



Pharmaceutical Powder X-ray Diffraction Symposium



*Organized by the
International Centre for Diffraction Data*

Acquisition and Use of X-ray Powder Diffraction Data
Polymorph Characterization by XRPD
Structure Determination, Indexing and Molecular Modeling
Preformulation, Formulation, Regulatory & Patent Issues



**Pharmaceutical Powder X-ray Diffraction Symposium
Newtown Square, Pennsylvania, U.S.A.**

27–29 September 1999

*Sponsored and Organized by the
International Centre for Diffraction Data
Cosponsored by
Glaxo Wellcome, Inc.*

***PPXRD Symposium
Scientific Organizing Committee***

Dr. John Faber

ICDD

Dr. Ron Jenkins

ICDD

Mr. Chris Kidd

Glaxo Wellcome, Inc.

Ms. Terry Maguire

ICDD

Dr. Raj Suryanarayanan

University of Minnesota

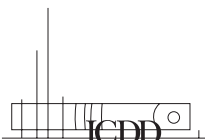
Dr. Peter Varl ashkin

Glaxo Wellcome, Inc.

Dr. Marek Zakrzewski

Rhône-Poulenc Rorer

This program is also available on the ***PPXRD Symposium*** web page at <http://www.ICDD.com/ppxrdsymp/>. The information contained in this program is current as of the date of printing. Changes will be communicated at the Symposium.



GlaxoWellcome

Symposium Program

ICDD Headquarters

Monday 27 September 1999

Morning ACQUISITION AND USE OF X-RAY POWDER DIFFRACTION DATA

Chris Kidd, Chair

8:30- 9:00 WELCOMING REMARKS & INTRODUCTIONS

R. Jenkins, International Centre for Diffraction Data, Newtown Square, PA

9:00- 9:45 THE ROLE OF XRPD IN THE CHARACTERIZATION OF PHARMACEUTICAL MATERIALS –
Invited

J. Bernstein, Ben-Gurion University of the Negev, Beer Sheva, Israel

9:45-10:30 ON THE OBTAINING OF HIGH QUALITY EXPERIMENTAL DATA WITH PHARMACEUTICAL
SPECIMENS – *Invited*

R. Jenkins, International Centre for Diffraction Data, Newtown Square, PA

10:30-11:00 *Break*

11:00-11:45 THE EFFECT OF DIFFERENT PREPARATIONS OF XRD SPECIMENS ON THE QUALITY OF THE
DIFFRACTION DATA – *Invited*

D. K. Smith, Emeritus, The Pennsylvania State University, University Park, PA

11:45-12:30 INVESTIGATION OF REACTIONS IN PHARMACEUTICAL SOLIDS BY TEMPERATURE AND
HUMIDITY CONTROLLED XRD – *Invited*

S. Rastogi, R. Suryanarayanan, University of Minnesota, Minneapolis, MN, and **M. Zakrzewski**, Philips
Analytical X-ray, The Netherlands. Present address: Rhône-Poulenc Rorer, Collegetown, PA

12:30-1:30 *Lunch*

Afternoon POLYMORPH CHARACTERIZATION BY XRPD

Peter Varlashkin, Chair

1:30-1:55 RAPID SCREENING OF POLYMORPHS BY DIFFRACTION METHODS

C. Lehmann, Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr, Germany

1:55-2:20 CHARACTERIZATION OF MULTIPLE POLYMORPHS / PSEUDOMORPHS OF A
DEVELOPMENTAL PHARMACEUTICAL USING THERMAL AND X-RAY POWDER
DIFFRACTION METHODS

R. Newman, D. Miller, Dow Chemical U.S.A., Midland, MI

2:20-2:45 CHARACTERIZATION AND INTERCONVERSION OF THE POLYMORPHS OF AN IP RECEPTOR
ANTAGONIST

Z. Chen, J. Lang, Roche Carolina Inc., Florence, SC

2:45-3:15 *Break*

3:15-3:40 POLYMORPH DETERMINATION OF GP IIB/IIIA ANTAGONIST, ROXIFIBAN, USING A
COMBINATION OF ELECTRON DIFFRACTION AND SYNCHROTRON X-RAY POWDER
DIFFRACTION TECHNIQUES

Z. Li, R. Harlow, C. Foris, DuPont Company, Central Research & Development, Wilmington, DE, and
H. Li, P. Ma, R. Vickery, M. Maurin, DuPont Pharmaceuticals Company, Wilmington, DE

3:40-4:05 QUANTITATION OF TWO POLYMORPHIC FORMS USING RIETVELD ANALYSIS,
SYNCHROTRON X-RAY POWDER DIFFRACTION, AND TRADITIONAL X-RAY POWDER
DIFFRACTION

A. Newman, M. Andres, G. Stahly, A. Thomas, Solid State Chemical Information, Inc., West Lafayette,
IN, and P. Stephens, State University of New York, Stony Brook, NY

4:05-4:30 POWDER X-RAY DIFFRACTION METHODS TO FIND VARIOUS HYDRATES OF A DRUG
SUBSTANCE

M. Davidovich, J. Gougoutas, J. DiMarco, R. Mueller, I. Vitez, Bristol-Myers Squibb Pharmaceutical
Research Institute, New Brunswick, NJ, and A. Newman, Solid State Chemical Information, Inc., West
Lafayette, IN

Symposium Program

ICDD Headquarters

Tuesday 28 September 1999

Morning INDEXING, STRUCTURE DETERMINATION, AND MOLECULAR MODELING

Marek Zakrzewski, Chair

8:10- 8:55 DEALING WITH MATERIALS THAT CONTAIN CRYSTALLINE AND AMORPHOUS CONSTITUENTS – *Invited*

J. Faber, International Centre for Diffraction Data, Newtown Square, PA

8:55- 9:40 MOLECULAR STRUCTURES FROM POWDERS: GLOBAL RIETVELD ANALYSIS – *Invited*

B. David, Rutherford Appleton Laboratory, Oxon, United Kingdom

9:40-10:00 *Break*

10:00-10:45 TEREPHTHALATE SALTS. SALTS OF MONOPOSITIVE CATIONS – *Invited*

J. Kaduk, BP Amoco PLC, Naperville, IL

10:45-11:30 APPLICATION OF STRUCTURE SOLUTION FROM POWDER PATTERNS – *Invited*

G. Stephenson, Eli Lilly and Company, Fishers, IN

11:30-11:55 30 YEARS OF RIETVELD ANALYSIS: THE NEXT GENERATION

A. Kern, A. Coelho, Bruker-AXS GmbH, Karlsruhe, Germany

11:55-12:20 POWDER SOLVE - A NEW METHOD FOR CRYSTAL STRUCTURE DETERMINATION FROM POWDER DATA

M. Wahle, G. Engel, S. Wilke, F. Leusen, Molecular Simulations Inc., San Diego, CA

12:20-12:45 SOLUTION OF FLEXIBLE MOLECULAR STRUCTURES FROM POWDER DIFFRACTION DATA USING SIMULATED ANNEALING

Y. Andreev, P. Bruce, University of St. Andrews, Fife, Scotland

12:45-1:45 *Lunch*

Afternoon Marek Zakrzewski, Chair

1:45-2:30 POLYMORPHS AND SALT FORMS OF PHARMACEUTICALS SOLVED FROM POWDER DIFFRACTION DATA – *Invited*

K. Shankland, Rutherford Appleton Laboratory, Oxon, United Kingdom

2:30-2:55 A SYSTEMATIC SEARCH STRATEGY FOR STRUCTURE DETERMINATION FROM X-RAY POWDER DIFFRACTION DATA: APPLICATION TO ANHYDROUS THEOPHYLLINE

E.D.L. Smith, R. Hammond, K. Roberts, Heriot-Watt University, Edinburgh, United Kingdom, and J. Cherryman, Zeneca Specialties Research Centre, Manchester, United Kingdom

2:55-3:20 DO MICROCRYSTAL DIFFRACTION FACILITIES MAKE STRUCTURE SOLUTION FROM POWDER DIFFRACTION DATA OBSOLETE?

C. Frampton, Roche Discovery Welwyn, Hertfordshire, United Kingdom

3:20-3:40 *Break*

3:40-4:25 APPLICATION OF SYNCHROTRON RADIATION TO PROBLEMS IN THE PHARMACEUTICAL SCIENCES – *Invited*

P. Stephens, State University of New York, Stony Brook, NY

4:25-5:10 POWDER DIFFRACTION FROM BIOLOGICAL MACROMOLECULES USING SYNCHROTRON RADIATION – *Invited*

F. Rotella, Argonne National Laboratory, Argonne, IL

Symposium Program

ICDD Headquarters

Wednesday 29 September 1999

Morning PREFORMULATION, FORMULATION, REGULATORY & PATENT ISSUES

John Faber, Chair

8:30-9:15 NEW METHODS FOR PERCENTAGE CRYSTALLINITY DETERMINATION – *Invited*
S. Bates, Kratos Analytical, Chestnut Ridge, NY

9:15-10:00 APPLICATIONS OF X-RAY POWDER DIFFRACTOMETRY IN PREFORMULATION AND FORMULATION – *Invited*
R. Suryanarayanan, University of Minnesota, Minneapolis, MN

10:00-10:30 ***Break***

10:30-11:15 THE IMPACT OF POLYMORPHISM ON DRUG DEVELOPMENT: A REGULATOR'S VIEWPOINT – *Invited*

W. DeCamp, Food and Drug Administration, Rockville, MD

11:15-12:00 XRD DATA AND PATENTS – *Invited*

G. Geist, US Patent & Trademark Office, Washington, DC

12:00-1:00 ***Lunch***

Afternoon *Ron Jenkins, Chair*

1:00-1:45 PPXRD: SWEAR BY YOUR RESULTS, NOT AT THEM – *Invited*

S. Tarling, Birkbeck College, London, United Kingdom

1:45-2:30 THE ROLE OF THE ORGANIC POWDER DIFFRACTION FILE IN THE PROVISION OF PHARMACEUTICAL DATA – *Invited*

J. Faber, R. Jenkins, R. Snyder, International Centre for Diffraction Data, Newtown Square, PA

2:30-3:15 XRPD PATENTS IN LITIGATION – *Invited*

S. Lee, Kenyon & Kenyon, New York, NY

3:15-3:35 ***Break***

3:35-4:15 Question and Answer Session

4:15-4:45 Future Topics and Wrap-up: ***Chris Kidd, Chair***

Poster Session

Sheraton Great Valley, Regency Ballroom
Monday, 27 September 1999
5:30 - 9:00 p.m.

The poster session will include the following:

- ENVIRONMENTALLY-CONTROLLED SAMPLE STAGE FOR SCINTAG'S SIX-POSITION XRD SAMPLE CHANGER
C. Buckner, C. Kidd, S. Long, **P. Varlashkin**, J. Zhu, Glaxo Wellcome, Inc., Research Triangle Park, NC
- PITFALLS IN THE AVAILABILITY OF MULTIPLE PDF ENTRIES
R. Jenkins, International Centre for Diffraction Data, Newtown Square, PA
- POWDER DIFFRACTION AT A SYNCHROTRON SOURCE
A. Mehta, J. Arthur, Stanford Synchrotron Radiation Laboratory, Stanford, CA
- TRADITIONAL EQUIPMENT FOR THE MEASUREMENT OF POWDER PATTERNS
R. Jenkins, International Centre for Diffraction Data, Newtown Square, PA
- NON-TRADITIONAL EQUIPMENT FOR THE MEASUREMENT OF POWDER PATTERNS
J. Faber, International Centre for Diffraction Data, Newtown Square, PA
- THE ICDD GRANT-IN-AID PROGRAM
T. Kahmer, R. Jenkins, International Centre for Diffraction Data, Newtown Square, PA
- CRYSTAL STRUCTURES OF SMALL ORGANIC MONOMERS
J. Kaduk, BP Amoco PLC, Naperville, IL
- STRUCTURAL DETERMINATION OF SODIUM PHENOXYACETIC ACID HYDRATE
J. Evans, K. Roberts, G. White, G. Rosair, Heriot-Watt University, Edinburgh, Scotland, and A. Kapitan, A. H. MARKS Ltd., West Yorkshire, England
- POWDER XRD IN THE PHARMACEUTICAL INDUSTRY - AN OVERVIEW
S. Robie, Scintag, Inc., Cupertino, CA
- REVIEW OF WIDELY USED INDEXING TECHNIQUES
P. Stephens, State University of New York, Stony Brook, NY
- X-RAY POWDER DIFFRACTOMETRY AND OTHER METHODS TO ESTABLISH THE PHARMACEUTICAL QUALITY OF GENERIC DRUG RAW MATERIALS AVAILABLE IN SOUTH AFRICA
M. De Villiers, W. Liebenberg, E. Swanepoel, E. Van Tonder, T. Dekker, Potchefstroom University for CHE, Potchefstroom, South Africa

Structure Determination Workshop

ICDD Headquarters
Thursday, 30 September 1999
9:00 a.m. – 4:00 p.m.

Lecturers Include: **John Faber**, ICDD, **Jason Hanko**, Molecular Simulations, Inc., **James Kaduk**, BP-Amoco PLC, **Steve Maginn**, Cambridge Crystallographic Data Centre, **Frank Rotella**, Argonne National Laboratory, **Peter Stephens**, State University of New York at Stony Brook, **Mark Wahle**, Molecular Simulations, Inc.

The Structure Determination Workshop is oriented to the elucidation of pharmaceutical materials. The workshop will be hands-on with the use of *Cerius2* (Molecular Simulations, Inc.). In addition to display and the determination of molecular structures, current plans are to use the new simulated annealing Monte Carlo module called *Powder Solve*. Do's and Don'ts for solutions to problems will be discussed.

Special Events

Sheraton Great Valley, Regency Ballroom
Monday, 27 September 1999

5:30-9:00 p.m.

Manufacturers' Exhibit and Poster Session

6:00-8:00 p.m.

Reception – Sponsored by Bruker AXS, Inc.

*Two hour social with carving station, hot and cold hors d'oeuvres,
trays of cheese, vegetables and fruits, wine, beer and sodas.*

Held in conjunction with Exhibit and Poster Session.

Exhibitor Information

Exhibits will be located in the Regency Ballroom on the Ground Floor of the Sheraton Great Valley on **Monday, 27 September from 5:30-9:00 p.m.** The following is a list of exhibitors registered to date:

Bruker AXS, Inc.

Cambridge Crystallographic Data Centre (CCDC)

INEL, Inc.

International Centre for Diffraction Data (ICDD)

Kratos Analytical, Inc.

LND, Inc.

Molecular Simulations, Inc.

Philips Analytical B.V.

Rigaku USA, Inc.

Scintag, Inc.

Solid-State Chemical/Pharmaceutical Information, Inc. (SSCI)

SPEX CertiPrep, Inc.

Accommodations & Travel

The PPXRD Symposium will be held at the ICDD Headquarters at 12 Campus Boulevard, Newtown Square, PA 19073, U.S.A. The Sheraton Great Valley, located at 707 East Lancaster Pike, Frazer, PA 19355, U.S.A., is the designated host hotel for the PPXRD Symposium.

Hotel Information

*Sheraton Great Valley, 707 East Lancaster Pike, Frazer, Pennsylvania 19355, U.S.A.
Tel: 610-524-5500, Fax: 610-594-8060.*

A block of rooms is reserved for Symposium guests for the nights of 26-29 September 1999. Rates are 123.00 \$US for a standard room, plus 6% tax. An upgraded room on the Executive Level is 143.00 \$US, plus 6% tax. Reservations must be made by 1 September 1999. Please mention PPXRD when you make your reservation. Check-in time is 4:00 p.m., and checkout is 12:00 noon. You must advise the hotel at least 24 hours in advance of a cancellation to avoid a charge of one night's room and tax.

All guest rooms offer the following amenities: coffee maker, hair dryer, iron & ironing board, work desk, two telephones, voice mail, computer access, nightly turndown service, and a daily newspaper delivered to your room. The Executive Level features upgraded room amenities (such as a bathrobe), use of the club lounge and complimentary wine and hors d'oeuvres in the evenings, and a continental breakfast in the mornings. The indoor swimming pool is open daily until 9:00 p.m., and the exercise facility is open 24 hours. The Sheraton offers same day dry cleaning, a self-serve guest laundry, safe deposit boxes, a gift shop, and complimentary local transportation (upon availability).

Transportation

During the Symposium and Workshop, the Sheraton will provide transportation to the ICDD each morning and return transportation to the Sheraton at the conclusion of each day's session. A map and directions for driving in the area are located on page 8.

Ground Transportation from Philadelphia Airport to Sheraton Great Valley:

Paoli Airport Limousine: 23.00 \$US per person each way; no reservation necessary; leaves 15 minutes after the hour until 10:15 p.m. Dial 11 from the Ground Transportation counter, located in the Baggage Claim area of the airport, or call 610-647-5466 from outside the airport.

Super Shuttle: 29.00 \$US for one passenger, 11.00 \$US each additional passenger; no reservation required; leaves frequently. Dial 43 from the Ground Transportation counter, located in the Baggage Claim area of the airport, or call 800-258-3826 from outside the airport.

Taxi: Available outside the Baggage Claim area. Fares are not regulated and vary widely with each driver. This mode of transportation is **not recommended** unless travelling to Center City Philadelphia.

Attire: Attire is informal for most activities.

Climate: Average range of temperatures is 55 to 75° F.

Finding Your Way Around

Directions to ICDD from Philadelphia International Airport

Take Airport Exit towards Delaware, merging onto I-95 South. Follow I-95 South for 5 miles to Exit 7 (I-476 North.) Follow I-476 North for 9 miles, and at Exit 4 turn left onto Route 3. Follow Route 3 for 4 miles, turning left onto Campus Boulevard at the traffic light, into the Newtown Square Corporate Campus. The ICDD is on the right at 12 Campus Boulevard.

Directions to ICDD from Sheraton Great Valley Hotel

Take 202 South to the Route 3 East (Newtown Square) exit. Follow Route 3 east for approximately 8.5 miles. Turn right (at traffic light) into the Newtown Square Corporate Campus on Campus Boulevard. ICDD is located on right at 12 Campus Boulevard.

Directions to Sheraton Great Valley Hotel from Philadelphia International Airport

Take I-95 South approximately 5 miles to Route 322 West. Take 322 West approximately 5 miles, turn left onto Route 1 South. Follow Route 1 South for ½ mile and turn right onto 202 North. Take Route 202 North 12 miles to Route 30 East (Frazer Exit). Turn right at end of ramp onto Route 30 East. Sheraton Great Valley will be on your left. Caution: Routes 202/322 separate just past the Holiday Inn. Make sure to go right. Also, do not take Route 30 West Exit which comes before the Route 30 East Frazer Exit.

Directions to Sheraton Great Valley Hotel from:

North - NJ Turnpike South to PA Turnpike West. Take Exit 24 from Turnpike to 202 South 12 miles to Route 30 Exit. Hotel is on left ½ mile.

South - Take I-95 North to Wilmington/West Chester 202-North Exit. Continue on 202 North to Route 30 Exit. Turn right off exit. Hotel is on immediate left.

East - From PA Turnpike West take Exit 24. Then take Route 202 South 12 miles to Route 30 East. Hotel is on left ½ mile.

West - From PA Turnpike East, take Exit 23 to 100 South. Take 100 South 4 miles to Route 30 East. Hotel is on left 2 miles.