NEWSLETTER OF *eurostar-science*

NO 3 – February 4, 2002

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3.1 EDITORIAL

Erwin Marti, President

The Meeting Place of our next PhandTA Conference will be for the second time the **Centro Stefano Franscini at Monte Verità, Ascona**. This Conference Site of the ETH Zürich is in a charming park above the Lago Maggiore and is as a combination of the hotel, the restaurant and the meeting locations rather ideal for a Conference of our conception.

In the name of the members of the OC of the PhandTA 6, I would like to invite to this Conference all who are interested in the combined subject of **Pharmacy and Applied Physical Chemistry**. The structure of the PhandTA 6 will be outlined according to our tradition with **Award and Plenary Lectures, Key and Short Communications** and **Poster Presentations.** The three **Workshops** on Thursday are an integrated part of the PhandTA 6.

The main idea of the PhandTA Conferences are scientific interactions on a high level which enable to present elucidations of a broad range of subjects within applied research and development work. The different sections of the conference are explained in detail at the Conference Website. At present almost 40 Oral Communications and Poster Presentations have been submitted or announced. You will find these Communications listed in this Newsletter.
Please, visit our Conference Website for further information. You will find there also the **Registration Forms** for both the **PhandTA 6** and for participation in the **Workshops** only.

I hope to see many of our scientific friends at Monte Verità.
Erwin Marti

3.2 NEWS

PhandTA 6 – News

- Next eurostar-science Newsletter is scheduled for June 2002, if you want to be informed about changes at PhandTA 6 and haven't done so far, please register for the PhandTA 6 eNewsticker
- Abstracts of the accepted contributions will be ongoingly published on the website
- In case you like to submit a Contributions for PhandTA 6, please register as soon as possible

PhandTA 6 - Current List of Contributions

Novel Carriers for Dry Powder Inhalation
D. Al-Hadithi, G. Buckton, S. Brocchini, D. Singh, N. Lowther
School of Pharmacy, London, UK

Biophysical Analytics of Single Molecules
D. Anselmetti
Universität Bielefeld, D

Flow Microcalorimetry: A Test Reaction for Instrument Performance Evaluation plus Theoretical and Practical Applications of the Technique
A.E. Beezer
NRI, University of Greenwich, Kent, UK

Solid State Characterization of Drug Substances Under High Pressure
E.E.V. Boldyreva
Novosibirsk State University, Rus

Non Thermally Driven Transformation of Molecular Compounds
M. Descamps, J.F. Willart, A. de Gusseme, S. Deprez
Université de Lille, Villeneuve d'Ascq, F

The Use of Organic Vapour Atmospheres to Quantify Amorphous Content in Pharmaceutical Substances by Isothermal Microcalorimetry
S. Garnier, M. Mutz, D. Giron
Novartis Pharma AG, Basel, CH

Characterization of Salts of Drug Substances
D. Giron
Novartis Pharma AG, Basel, CH

Cyclodextrin Chemistry: Review of Results by Thermal Analysis
B. Glass and M. Brown
Rhodes University, Grahamstown, South Africa

Nucleotide / Protein Interaction: Energetic and Structural Features
E. Grell, E. Lewitzki
Max-Planck-Institut für Biophysik, Frankfurt / M., D

Moister Sorption
U. Griesser
Universität Innsbruck, A

The Combination of UV/VIS/IR Spectroscopy with Isothermal Fluxmetry and Isoperibolic Calorimetry to Perform and Monitor Polymerization in Organic Media
F. Dan, J.-P. Grolier
Université Blaise Pascal, Aubiere, F

High Throughput Polymorphism Screening: Just the first Step for Integrated Crystal Ingeneering
R. Hilfiker, U.Ch. Hofmeier
Solvias AG, Basel, CH

Relation of Drug Substances to Solvents: Free Solvent, Adsorption, Inclusion and Intercalation
E. Kaisersberger and E. Marti
Netzsch Gerätebau GmbH, Selb, D

Characterization of Drug Substances by Physicochemical Methods
E. Marti
c/o Novartis Pharma AG, Basel, CH

Physical Characterization of Pharmaceutical Hydrates
M. Mutz
Novartis Pharma AG, Basel, CH

Simultaneous Coupling of DSC and Time-Resolved Synchroton X-ray Diffraction for the Study of Colloids of Pharmaceutical Interest
M. Ollivon
Université Paris Sud, Châtenay-Malabry, F

Oscillating Crystallisation of a Chiral Compounds in Quasi-racemic Solution; Evidence of a Multiepitaxy Crystal Growth Mechanism and Influence of Stirring
C. Gervais, St. Beilles, S. Petit, G. Coquerel
Université de Rouen, Mont Saint Aignan, F

Polymorphism Investigations and Structure Elucidation of Pharmaceuticals in Development
S. Pfeffer-Hennig, E. Tedesco, P. Piechon, M. Bellus, C. Goldbronn
Novartis Pharma AG, Basel, CH

Freeze Drying of Pharmaceuticals: A Review of Critical Parameters
M.J. Pikal
University of Connecticut, USA

Development- and Quality-Control for Molecules of Pharmaceutical Interest by MID-IR and NIR Techniques
A. Rager, M. Boese and H. Weiler
Bruker Optik GmbH, Ettlingen, D

Enzyme Immobilization in Silica-Hardened Organogels
M. Schuleit, P.L. Luisi
Novartis Pharma AG, Basel, CH

New Advances in the Application of Inverse Gas Chromatography (IGC) for the Physical Characterisation of Pharmaceuticals
F. Thielmann, D. Williams, C. Levoguer, S. Reutenauer
Surface Measurement Systems Ltd., London, UK

Anti-Thermodynamic Transitions of Sulphathiazole Polymoprhs
T.L. Threlfall
University of York, UK

Industrial Crystallization: Some Fields of Problems - Polymorphs, Pseudopolymorphs and Impurities
J. Ulrich
Martin-Luther-Universität Halle-Wittenberg, D

Microemulsions as Reactors for Nanoscopic Materials
A. Weidenkaff and A. Reller
Universität Augsburg, D

Hydrophobic Interactions: Selected Thermodynamic Results on Simple Solute/Solvent Systems
E. Wilhelm
Universität Wien, A

Particle Design for Drug Delivery Systems
P. York
University of Bradford, UK

Further Communications

Efficient use of TG-MS Coupled Technique in Pharmaceutical Development
D. Giron, P. Piechon, S. Pfeffer
Novartis Pharma AG, Basel, CH

Supramolecular Structures with Peroxides as possible Active Long-Lived Drug Substances
E.G. Ippolitov, T.A. Tripolskaya, G.P. Pilipenko, I.V. Pokhabova
Kurnakov Institute, Moscow, Rus

Polymorphic Studies on Selected Pharmaceutical Substances
A. Kutner
Pharmaceutical Research Institute, Warsaw, Poland

Thermal Characteristics of Macroalgae Spirulina Platensis Cells at Various Values of pH Medium in Temperature Range 5-55 C. DSC Investigation
J. Monaselidze, Sh. Barbakadze, T. Kvirikashvili, L. Topchishvili
Georgian Academy of Sciences, Tbilisi, Republic of Georgia

Thermal Investigation of Morphine and its Derivates
Cs. Novak, O. Bene, S. Hosztafi, J. Sztatisz, S. Gal
Technical University of Budapest, H

Formation of New Crystalline Phases by means of Solvent Exchange and Growth of Whisker-like Crystals
F. Mallet, S. Petit, S. Laffont, P. Billot, G. Coquerel
Université de Rouen, Mont Saint Aignan, F

Application of Raman and IR Spectroscopy in Pharmaceutical Development
S. Pfeffer and M. Bellus
Novartis Pharma AG, Basel, CH

Comparative Study about some antithermal Drugs produced by different Companies
V. Popescu, S. Birghila, G. Solomon
Ovidius University of Constantza, Rom

PhandTA 6 - Current List of Exhibitors

- Solvias AG
- Witec AG / Thermometric
- Mettler – Toledo
- TA Instruments
- Porotec
- Quantachrome
- Netzsch Gerätebau
- Bruker Optik
- Micromeritics
- Setaram

Announcements

- Netzsch Gerätebau GmbH
  - Preview to the 5th SKT 2003
    http://www.skt2000.com
  - Thermoanalytical Characterization of Pharmaceuticals
    www.ngb.netzsch.com/annual_00.htm

- Solvias AG
  - Crystal Engineering: Our new Service
  - Computerized System Validation (CSV)
    http://www.solvias.com

3.3 OUR SPONSORS. NETZSCH GERÄTEBAU

The DSC World of NETZSCH

Stephan Knappe and Jürgen Blumm
NETZSCH-Gerätebau GmbH, Selb, Germany

NETZSCH-Gerätebau GmbH was founded in 1962 as a company developing and manufacturing instruments for the thermoanalytical characterization of materials.
Nowadays NETZSCH offers a complete range of testing systems for thermoanalytical and thermophysical properties characterization of materials between -260 and 2800°C. Additionally special software packages are developed for the advanced analysis of the measured data.

Differential Scanning Calorimetry
One of the most frequently used techniques in the field of thermal analysis is differential scanning calorimetry (DSC). Material properties such as glass transitions, melting temperatures, transition enthalpies, polymorphism, specific heat or oxidative stability can be analyzed employing DSC. It is a fast and easy-to-operate method according to industrial standards (ASTM E 793, ASTM E 1356 or DIN 51007). It is used for research and development, quality management, failure analysis and process optimization of a wide range of materials.
The DSC technique is used in many laboratories for characterizing e.g. polymers, pharmaceuticals, textiles, foods, ceramics, minerals, composites or metals.
For solving nearly all different questions NETZSCH offers a wide range of differential scanning calorimeters.

The cost-effective **DSC 200 PC *Phox*®** is used mainly for quality control and quality assurance in a temperature range from -150 to 600 °C.

The design of the high performance **DSC 204 *Phoenix*®** from –180 to 700°C is demonstrated in Fig. 1. The gold-plated silver furnace guarantees a long durability even in rough day-to-day routines. Due to an interchangeable DSC sensor nearly all possible applications can be solved. The robust σ-Sensor provides a high sensitivity and good peak separation on e.g. polymer blends. The τ-Sensor is ideal for highest resolution due to its fast response time.

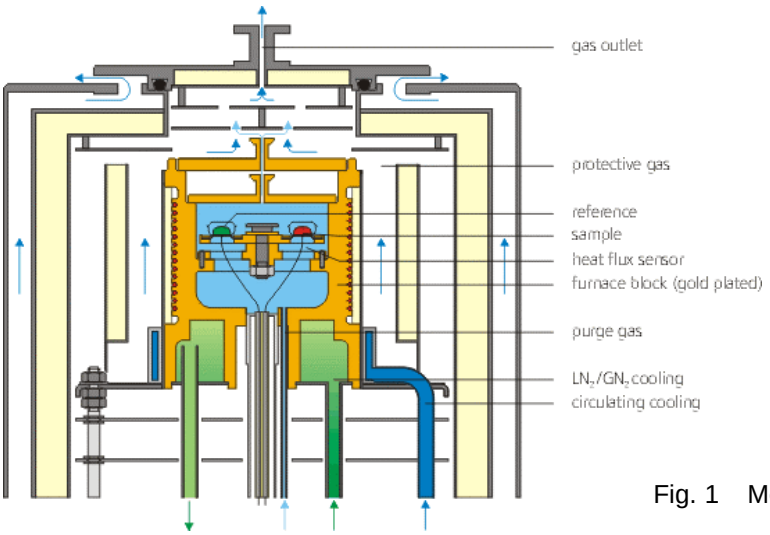

Fig. 1 Measuring cell **DSC 204 *Phoenix*®**

Offering both outstanding sensitivity and excellent resolution simultaneously, the µ-Sensor guarantees comprehensive measurement results, especially if only a small sample mass is available. This newly developed sensor which works in a temperature range from –150 to 400°C is ideal for pharmaceuticals, biomaterials and foods.

For demonstrating the high signal-to-noise ratio of the new µ-Sensor, 0.27 mg of 4,4'-azoxyanisole were measured in a closed standard aluminum crucible at a heating rate of 1 K/min according to the sensitivity test in [1]. This substance shows two transitions: a large solid to liquid crystal transition at

about 117°C and a much smaller liquid crystal to isotropic liquid transition at about 134°C. Fig. 2 illustrates the raw data with an endothermal peak of the second transition at 134.6°C with a peak height of 0.05 mW in comparison to a peak-to-peak noise of only 0.5 µW.

Various cooling devices and an automatic sample changer for up to 64 different sample and reference crucibles round off this versatile NETZSCH DSC system.

The ***Phoenix***® is also available as the high-pressure version **DSC 204 HP** for applications under a controlled pressure up to 15 MPa (150 bar).

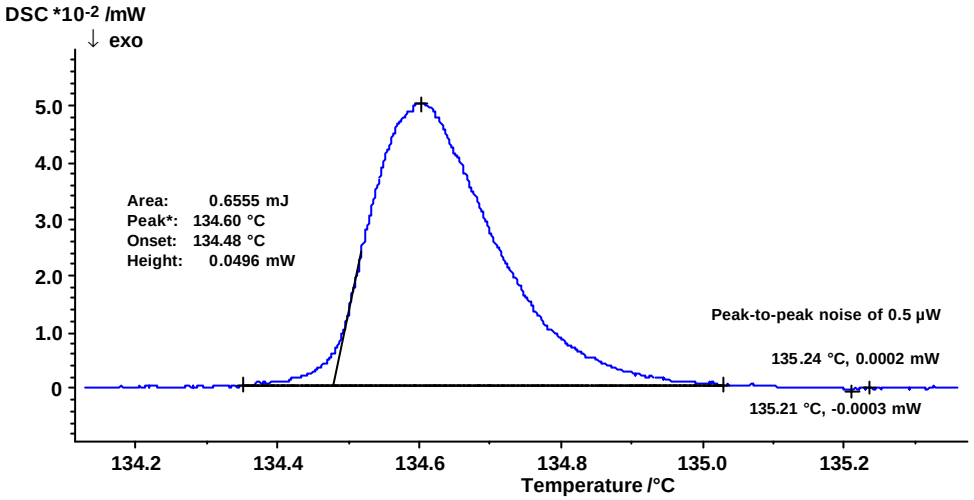

Fig. 2 Liquid crystal to isotropic liquid transition of 4,4'-azoxyanisole at 1 K/min

The **DSC 404 C *Pegasus***® is a system for measurements up to high temperatures (1650°C). Due to the vacuum-tight design materials sensitive to oxygen can easily be analyzed. The schematic design of the ***Pegasus***® is depicted in Fig. 3. The furnace is mounted on a motorized hoist allowing reproducible placement of the furnace in the system. The different available furnaces are user exchangeable. For subambient temperatures a furnace with an integrated cooling coil can be employed. Connection of a liquid nitrogen cooling device allows measurements between -120 and 750°C. For temperatures up to 1650°C, another furnace with rhodium heating elements can be used. The special design of the heating elements in the furnaces allows homogeneous heating of the sensor head over the entire temperature range. Homogeneous heat flow from the tube furnace to the sensors is crucial for a stable and reproducible baseline.

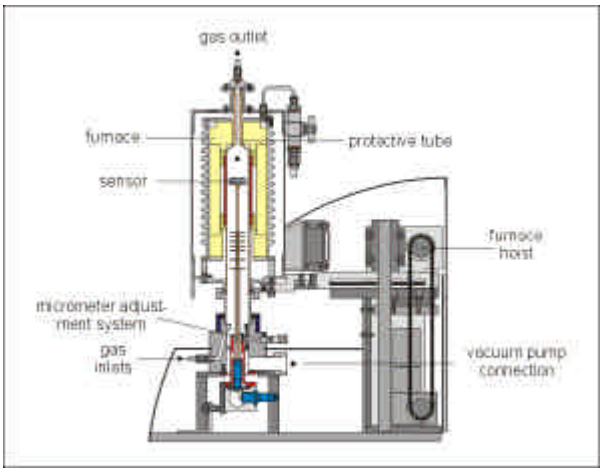

Fig.3 **DSC 404 C *Pegasus***®, 1650°C-Version

In Fig.4 the apparent specific heat of a partially amorphous Ti60Cr40-alloy is shown between room temperature and 1500°C [2]. Titanium alloys are well-known for being extremely sensitive to oxygen at elevated temperatures. The alloy was measured using platinum crucibles with alumina liners and lids. The inner surface of the crucibles was coated with an yttria spray to avoid reactions between the titanium alloy and the alumina liner. For the tests the DSC was evacuated with a turbo molecular

pump system several times and backfilled with a highly pure argon atmosphere. During heating an exothermal effect was detected in the apparent specific heat at 723°C (peak temperature). This effect is due to the cold crystallization of the partially amorphous sample. Between ≈900°C and ≈1250°C a phase transition was detected. Melting of the sample was measured at 1400°C (extrapolated onset). The heat of fusion was 282.3 J/g. Outside the transition ranges a good agreement was achieved between the heating and cooling runs.

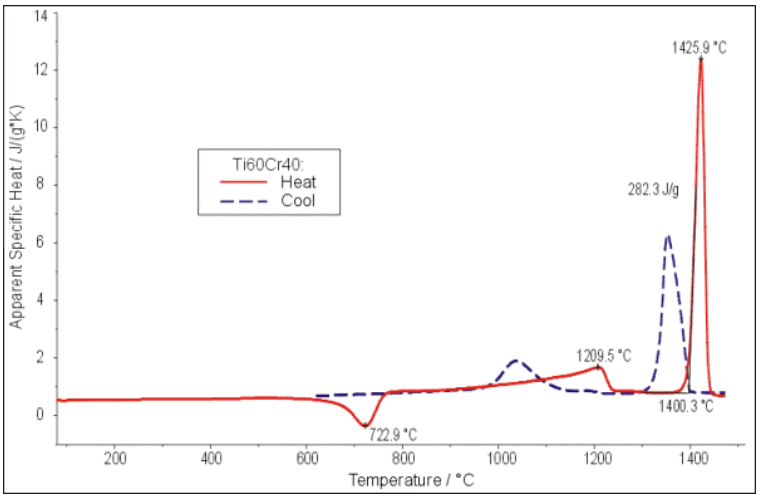

Fig. 4 Apparent specific heat of partially amorphous Ti60Cr40 between room temperature and 1500°C (heat and cool)

The following table gives an overview of the different DSC models by NETZSCH.

	DSC 404 C *Pegasus*®	**DSC 204 *Phoenix*®**	**DSC 204 HP *Phoenix*®**	**DSC 200 PC *Phox*®**
interchangeable furnaces	yes	no	no	no
temperature range	-120°C - 1650°C	-180°C - 700°C	RT - 600°C	-150°C - 600°C
heating rate	0 -50 K/min	0 - 100 K/min	0 - 50 K/min	0 - 100 K/min
interchangeable sensors	yes	yes	no	no
calorimetric sensitivity	0.5 - 16 µV/mW	3.5 - 65 µV/mW	2 - 3 µV/mW	4 - 4.5 µV/mW
signal time constant	3 - 15 s	0.6 - 3 s	2 - 4 s	3 s
pressure	10^{-4} - 1030 mbar	1030 mbar	10^{-2} mbar - 150 bar	1030 mbar
atmosphere	oxidizing reducing inert	oxidizing inert	oxidizing reducing inert	oxidizing inert
cooling options	forced air LN_2/GN_2	forced air refrigerated bath circulator mechanical cooling LN_2/GN_2	forced air	forced air mechanical cooling LN_2
autosampler	no	yes	no	no

It should be pointed out that differential scanning calorimeters can be combined with a thermobalance allowing measurement of mass changes and caloric effects on one sample in one test run at the same time: Simultaneous Thermal Analysis (STA). Different instruments are available for the temperature range between -160 and 2400°C.

References:

[1] P. J. van Ekeren, C. M. Holl and A J. Witteveen: A comparative test of differential scanning calorimeters, Journal of Thermal Analysis, Vol. 49 (1997) 1105 – 1114.
[2] J. Blumm and E. Kaisersberger: Accurate measurement of transformation energetics and specific heat by DSC in the high-temperature region, Journal of Thermal Analysis and Calorimetry, Vol. 64 (2001) 385-391.