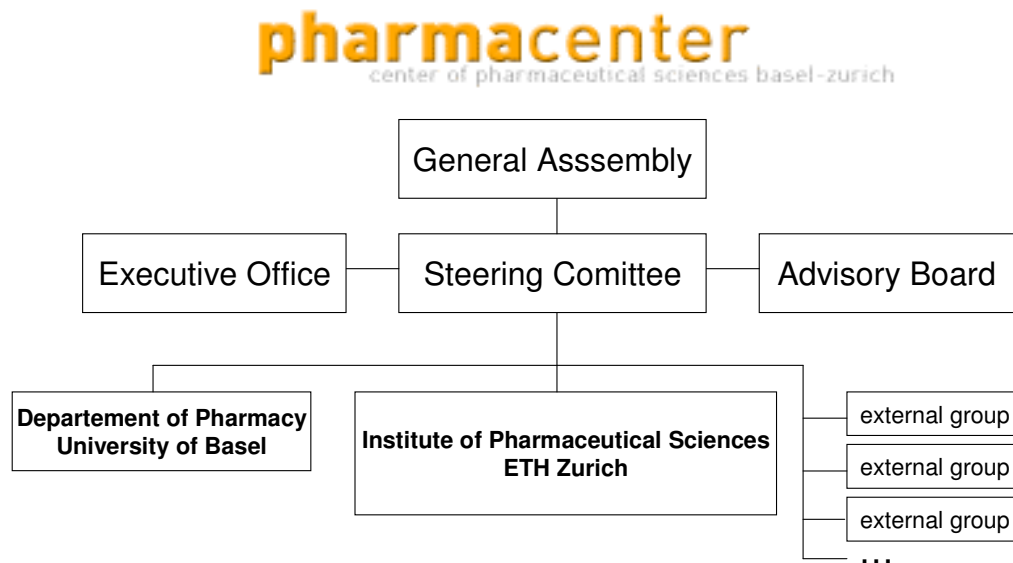
I.2.4 Total Support

Year 2001 **CHF** **586'000.-**

Year 2002 **CHF** **645'200.-**

ATTACHMENT

J. Organization charts



Organisation

www.pharmacenter.ch

Steering Committee Members 2001

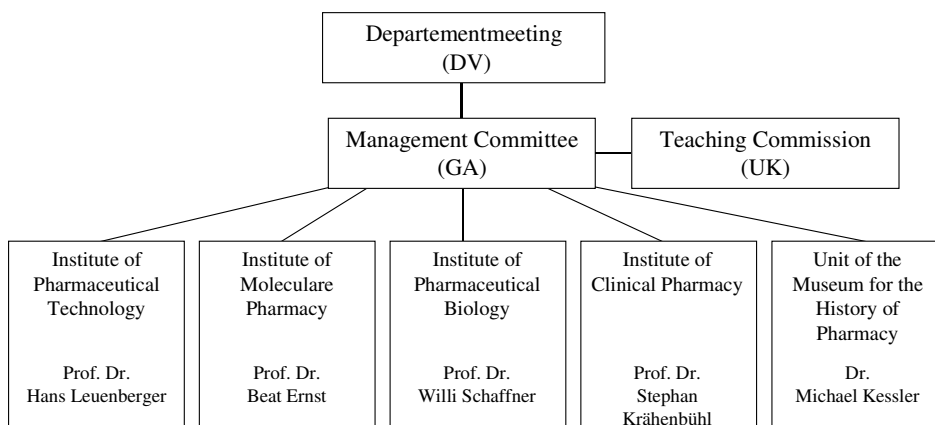
- G. Folkers, President
- H. Wunderli (ETH)
- H. Leuenberger
- A. Eberle (external groups)

Executive Office

- H.P. Wessels, Managing Director

ORGANISATION

DEPARTMENT of PHARMACY



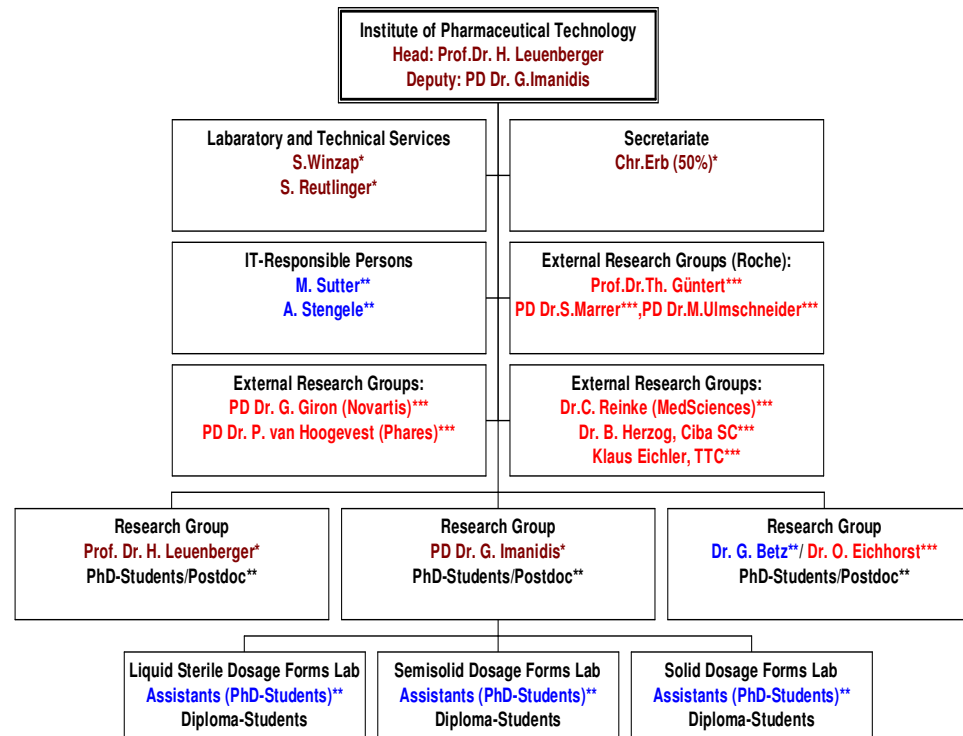
Management Committee 2001

- H. Leuenberger (Vorsitz),
- B. Ernst
- W. Schaffner
- J. Krähenbühl

Teaching Commission

- B. Ernst (Vorsitz)

Organisation; Institute of Pharm.Tech.



***Employees of the University**

****PhD/Postdoc students**
(non permanent positions, support by University, SNF, private grants etc.)

*****External docents**
(not employees of the University)

Geist und Geld

Für einen gemeinsamen Aufbruch in Lehre und Forschung

Von Hans Leuenberger*

Der internationale Wettbewerb hat der Wissenschaftspolitik wieder grössere Bedeutung verschafft. Der Autor des nachstehenden Diskussionsbeitrags fragt nach den sich abzeichnenden inhaltlichen Richtungen, ohne sich auf solche Trends zu fixieren. Vor allem plädiert er für stärkere finanzielle Anstrengungen, aber auch für eine offene Zusammenarbeit unterschiedlicher Forschungsdisziplinen im Interesse der Innovation.

Alles ist heute in Bewegung. Alles strebt vorwärts, Stehenbleiben bedeutet bereits Rückschritt. Auch die Forschungsentwicklung ist davon nicht ausgenommen. Der reale Rückgang unserer staatlichen Forschungsförderung kann sich schon bald sehr nachteilig für den Denk- und Arbeitsplatz Schweiz auswirken. Es besteht die Gefahr, dass die Schweiz den Anschluss an die moderne Forschungsentwicklung verpasst.

Wirtschaftskraft und Forschungspolitik

Im Wettstreit um die Position eines Landes spielt die wirtschaftliche Stärke eine wichtige Rolle. In vielen Ländern wird die Kooperation zwischen der Industrie und staatlichen Forschungslabors beziehungsweise den Universitäten gefördert. In den USA kann der Kongress zusätzliche Mittel bewilligen, um im Rahmen einer nationalen Initiative einen bestimmten Forschungszweig an den Hochschulen zu fördern. Kooperationen zwischen staatlichen und privatwirtschaftlichen Institutionen sind in den USA ebenfalls keine Seltenheit. So wurde beispielsweise zur Förderung der Nutzung von Daten des menschlichen Genoms zwischen den Sandia National Laboratories und der privaten Celera Genomics Corporation ein Zusammenarbeitsvertrag unterschrieben, wobei die Compaq einen Supercomputer bauen soll, der beträchtlich schneller als irgendein heute funktionierender Computer sein soll.¹

Die Biotechnologie sowie die Informations- und Kommunikationstechnologie wurden in den USA durch nationale Forschungsinitiativen speziell gefördert. Vor kurzem bewilligte der Kongress für die Nanowissenschaften eine weitere nationale Forschungsinitiative. Der Autor hatte die Gelegenheit, am vorbereitenden Workshop² dieser Initiative teilzunehmen. Die Veranstaltung beeindruckte durch den kooperativen Stil der Vertreter der konkurrierenden staatlichen Forschungsinstitutionen und der amerikanischen Industrie (Biotechnologie, Chemie, Elektronik usw.), durch den erfolgreichen Ansatz «von unten nach oben» sowie durch das Verschwinden der Grenzen zwischen den klassischen Disziplinen Physik, Biologie und Chemie im Bereich der Nanowissenschaften.

Auf Grund der schon bekannten Megatrends in Forschung und Wissenschaft, der zunehmend

* Der Autor, Professor für Pharmazie in Basel und Mitglied des Leitenden Ausschusses des Zentrums für Pharmazeutische Wissenschaften der Universität Basel und der ETH Zürich, ist Vizepräsident der Schweizerischen Akademie der technischen Wissenschaften.

dominierenden Stellung der Wirtschaft mit Globalisierungs- und Shareholder-Value-Politik, der wachsenden Bedeutung der Computerwissenschaften und der Informatik im beruflichen und privaten Sektor, der demographischen Entwicklung und der damit verbundenen Migrationsbewegungen sind tiefgreifende technologische und soziale Umwälzungen zu erwarten.

Die grossen Trends

An einem Symposium des Rats der vier schweizerischen Akademien (Cass) über «Aufstieg und Fall von Megatrends in der Wissenschaft» wurden Ende des letzten Jahres die sich abzeichnenden, zunehmend miteinander zusammenhängenden Megatrends der nächsten Jahrzehnte von Michael C. Roco, Mitglied des Nationalen Wissenschafts- und Technologierats, Washington, wie folgt zusammengefasst:³

- Informations- und Kommunikationstechnologie, Computerwissenschaften;
- Biologie und Bio-Umweltwissenschaften;
- Nanowissenschaft und -technologie;
- medizinische Wissenschaften und Technologien, die eventuell die physischen menschlichen Fähigkeiten verbessern;
- kognitive Wissenschaften, die sich mit der Erforschung und Verbesserung der intellektuellen menschlichen Fähigkeiten befassen;
- Erforschung des kollektiven Verhaltens und Systemlehre.

Durchlässigkeit und Vielfalt

Will die Schweiz den Anschluss nicht verpassen, muss sie sich mit diesen Megatrends auseinandersetzen und in diesen Bereichen interessante Nischen ausfindig machen, auf Komplementarität achten und Duplizitäten vermeiden. Da Innovationen eher in solchen Gebieten stattfinden, wo sich verschiedene Disziplinen überlappen (Querschnittsdisziplinen), stellt sich die Frage, wie die Grenzen zwischen verschiedenen Disziplinen durchlässiger gemacht werden können. Multidisziplinäre Forschungsgruppen könnten für den Wettlauf um neue Forschungsdurchbrüche entscheidend sein.

Auf Grund nicht vorhersehbarer Entwicklungen in der Forschung dürften bis zum Jahre 2008 neue Megatrends entstehen. Zur Bewahrung der Forschungsvielfalt sollten deshalb genügend Mittel für die Pflege von Wissenschaftszweigen ausserhalb der Megatrends bereitgestellt werden. Zudem sollten auch Forschungsbereiche mit hoher gesellschaftlicher oder nationaler Relevanz unterstützt werden. Dazu gehören beispielsweise Umweltschutz, Nachhaltigkeit, Energieforschung («saubere Energie»), Verkehr oder gesellschaftlicher Zusammenhalt.

Mehr Mittel und mehr Synergien

Für eine optimale Lehre und Forschung braucht es nicht nur Geist, sondern auch Geld. Während es bei uns in der Regel selbstverständlich ist, dass Primar-, Sekundar-, Real- und Mittelschulen zusätzliche Mittel erhalten, nehmen an den Hochschulen die zur Verfügung stehenden Mittel für Lehre und Forschung ab. Um der jetzigen und der kommenden Situation gerecht zu werden, müssen wir diese Budgets jedoch wesentlich aufstocken, denn das Potenzial der «grauen

Zellen» stellt die einzige Ressource dar, auf die das Land zurückgreifen kann. Die Idee einer Bildungsinitiative – beispielsweise durch Verwendung nicht benötigter Goldreserven – ist zu unterstützen.

Nachfolgend sind einige Ideen zusammengefasst, wie Synergien genutzt werden könnten:

- Förderung und Verstärkung der regionalen und nationalen Zusammenarbeit zwischen den Hochschulen (ohne die internationale Zusammenarbeit zu vernachlässigen). Beispiele: Arc lémanique, Bern - Neuenburg - Freiburg (Benefri), Basel - Zürich - St. Gallen?
- Förderung der regionalen Zusammenarbeit zwischen den Fachhochschulen und den Universitäten.
- Förderung der internationalen Zusammenarbeit in der Graduiertenausbildung, unter anderem durch Umstellung auf Englisch als Unterrichtssprache.
- Prüfung einer Zusammenlegung der Kommission für Technologie und Innovation und des Schweizerischen Nationalfonds sowie Eingliederung der Büros für die Beteiligung an europäischen und internationalen Förderungsprogrammen.
- Förderung der Zusammenarbeit unterschiedlicher Disziplinen, zum Beispiel Physik/Biologie/Chemie oder Physik/Philosophie/Mathematik (Matrix-Organisation, flache Hierarchien an Hochschulen), durch Clusterbildung in Forschungsbereichen und Förderung der Querschnittsdisziplinen wie Nanowissenschaften, Bionik, Pharmazeutische Wissenschaften, Komplexe Systeme.
- Breite Förderung der Anwendung von Computational Science, von neuen Lehr- und Lerntechnologien und allen Aktivitäten in elektronischer Information und Kommunikation.
- Schaffung eines schweizerischen Forums als Treffpunkt für Industrie und Hochschulen.

«Campus Schweiz» im Wettbewerb

Die Schweizer Forschungspolitik braucht endlich wieder einen Aufbruch – eine ähnliche Stimmung, wie sie unsere Vorfahren zur Zeit des Eisenbahnbaues gekannt haben. Um diese kreative Atmosphäre herbeizuführen, müssen Sonderinteressen überwunden und ein «Campus Schweiz» geschaffen werden, in dem für alle Forscherinnen und Forscher optimale Rahmenbedingungen herrschen. Damit dies gelingt, muss nicht nur ein Blick über den Zaun des eigenen «Forschungskönigreiches» gewagt werden, sondern dieser Zaun muss fallen, und im nahen – interessanterweise oft komplementären – Umfeld muss nach Partnerschaften gesucht werden. Es braucht die Einsicht aller Forscherinnen und Forscher, dass eine landesweite, «multikulturelle» beziehungsweise multidisziplinäre Zusammenarbeit ein spannendes Experiment ist und dass die Konkurrenz sich nicht innerhalb unseres Landes, sondern primär ausserhalb unserer Grenzen befindet.

In diesem Zusammenhang ist es wichtig, eine exzellente Forschungsinfrastruktur aufzubauen, die bei Bedarf gemeinsam genutzt werden kann. Dieses Ziel wird beispielsweise durch das hochschulübergreifende «Zentrum für Pharmazeutische Wissenschaften» der Universität Basel und der ETH Zürich verfolgt, welches ähnliche Bestrebungen in benachbarten Gebieten gerne fördern wird. – Erfolg ist zwar nicht planbar, sicher ist jedoch, dass es neben viel Geist und Kooperation eben auch viel Geld braucht.

¹ «The Washington Post», 19. 1. 2001, S. E1, E6.

² Nanotechnology Research Directions: IWGN Workshop Report. Kluwer Academic Publishers, Dordrecht, Boston, London 2000.

³ M. C. Roco: Coherence and Divergence of Megatrends in Science and Engineering. Abstract. Cass-Symposium vom 30. 11./1. 12. 2000.

K. Reports / Contributions from External Docents

K. 1. PD Dr. Peter van Hoogevest

K.1.1 Publication

- Leigh M., van Hoogevest P., Tiemessen H., Optimising the oral bioavailability of the poorly water-soluble drug cyclosporin A using membrane lipid technology in: Drug Delivery systems & sciences 2001, vol 1, no 3, pp 73-77

K. 2. PhD Dr. Stephan Marrer

K.2.1 Promotion of Stephan Marrer, PhD, Private Docent

Dr. Stephan Marrer received in 2001 the VENIA LEGENDI of the University of Basel and has been promoted to become PD [Private Docent].

K.2.2 Contribution of F. Hoffmann-La Roche Ltd., Basel

The new Pharma Centre includes facilities for the sterile operations. It is planned to use these facilities in research and education. Sonja Reutlinger, Institute of Pharm. Technology, working in the sterile facilities, was trained in sterile operations and handling at F. Hoffmann-La Roche Ltd., Basel.

The PhD-Day of the PhD Candidates of the Centre of Pharmaceutical Science University of Basel and of Federal Institute of Technology Zürich, October 24, 2001 was sponsored by and carried out at F. Hoffmann-La Roche Ltd., Basel.

K. 3. PD Dr. D. Giron

K.3.1 Activities

Organisation or co-organisation of Symposium

- 28.03.01, ETH Zurich, 25 years swiss thermal analysis and calorimetry (STK)
- 11.9-13.9.01, Munich, GEFTA, eurostar-science and STK associations
- 14.11-16.11.01, Lyon, Colloque: apport de l'analyse thermique et de la calorimétrie dans les industries chimiques, pharmaceutiques et cosmétiques
- President of the swiss thermal analysis and calorimetry society activities
- Member of Scientific Technology Forum in TRD in Novartis

Invited lectures at international meetings

September 9	Symposium rational design of drug materials and drug delivery systems, EUFEPS, Strasbourg	Solid properties relevant in salt selection
November 14	Lyon, Colloque: apport de l'analyse thermique et de la calorimétrie dans les industries chimiques, pharmaceutiques et cosmétiques	Conférence introductive

Workshops, lectures at university

Date, 2001	Location	Title
May 17, 1/2 day	Pharmaceutical Institute, Nancy	Développement du principe actif
May 14-16, May 28-30, June 25-27	Workshop for students in 4 th year, Pharmaceutical Institute Basel, (45 h)	Thermische Analyse
November 14 1 day	Chemical and Physical Institute Lyon, Formation continue	Analyse thermique appliquée à la pharmacie

K.3.2 Publications

- D.Giron and D.J.W. Grant, Chapter 3, "Evaluation of solid state properties of salts", IUPAC Monograph "Pharmaceutical Salt Selection" H. Stahl and C. Wermuth Eds, In Press by Helvetica Chim.Acta
- D. Giron, Chapter: Thermal Analysis of Drugs and Drug Products, Encyclopedia of Pharmaceutical Technology, J.Swarbrick and J.C. Boylan eds, In Press by Marcel Dekker
- D. Giron, Applications of thermal analysis and coupled techniques in pharmaceutical industry, accepted by Journal of Thermal Analysis and Calorimetry
- D. Giron, C. Goldbronn, M. Mutz, S. Pfeffer, P. Piechon and O. Schwab, Solid state characterizations of pharmaceutical hydrates, accepted by Journal of Thermal Analysis and Calorimetry
- D. Giron, Investigation of polymorphism and pseudo-polymorphism in pharmaceuticals by combined thermoanalytical techniques, J. Therm. Anal. Calorim., (2001), 64, 37-60

K.3.3 Award

- Leading scientist at Novartis, 3.12.01

K. 4. Prof. Dr. Th. Güntert

In addition to the lectures in Biopharmaceutics, Drug Metabolism and Instrumental Analysis, extensive restructuring took place to achieve a higher degree of coordination within the Pharmacy curriculum.

K.4.1 List of Dissertations, Publications, Talks/Posters

Dissertations

Ongoing Dissertations:

- Susan Grange, University Basel, Pharmacokinetic-pharmacodynamic modeling as a tool to extrapolate dose-effect relationships from animal to man. (Beginning 1996)
- Stefanie Lerch, University Bern, Ifosfamidtherapie assoziierte Enzephalopathie und ihre Interaktion mit Benzodiazepinrezeptoren (Beginning 2000)
- Olivier Luttringer, University Basel, Physiologically-based Modeling of Active Transport Processes. (Beginning 2000)
- Shiva Neysari, University Basel, Characterization of the functional coupling and binding mode of Neuropeptide-Tyrosine (NPY) Y2 and Y5 receptors: Implications for their functional role (Beginning 2000)

Completed Dissertation:

- Jürg Nyfeler, University Basel, Nitric oxide as a possible marker for vascular endothelial health.

Publications

- S. Grange, N.H.G. Holford, T.W. Guentert: A pharmacokinetic model to predict the PK interaction of L-dopa and benserazide in rats. *Pharm. Res.*, 18, 1174-1184 (2001).
- O.G. Nilson, K. Aasarød, T.E. Widerøe, T.W. Guentert: Single and multiple dose pharmacokinetics, kidney tolerability and plasma protein binding of tenoxicam in renally impaired and healthy subjects. *Pharmacology and Toxicology*, 89, 265-272, 2001.

Presentations

- W.F. Richter, A. Tobler, L. Gand, V. Starke, A. Philippe, T.W. Guentert: Use of an Ussing chamber model for the study of intestinal first-pass metabolism of midazolam in the rat. AAPS Meeting, Denver CO USA, October 2001,
- O. Luttringer, F.-P. Theil, T. Lavé, T.W. Guentert, K. Wernli Kuratli, A. de Saizieu: Differential expression at messenger RNA level of genes encoding membrane transporters in different primary culture of rat hepatocytes. Pharmaconference on Membrane Transporters Interlaken, Switzerland, August 5-9 2001,
- O. Luttringer, F.-P. Theil, T. Lavé, T. Guentert, A. De Saizieu: Impact of dexamethasone on messenger RNA levels of genes encoding liver specific transporters in sandwich culture of rat hepatocytes. Sixth International ISSX meeting, Munich Germany, October 8-11 2001

K.4.2 Invited Speaker

July 2001	University Leiden The Netherlands	The Role of Pharmacokinetics and Pharmacodynamics in Drug Discovery and Development;
September 12 – 15	5th Congress EACPT. Odense Denmark	Linking Preclinical and Clinical Studies More Effectively
October 2 – 4, 2001;	5th ECPM Course “The Future of Drug Development”: Basel, Switzerland	Predictive Models - Key to High Chance of Success.

K.4.3 External Courses

- Faculty Member in Workshop in Basic Pharmacokinetics, Dept. of Pharmacy, Univ. Manchester.
- Arosa July, 7 - 12, 2001

K.4.4 Research 2001

- In vitro absorption models
- Influence of galenic factors on drug absorption
- Prediction of drug behaviour in humans based on animal and in vitro data
Simulation techniques
Pharmacogenomics



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Basel, 31.1.2002 gez. Prof. Dr. H. Leuenberger