MATERIAL IDENTIFICATION AND CHARACTERIZATION

10 YEARS OF DEVELOPMENT
PDF-4/Organics Database

Timothy G. Fawcett, Soorya N. Kabbekodu,
Fangling Needham and Cyrus E. Crowder
International Centre for Diffraction Data,
Newtown Square, PA, USA

Experimental X-Ray Diffraction Data
provided by ICDD members and ICDD grantees

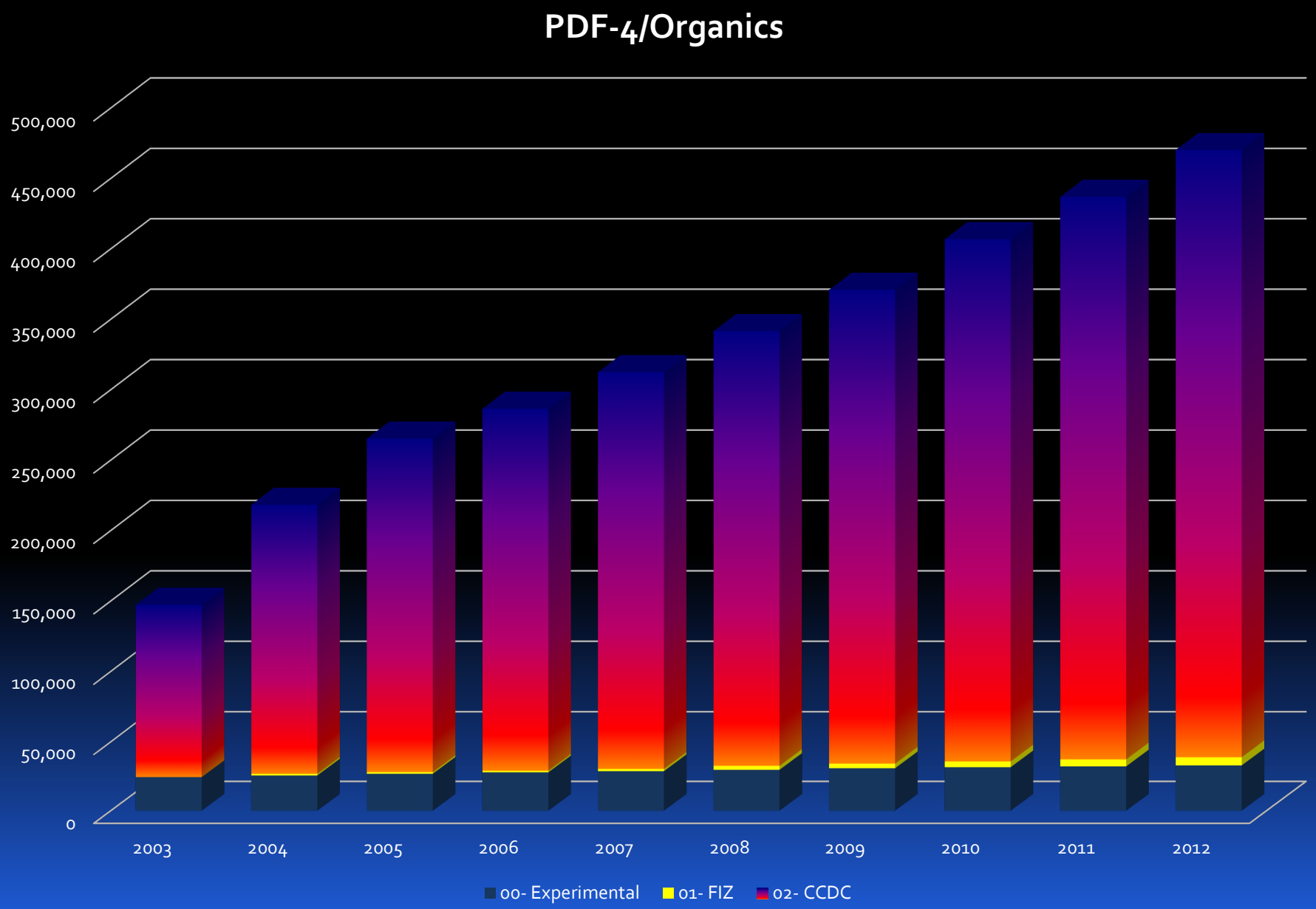
MATERIAL IDENTIFICATION AND CHARACTERIZATION

- All entries have powder patterns
  - Most have spot, ring, EBSD patterns
- Database contains organic, organometallic, polymer and inorganic materials

(Drugs, excipients, packaging materials, common salts, common corrosion phases)

- Database has a relational database design
  - Entries contain physical properties
  - Entries contain instrumental and experimental conditions
  - Entries contain bibliographic information
  - Entries contain crystallographic information
  - ***All entries have been standardized***
  - ***All entries have been evaluated for quality***
  - **Searches based on chemistry, crystallography *and analytical data***

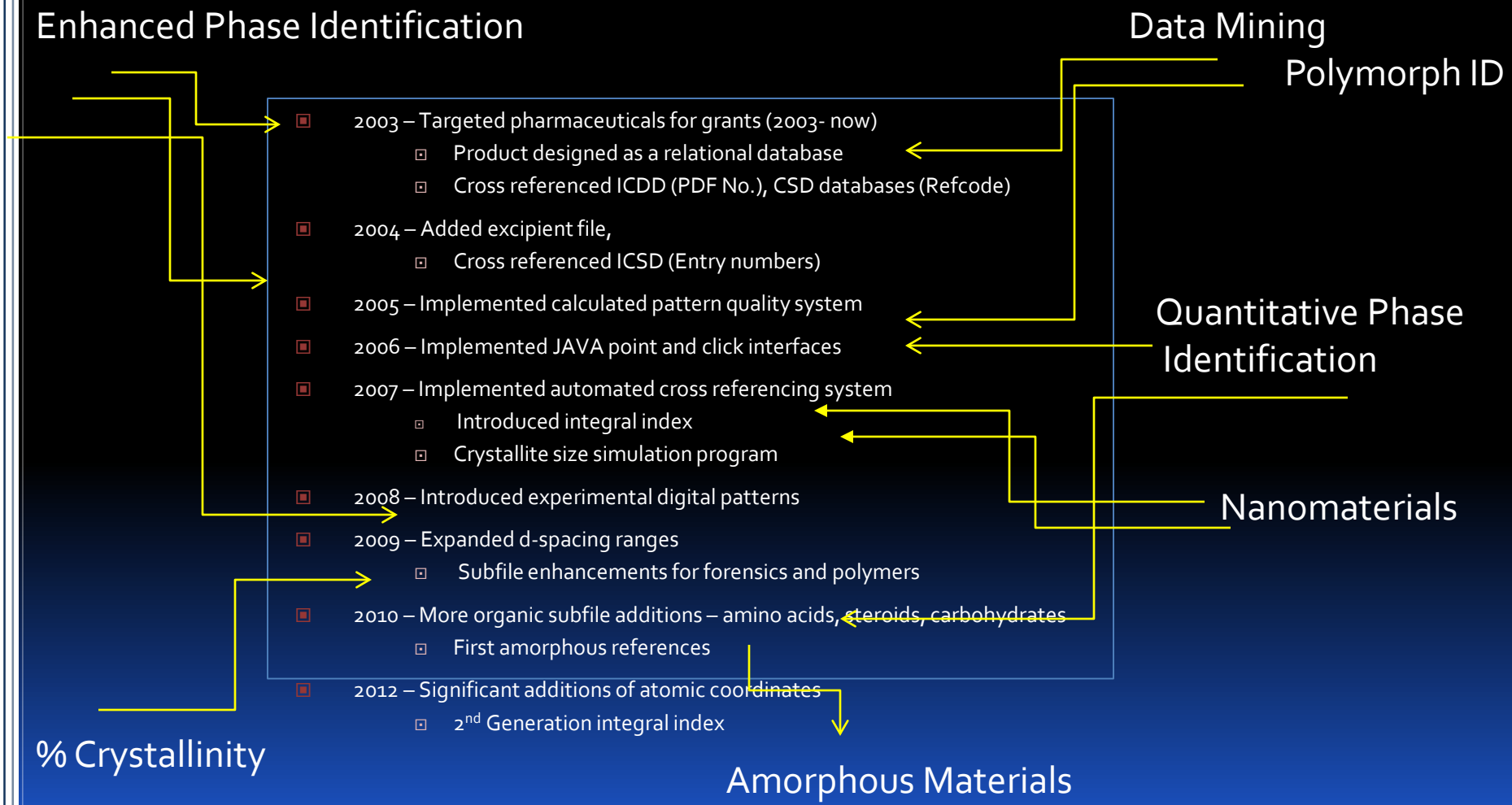
10 Year Growth



History of Continuous Improvements

- 2003 – Targeted pharmaceuticals for grants (2003- now)
  - Product designed as a relational database
  - Cross referenced ICDD (PDF No.), CSD databases (Refcode)
- 2004 – Added excipient file,
  - Cross referenced ICSD (Entry numbers)
- 2005 – Implemented calculated pattern quality system
- 2006 – Implemented JAVA point and click interfaces
- 2007 – Implemented automated cross referencing system
  - Introduced integral index
  - Crystallite size simulation program
- 2008 – Introduced experimental digital patterns
- 2009 – Expanded d-spacing ranges
  - Subfile enhancements for forensics and polymers
- 2010 – More organic subfile additions – amino acids, steroids, carbohydrates
  - First amorphous references for % crystallinity determinations
- 2012 – Significant additions of atomic coordinates
  - 2nd Generation integral index

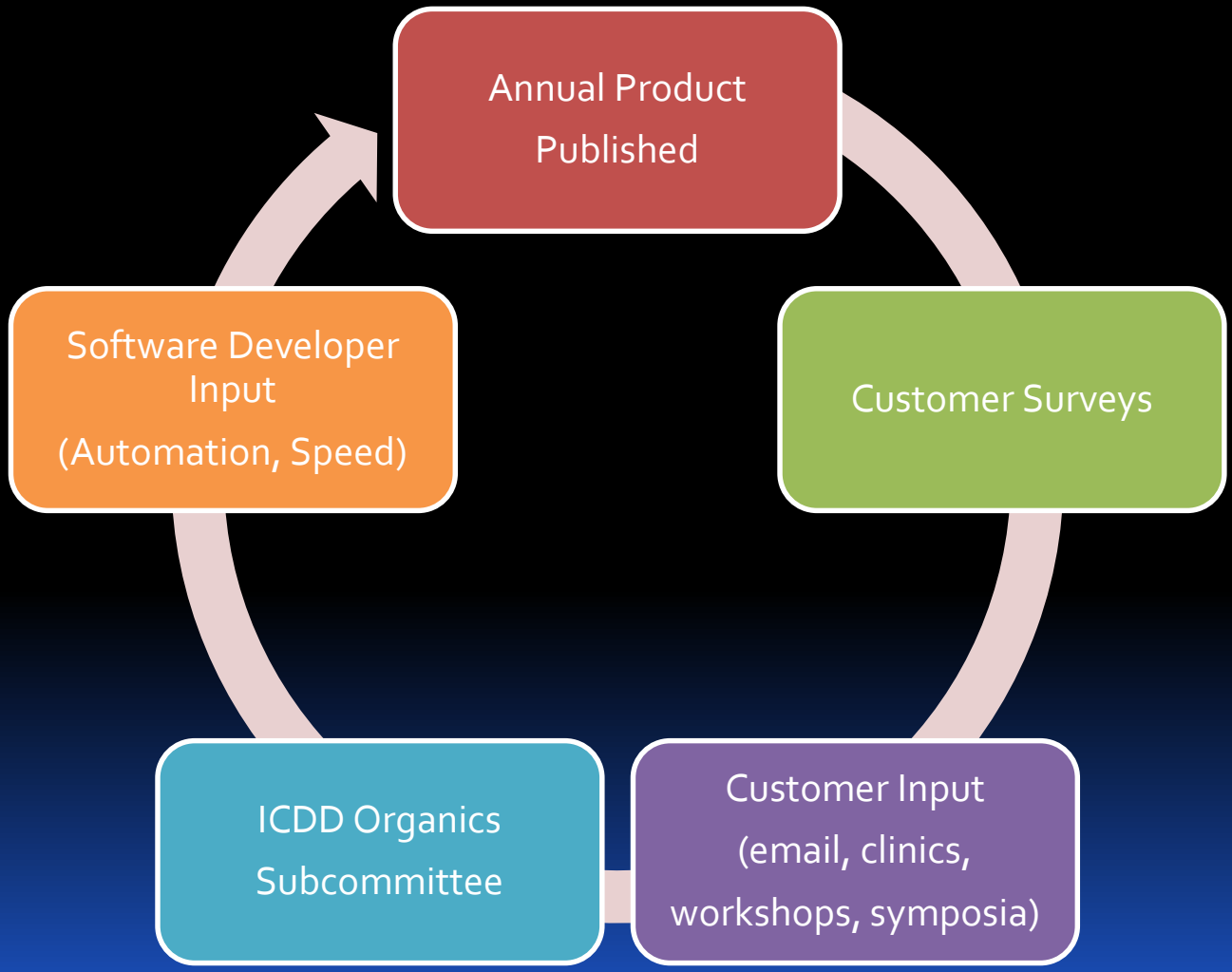
PDF-4/Organics



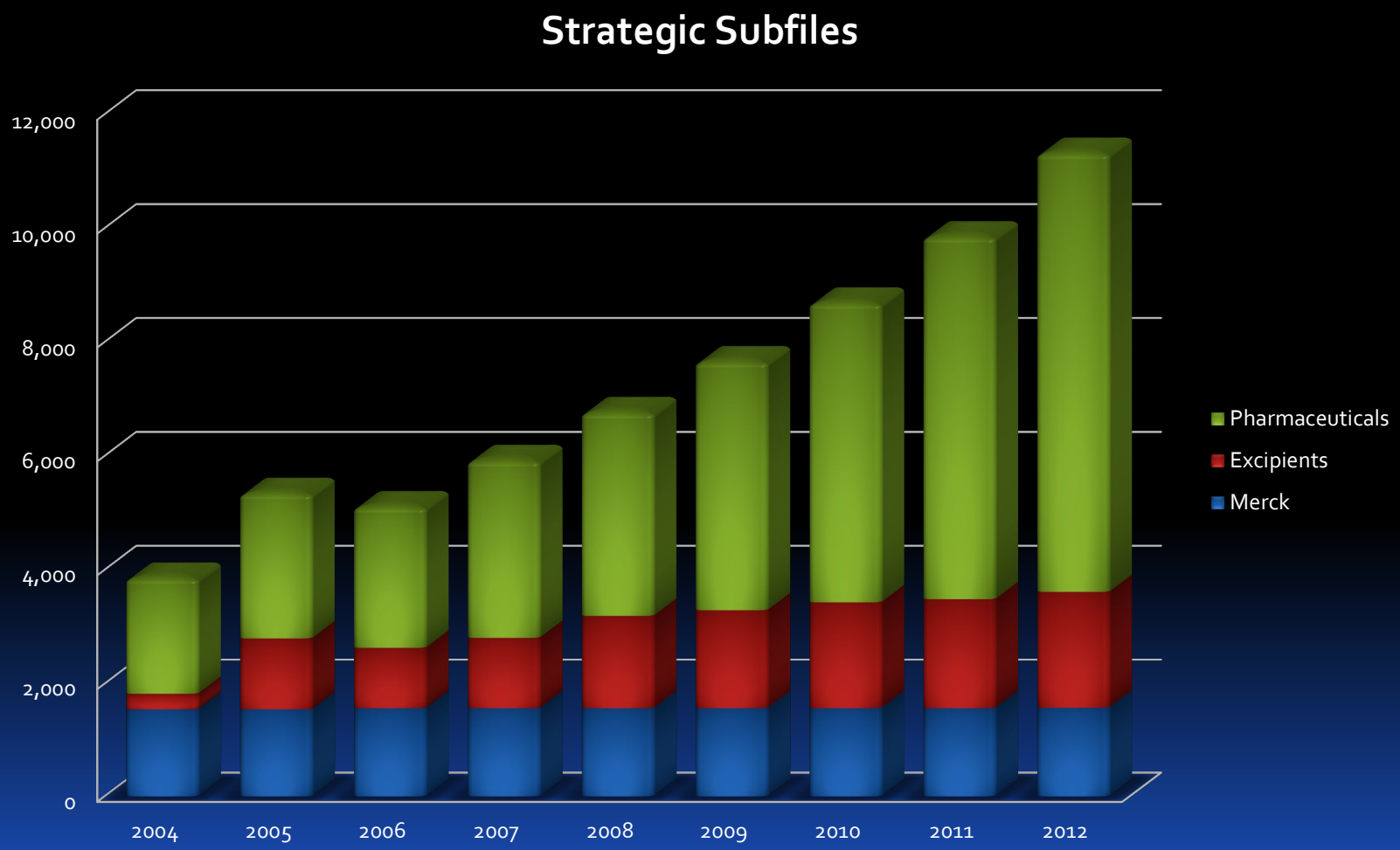
Material Identification and Characterization

FORMULATION ANALYSES OF OFF THE SHELF PHARMACEUTICALS	PPXRD-3	Formulation Analysis (Excipients, Quality System)
FORMULATION ANALYSES OF COMMON HEALTH SUPPLEMENTS	PPXRD-4	
ANALYSES OF PHARMACEUTICAL FORMULATIONS	PPXRD-5	
MAPPING DRUG CHEMISTRY USING CLUSTER ANALYSIS AND DIFFRACTION DATABASES	PPXRD-4	Polymorph Identification (Digital Calc. Patterns)
RESOLVING POLYMORPH CHEMISTRY IN THE CA-O-P-H SYSTEM	PPXRD-5	
POLYMORPH ANALYSES: TOOLS AND RESULTS	PPXRD-7	
MATERIAL IDENTIFICATION: THE DESCRIPTIVE STATISTICS OF PHASE IDENTIFICATION	PPXRD-8	Trace Phase Identification with Data Mining (Searches)
SUCCESSFUL MATERIAL IDENTIFICATION	PPXRD-9	
THE ANALYSIS OF NANOMATERIALS, AMORPHOUS MATERIALS AND SEMICRYSTALLINE MATERIALS	PPXRD-7	Nano materials Amorphous Materials (Digital Experimental Patterns)
DIFFRACTION, NON-CRYSTALLINITY, AND THE PDF DATABASE	PPXRD-8	
DIGITAL PATTERN ANALYSES	PPXRD-11	

Database Development

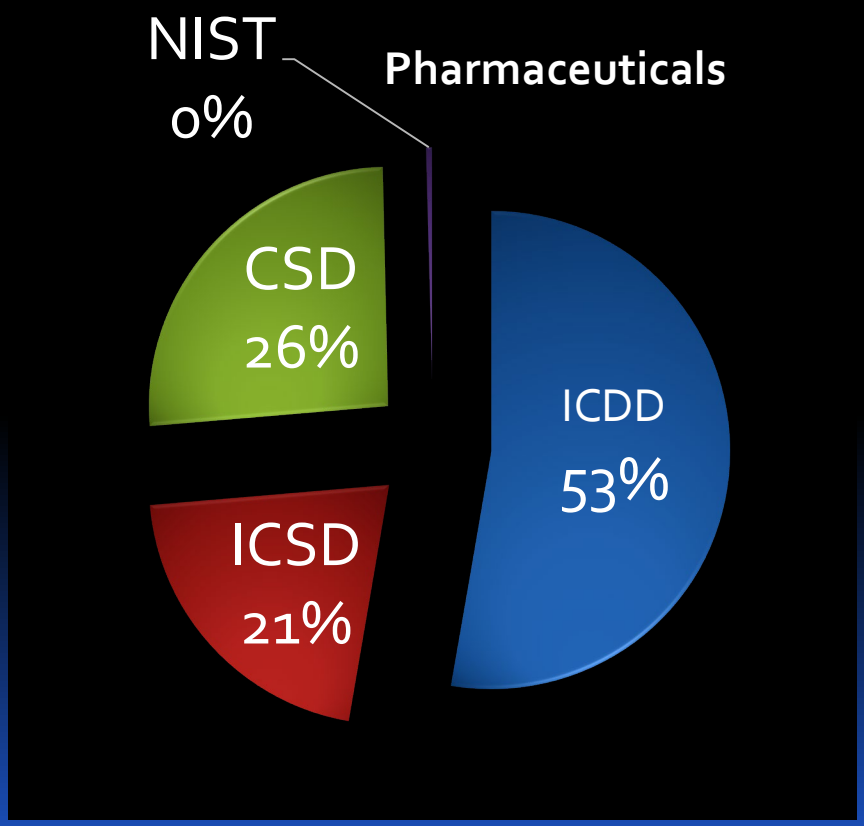


Development of Strategic Subfiles

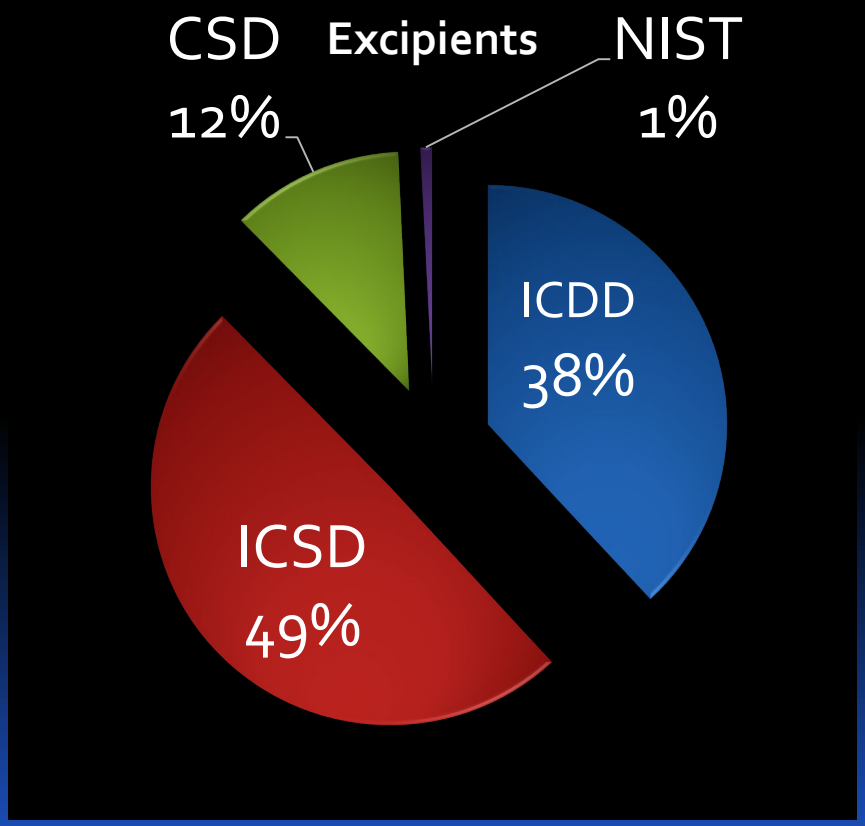


Pharmaceutical Materials – Release 2011

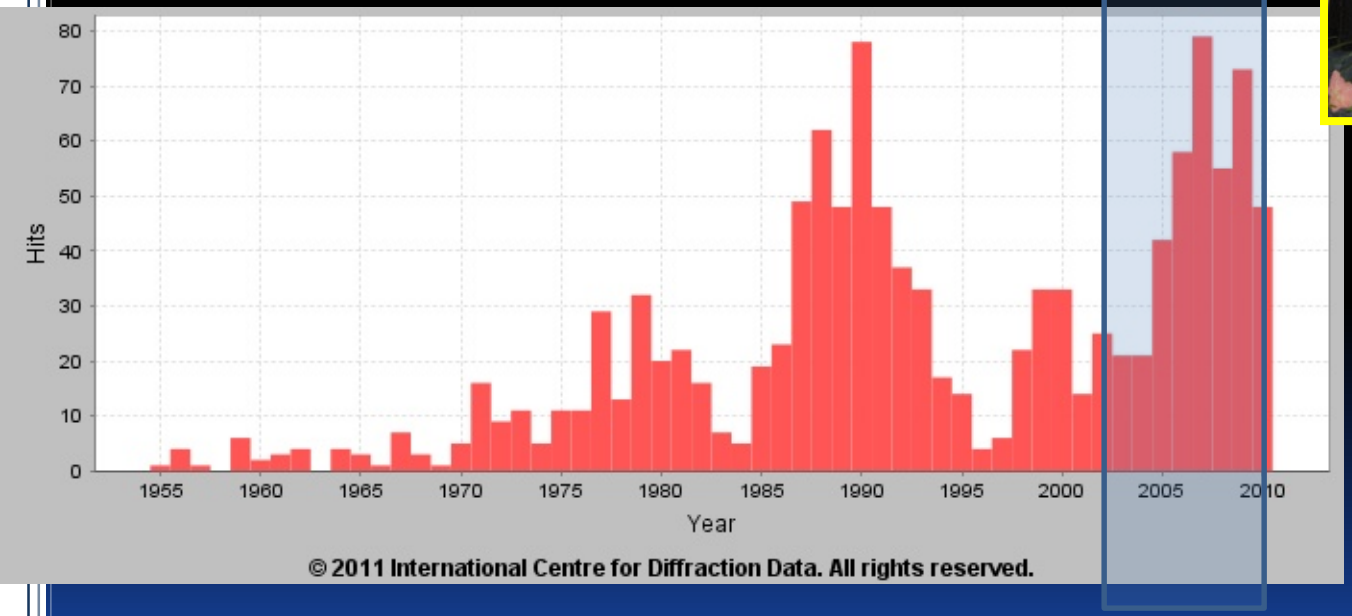
Pharmaceuticals -6,370

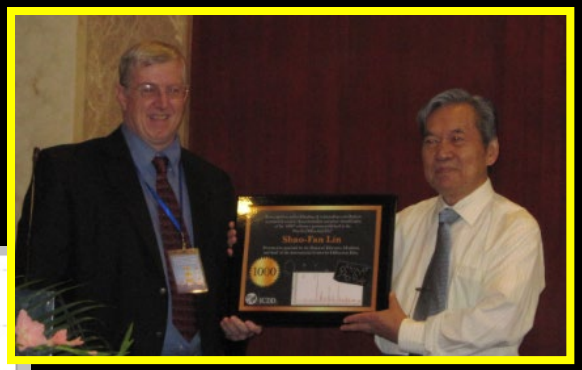


Excipients – 1,916



ICDD Grant Programs
1,396 Pharmaceutical Phases

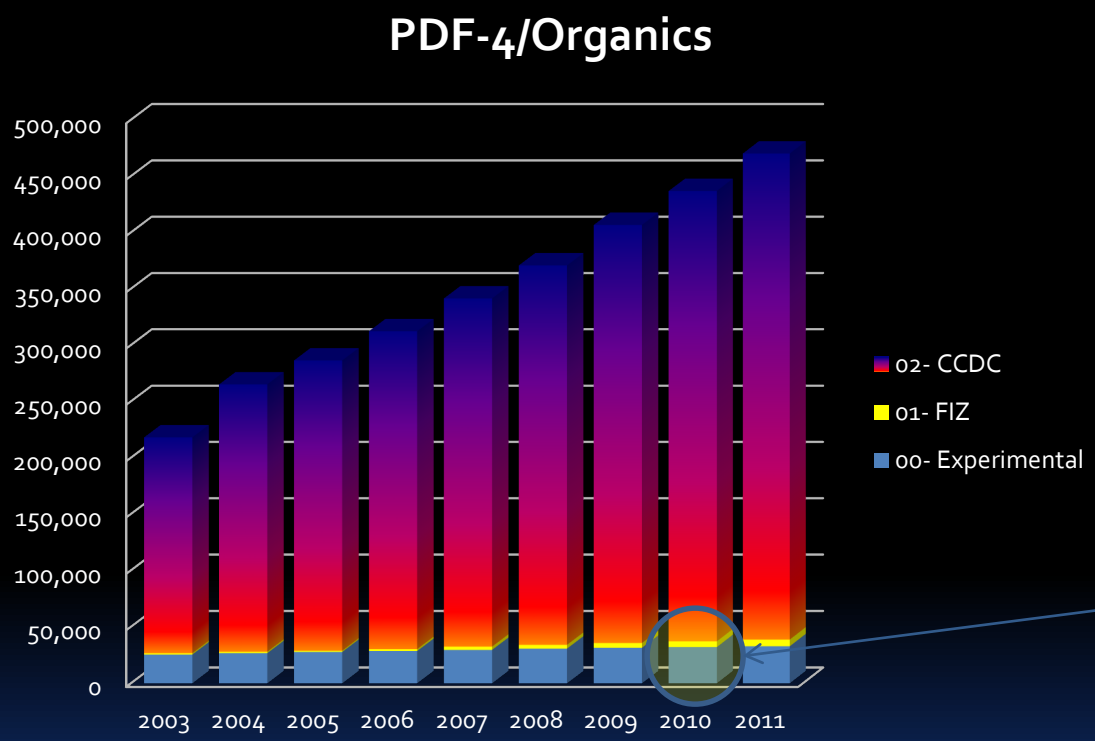




Prof. Shao Fan Lin

18 % of all known XRD patterns of pharmaceuticals, both single crystal and powder, have come from the ICDD grant program

10 Year Growth

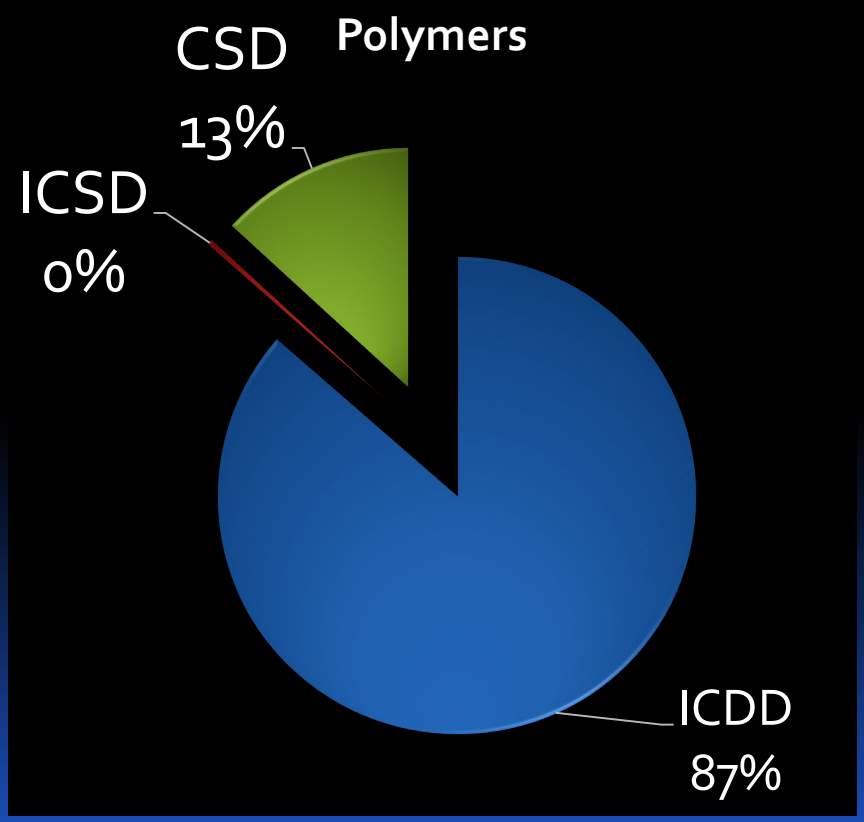


FIZ (01) contributes
49 % of all excipients,
21 % pharmaceuticals

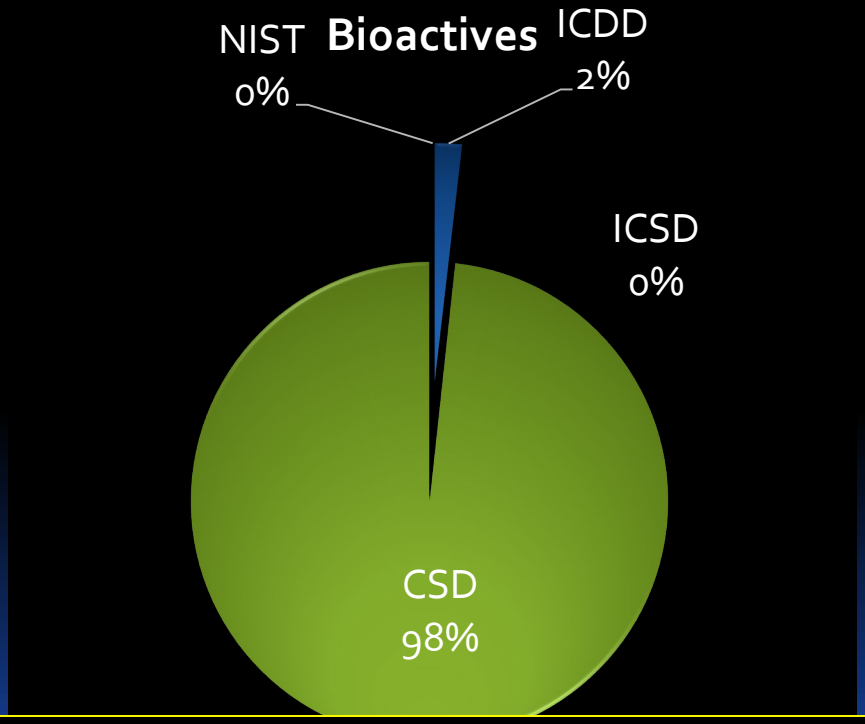
ICDD (00) experimental
contributes 53 % of
all pharmaceuticals,
38 % of excipients

Pharma associated Subfiles

Polymers – 1,302

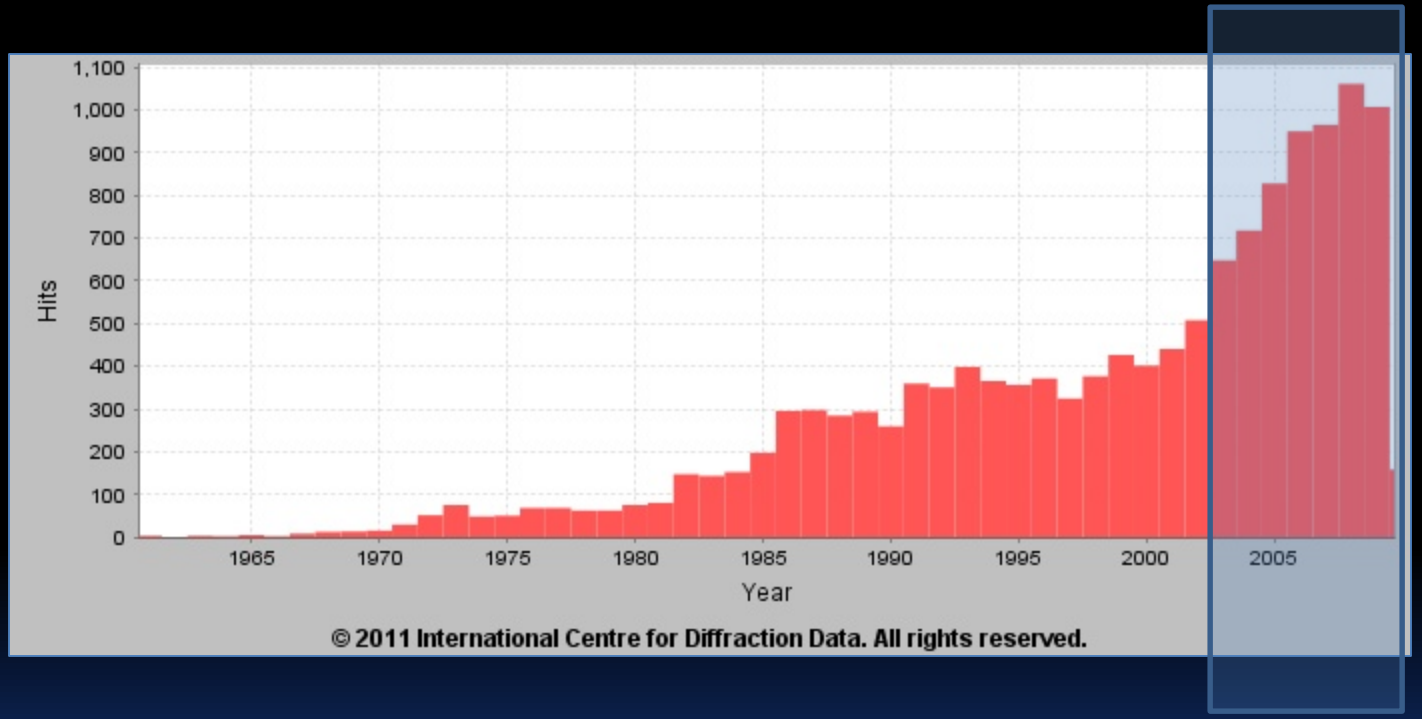


Bioactives -13,145



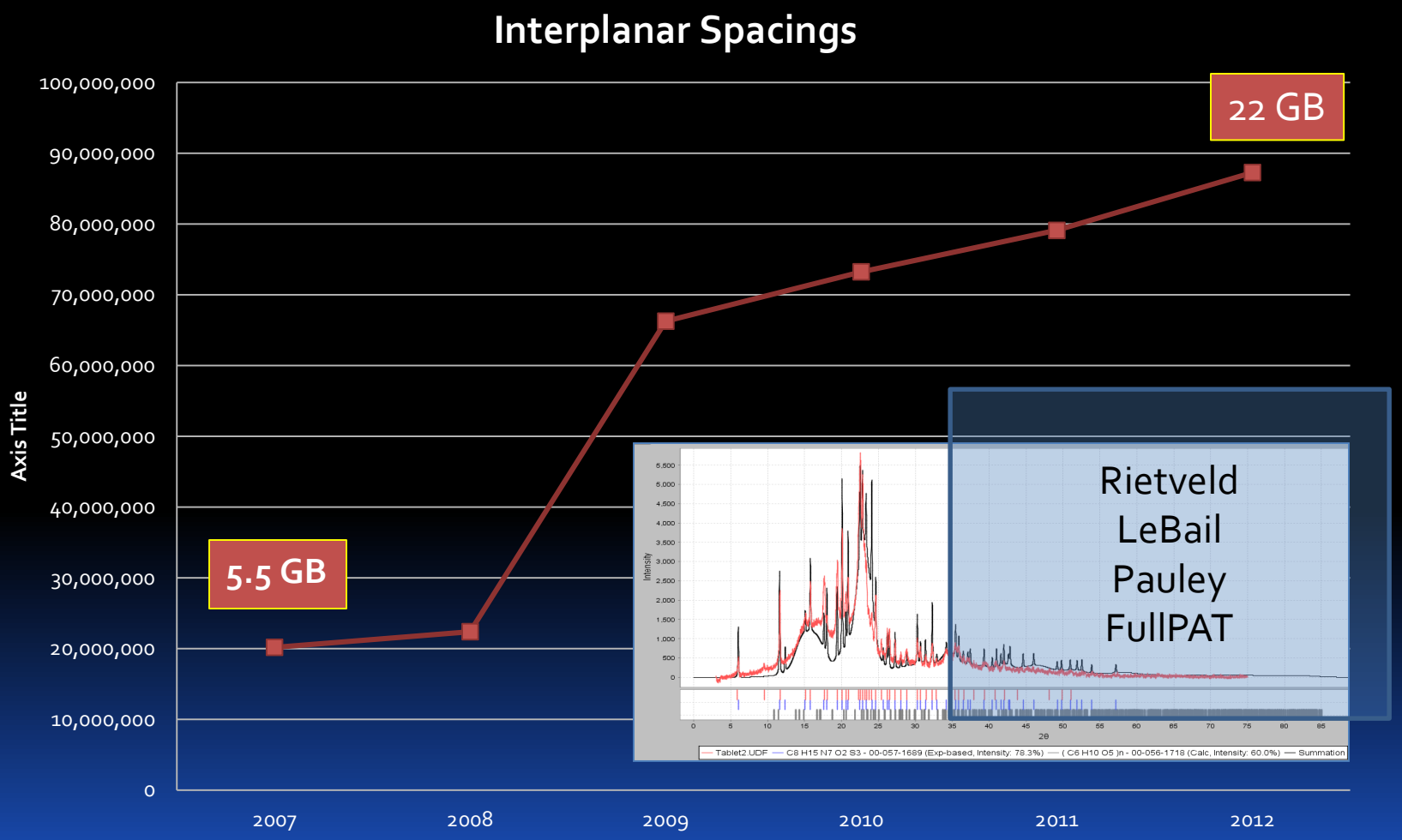
Bioactives are materials that exhibit some Bioactive behavior

Bioactives by Publication Year 13,864 Bioactives



Would include exploratory drugs, drug salts, herbicides, pesticides, gramicides

File Size and 2θ Range - For full pattern methods



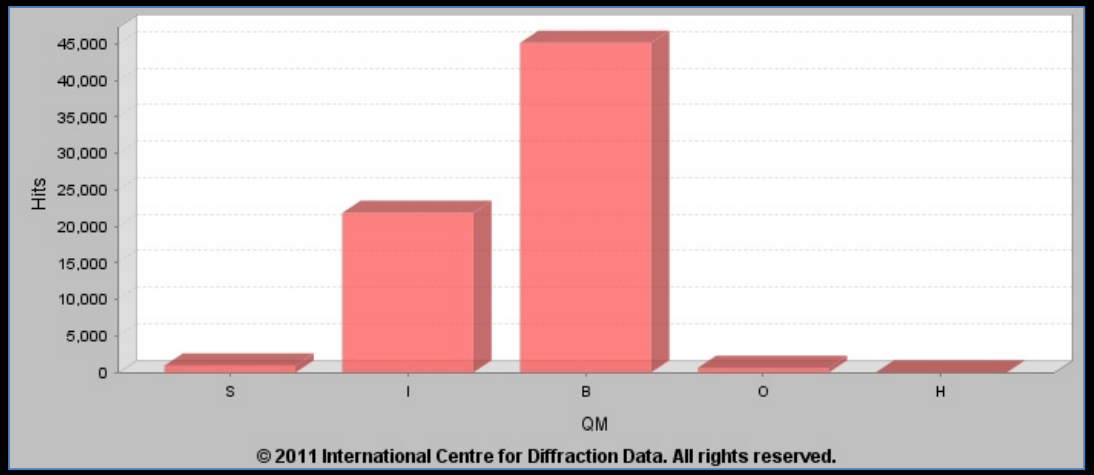
Quality System – Disordered Structures

68,608 published, most with low quality marks

Missing electron density

Is the powder pattern accurate

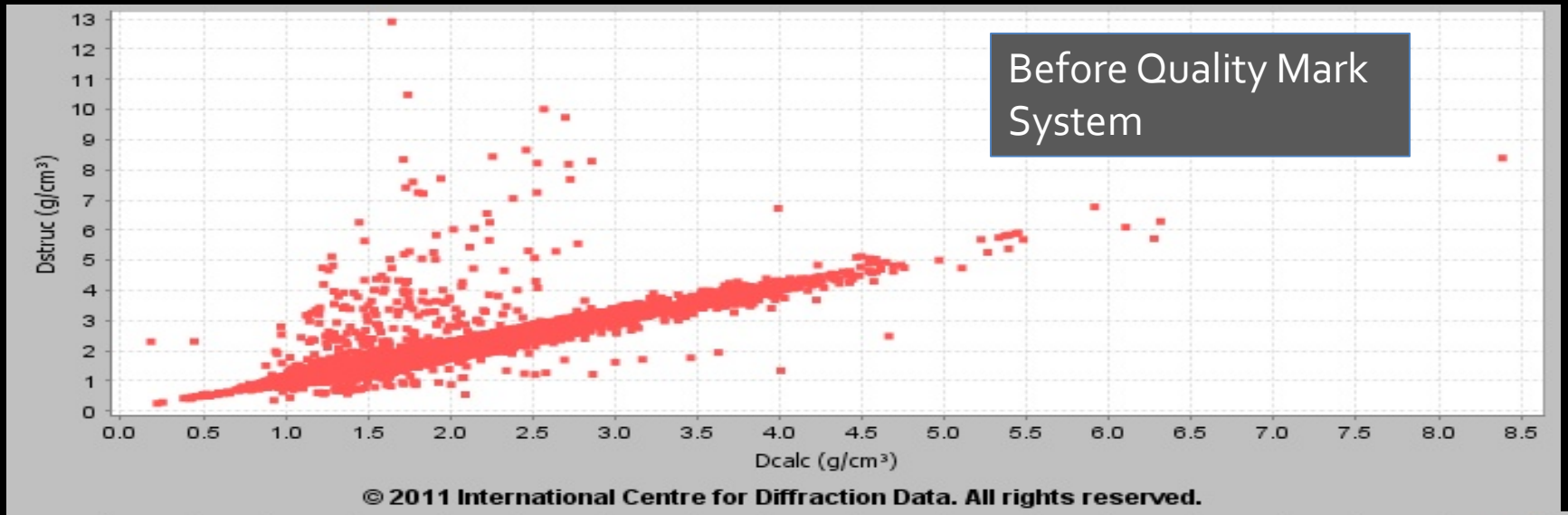
How much electron density is missing ?

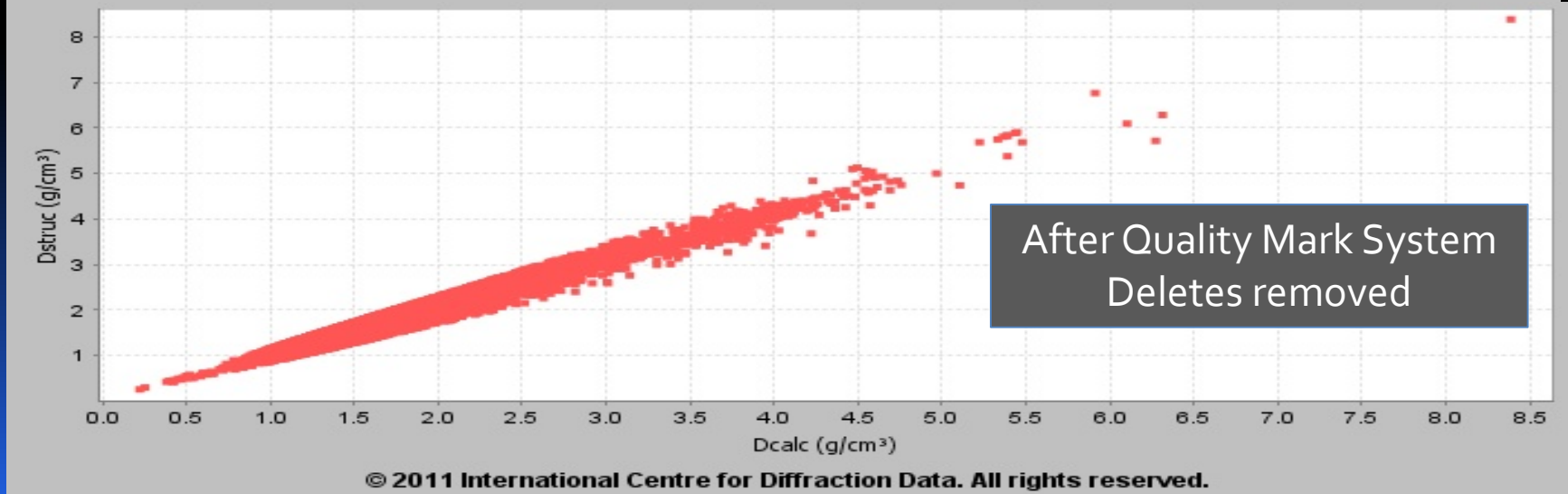


0 % 1-3 % 4-15 %

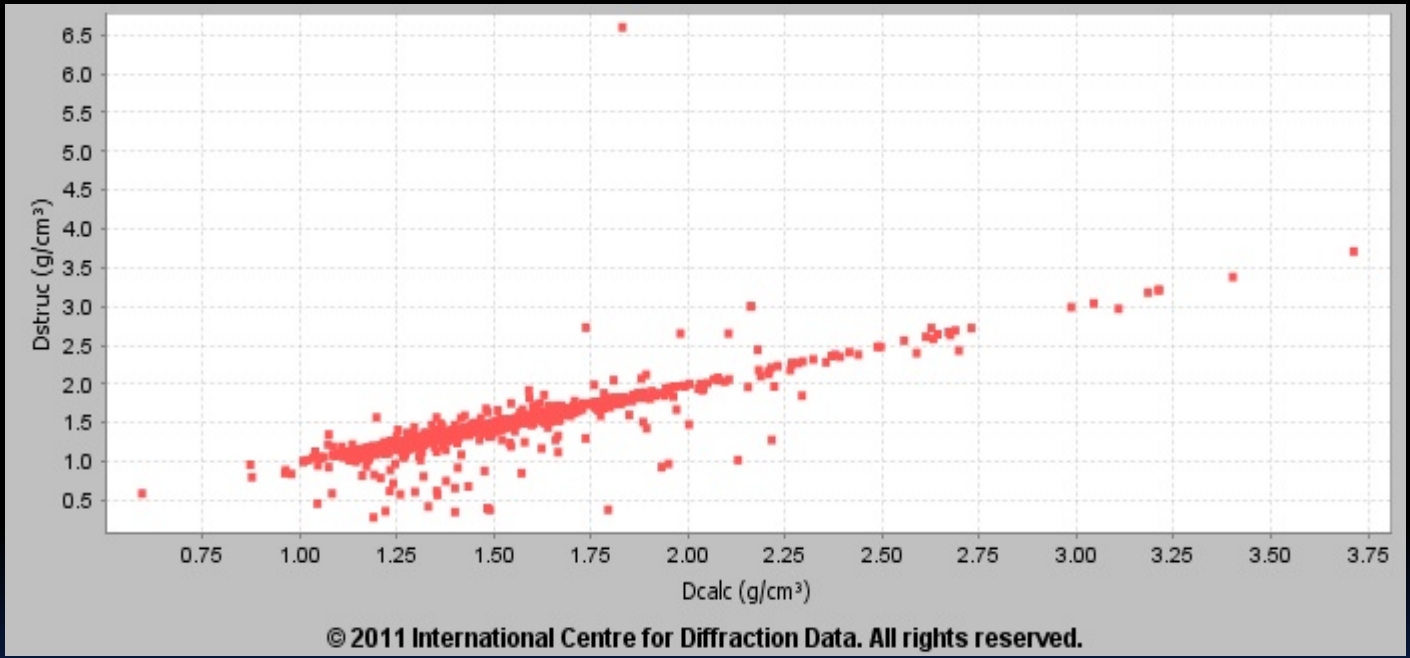
> 15 % 50,757 not published !

Disordered Structures Calculated vs Structural Density

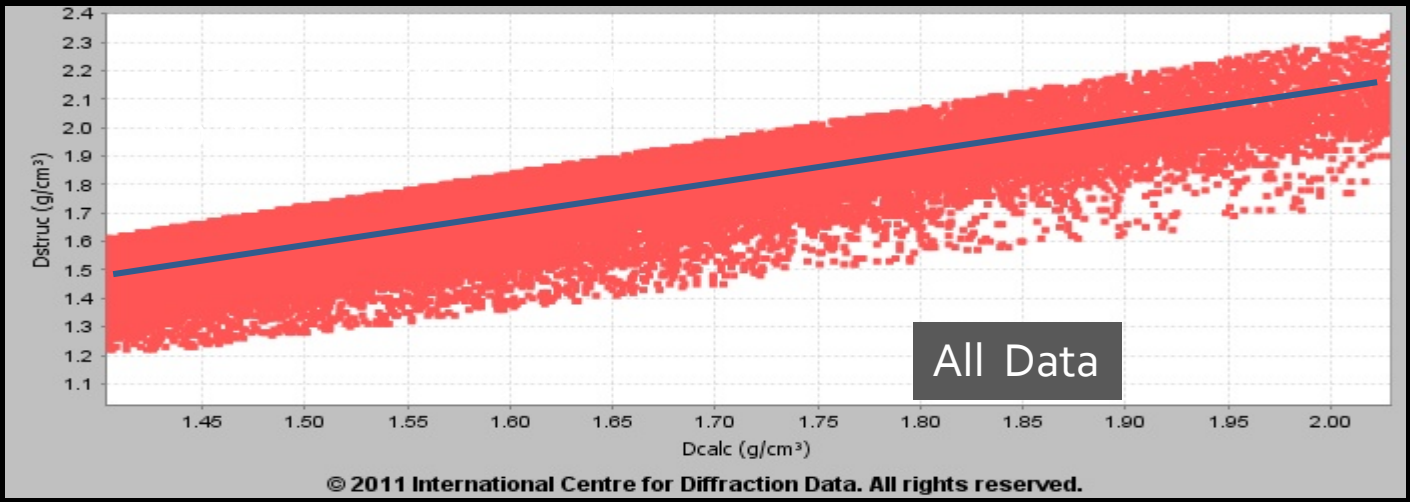


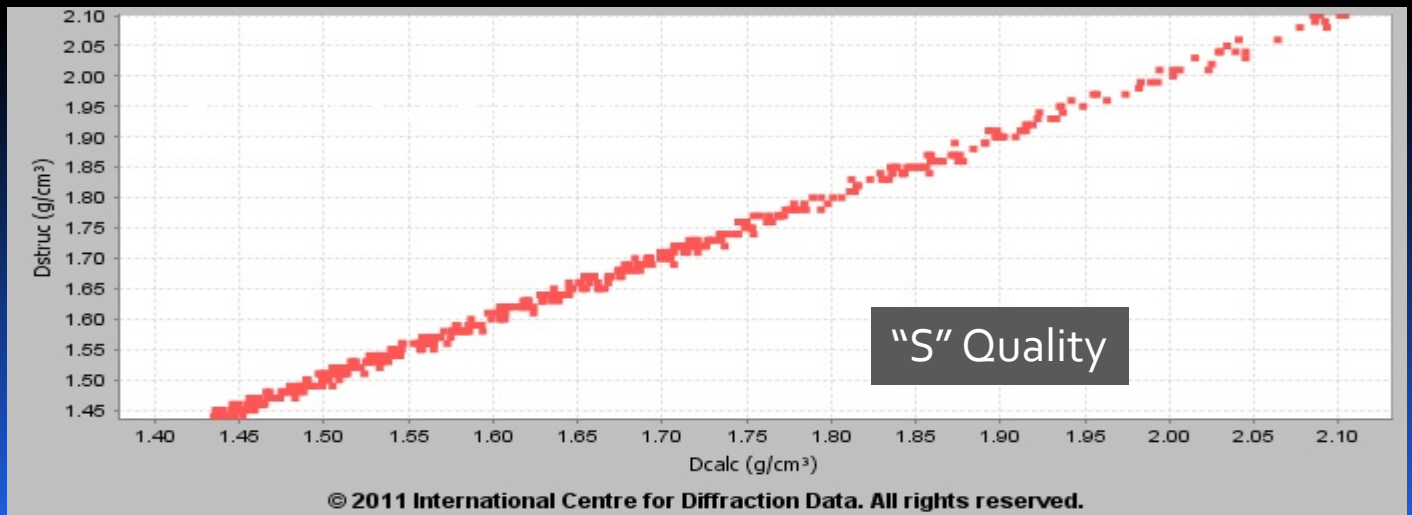


Missing H atoms

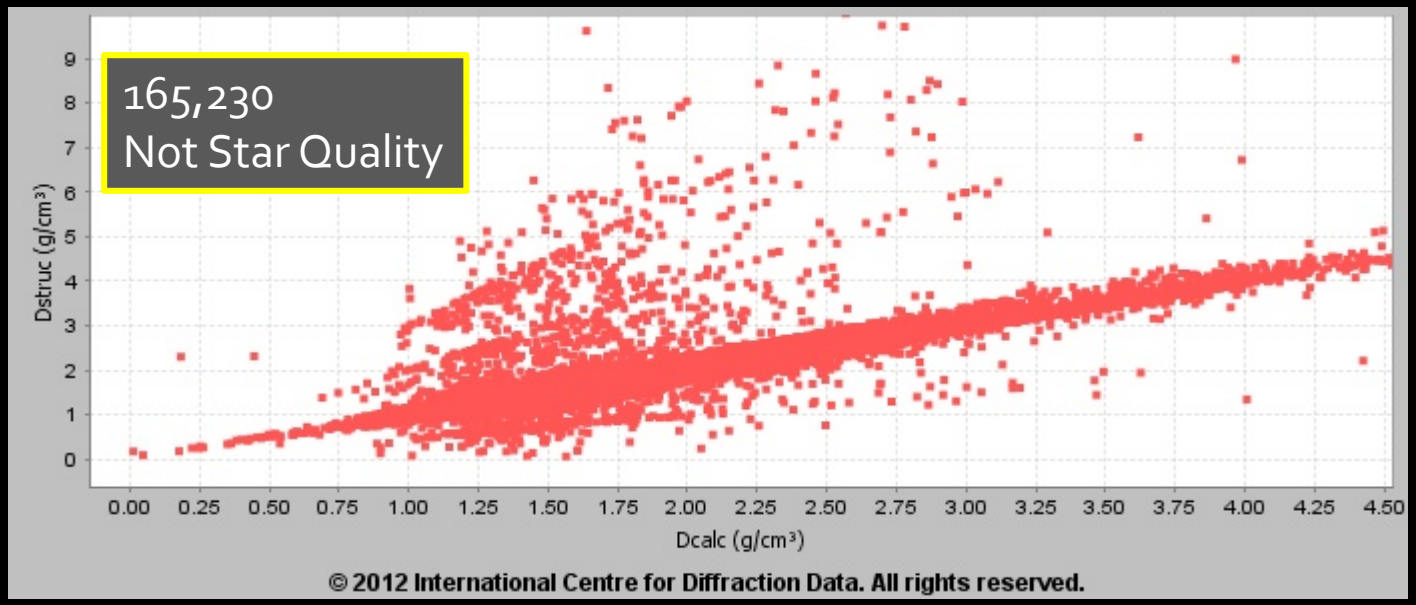


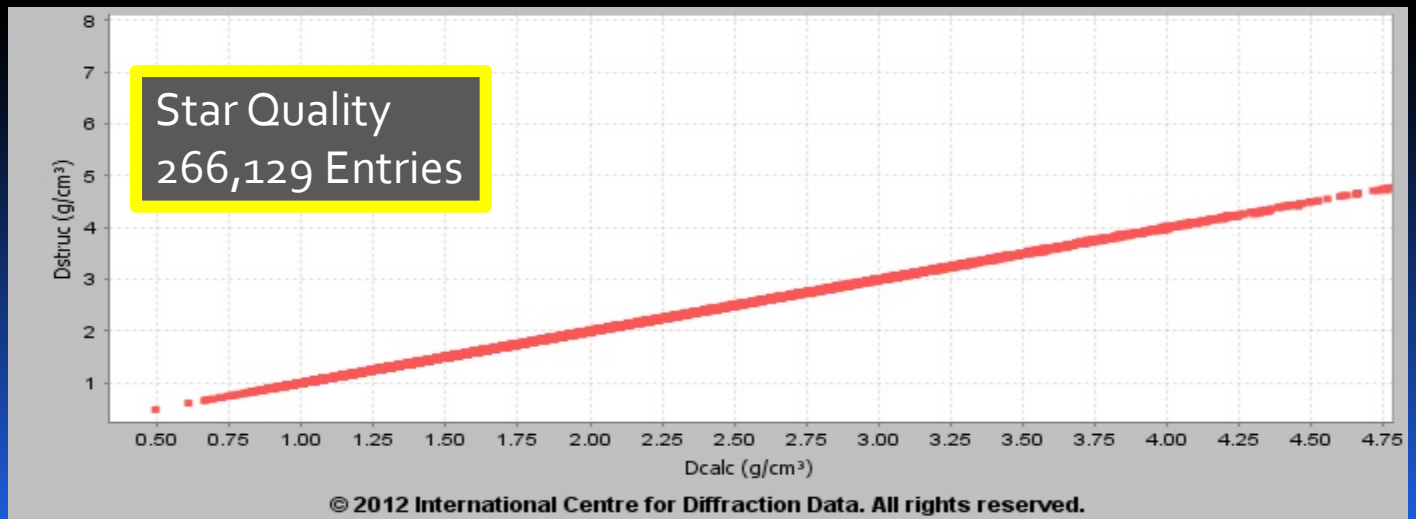
Quality System – Disordered Structures





Quality of CSD sourced Data





Sources of errors

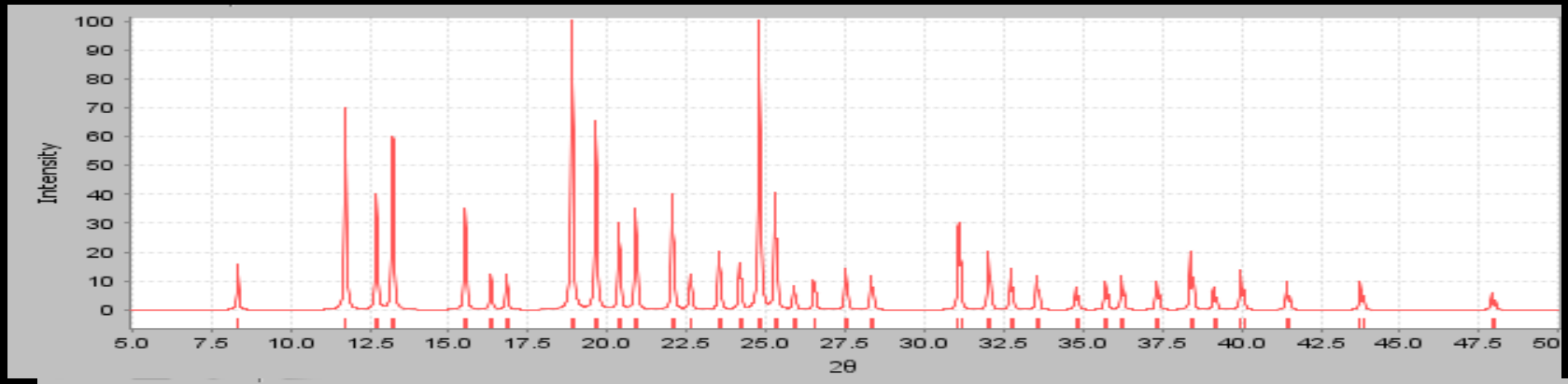
Missing electron density
- disorders
- missing hydrogens
- missing molecules (water, other solvates)

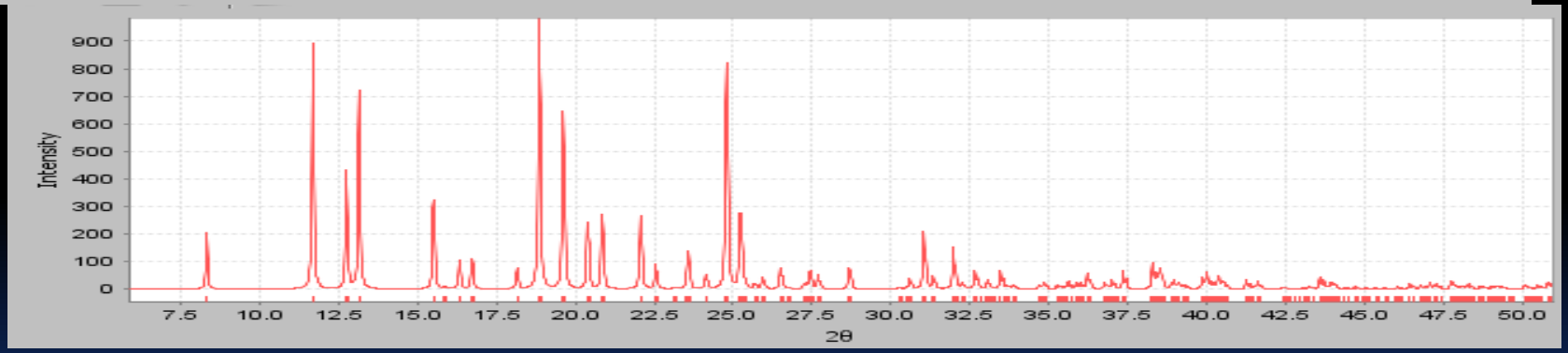
Non positive thermal displacement parameters

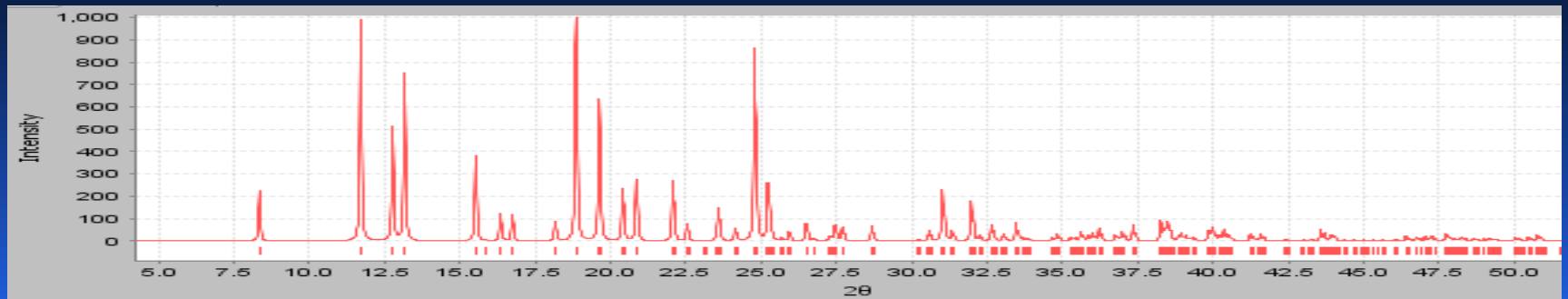
Unrealistic bond angles and distances

Chemical analysis does not match crystallographic determination
(Author formula vs calculated formula)

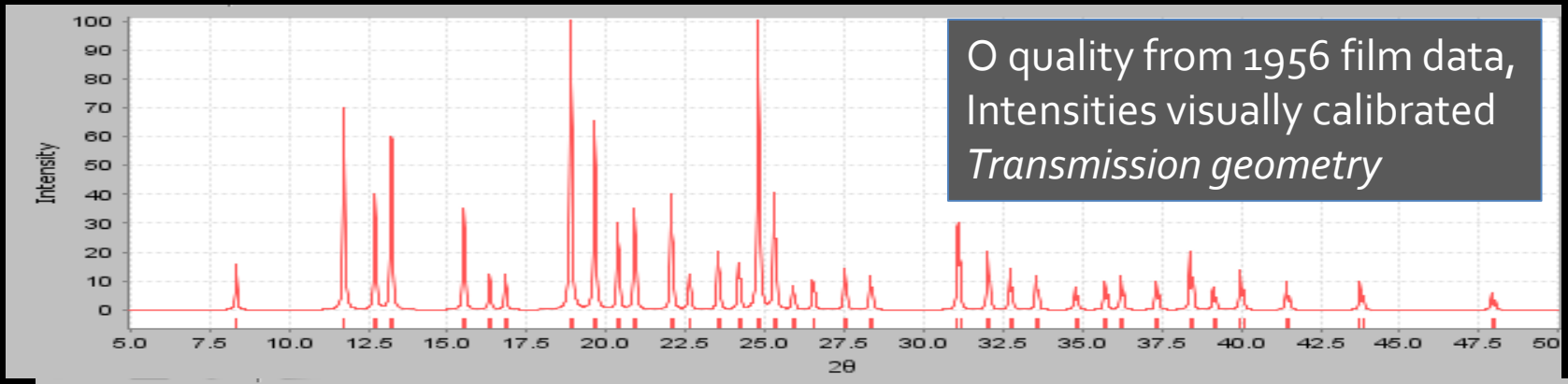
Sucrose – Which one is correct ?



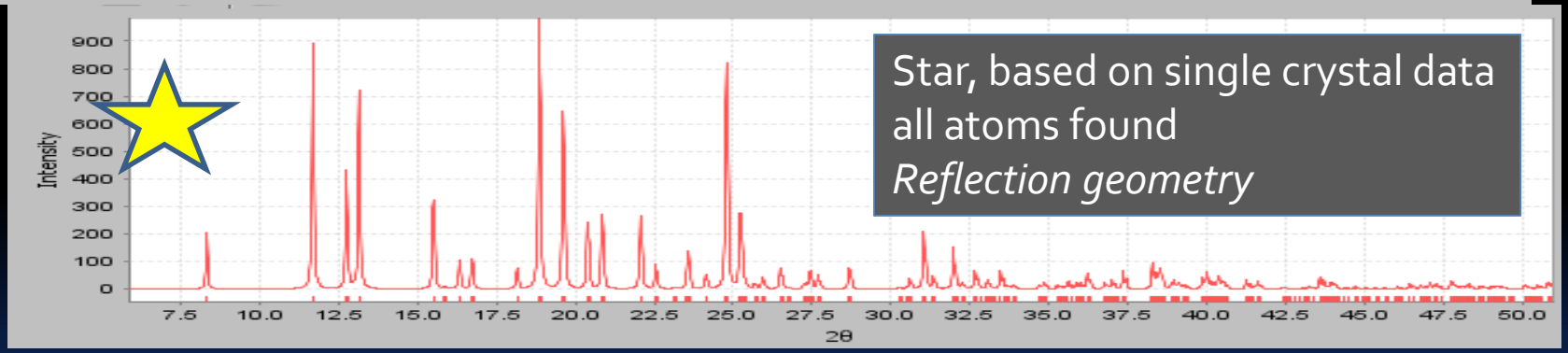




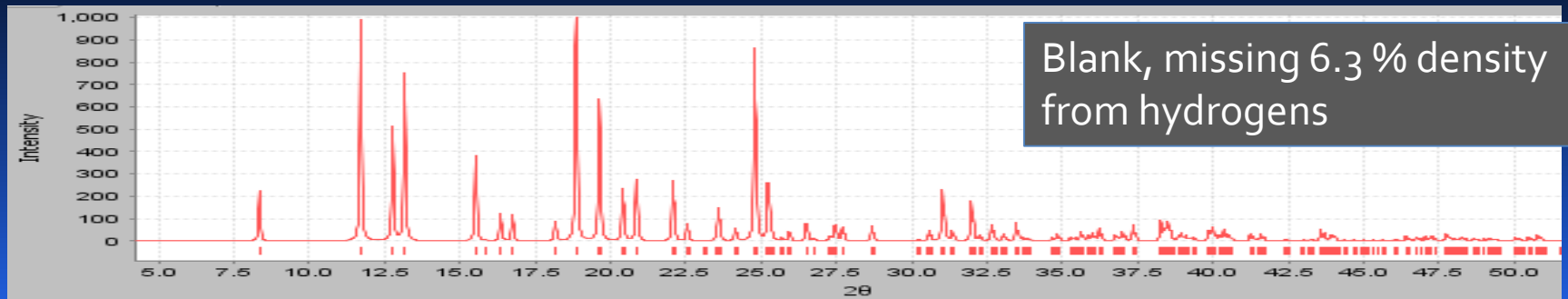
Sucrose – Which one is correct ?



O quality from 1956 film data,
Intensities visually calibrated
Transmission geometry

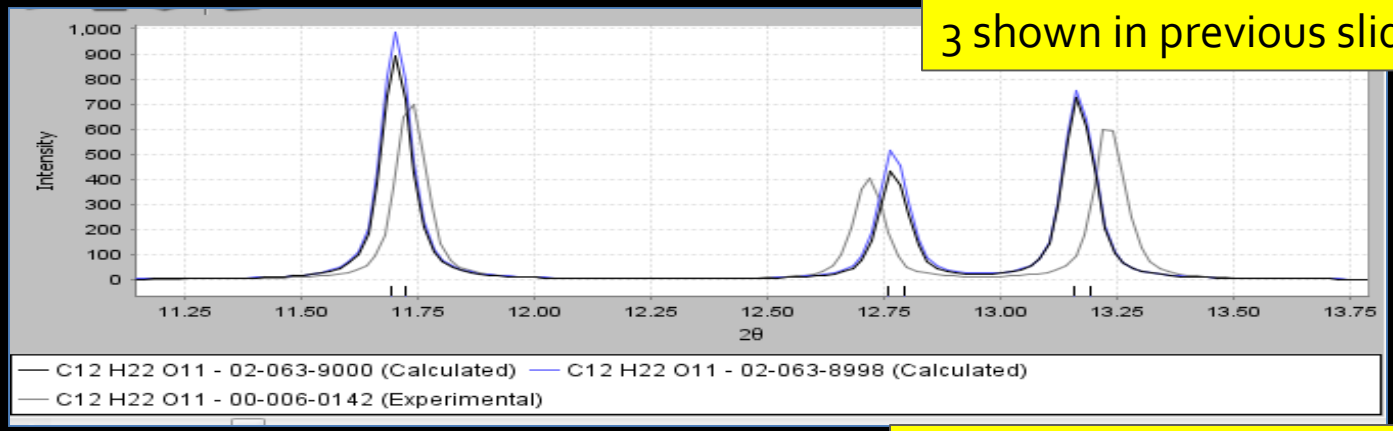


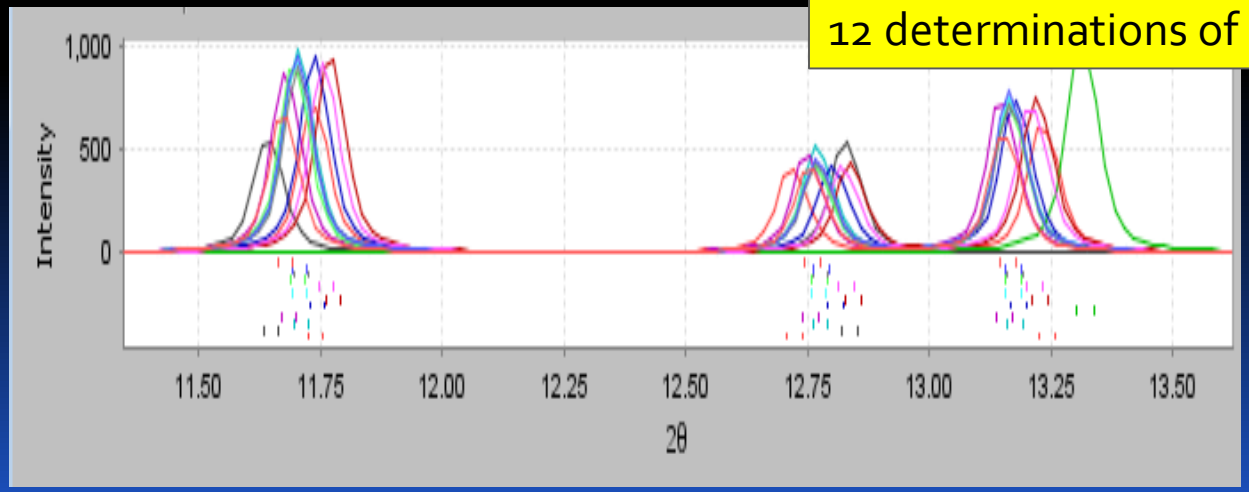
Star, based on single crystal data
all atoms found
Reflection geometry



Blank, missing 6.3 % density
from hydrogens

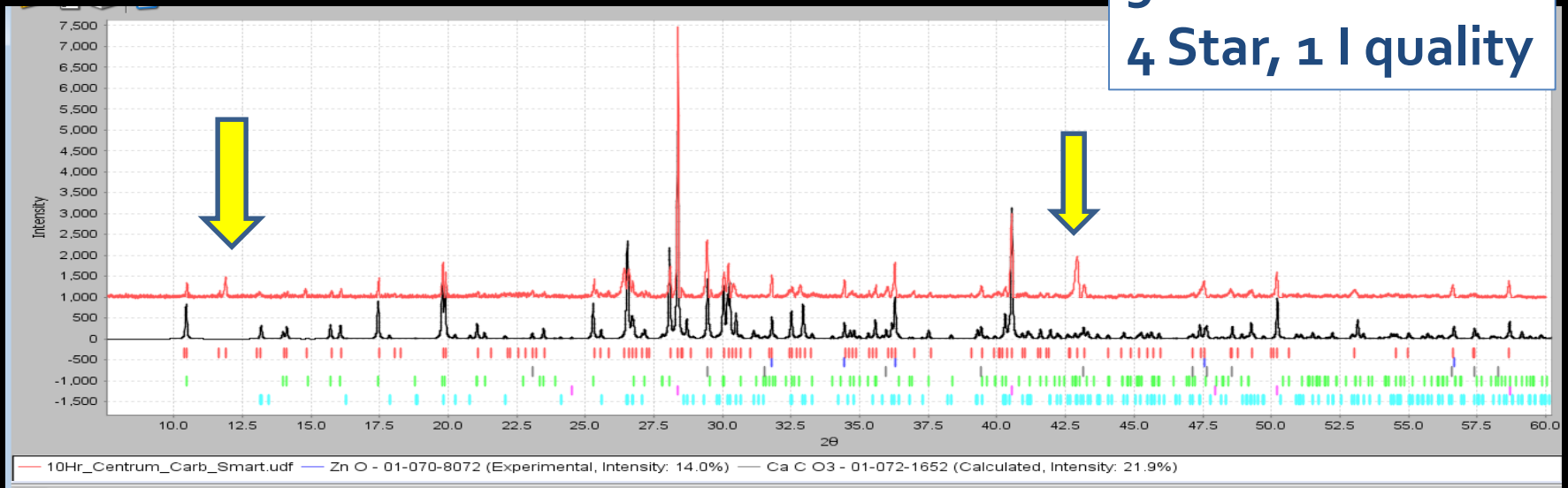
Closer Inspection



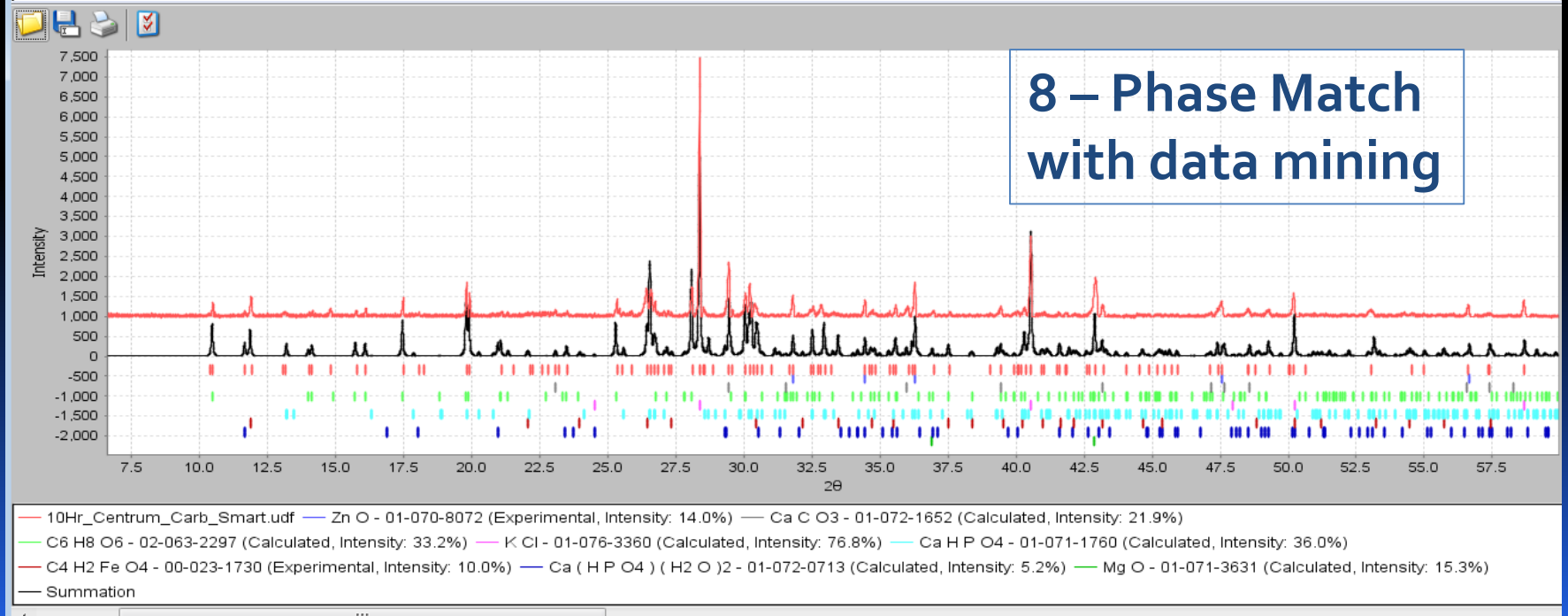


Multiphase Analyses

5- Phases
4 Star, 1 I quality

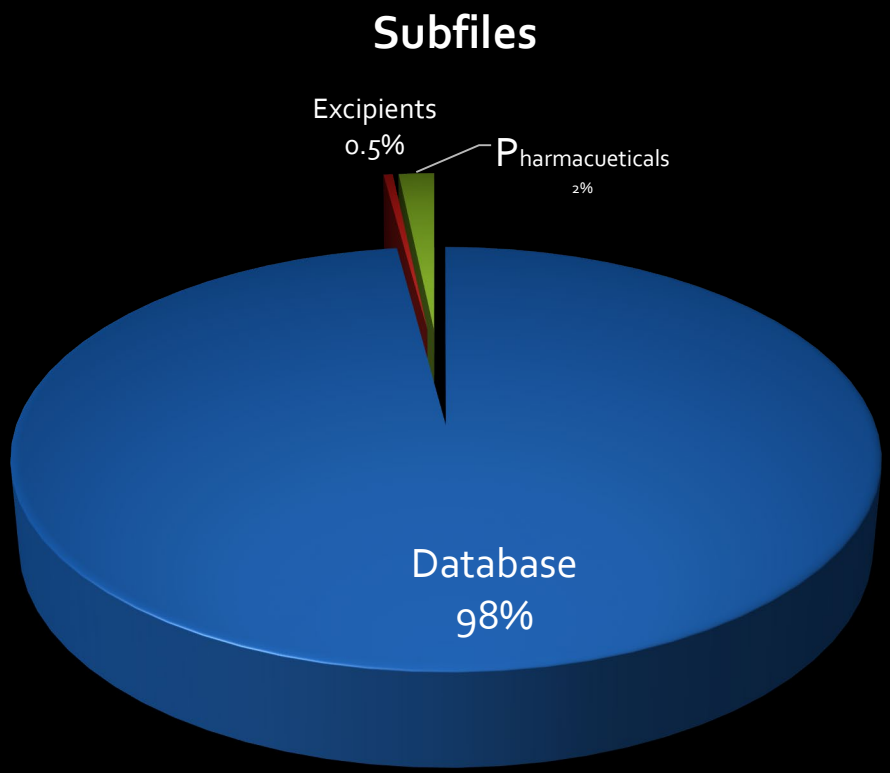


8 – Phase Match with data mining



Subfiles and Data Mining

Dave Rendle, UK



Fangling Needham

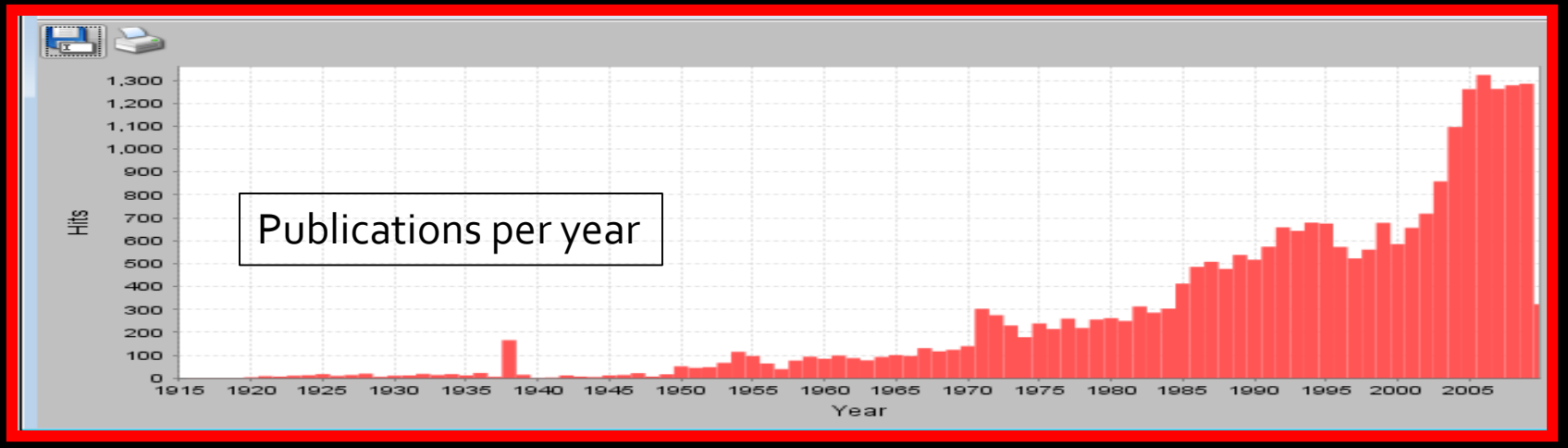
What is in a pharmaceutical tablet ?

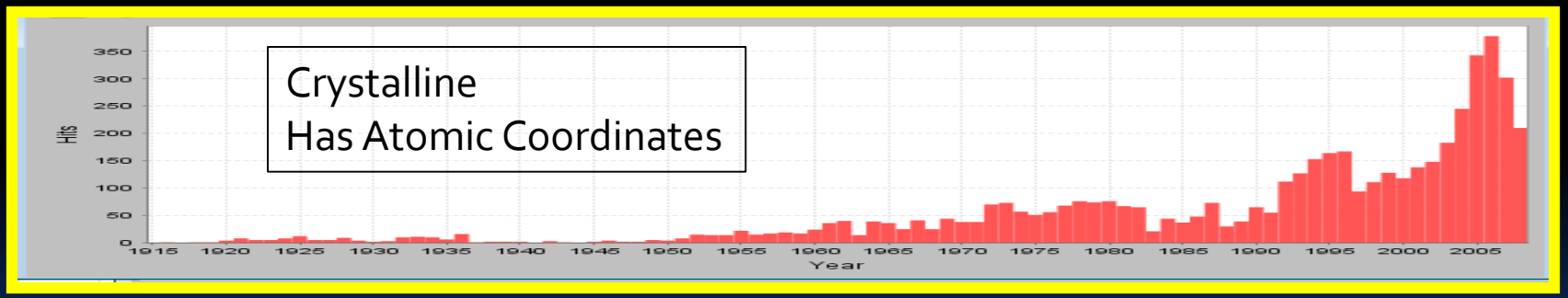
Subfiles

Target Subfiles

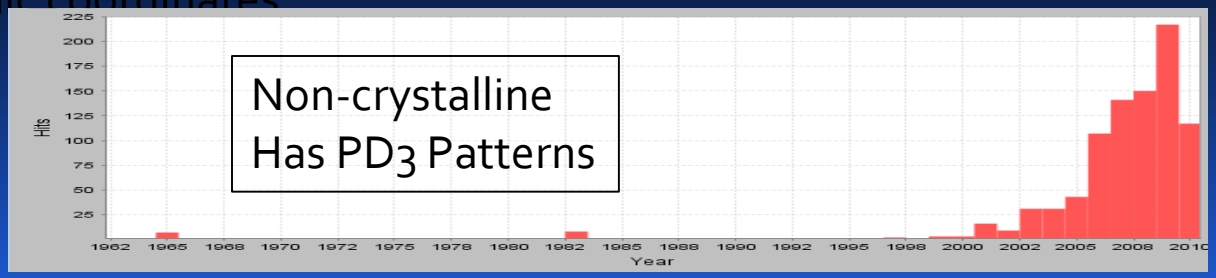
- Alkaloids
- Amino Acids, Peptides & Complex
- Battery Material
- Bioactivity
- Carbohydrate
- Cement and Hydration Product
- Ceramic
- Common Phase
- Education
- Excipient
- Explosive
- Forensic
- Inorganic
- Intercalate
- Ionic Conductors
- Merck
- Metals & Alloys
- Micro & Mesoporous
- Mineral Related
- Modulated Structure
- NBS
- Nucleosides & Nucleotides
- Organics
- Pharmaceutical
- Pigment
- Polymer
- Porphyrins, Corrins & Complexes
- Steroids
- Superconducting Material
- Terpenes
- Thermoelectric Material

Target Materials

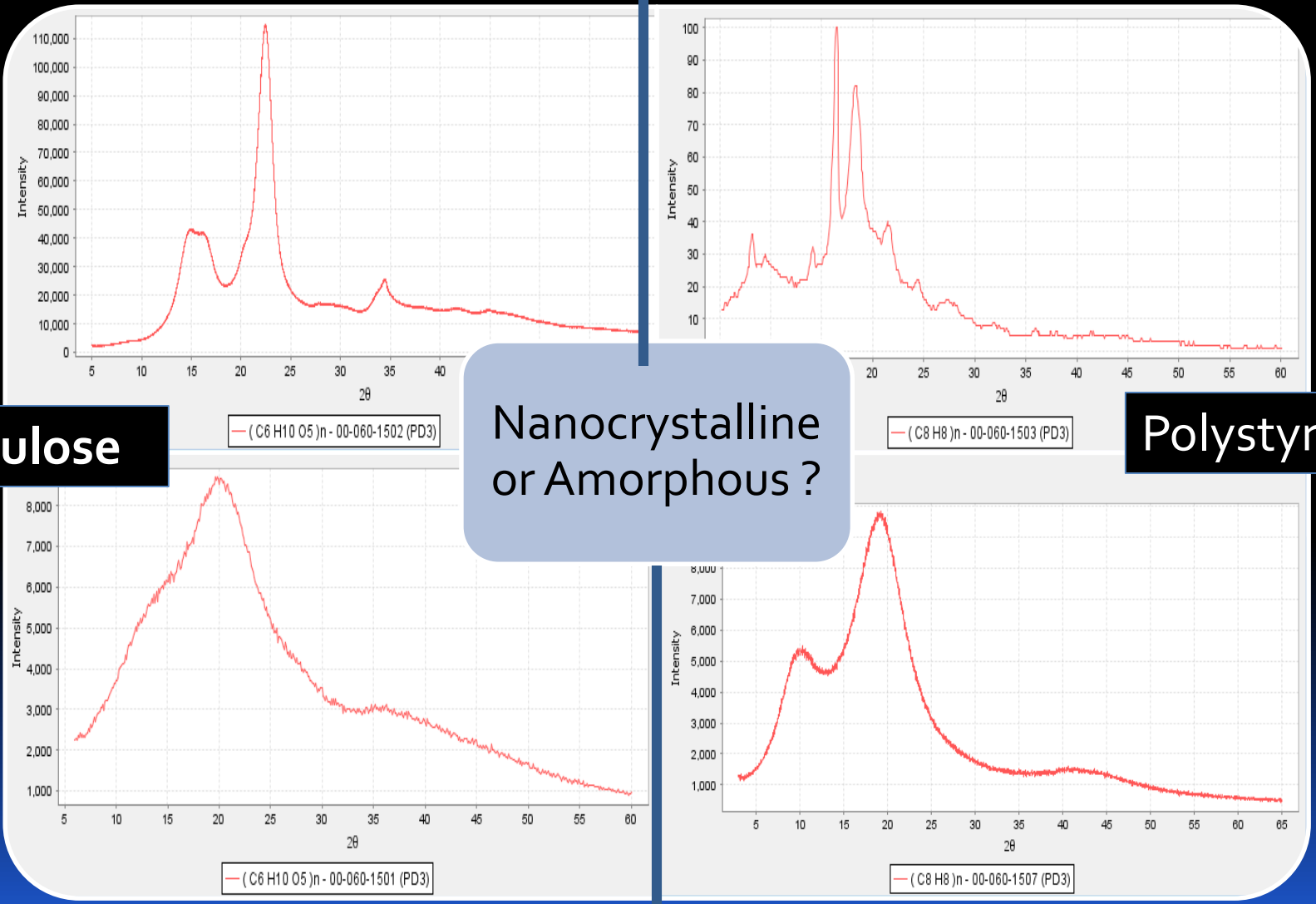




Have atomic coordinates



Experimental digital patterns



Cellulose

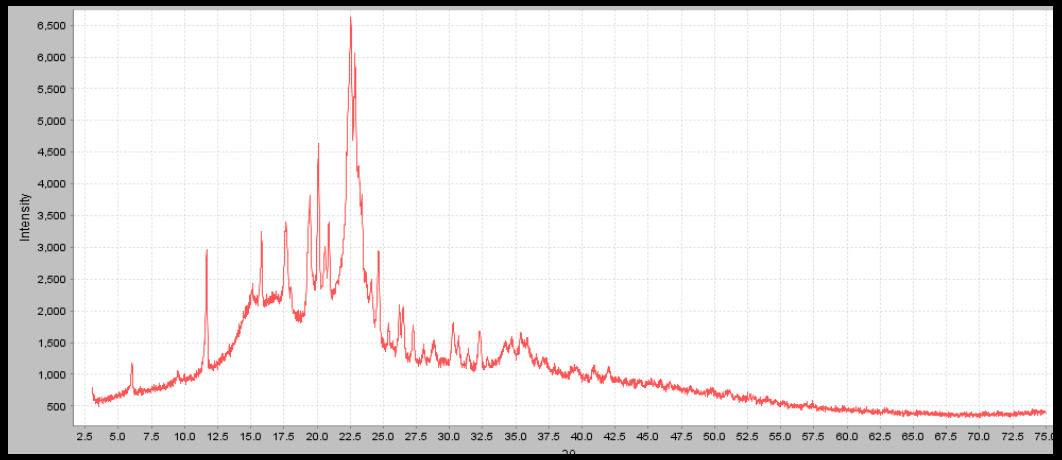
Nanocrystalline or Amorphous ?

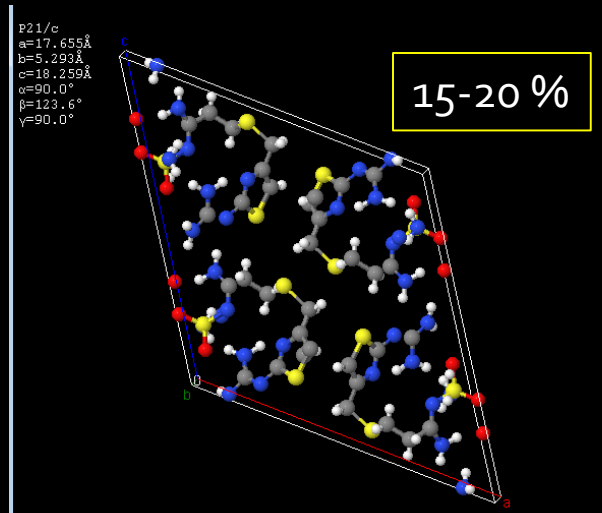
Polystyrene

Targeted Development

- Include all target subfiles
- Add atomic coordinate data sets through bibliographic extraction
- Fix disorders – site occupancies included
- Add anisotropic thermal displacement parameters
- Extract supporting analytical data

Pepcid AC - 2012





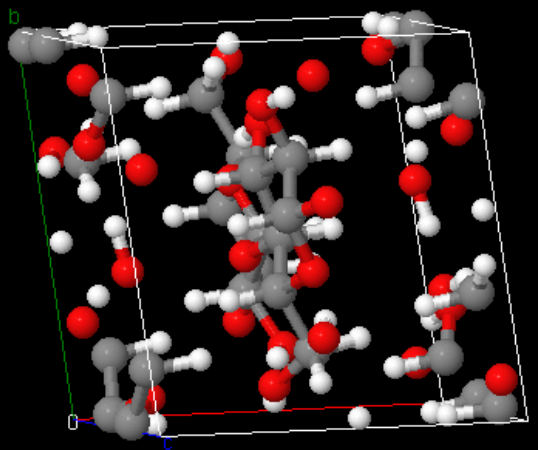
15-20 %

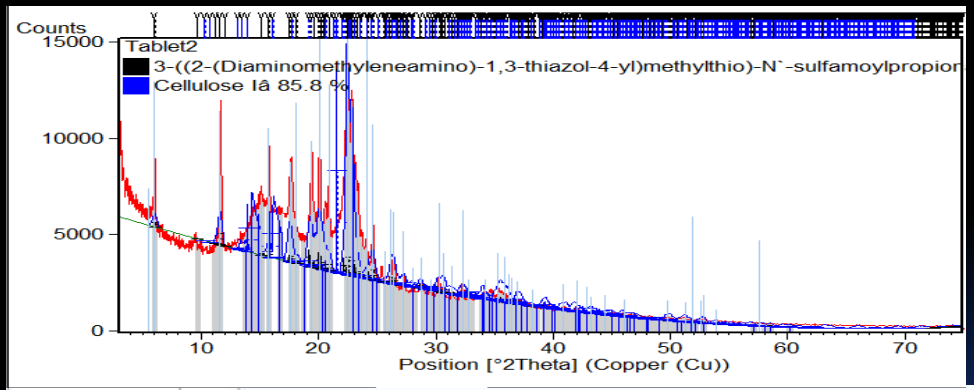
McBride, Shankland, David Shankland, Steele

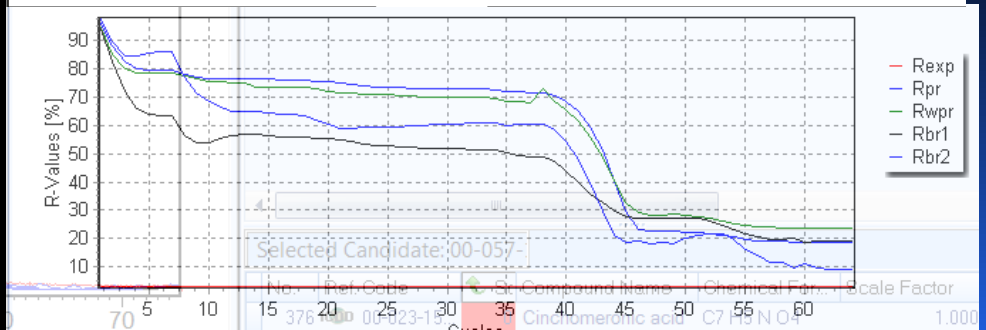
HM:P21
a=7.784Å
b=8.201Å
c=10.380Å
α=90.0°
β=90.0°
γ=96.5°

Kaduk & Langan

80-85 %

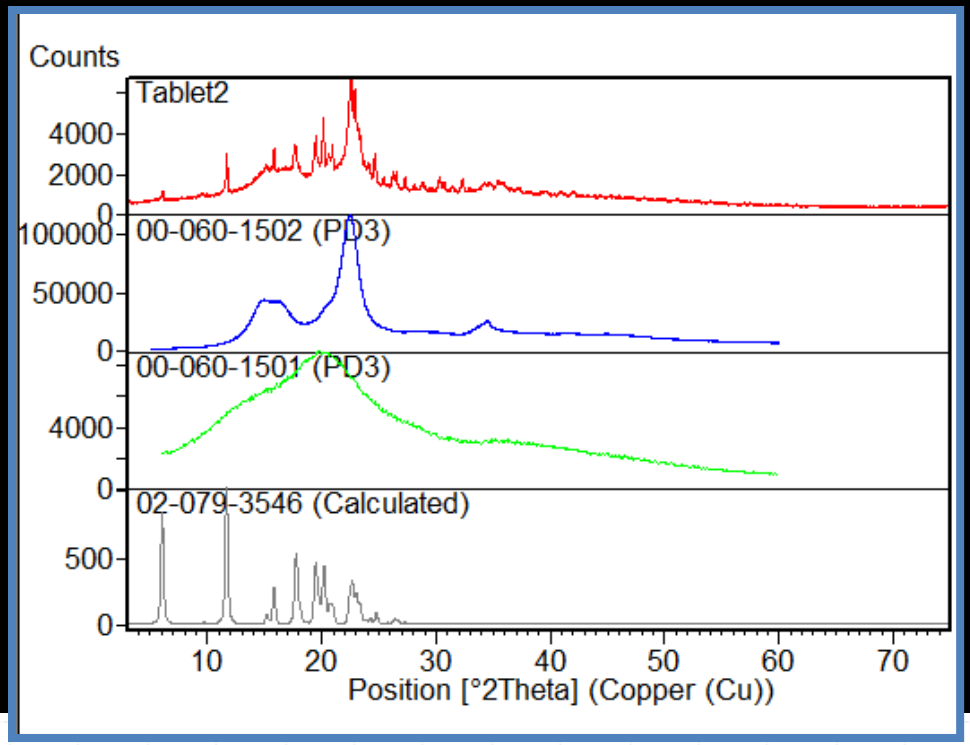


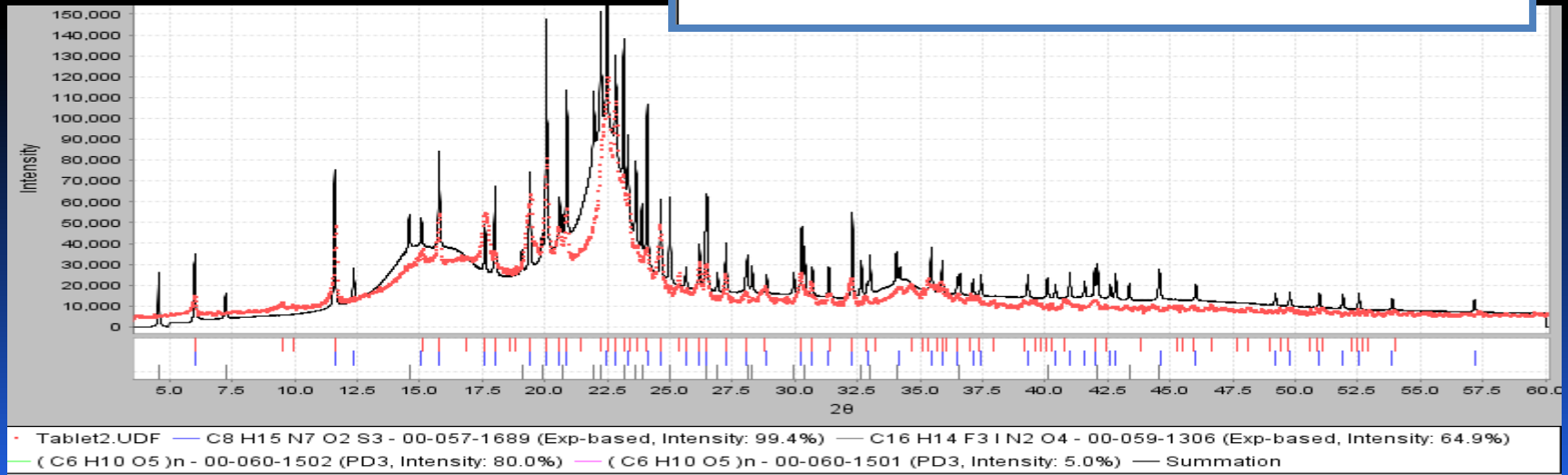




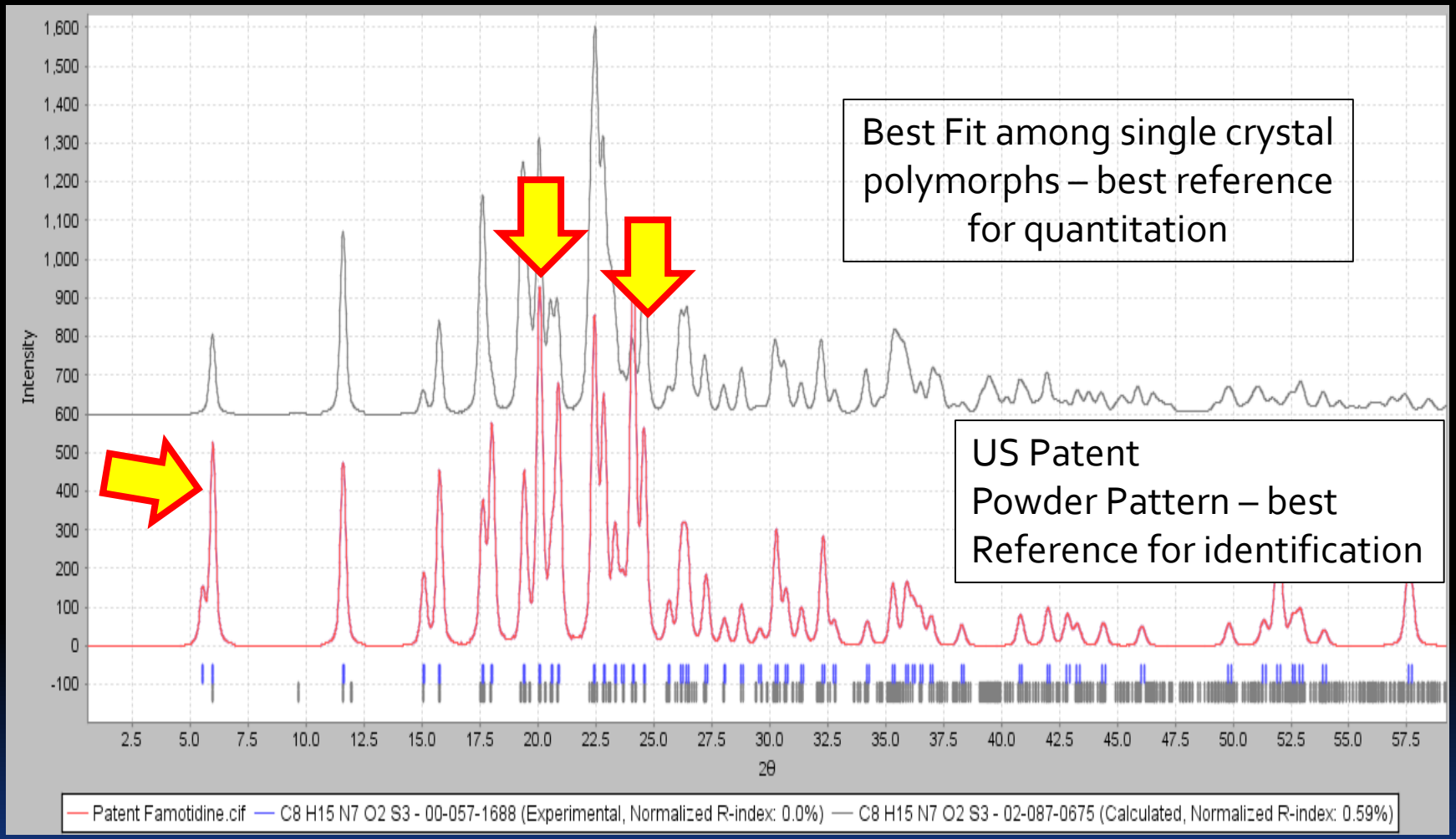
Pepcid AC

Calculated pattern
Experimental amorphous pattern
Experimental nano pattern





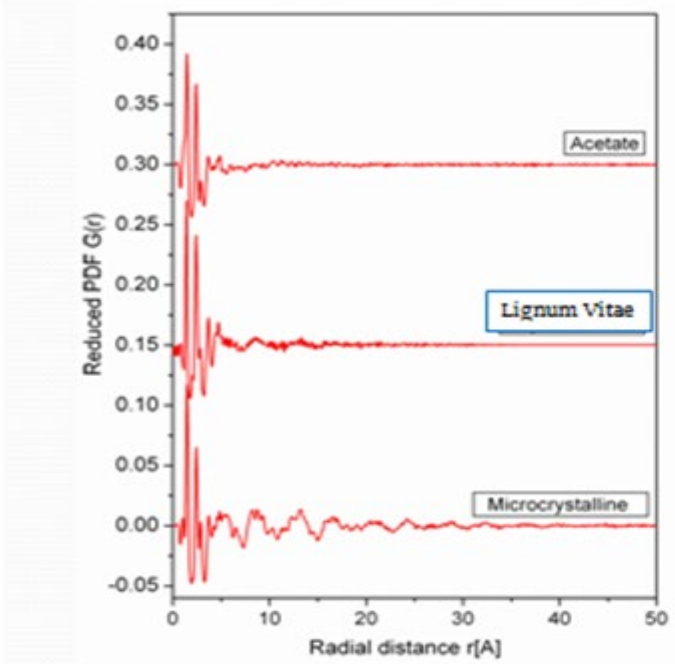
Famotidine – Similarity Index

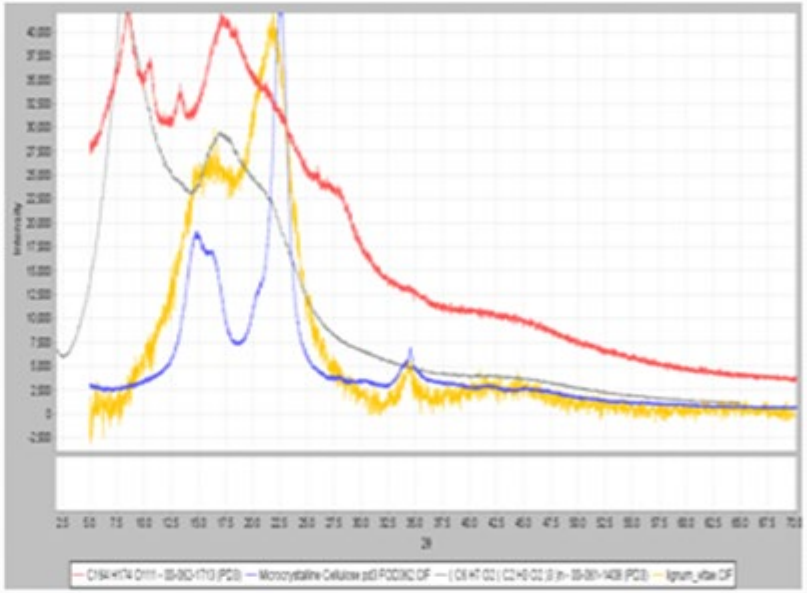


Patent exhibits orientation along (h o o)

Data on Pepcid AC matches patent data over single crystal !

Amorphous and nanocrystalline patterns





Often requires support analytical data to help with the diffraction pattern interpretations. In this case the PDF confirms that in some cases the materials are nanocrystalline and in other cases the materials are amorphous. In these cases the support data are included with the PDF reference.

Conclusions

- PDF-4/Organics is designed for material identification and characterization
- Database, data mining and identification software are all being continuously improved – expanding analysis capabilities for identification and characterization
- Feedback from users and members redesigns the database

(2012 Global User Survey)

PDF-4/Organics

PUBLICATION

Theresa Kahmer, *Publication Manager*
Saorya Kabekkodu, *Editor-in-Chief*
Stacy Gates, *Senior Scientific Editor*
Amy Gindhart, *Senior Scientific Editor*
Michael Carr, *Scientific Editor*
Diane Sagnella, *Senior Scientific Programmer*
Lisa Lanna, *Editorial Coordinator*
Vesna Bosnic, *Senior Database Programmer*
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Jackie Hollencamp, *PDF Technician*
Beverly Dickson, *Publishing Manager*

SCIENCE

Cyrus Crowder, *Principal Scientist*
Fanglin Needham, *Senior Scientist*
Joseph Sunseri, *Information Technology Manager*
Greg Haschak, *Desktop Support Specialist*
Monika Kottenhahn, *Webmaster*
Charles Weth, *Senior Software Engineer*
Yuming Si, *Senior Software Engineer*
Justin Blanton, *Senior Software Engineer*
David Crane, *Software Engineer*
John Torbet, *Software Engineer*

CONFERENCE SERVICES

Theresa Maguire, *Manager of Conference Services*
Denise Flaherty, *Conference Coordinator*
Eileen Jennings, *Education Coordinator*
Tess Kozul, *Conference Assistant*