X-RAY POWDER DIFFRACTION DATABASE TOOLS FOR THE PHARMACEUTICAL SCIENTIST: NEW CAPABILITIES

C. E. Crowder, F. Needham, T. G. Fawcett,
S. Kabekkodu, J. Blanton, D. Crane, C. Weth

International Centre for Diffraction Data

This document was presented at PPXRD - Pharmaceutical Powder X-ray Diffraction Symposium

Sponsored by The International Centre for Diffraction Data

PPXRD Website – www.icdd.com/ppxrd

ICDD Website - www.icdd.com

PDF Databases

The Powder Diffraction File

Data Entry Source	2009 PDF-2	2009 PDF-4+	2009 PDF-4/Minerals	2010 PDF-4/Organics
00- ICDD	104,056	104,056	11,180	31,534
01- FIZ	104,487	64,090*	12,727*	4,181
02- CCDC	0	0	0	371,031*
03- NIST	10,067	4,480*	237*	27
04- MPDS	0	118,814	10,068	0
Total No. of Data Sets	218,610	291,440	34,212	406,773
New Entries in 2009	7,503	19,354**	4,605	35,929
Total No. with atomic coordinates	0	125,329	10,762	452

DDView+ is database access / data mining software that is packaged with the three PDF-4 databases

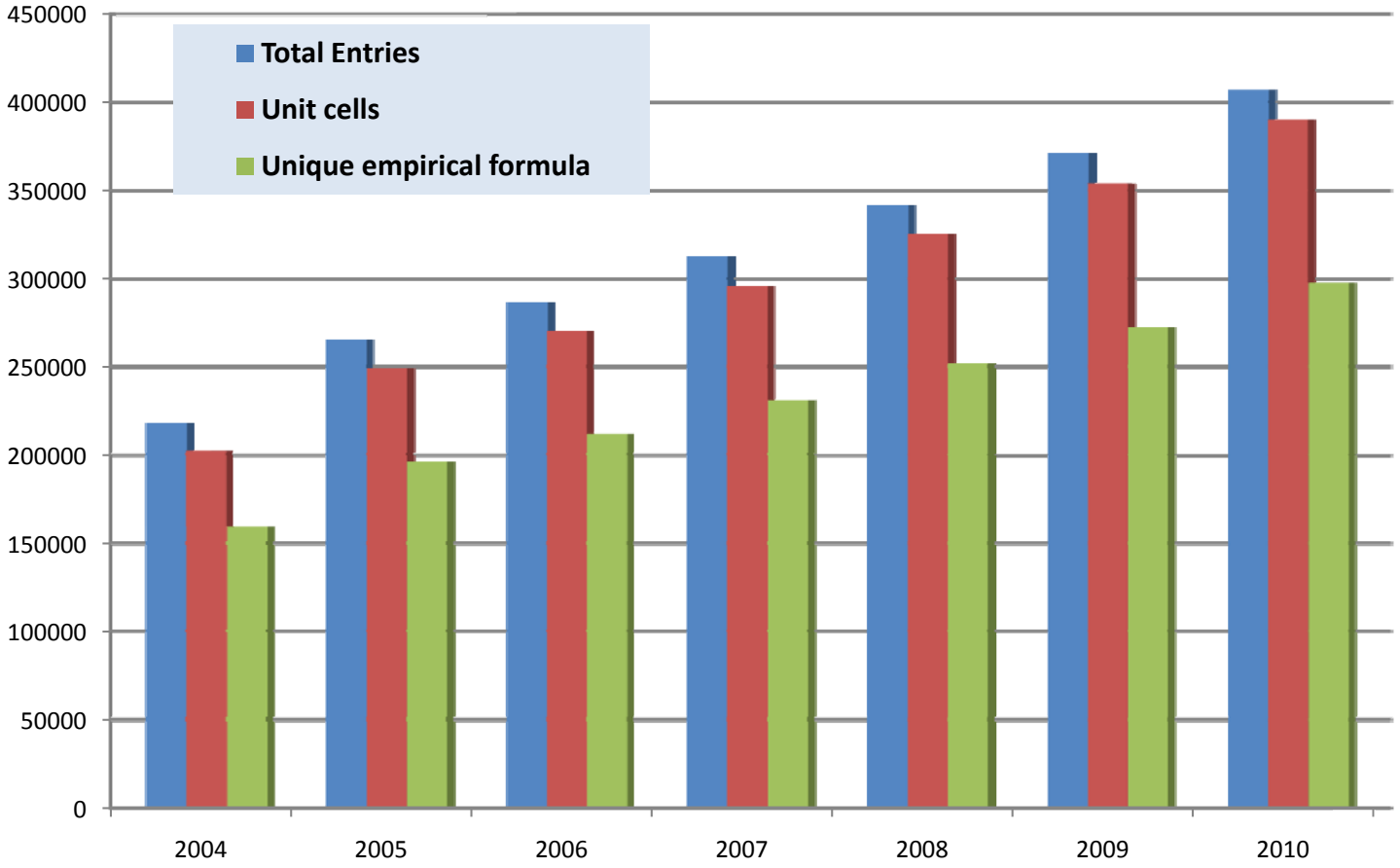
SIeve+ is search/match software designed to work with the three PDF-4 databases

DDView and SIeve are the corresponding products designed to work with the PDF-2 database

ISO 9001:2008 QUALITY ASSURED COMPANY CERT.NR. 11409.1

ICDD

Growth of Organics PDF Database

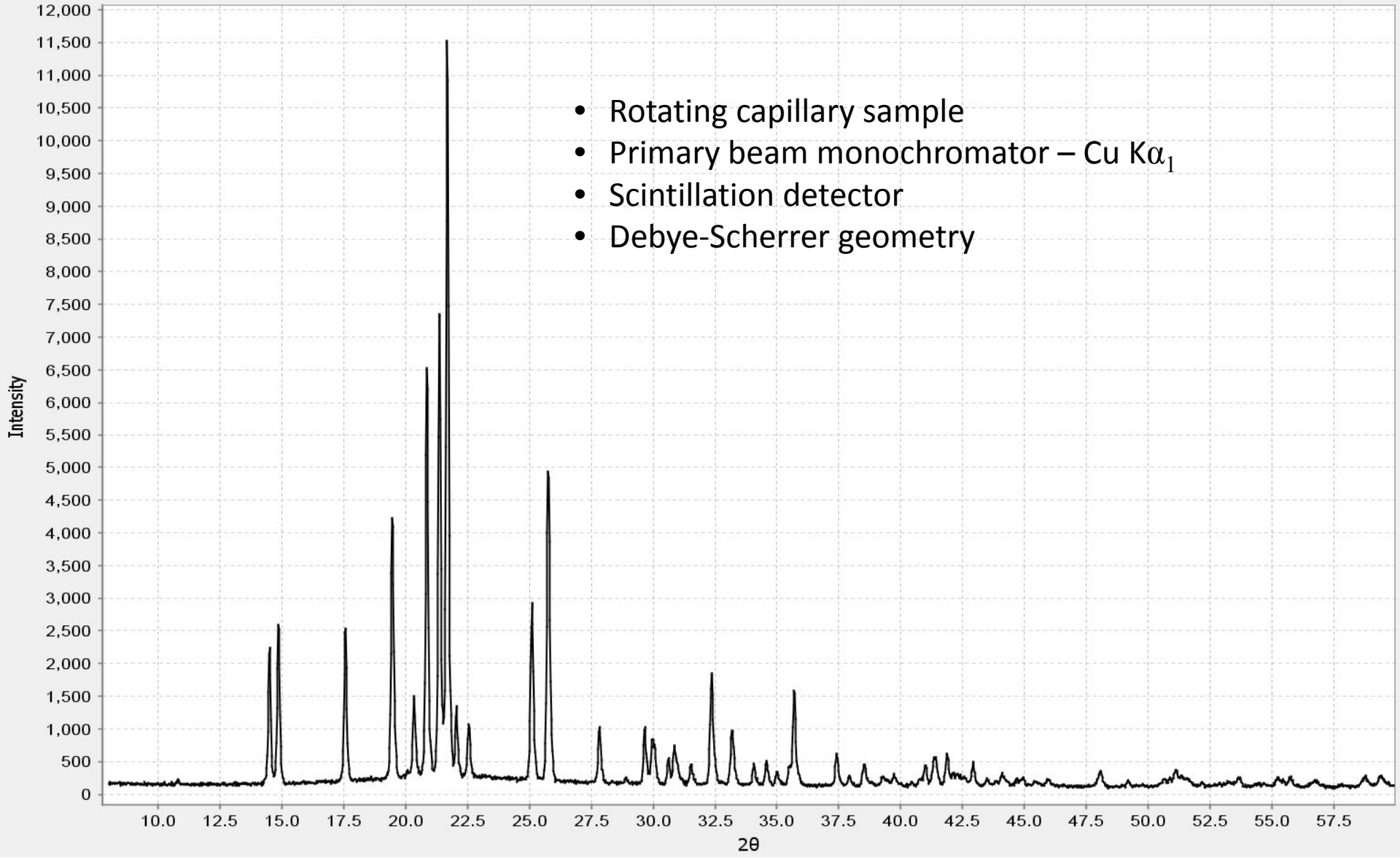


PDF-4 Organics Improvements

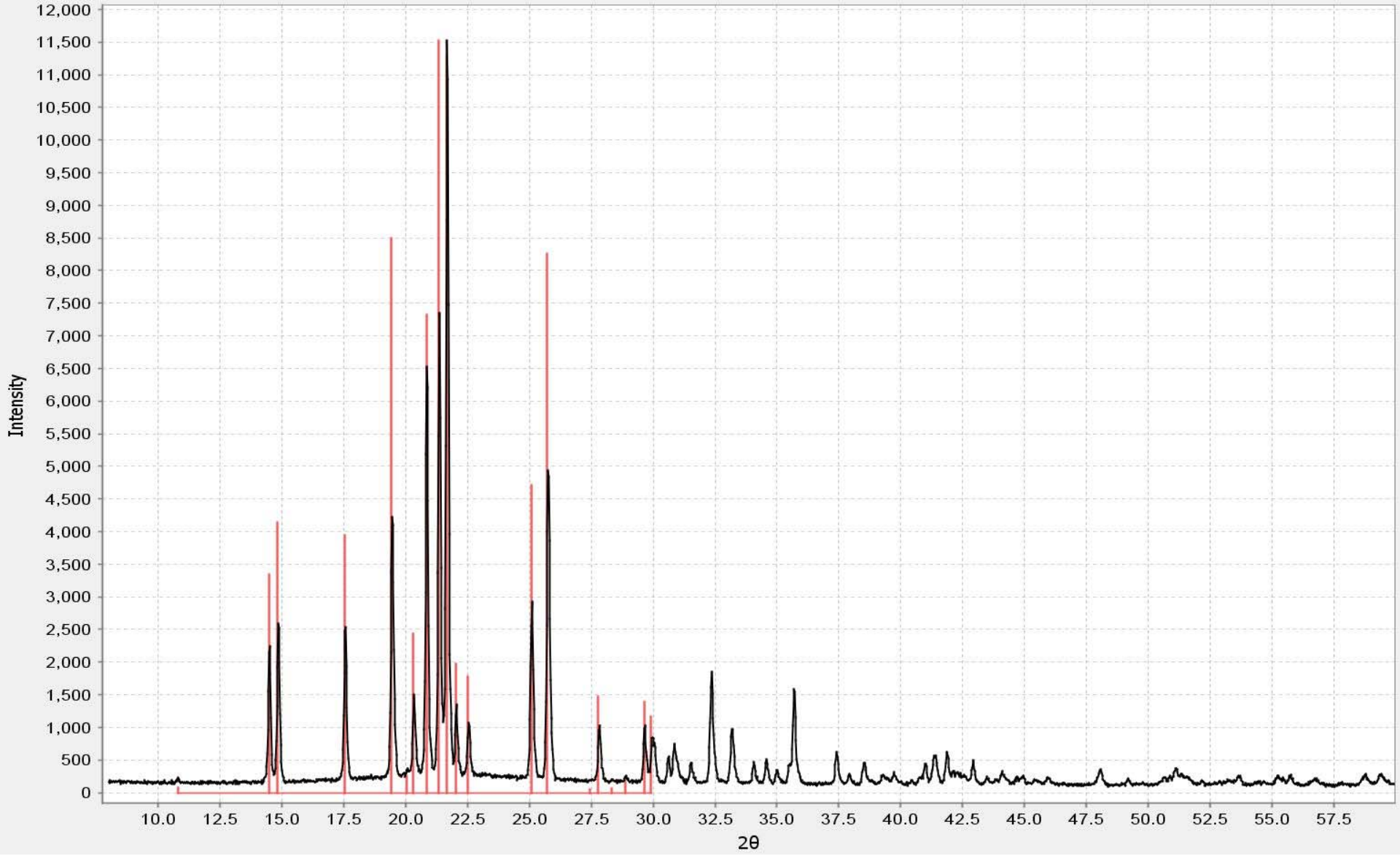
- Calculated patterns now extend to 60° 2θ (1.54 Å)
- New subfile designations
- Common reference standards added
- Raw data included for selected patterns (PD3)
- Peak profile parameters for instrument and/or crystallite size broadening functions are available for pattern simulations
- 2D ring pattern and electron diffraction spot pattern simulations
- Extensive data mining capabilities – polymorph mining

Calculated patterns now extend to 60° 2θ (1.54 Å)

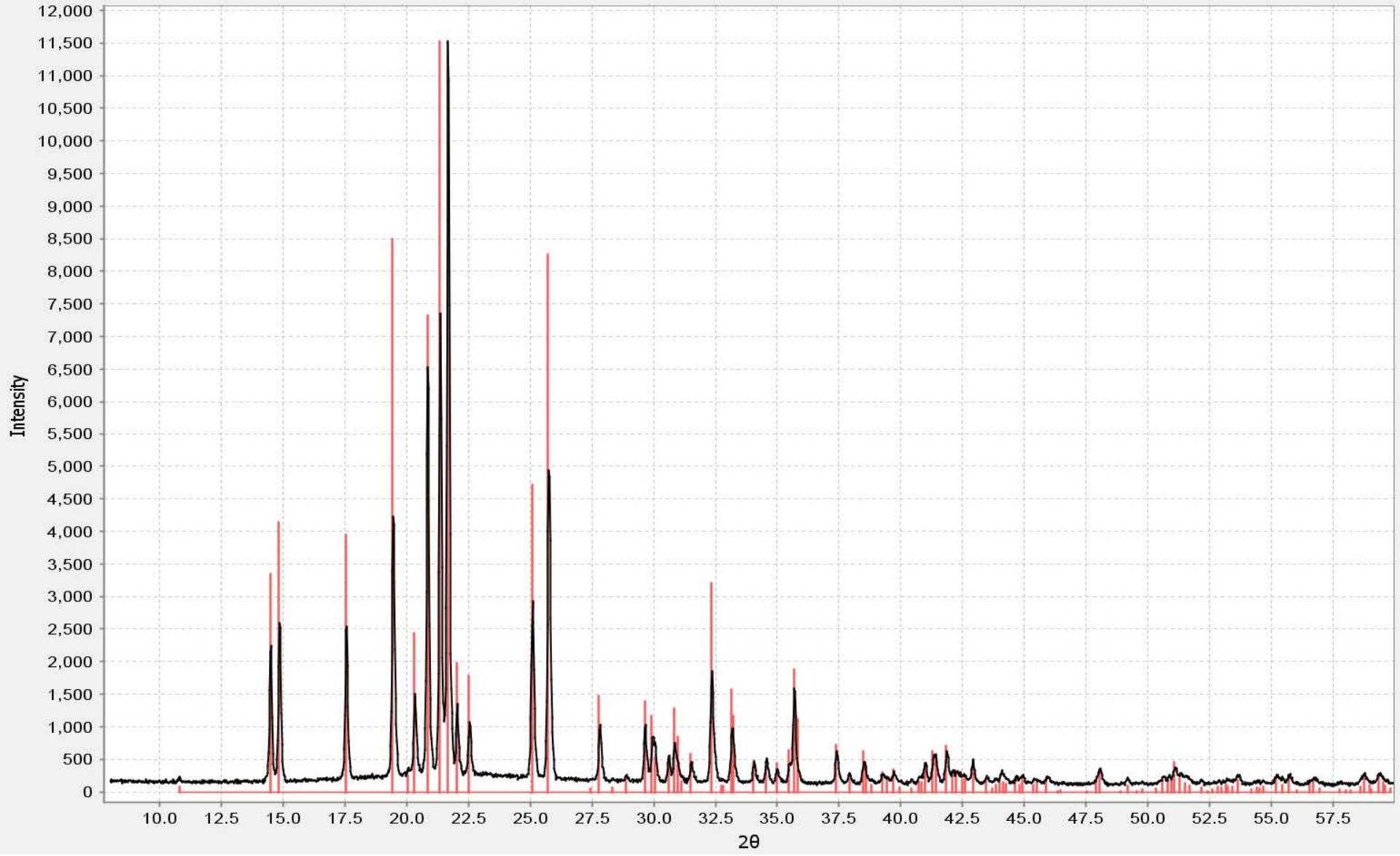
- Majority of the PDF-4 Organics database is derived from the Cambridge Structural Database (CSD)
- These calculated powder patterns were expanded for the 2009 product to include peak positions out to 60° 2θ (Cu Kα)
- Number of compiled d-spacings jumped from 22,389,668 in 2008 to 66,275,578 in 2009. The 2010 product includes 73,236,747 d-spacings



Piracetam (2-oxo-1-pyrrolidine acetamide) - enhances cognition and memory, slows brain aging, increases blood flow and oxygen to the brain. Used for stroke recovery and ameliorating Alzheimer's, Down's syndrome, dementia, and dyslexia.

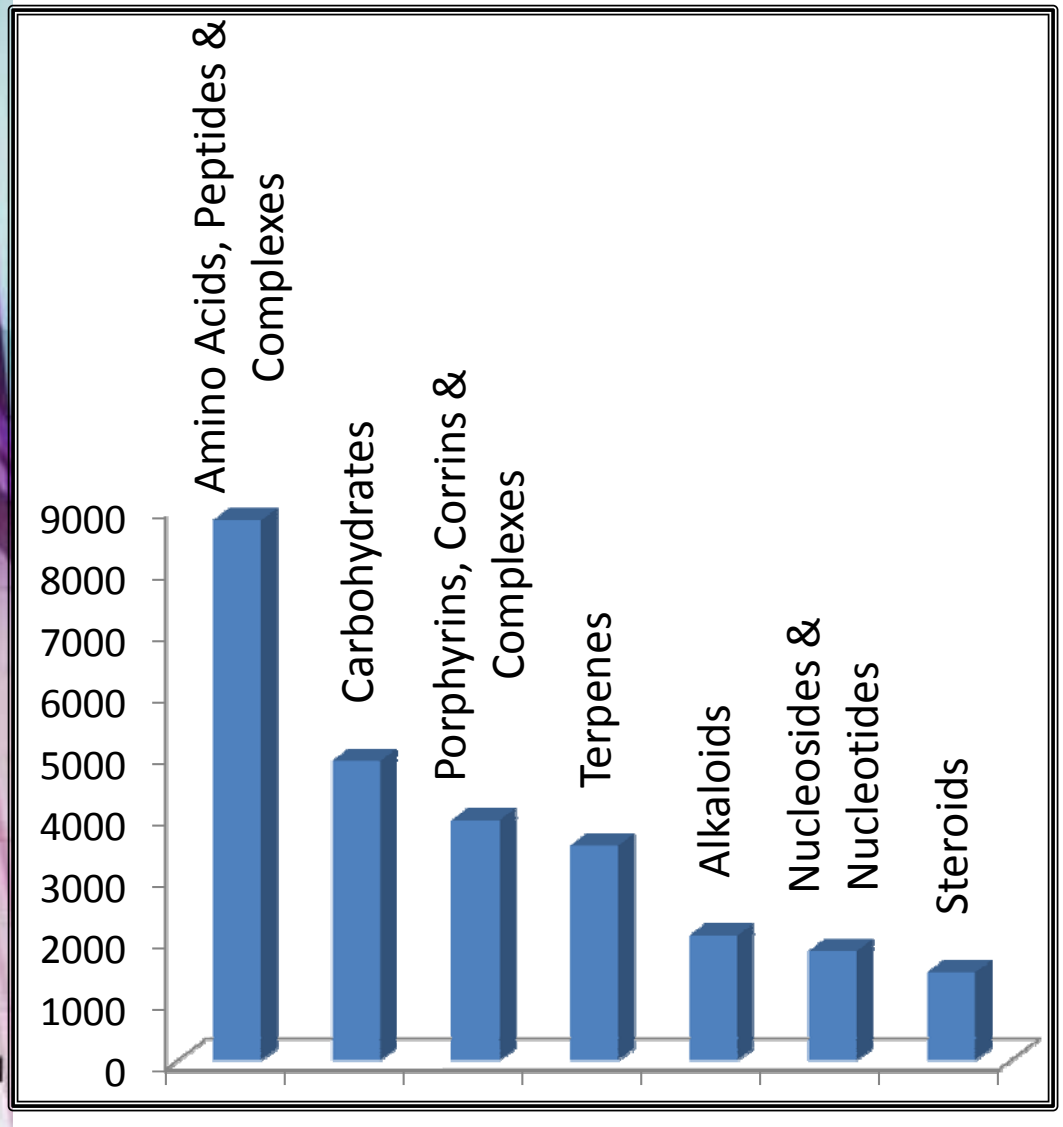


First 30° confirms identity of Piracetam, but does not confirm that all peaks belong to this phase, i.e., does not confirm purity.



With reference lines to 60° 2θ, single phase purity is more definitely confirmed.

New Subfile Designations



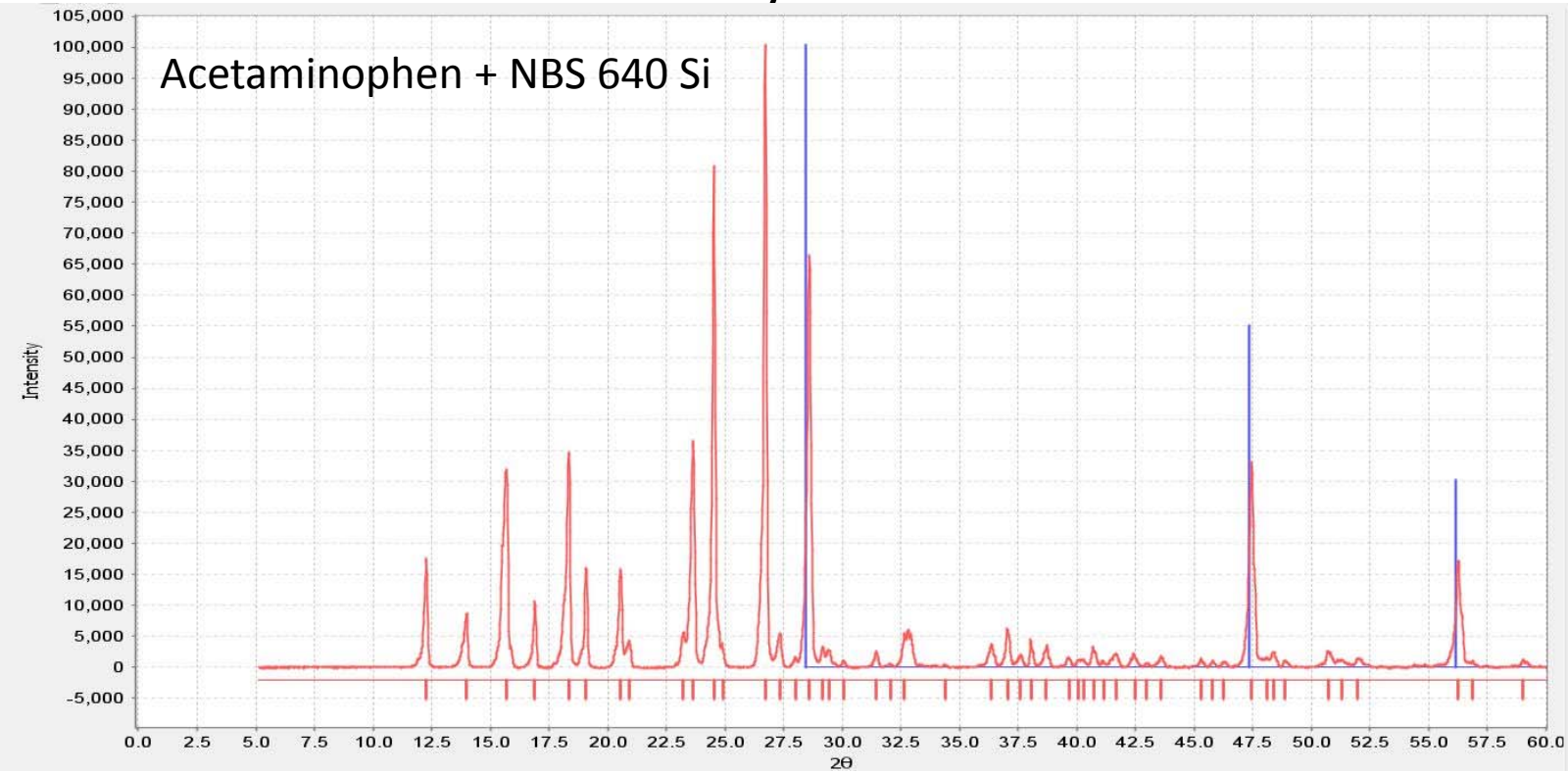
For the PDF-4+ Organics 2010, these 7 subfile designations have been added from the Cambridge Structural Database for PDF database screening and mining applications.

Subfiles already existing:

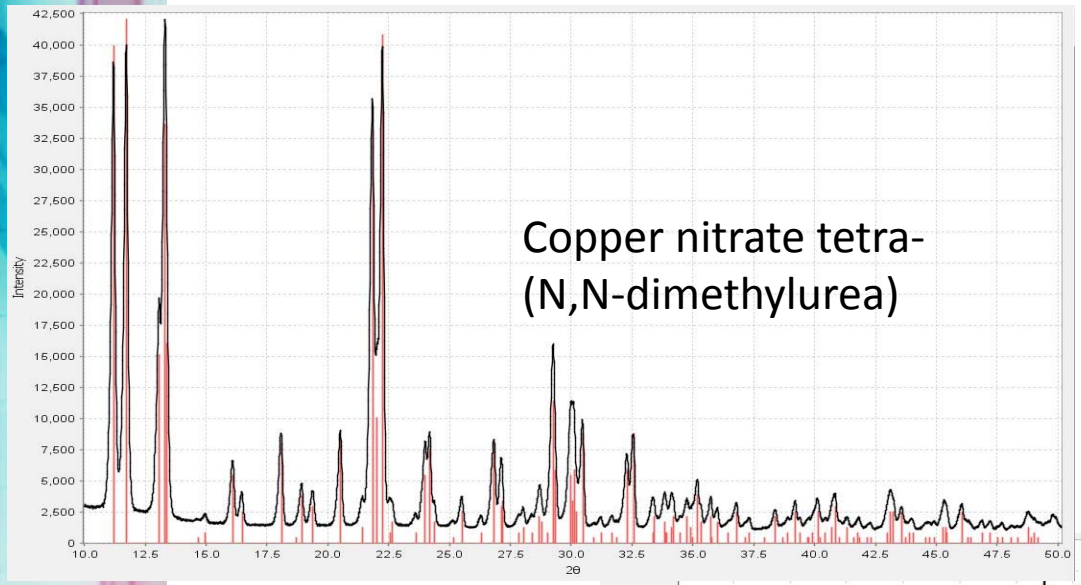
- Pharmaceutical – 5262
- Excipients – 1861
- Merck index – 1574

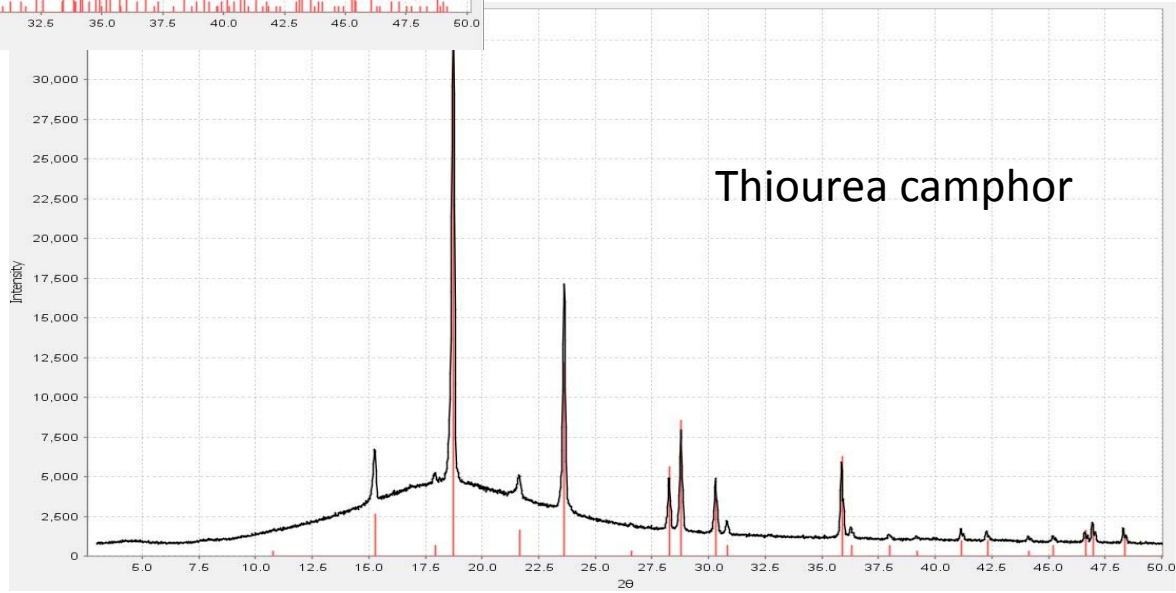
Reference Materials Added

204 standard reference patterns produced by NBS between 1953 and 1988 for commonly-used internal standards have been added to the PDF-4+ Organics database. This has been done to make the database more stand-alone in an analytical environment.



Raw data has been included with 1,892 entries in the PDF-4+ Organics 2010 database

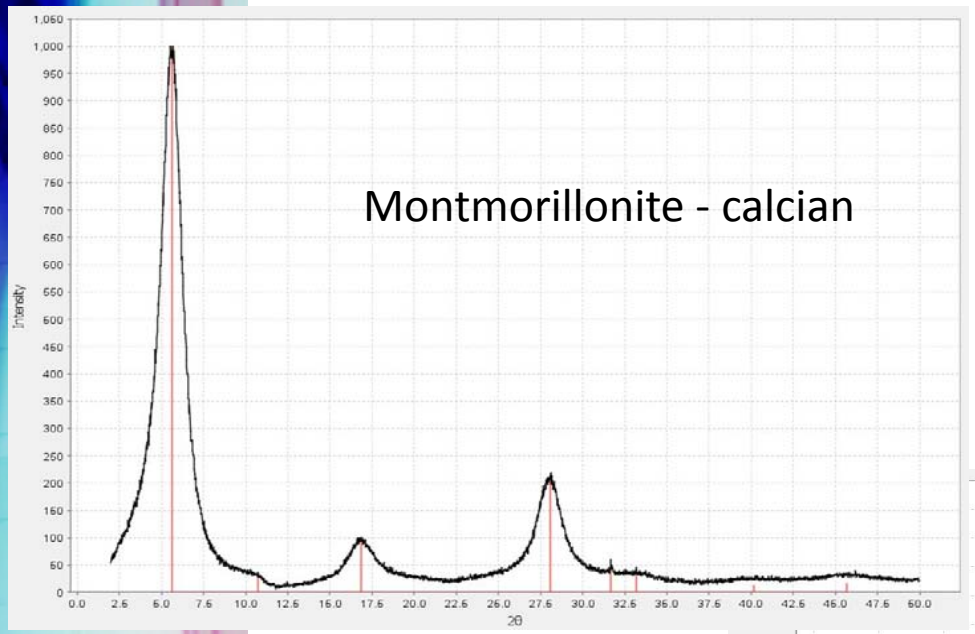


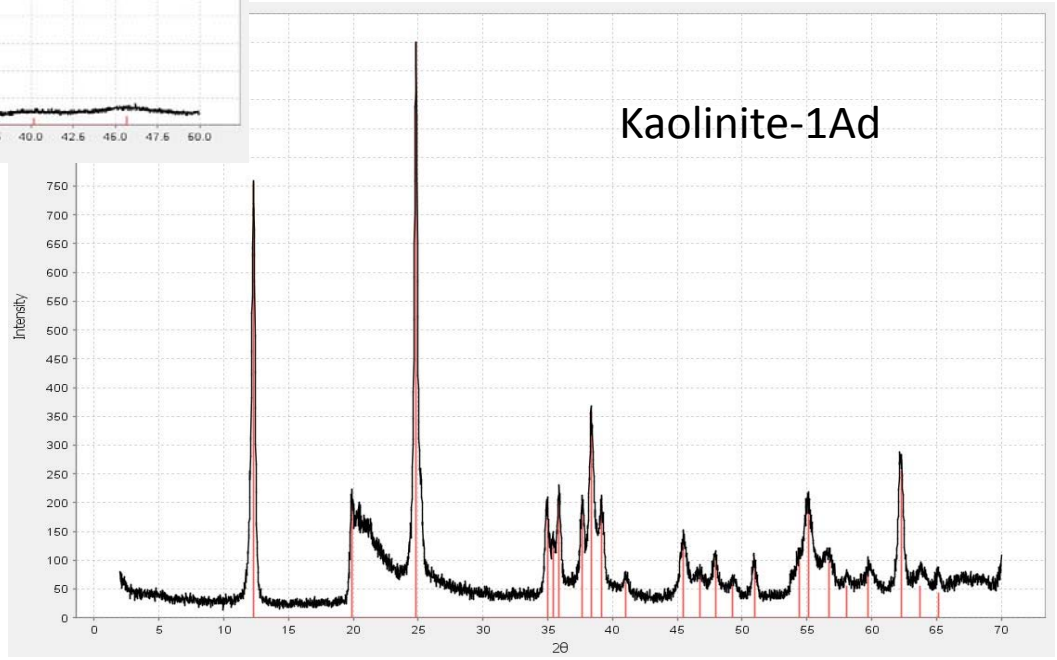


ISO 9001:2008 QUALITY ASSURED COMPANY CERT. NR. 11409.1

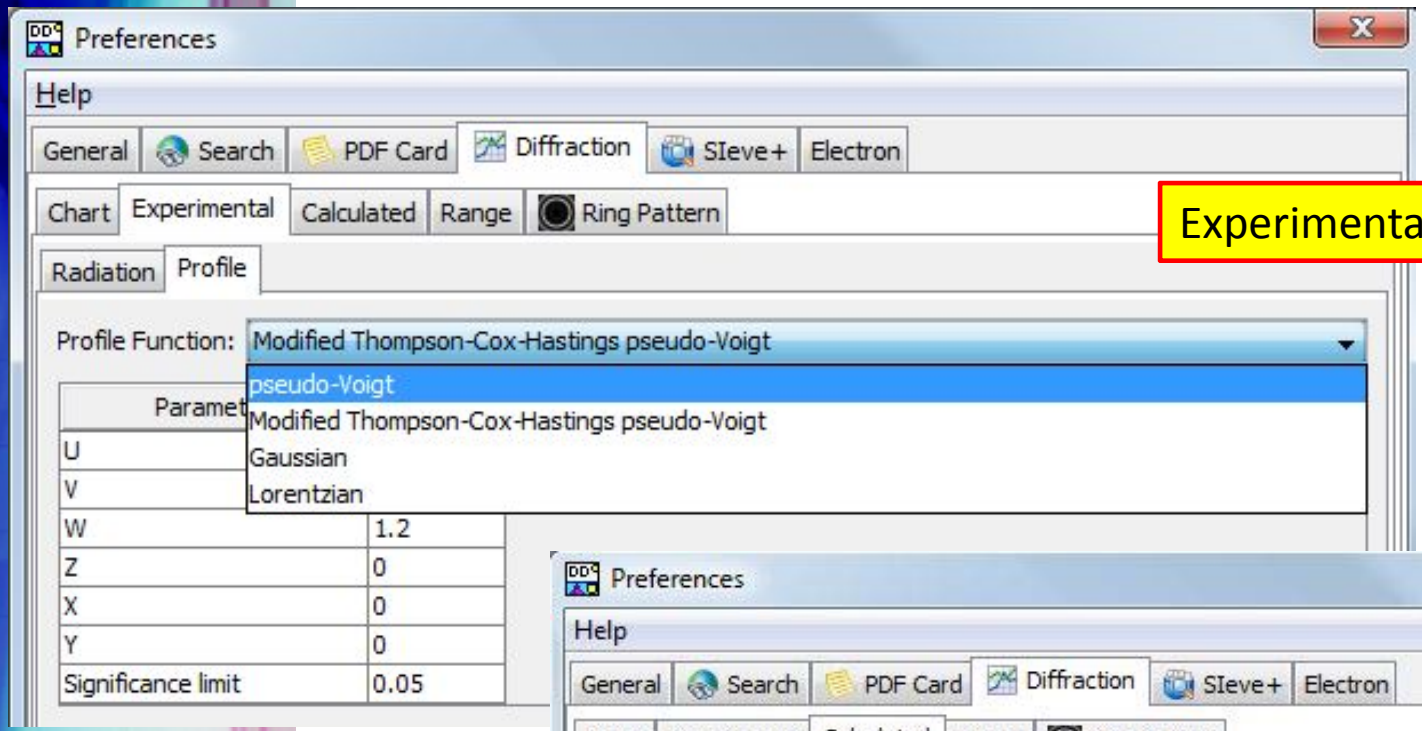
ICDD

Examples of Clay Mineral PD3 Patterns from the PDF-4+ 2009 Inorganic Database

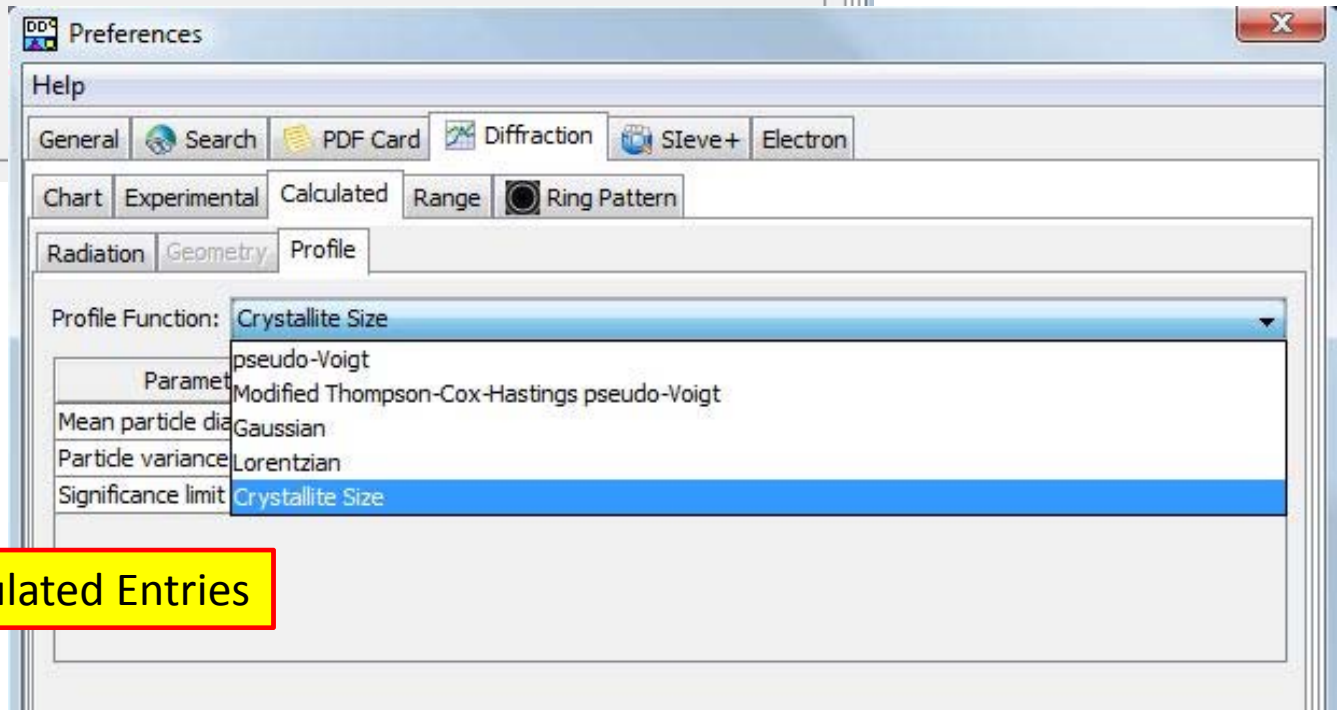




User Control of Pattern Simulation

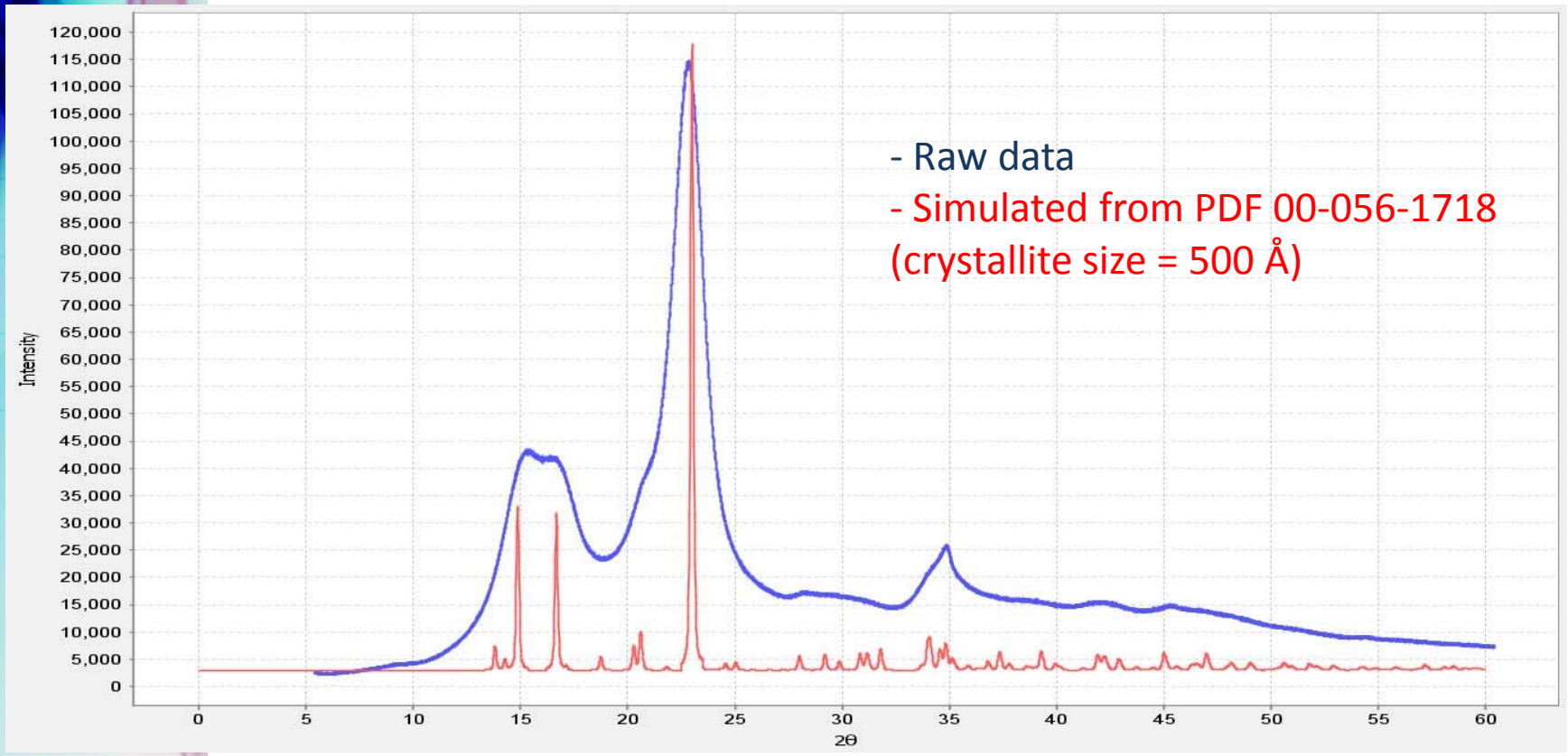


Experimental Entries

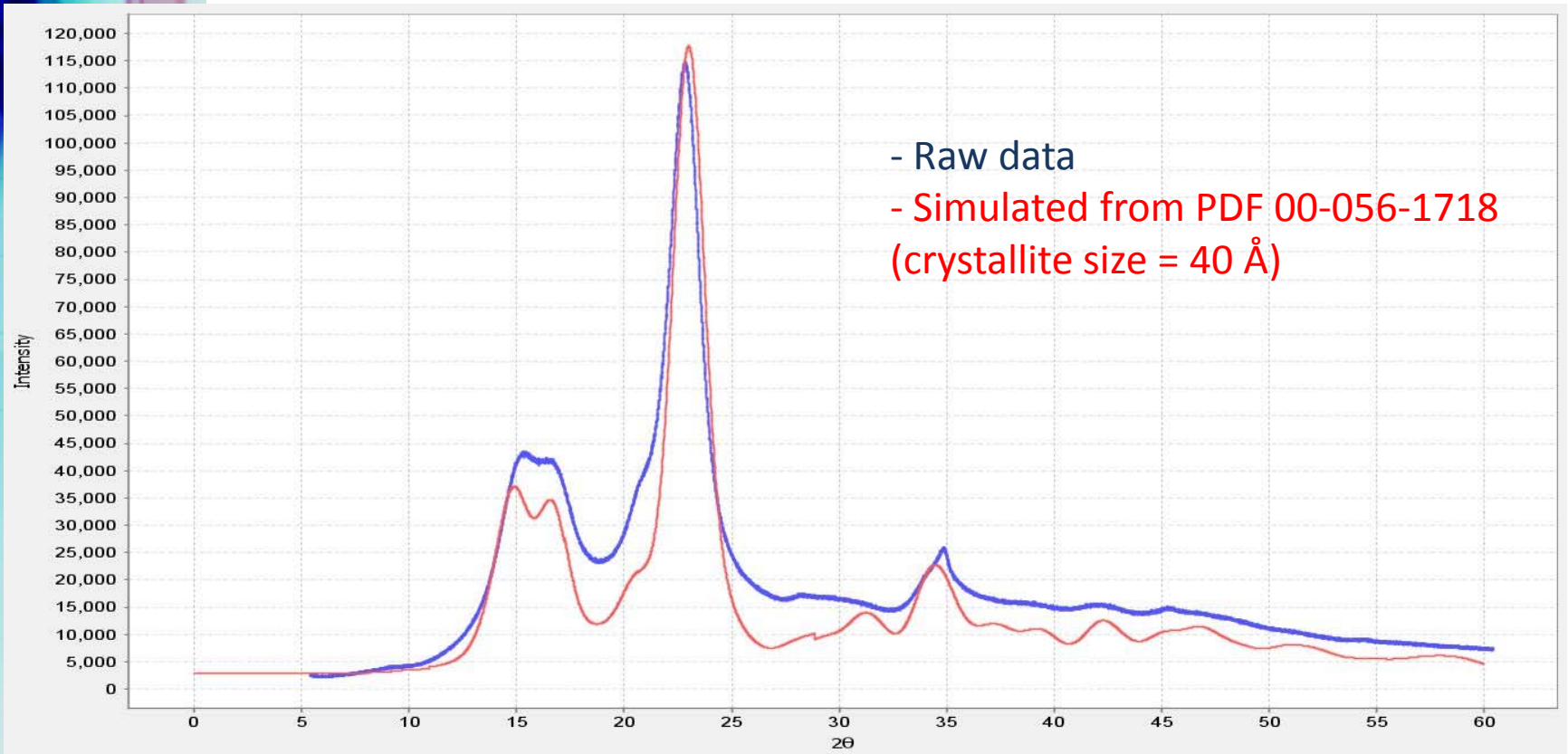


Calculated Entries

Cellulose 1β



Cellulose 1β



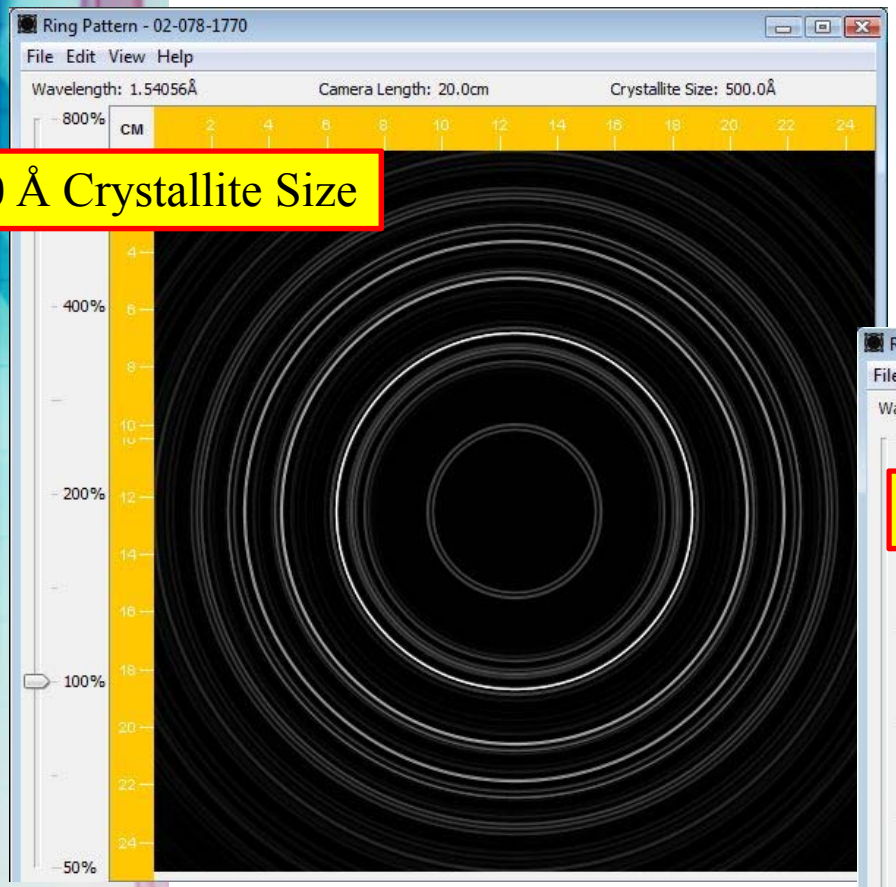
New Simulation Tools

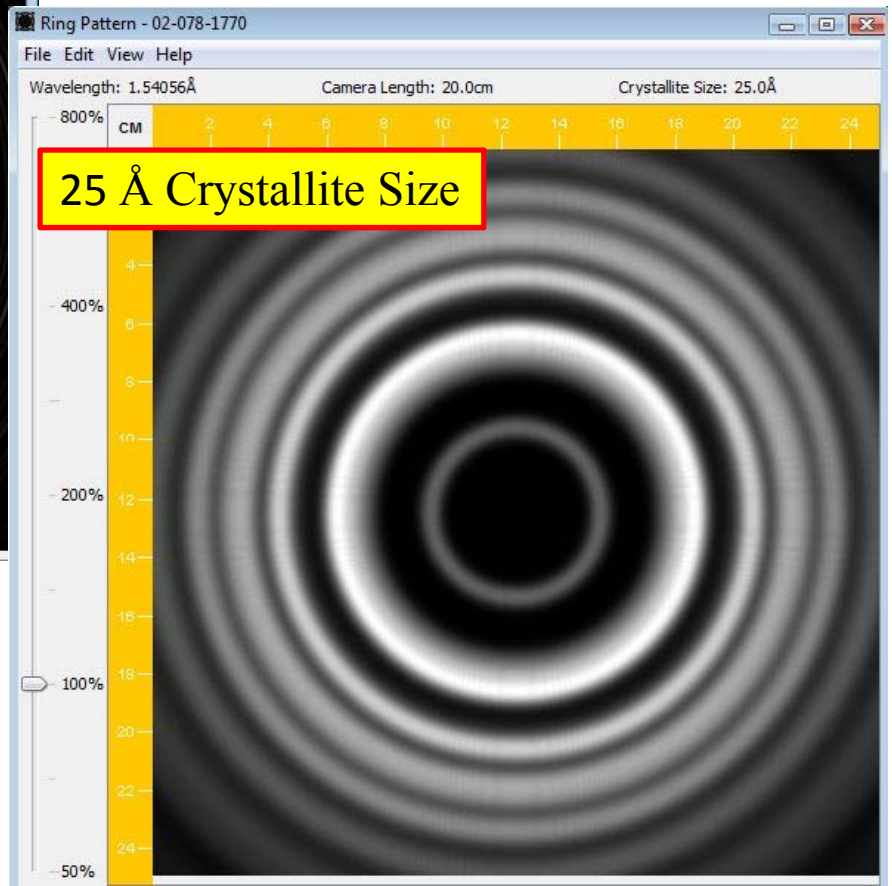
Ring Patterns

2-dimensional simulations of X-ray patterns can be performed for a given phase to show how it would appear on a flat 2-dimensional detector such as photographic film, phosphor image plates, or solid state arrays.

The current version of the simulation assumes no preferred orientation in the specimen, uniaxial positioning of the detector (transmission geometry with incident beam centered) and an infinite number of randomly oriented crystallites.

Ring Pattern for Ranitidine Hydrochloride Polymorph II





Selectable Parameters

- Wavelength
- Plot size
- Camera length
- Crystallite size

ISO 9001:2008 QUALITY ASSURED COMPANY CERT.NR. 11409.1

ICDD

New Simulation Tools

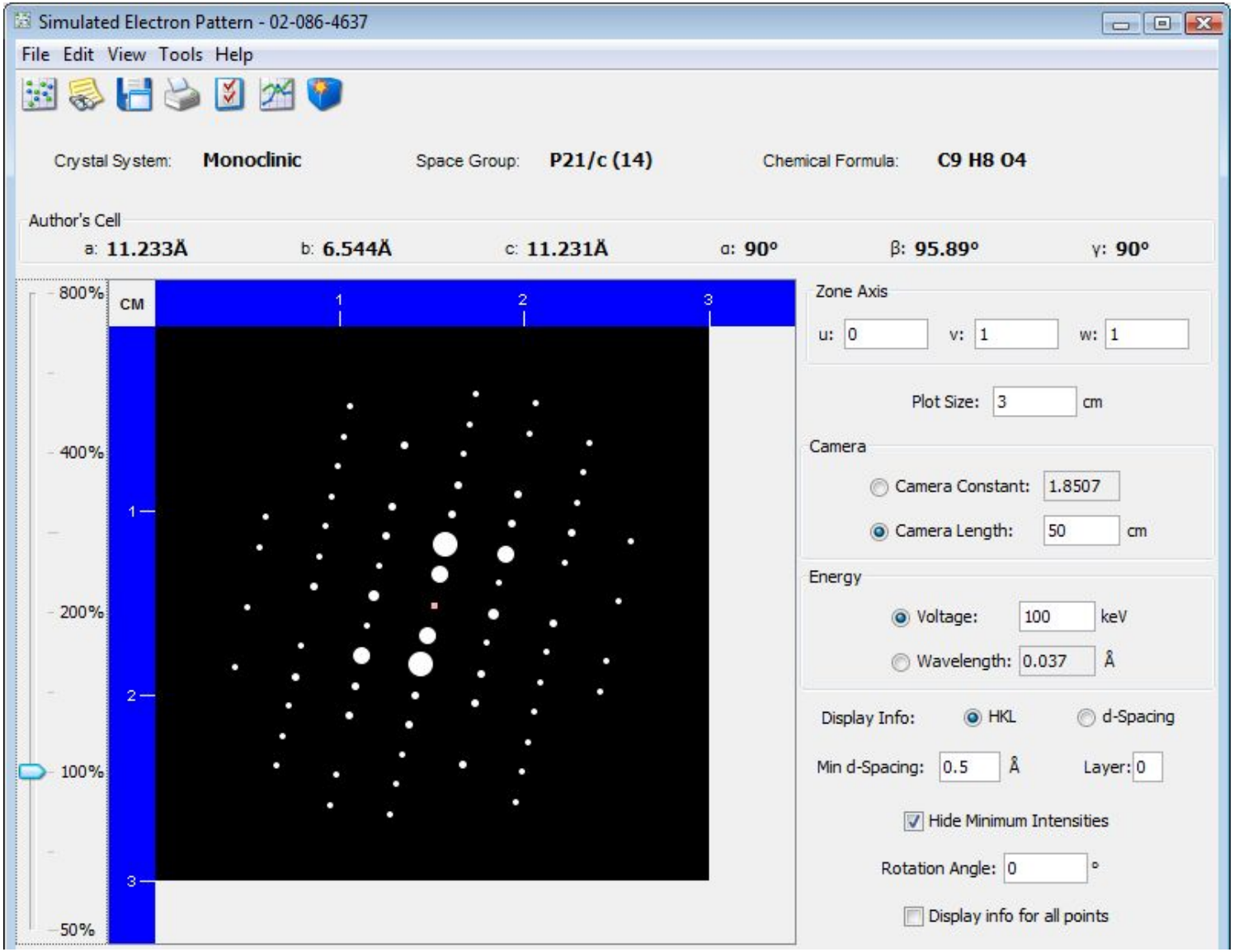
Electron Diffraction Spot Patterns

Positions and kinematic spot intensities are simulated for a given zone for any entry in the database. If the entry is derived from a single crystal structure, true electron scattering structure factors are used to compute the spot intensity.

For experimental X-ray entries, the electron spot intensity is approximated using the given X-ray line intensity divided by the multiplicity.

A concurently displayed parameter form allows for quick modifications of the simulation.

Simulated Electron Diffraction Pattern Aspirin 011 Zone Axis



Data Mining Capabilities

More search criteria including . . .

- Elemental weight%
- Elemental atomic %
- Literature reference volume & page
- Presence of atomic coordinates
- Presence of raw XRPD pattern

Search Criteria

Database/Subfile
- Database (5)
- Status (3)
- Ambient/Non-ambient (4)
- Quality Mark (8)
- Subfile/Subclass (27/13)

Names Search
- ***Compound Name***
- ***Common Name***
- Mineral Name
- ***All Names***

Miscellaneous Searches
- ***First 3 d-spacings***
- ***Strongest 3 d-spacings***
- ***Density, measured or calculated***
- I/I_c
- Melting Point
- Color
- ***Organic Functional Group***
- ***Comments (words, phrases)***

Full Periodic Table Element Search
- ***103 elements with 'And', 'Or', 'Only', 'Just', and 'Not' Boolean operators & combinations***

Reference Search
- Author, Journal, Journal Coden, Title, CAS#, Year, Volume, Page

Formula Search
- ***Empirical Formula***
- Formula Type (i.e., AB_3)
- ***Weight% Composition***
- ***Atomic% Composition***
- # of Elements

Crystal Information Search
- ***Author-Defined Space Group***
- ***Crystal Symmetry***
- ***Author's Cell - a, b, c, α, β, γ, Volume, Molecular Volume, c/a, a/b, c/b***
- ***Crystal Data Cell - a, b, c, α, β, γ, Volume***
- ***Reduced Cell - a, b, c, α, β, γ, Volume***
- Centrosymmetric/Non-centrosymmetric
- Pearson Symbol Codes
- Atomic Coordinates Present
- Prototype Structure

Using Supporting Analyses

C, H, & N analysis:

81.5 % C

8.7 % H

3.0 % N

Using ± 0.2% . . .

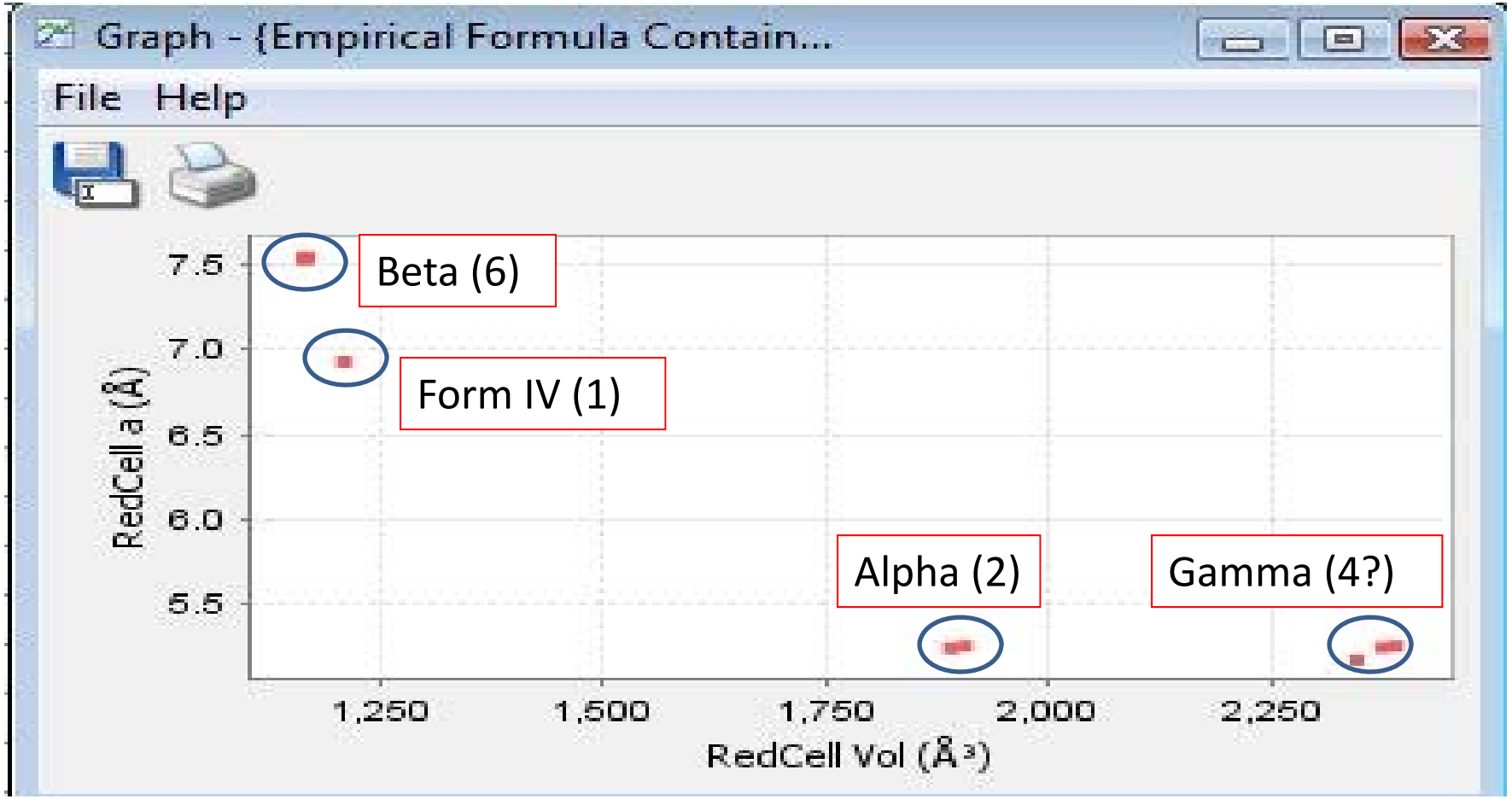
PDF #	Empirical Formula	Chemical Formula	Compound Name
00-041-1943	C32 H41 N O2	C32 H41 N O2	Terfenadine
00-053-1940	C32 H41 N O2	C32 H41 N O2	Terfenadine
02-078-8973	C31 H39 N O2	C31 H39 N O2	11beta-(4-(N,N-Dimethylamino)phenyl)-17...

Searching for Known Polymorphs: Carbamazepine

- Searched: All Names = 'carbamazepine', and Empirical Formula = 'C_{15} H_{12} N_2 O'
- 19 hits in PDF-4+ Organics 2010 database
- 12 have cell parameter and space group information
- 5 different space group designations (1,2,14,15,148)

PDF # ▲	Empirical Formula	Compound Name	Common Name	SPGR	SG #	RedCell c	RedCell b	RedCell a	RedCell Vol
00-033-1565	C15 H12 N2 O	β-Carbamazepine	β-5H-dibenz(b,f)azepine-5-carboxamide	P21/n	14	13.918	11.159	7.543	1170.07
00-033-1566	C15 H12 N2 O	α-Carbamazepine							
00-040-1554	C15 H12 N2 O	β-Carbamazepine	β-5H-dibenz(b,f)azepine-5-carboxamide	P21/n	14	13.912	11.156	7.537	1168.30
00-043-1988	C15 H12 N2 O	α-Carbamazepine	α-5H-dibenz(b,f)azepine-5-carboxamide						
00-043-1989	C15 H12 N2 O	β-Carbamazepine	β-5H-dibenz(b,f)azepine-5-carboxamide						
00-043-1997	C15 H12 N2 O	β-Carbamazepine	β-5H-dibenz(b,f)azepine-5-carboxamide						
00-043-1998	C15 H12 N2 O	α-Carbamazepine	α-5H-dibenz(b,f)azepine-5-carboxamide	R-3	148	20.544	20.544	5.253	1906.09
00-046-1813	C15 H12 N2 O	Carbamazepine	5H-dibenza(b,f)azepine-5-carboxamide						
00-051-2106	C15 H12 N2 O	β-Carbamazepine	5H-dibenz(b,f)azepine-5-carboxamide	P21/n	14	13.918	11.156	7.539	1169.22
00-054-2015	C15 H12 N2 O	Carbamazepine	5H-dibenz(6,f)azepine-5-carboxamide, ca...	P1	1	22.258	20.520	5.245	2374.48
00-056-1968	C15 H12 N2 O	γ-Carbamazepine	5H-dibenz(b,f)azepine-5-carboxamide	P-1	2	22.294	20.584	5.253	2388.71
00-057-1449	C15 H12 N2 O	Carbamazepine	5H-dibenz(b,f)azepine-5-carboxamide	P-1	2	22.245	20.574	5.170	2344.82
00-058-1418	C15 H12 N2 O	Carbamazepine	5H-dibenz(b,f)azepine-5-carboxamide	R		20.484	20.484	5.240	1890.23
00-058-1419	C15 H12 N2 O	Carbamazepine	5H-dibenz(b,f)azepine-5-carboxamide						
02-060-9919	C15 H12 N2 O	5H-Dibenz(b,f)azepine-5-carboxamide	Carbamazepine	P21/c	14	13.902	11.148	7.529	1165.34
02-060-9920	C15 H12 N2 O	5H-Dibenz(b,f)azepine-5-carboxamide	Carbamazepine	P21/n	14	13.912	11.156	7.537	1168.30
02-064-1948	C15 H12 N2 O	5-Carbamoyl-5H-dibenzo(b,f)azepine	Carbamazepine	P21/n	14	13.917	11.150	7.534	1167.55
02-084-2534	C15 H12 N2 O	Carbamazepine	5H-Dibenz(b,f)azepine-5-carboxamide	P-1	2	22.245	20.574	5.170	2344.82
02-086-6230	C15 H12 N2 O	Carbamazepine		C2/c	15	13.957	13.748	6.927	1210.96

Carbamazepine – Separating the Polymorphs: a-axis Length vs Reduced Cell Volume

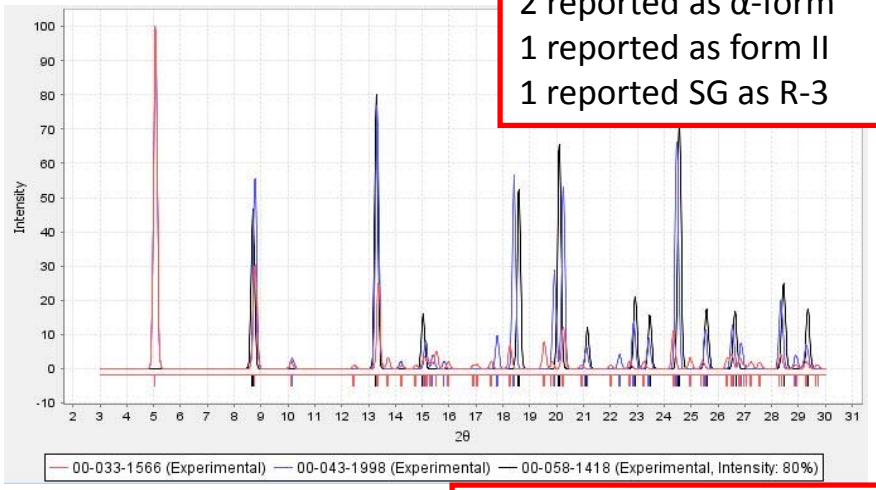


Here, the groupings have been labeled based on information from the 'Compound Name' or 'Comments' field from at least one member of the group

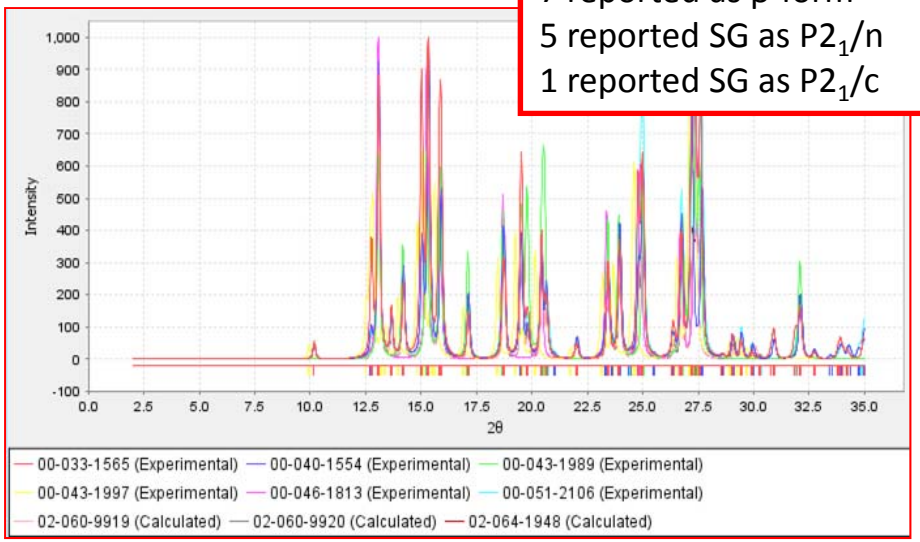
Grouping of Similar XRPD Patterns for 19 Carbamazepine PDF Entries

One can overlay the simulated patterns for all 19 PDF entries to establish four groups of similar patterns.
Note: Several entries with no space group or polymorphic form information have been reasonably assigned to one of these four groups.

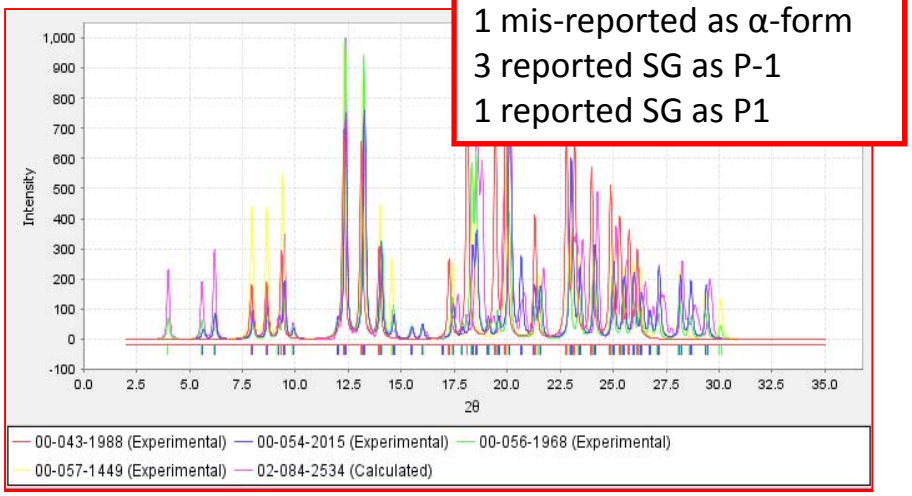
<u>3 entries</u> (no CSD entry)
2 reported as α-form
1 reported as form II
1 reported SG as R-3



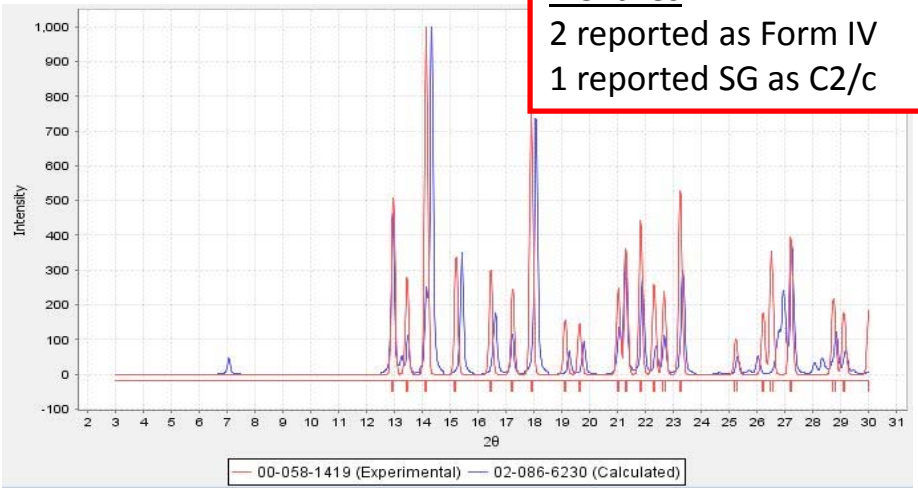
<u>9 entries</u>
7 reported as β-form
5 reported SG as $P2_1/n$
1 reported SG as $P2_1/c$



<u>5 entries</u>
1 reported as γ-form
1 mis-reported as α-form
3 reported SG as P-1
1 reported SG as P1



<u>2 entries</u>
2 reported as Form IV
1 reported SG as C2/c



Summary

- The PDF-4 Organics database continues to expand in size and scope
- The ICDD, along with many of our developer partners, have designed tools to take advantage of these added features
- The result is improved capability for solving pharmaceutical problems with XRPD.