

# Excipient Reference Data in the Powder Diffraction File (PDF®) for Phase Identification in Pharmaceutical Formulations

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# Why have excipients in ICDD® databases?

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The formulation of pharmaceutical drugs is a combinative process that incorporates a multitude of chemical constituents, which may be organic, inorganic, or polymeric in nature.

While the Active Pharmaceutical Ingredient (API) in a formulation is the key component that provides a drug its therapeutic functionality, excipients are generally the bulk of the content.

Due to the potential complexity of a diffraction pattern obtained from the analysis of a multiphase pharmaceutical drug, it is often necessary to analyze and identify all excipients before one can make an accurate identification of an API.

Currently, ICDD maintains an excipient subclass in the PDF that follows the list provided by the United States Pharmacopeia (USP). In PDF-4/Organics Release 2016, there are over 2,600 entries for excipient phases.

# Excipients

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Tablet and capsule formulations include

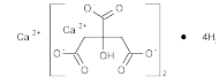
1. Diluents/fillers – increase the bulk content of the dosage form
2. Binders – promote cohesive compact during direct compression.
3. Disintegrants - breaks the dosage form into smaller particles when it comes in contact with a liquid
4. Lubricants - used to reduce the friction between the tablet and die cavity
5. Glidants - used to improve the flow property of the formulation
6. Coatings – applied to make swallowing easier, control release rate, extend storage life
7. Misc.
  - Flavorants - improve the flavor or give a pleasant taste to the formulation
  - Colorants - added to the formulation for visual appeasement and increase the patent compliance or for identification of the formulation
  - Adsorbants - used when there is an need to add a liquid or semisolid ingredient in the formulation

# Excipient reference - USP-NF



The USP 39-NF 34 is a combination of two compendia, the United States Pharmacopeia (USP) and the National Formulary (NF). It contains standards for medicines, dosage forms, drug substances, **excipients**, biologics, compounded preparations, medical devices, dietary supplements, and other therapeutics.

## Calcium Citrate



$\text{C}_{12}\text{H}_{10}\text{Ca}_3\text{O}_{14} \cdot 4\text{H}_2\text{O}$  570.49  
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, calcium salt (2:3), tetrahydrate;  
Calcium citrate (3:2), tetrahydrate [5785-44-4].

### DEFINITION

Calcium Citrate contains four molecules of water of hydration. When dried at 150° to constant weight, it contains NLT 97.5% and NMT 100.5% of  $\text{Ca}_3(\text{C}_6\text{H}_5\text{O}_7)_2$ .

### IDENTIFICATION

- A.** Analysis: Dissolve 0.5 g in a mixture of 10 mL of water and 2.5 mL of 2 N nitric acid. Add 1 mL of mercuric sulfate TS, heat to boiling, and add 1 mL of potassium permanganate TS.  
Acceptance criteria: A white precipitate is formed.

- B.** Sample: 0.5 g of Calcium Citrate  
Analysis: Ignite completely the *Sample* at as low a temperature as possible, cool, and dissolve the residue in dilute glacial acetic acid (1:10). Filter, and add 10 mL of ammonium oxalate TS to the filtrate.  
Acceptance criteria: A voluminous white precipitate that is soluble in hydrochloric acid is formed.

### ASSAY

#### PROCEDURE

Sample solution: Dissolve 350 mg of Calcium Citrate, previously dried at 150° to constant weight, in 12 mL of 0.5 M hydrochloric acid, and dilute with water to about 100 mL.

and 10 mL of 0.2 M edetate disodium. If necessary, adjust with 1 N sodium hydroxide or 1 N hydrochloric acid to a pH of 5.5. Transfer to a 100-mL volumetric flask, and dilute with water to volume. This solution contains 0.05 µg/mL of fluoride.

**Linearity solution B:** Transfer 5.0 mL of the *Standard solution* to a 250-mL plastic beaker, and proceed as directed for *Linearity solution A* beginning with "Add 50 mL of water,". This solution contains 0.25 µg/mL of fluoride.

**Linearity solution C:** Transfer 10.0 mL of the *Standard solution* to a 250-mL plastic beaker, and proceed as directed for *Linearity solution A* beginning with "Add 50 mL of water,". This solution contains 0.50 µg/mL of fluoride.

**Sample solution:** Transfer 1.0 g of Calcium Citrate to a 100-mL beaker. Add 10 mL of water and, while stirring, 10 mL of 1 N hydrochloric acid. When dissolved, boil rapidly for 1 min, transfer the solution to a 250-mL plastic beaker, and cool in ice water. Add 15 mL of 1.0 M sodium citrate and 10 mL of 0.2 M edetate disodium, and adjust with 1 N sodium hydroxide or 1 N hydrochloric acid to a pH of 5.5. Transfer this solution to a 100-mL volumetric flask, and dilute with water to volume.

**Electrode system:** Use a fluoride-specific, ion-indicating electrode and a silver-silver chloride reference electrode connected to a pH meter capable of measuring potentials with a minimum reproducibility of ±0.2 mV (see *pH* (791)).

### Analysis

**Samples:** *Linearity solution A*, *Linearity solution B*, *Linearity solution C*, and *Sample solution*  
Transfer 50 mL of each *Linearity solution A*, *Linearity solution B*, and *Linearity solution C* to separate 250-mL plastic beakers, and measure the potential of each solution with the *Electrode system*. Between each reading wash the electrodes with water, and absorb any residual water by blotting the electrodes dry. Plot the logarithms of the fluoride concentrations (0.05, 0.25, and 0.50 µg/mL, respectively) versus potential to obtain a Standard response line.

Transfer 50 mL of the *Sample solution* to a 250-mL plastic beaker, and measure the potential with the *Electrode system*. From the measured potential and the Standard re-

# Excipient – XRD method reference



USP-NF | Online

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## A. X-RAY DIFFRACTION (941)

**Sample A:** Add 2 g in small portions to 100 mL of water, with intense agitation. Allow to stand for 12 h to ensure complete hydration. Place 2 mL of the mixture so obtained on a suitable glass slide, and allow to air-dry at room temperature to produce an oriented film. Place the slide in a vacuum desiccator over a free surface of ethylene glycol. Evacuate the desiccator, and close the stopcock so that the ethylene glycol saturates the desiccator chamber. Allow to stand for 12 h.

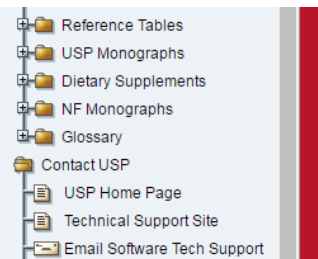
**Sample B:** Prepare a random powder specimen of Bentonite.

### Analysis

**Samples:** *Sample A* and *Sample B*

Record the X-ray diffraction pattern of the samples, and determine the  $d$  values.

**Acceptance criteria:** The largest peak in the pattern of *Sample A* corresponds to a  $d$  value between 15.0 and 17.2 Å. The major peak in the region between 1.48 and 1.54 Å from the pattern of *Sample B* is between 1.492 and 1.504 Å.



**Sample A:** Add 2 g in small portions to 100 mL of water, with intense agitation. Allow to stand for 12 h to ensure complete hydration. Place 2 mL of the mixture so obtained on a suitable glass slide, and allow to air-dry at room temperature to produce an oriented film. Place the slide in a vacuum desiccator over a free surface of ethylene glycol. Evacuate the desiccator, and close the stopcock so that the ethylene glycol saturates the desiccator chamber. Allow to stand for 12 h.

**Sample B:** Prepare a random powder specimen of Bentonite.

### Analysis

**Samples:** *Sample A* and *Sample B*

Record the X-ray diffraction pattern of the samples, and determine the  $d$  values.

**Acceptance criteria:** The largest peak in the pattern of *Sample A* corresponds to a  $d$  value between 15.0 and 17.2 Å. The major peak in the region between 1.48 and 1.54 Å from the pattern of *Sample B* is between 1.492 and 1.504 Å.





# PDF-4/Organics database - pharmaceutical

Results - [Subfile (Pharmaceutical)] And [Status (Primary, Alternate, Deleted)]

File Edit Fields Similarity Index Help

Preferences
  Open PDF Card
  Simulated Profile

Results: 10,780 of 501,964 CDD Defaults

PDF #	QM	Chemical Formula	Compound Name	D1 (Å)	D2 (Å)	D3 (Å)	SYS
05-006-4528	I	C15 H24 O	2,6-Di-tert-butyl-p-cresol	6.171470	5.088900	4.299360	O
05-006-4530	S	C22 H24 Cl Co N8 O7	bis(N-(2-(4-Imidazolyl)ethyl)pyridine...	6.717000	11.634200	4.105130	H
05-006-4531	I	C15 H38 N4 O8.5	O- $\alpha$ -D-2,6-Diamino-6-methyl-2,3,4,6...	7.099220	4.506350	7.867410	O
05-006-4532	I	C18 H22 O2	Estrone	4.314430	6.750170	4.396490	M
05-006-4537	S	C17 H16 Cl N3 O	{2-Chloro-11-(1-piperazinyl)dibenz(...	4.360060	3.956840	6.497700	O
05-006-4539	S	C6 H12 O6	$\alpha$ -D-Mannopyranose	5.030970	4.535910	4.046640	O
05-006-4559	S	C20 H16 N4 O2 S	N-methyl-N-(3-{3-(2thienylcarbonyl)...	5.199250	3.511100	3.385450	M
05-006-4621	S	C11 H10 Cl F O2	2-Chloro-1-(6-fluoro-3,4-dihydro-2H...	3.380140	3.397810	5.290960	M
05-006-4624	B	C21 H34 N3 O6	{(1-((1-(tert-butoxy carbonyl)pyrrolidi...	10.230000	4.504810	4.491540	O
05-006-4625	B	C23 H38 N3 O6	{(1-((1-(tert-butoxy carbonyl)pyrrolidi...	5.097400	4.565470	4.584290	O
05-006-4719	S	C27 H35 N2 O7 · Cl · C2 H3 N	((2S)-1-((3S)-3-carboxy-6,7-dimeth...	7.531660	8.969120	5.201270	M
05-006-4748	B	C4 H12 N O3 · C22 H25 O4 · H2 O	7-Phenyl-7-(2,4,5-trimethyl-3,6-diox...	23.442200	3.911940	7.348480	M
05-006-4765	B	C48 H58 O4 · C2 H3 N	1,4-bis(4-estren-17 $\alpha$ -ethynyl-18a-h...	5.956240	6.639670	6.022630	M
05-006-4766	B	C48 H56 F2 O4 · C2 H3 N	1,4-bis(18a-Homo-17 $\beta$ -hydroxy-17 $\alpha$ ...	6.003160	3.722570	4.731350	M
05-006-4767	B	C46 H52 F2 O4	1,4-bis(17 $\beta$ -hydroxy-17 $\alpha$ -ethynyl-4...	11.982600	12.307300	8.735050	M
05-006-4768	S	C7 H8 N4 O2 · C7 H6 O3	theopylline 3-hydroxybenzoic acid c...	3.315460	3.360570	3.558200	A
05-006-4769	B	C7 H8 N4 O2 · C7 H6 O4	theopylline 2,3-dihydroxybenzoic aci...	6.903530	3.308980	7.355580	M
05-006-4770	S	C7 H8 N4 O2 · C7 H6 O4	theopylline 2,4-dihydroxybenzoic aci...	7.177710	3.187240	3.330770	M
05-006-4771	I	C7 H9 N4 O2 · C7 H5 O4 · H2 O	theopylline 2,6-dihydroxybenzoic aci...	3.279150	7.311410	7.124660	M
05-006-4772	S	C7 H8 N4 O2 · C7 H6 O4	theopylline 3,4-dihydroxybenzoic aci...	3.187060	5.519520	7.553580	A
05-006-4773	I	C7 H8 N4 O2 · C7 H6 O4	theopylline 3,5-dihydroxybenzoic aci...	3.187780	7.850200	6.236990	A
05-006-4992	B	C26 H27 Cl5 N2 O Ru S	Dichlorido( $\eta$ 6-p-isopropyltoluene)(1-...	12.069200	9.410600	11.469600	A
05-006-4993	B	C54 H48 Cl3 N4 Ru · F6 P · 2 C H2 ...	Chlorido( $\eta$ 6-p-isopropyltoluene)bis(...	6.041510	11.834900	5.552620	A
05-006-4994	S	C16 H13 Cl3 N2 O S	1-(2-((2-chlorothiophen-3-yl)methox...	3.919640	3.223840	4.908550	M

Search Description: [Subfile (Pharmaceutical)] And [Status (Primary, Alternate, Deleted)]

Calculations: Mean: Median: ESD:



# PDF-4/Organics database - excipients

The screenshot shows the ICDD database search interface. The search criteria are:

- Subfile: Synthetic
- Environment: Ambient, Press. (Non-ambient), Temp. (Non-ambient), Press. & Temp. (Non-ambient), Atomic Coordinates, Raw Diffraction Data
- Status: Primary, Alternate, Deleted
- Quality Mark: Star, Rietveld, Good, Indexed, Calculated, Prototyping, Minimal Acceptable, Blank, Low-Precision, Hypothetical
- Database: ICDD (00), ICSD (01), CSD (02), NIST (03), LPF (04), ICDD Crystal Data (05)

The search results are displayed in a periodic table format. The search query is: [Subfile/Subclass (Pharmaceutical/Excipient)] And [Status (Primary, Alternate)]

Periodic Table	IA	IIA	IIIB	IVB	VB	VIB	VIIIB	VIIIB	IB	IIB	IIIA	IVA	VA	VIA	VIIA	VIIIA		
Formula/Name	1 H															2 He		
Classifications	1.008															4.003		
Crystallography	3 Li	4 Be									5 B	6 C	7 N	8 O	9 F	10 Ne		
Modulated	6.941	9.012									10.811	12.01	14.007	15.999	18.998	20.180		
Diffraction	11 Na	12 Mg									13 Al	14 Si	15 P	16 S	17 Cl	18 Ar		
Physical Properties	22.990	24.305									26.982	28.086	30.974	32.065	35.453	39.948		
Reference	19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
Comments	39.098	40.078	44.956	47.887	50.941	51.996	54.938	55.845	58.933	58.693	63.546	65.409	69.723	72.64	74.922	78.96	79.904	83.798
	37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
	85.468	87.62	88.906	91.224	92.906	95.94	[98]	101.07	102.908	106.42	107.868	112.41	114.818	118.71	121.76	127.6	126.904	131.293
	55 Cs	56 Ba		72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
	132.905	137.327		178.49	180.948	183.84	186.207	190.23	192.217	195.078	196.967	200.59	204.383	207.2	208.98	[209]	[210]	[222]
	67 Fr	68 Ra		104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Cn	113 Uut	114 Fl	115 Uup	116 Lv	117 Uus	118 Uuo
	[223]	[228]		[261]	[262]	[266]	[264]	[277]	[268]	[271]	[272]	[285]	[293]	[289]	[289]	[289]	[294]	[294]
La:			57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu	
			138.906	140.116	140.908	144.242	[145]	150.36	151.964	157.25	158.925	162.5	164.93	167.259	168.934	173.04	174.967	
Ac:			89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr	
			[227]	232.038	231.038	238.029	[237]	[244]	[243]	[247]	[247]	[251]	[252]	[257]	[258]	[259]	[262]	

# PDF-4/Organics database – excipients

Results - [Subfile/Subclass (Pharmaceutical/Excipient)] And [Status (Primary, Alternate, Deleted)]

File Edit Fields Similarity Index Help

Preferences: Open PDF Card Simulated Profile

Results: 2,667 of 501,964

PDF #	QM	Chemical Formula	Compound Name	D1 (Å)	D2 (Å)	D3 (Å)	SYS
02-063-1767	● S	C10 H14 O	2-Isopropyl-5-methylphenol	11.168600	4.719940	5.323980	R
02-063-2175	● S	C4 H4 N O4 S · K	Potassium 6-methyl-1,2,3-oxathiazin...	10.515600	4.656410	3.546590	M
02-063-2271	● B	C12 H22 O11 · H2 O	alpha-Lactose monohydrate	4.466030	4.547100	4.651660	M
02-063-2272	● S	C12 H22 O11 · H2 O	4-O-beta-D-Galactopyranosyl-alpha...	4.434390	4.527190	4.630340	M
02-063-2295	● I	C6 H8 O6	L-Ascorbic acid	3.176500	2.973560	4.483100	M
02-063-2296	● I	C6 H8 O6	0.42-Deutero-L-ascorbic acid	3.176500	2.973560	4.483100	M
02-063-2297	● S	C6 H8 O6	L-Ascorbic acid	3.176500	2.973560	4.483100	M
02-063-2345	● I	C5 H10 N O4 · Cl	L-Glutamic acid hydrochloride	3.878700	3.724620	3.366970	O
02-063-2619	● B	C4 H4 O4	Maleic acid	3.189610	5.075000	3.971510	M
02-063-2620	● I	C4 H4 O4	Maleic acid	3.189610	5.050000	3.959500	M
02-063-2621	● S	C4 H4 O4	Maleic acid	3.176710	5.049000	3.952830	M
02-063-2638	● I	C12 H22 O11 · H2 O	beta-Maltose monohydrate	4.463670	6.182130	4.070970	M
02-063-2639	● S	C12 H22 O11 · H2 O	beta-Maltose monohydrate	4.413050	4.050630	6.147350	M
02-063-2640	● I	C12 H22 O11	alpha-Maltose	4.038320	4.332030	7.000590	O
02-063-2888	● S	C15 H24 O	2,6-Di-t-butyl-4-methylphenol	4.410220	6.010410	8.240430	M
02-063-2889	● I	C15 H24 O	2,6-Di-t-butyl-4-methylphenol	6.171470	7.675430	5.088900	O
02-063-3451	● B	C4 H10 O4	meso-Erythritol	4.383910	4.529020	6.013110	T
02-063-3452	● B	C4 H10 O4	meso-Erythritol	4.526190	4.389470	6.030830	T
02-063-3544	● B	C H4 O	Methanol	3.349800	4.807670	3.215000	O
02-063-4972	● I	C2 H3 O2 · Na · 3 ( H2 O )	Sodium acetate trihydrate	3.039690	7.720300	3.953170	M
02-063-4973	● S	C2 H3 O2 · Na · 3 ( H2 O )	Sodium acetate trihydrate	3.002060	7.733770	3.944940	M
02-063-5052	● B	C5 H9 N O3 S	N-Acetyl-L-cysteine	3.382790	4.231290	4.502990	A
02-063-5053	● S	C5 H9 N O3 S	N-Acetyl-L-cysteine	3.228170	4.153140	3.813970	A

Search Description: [Subfile/Subclass (Pharmaceutical/Excipient)] And [Status (Primary, Alternate, Deleted)]

Calculations: Mean: Median: ESD:

# PDF-4/Organics database – excipients – data mining

The screenshot shows the ICDD search interface with the following filters:

- Subfile:** Inorganic
- Environment:** Ambient, Press. (Non-ambient), Temp. (Non-ambient), Press. & Temp. (Non-ambient), Atomic Coordinates, Raw Diffraction Data
- Status:** Primary, Alternate, Deleted
- Quality Mark:** Star, Rietveld, Good, Indexed, Calculated, Prototyping, Minimal Acceptable, Blank
- Database:** ICDD (00), ICSD (01), CSD (02), NIST (03), LPF (04), ICDD Crystal Data (05)

The periodic table is visible with elements H, Li, Be, B, C, N, O, F, Ne highlighted in various colors.

[Subfile/Subclass (Pharmaceutical/Excipient) And Subfile (Inorganic)] And [Mg] And [Status (Primary, Alternate)]

The screenshot shows the search bar containing the query: [Subfile/Subclass (Pharmaceutical/Excipient) And Subfile (Inorganic)] And [Mg] And [Status (Primary, Alternate)]. The search bar is circled in red.

# PDF-4/Organics database – excipients – data mining

Results - [Subfile/Subclass (Pharmaceutical/Excipient) And Subfile (Inorganic)] And [Mg] And [Status (Primary, Alternate)]

File Edit Fields Similarity Index Help

Results: 63 of 501,964

ICDD Defaults

PDF #	QM	Chemical Formula	Compound Name	D1 (Å)	D2 (Å)	D3 (Å)	SYS
00-004-0829	S	Mg O	Magnesium Oxide	2.106000	1.489000	0.941900	C
00-011-0273	I	Mg Si O3	Magnesium Silicate	3.170000	2.908000	2.551000	O
00-013-0558	I	Mg3 Si4 O10 ( O H )2	Magnesium Silicate Hydroxide	9.340000	3.116000	4.660000	M
00-013-0595	I	Mg4 Si6 O15 ( O H )2 ·6 H2 O	Magnesium Silicate Hydroxide Hydr...	12.100000	2.560000	4.310000	O
00-019-0770	I	Mg3 Si4 O10 ( O H )2	Magnesium Silicate Hydroxide	9.350000	1.529000	4.590000	M
00-026-1226	I	Mg4 Si6 O15 ( O H )2 ·6 H2 O	Magnesium Silicate Hydroxide Hydr...	3.360000	3.760000	3.200000	O
00-029-1492	O	Mg4 Si6 O15 ( O H )2 ·6 H2 O	Magnesium Silicate Hydroxide Hydr...	12.800000	2.580000	4.410000	O
00-029-1493	B	Mg3 Si4 O10 ( O H )2	Magnesium Silicate Hydroxide	9.310000	3.120000	4.550000	M
00-030-0794	O	Mg O	Magnesium Oxide	3.050000	2.040000	1.174000	C
00-041-0486	O	Mg Si O3 · H2 O	Magnesium Silicate Hydrate	3.000000	1.610000	1.496000	X
00-045-0946	S	Mg O	Magnesium Oxide	2.105640	1.489050	0.941716	C
00-058-2010	B	Na0.3 ( Al , Mg )2 Si4 O10 ( O H )2 ...	Sodium Aluminum Magnesium Silicat...	12.522800	3.118450	4.452390	O
00-058-2011	B	Na0.3 ( Al , Mg )2 Si4 O10 ( O H )2 ...	Sodium Aluminum Magnesium Silicat...	12.803800	3.164290	6.232400	O
00-059-0649	I	( Al11.1 Fe1.9 O4 ( O H )24 )0.152 (...)	Magnesium Iron Aluminum Silicate O...	18.683000	4.568000	1.528000	M
00-059-0650	B	( Al18.6 Fe4.4 O4 ( O H )24 ( H2 O )...	Magnesium Iron Aluminum Silicate O...	18.248000	4.563000	1.528000	M
00-059-0651	I	( ( Al2 O3 )0.84 ( Fe2 O3 )0.14 ) ( Si...	Magnesium Iron Aluminum Silicate O...	18.156000	4.567000	1.528000	M
00-059-0652	B	( ( Al2 O3 )0.88 ( Fe2 O3 )0.54 ) ( Si...	Magnesium Iron Aluminum Silicate O...	18.249000	4.581000	1.529000	M
01-070-9183	H	Mg O	Magnesium Oxide	2.117800	1.497510	1.222710	C
01-071-1176	S	Mg O	Magnesium Oxide	2.108500	1.490930	0.942950	C
01-071-3631	S	Mg O	Magnesium Oxide	2.107000	1.489870	0.942279	C
01-071-3777	I	Mg O	Magnesium Oxide	2.105950	1.489130	2.431740	C
01-071-4938	I	Mg O	Magnesium Oxide	2.108000	1.490580	2.434110	C
01-071-6452	I	Mg O	Magnesium Oxide	2.125300	1.502810	1.227040	C

Search Description: [Subfile/Subclass (Pharmaceutical/Excipient) And Subfile (Inorganic)] And [Mg] And [Status (Primary, Alternate)]

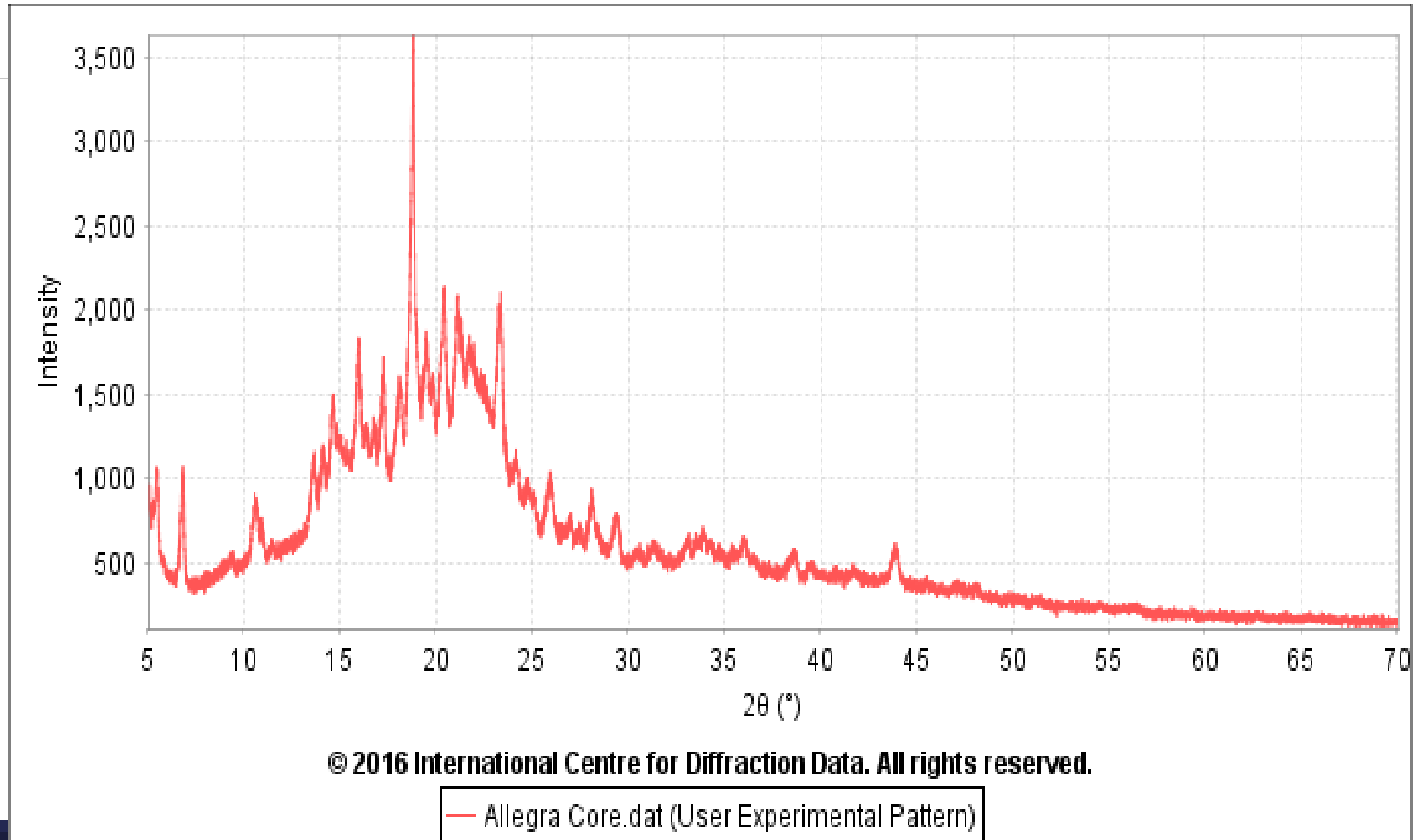
Calculations: Mean: Median: ESD:



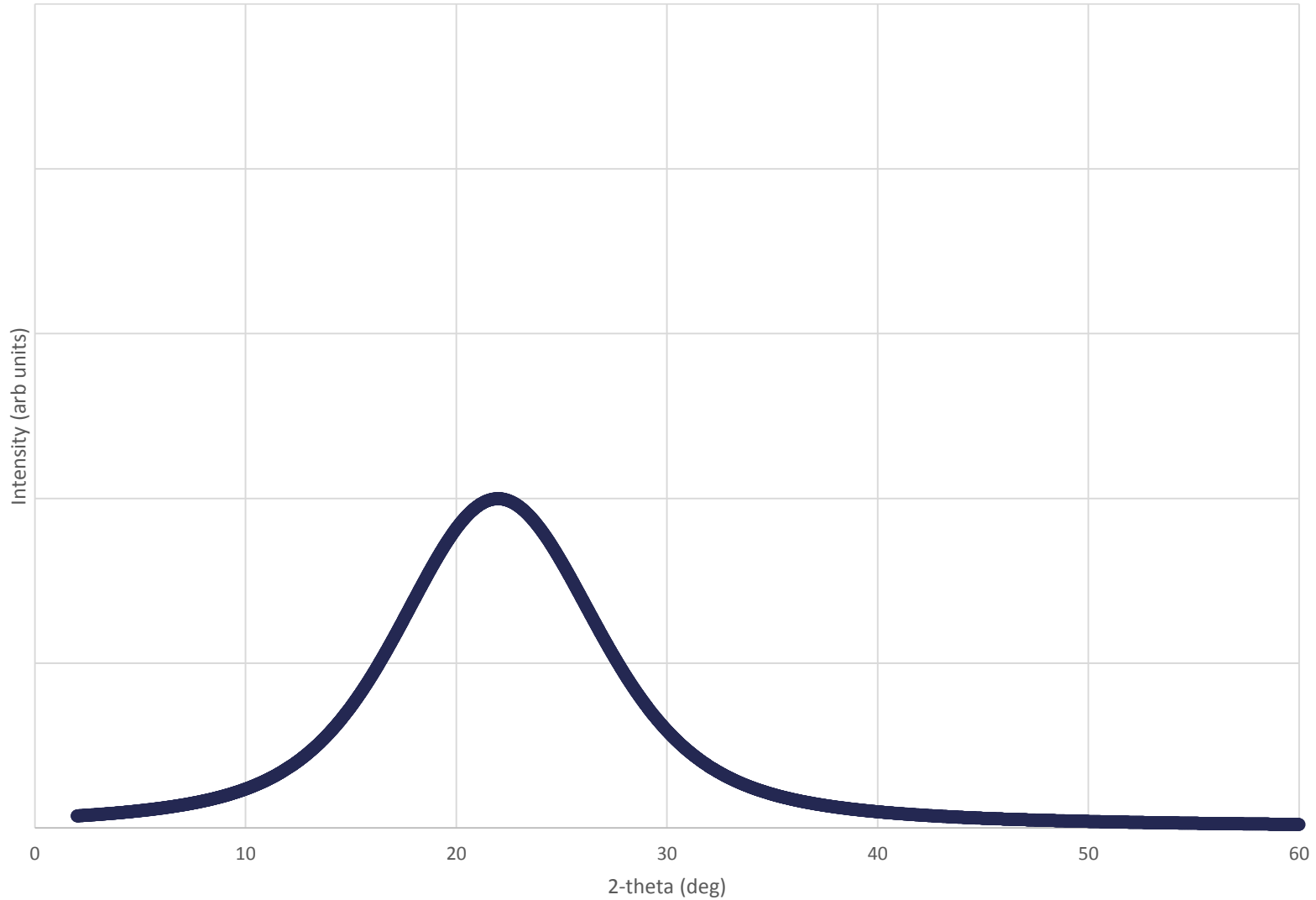




# XRD pattern of Allegra<sup>®</sup>, antihistamine

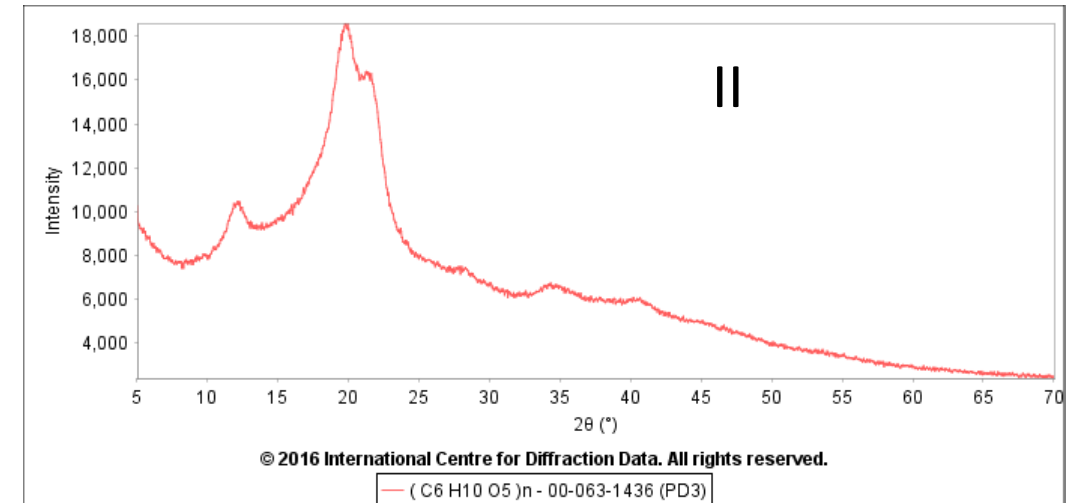
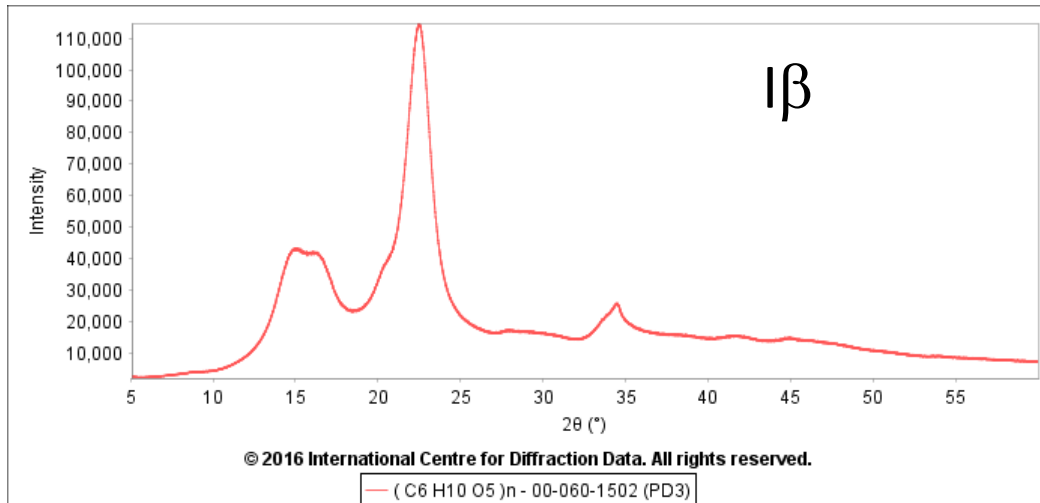
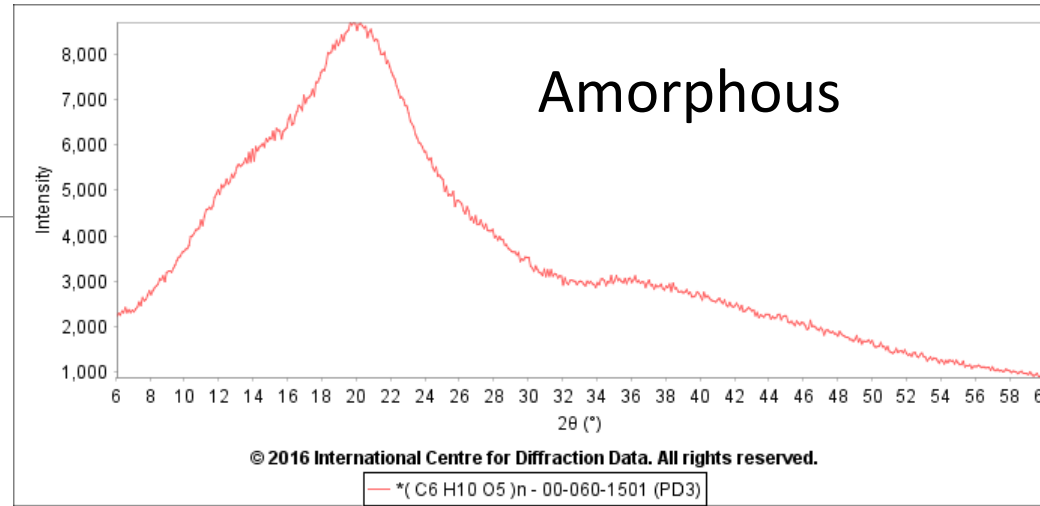


# Can I just model the polymer amorphous component as a single peak?

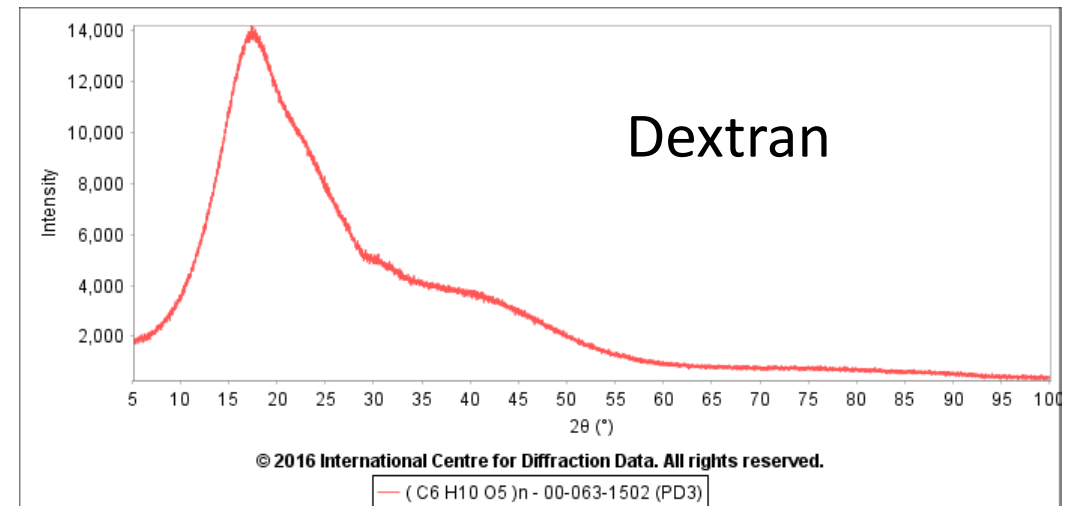
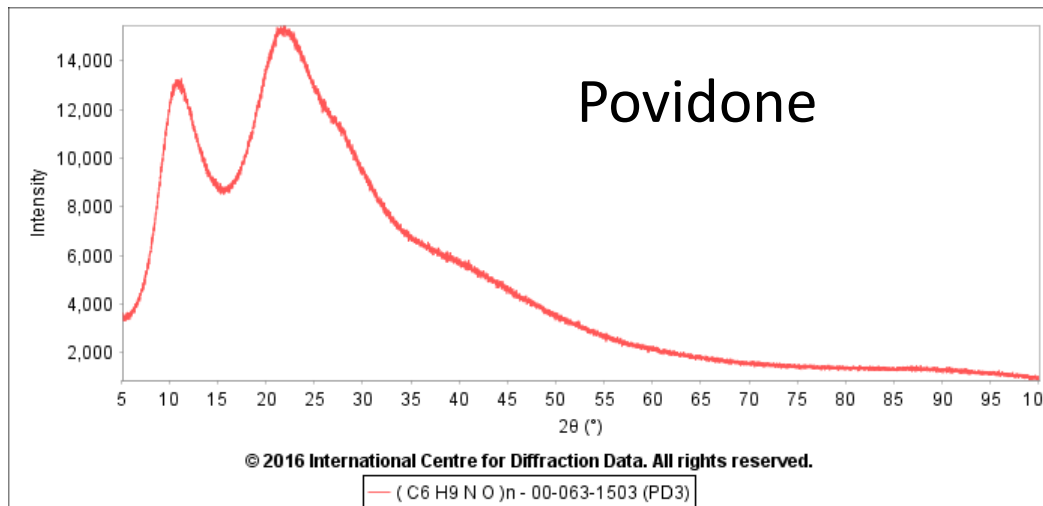
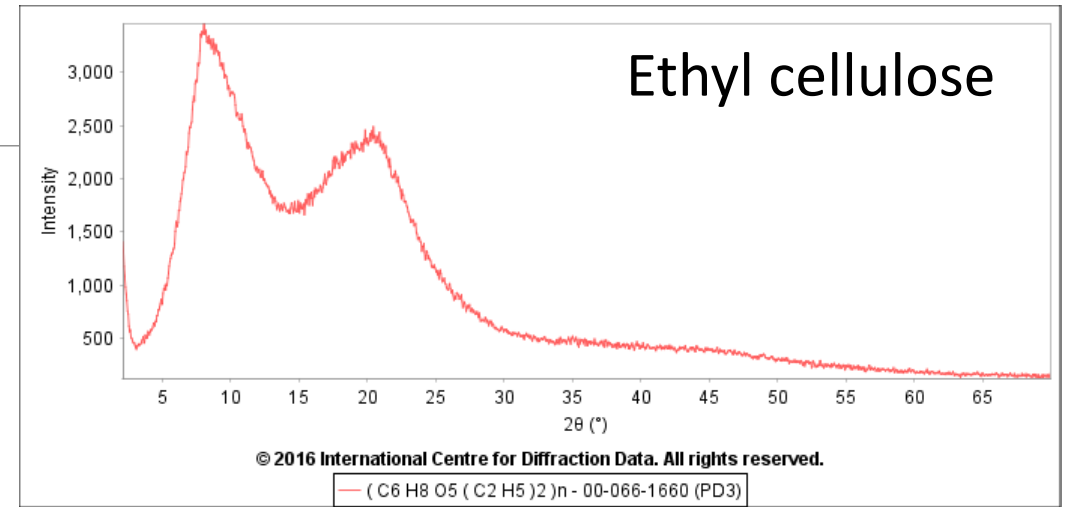
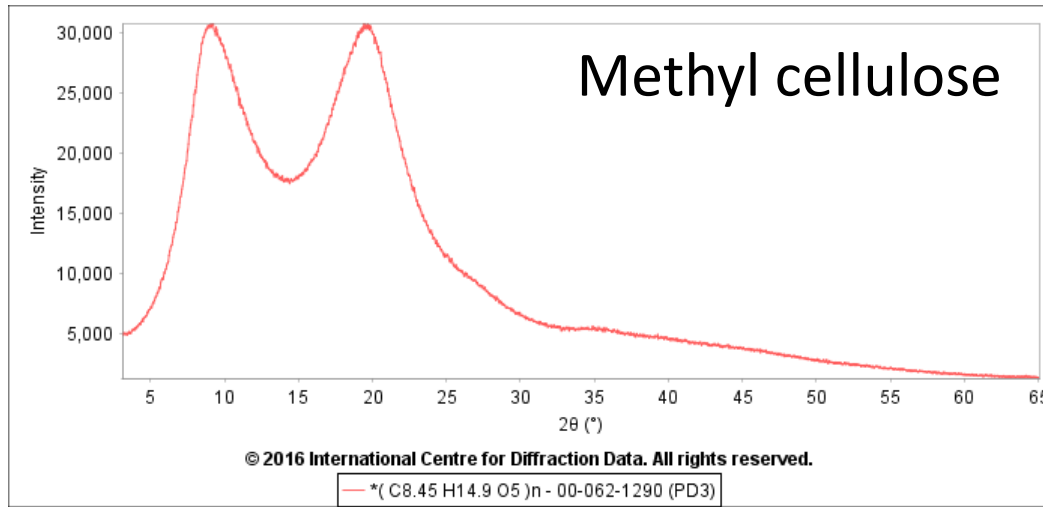


# Excipient polymers PDF raw data patterns (PD3)

Cellulose



# Excipient polymers PDF raw data patterns (PD3)



# XRD analysis of Suprax<sup>®</sup>

---

Suprax (API: Cefixime 3H<sub>2</sub>O ) is an antibiotic used for the treatment bacterial infections



Once-a-day  
**Suprax<sup>®</sup>**  
cefixime

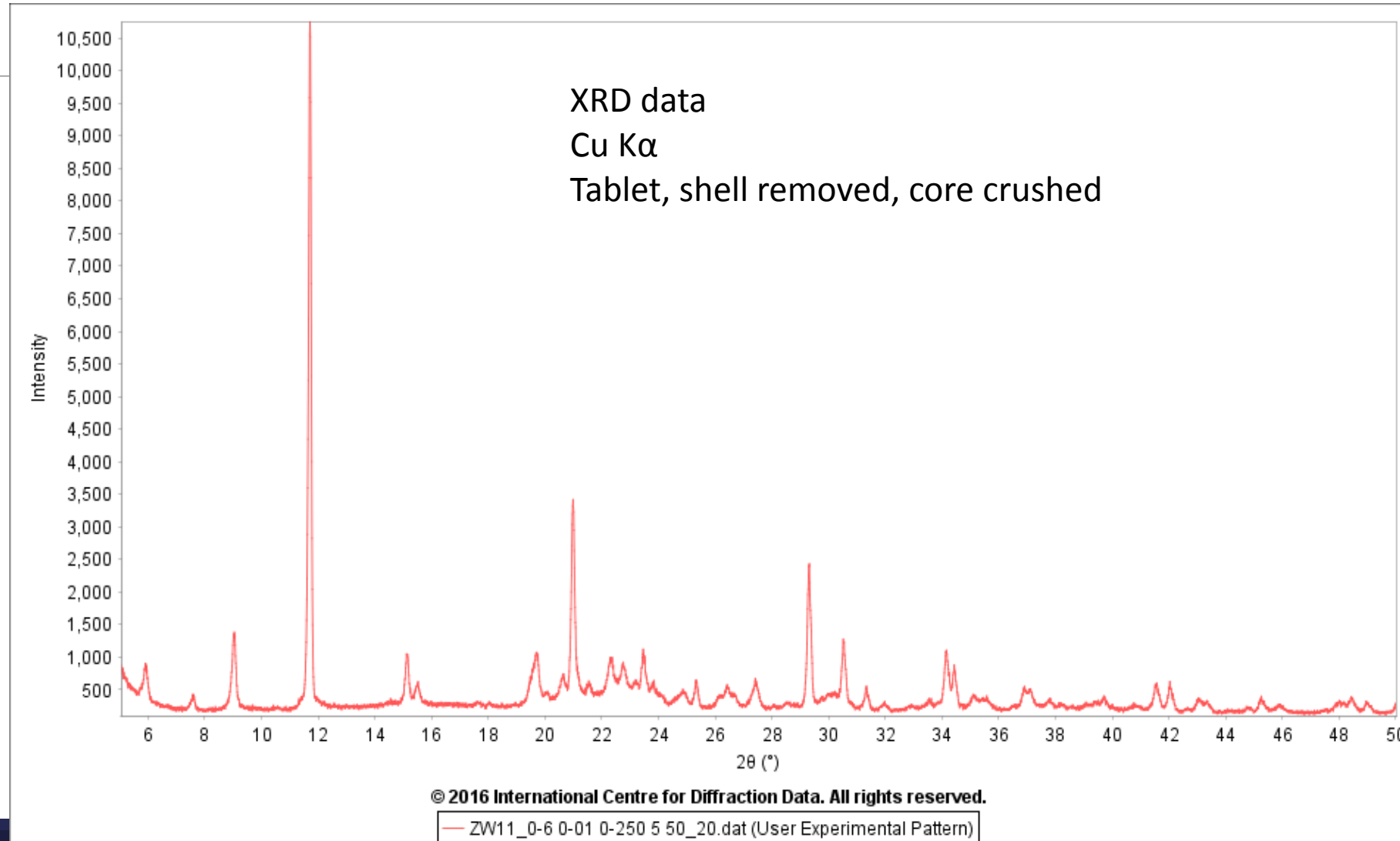
Click here to download a card  
for instant savings

ORAL  
SUSPENSION  
AND  
CHEWABLE  
TABLETS

The image shows a promotional graphic for Suprax. On the left, the text reads "Once-a-day Suprax<sup>®</sup> cefixime". Below this, there is a call to action: "Click here to download a card for instant savings". On the right, there is a wooden A-frame sign with a pink sign that says "ORAL SUSPENSION AND CHEWABLE TABLETS".



# Phase identification – Suprax core



# Phase identification – Suprax core

Slewe+ - ZW11\_0-6 0-01 0-250 5 50\_20.xml

File Edit Matches Phases Help

Import (1D) Import (2D) Open Session Save Session Print Preferences Accept Phase Remove Last Phase Matches Filter: [Any Name Contains Fragments 'cefixime'] And [Status (Primary, Alternate)]

Matches (0 of 1)

GOM	PDF #	QM	Status	Coords	I/Ic	Compound Name	Mineral Name	Phase	Chemical Formula	D1 (Å)	D2 (Å)	D3 (Å)

Experiment  
 Search Lines: 7.628866 Å D1 Range: 7.530 Å - 7.727 Å Rotation: All

Preferences  
 Radiation: X-ray Wavelength: Cu Kα1 1.54056 Å Search Method: Hanawalt Search Window: 0.15° Match Window: 0.15°  
 Use Residual Intensities  2nd Pass Filter  Weight d-Spacings  
 Lowest Allowable GOM: 2000

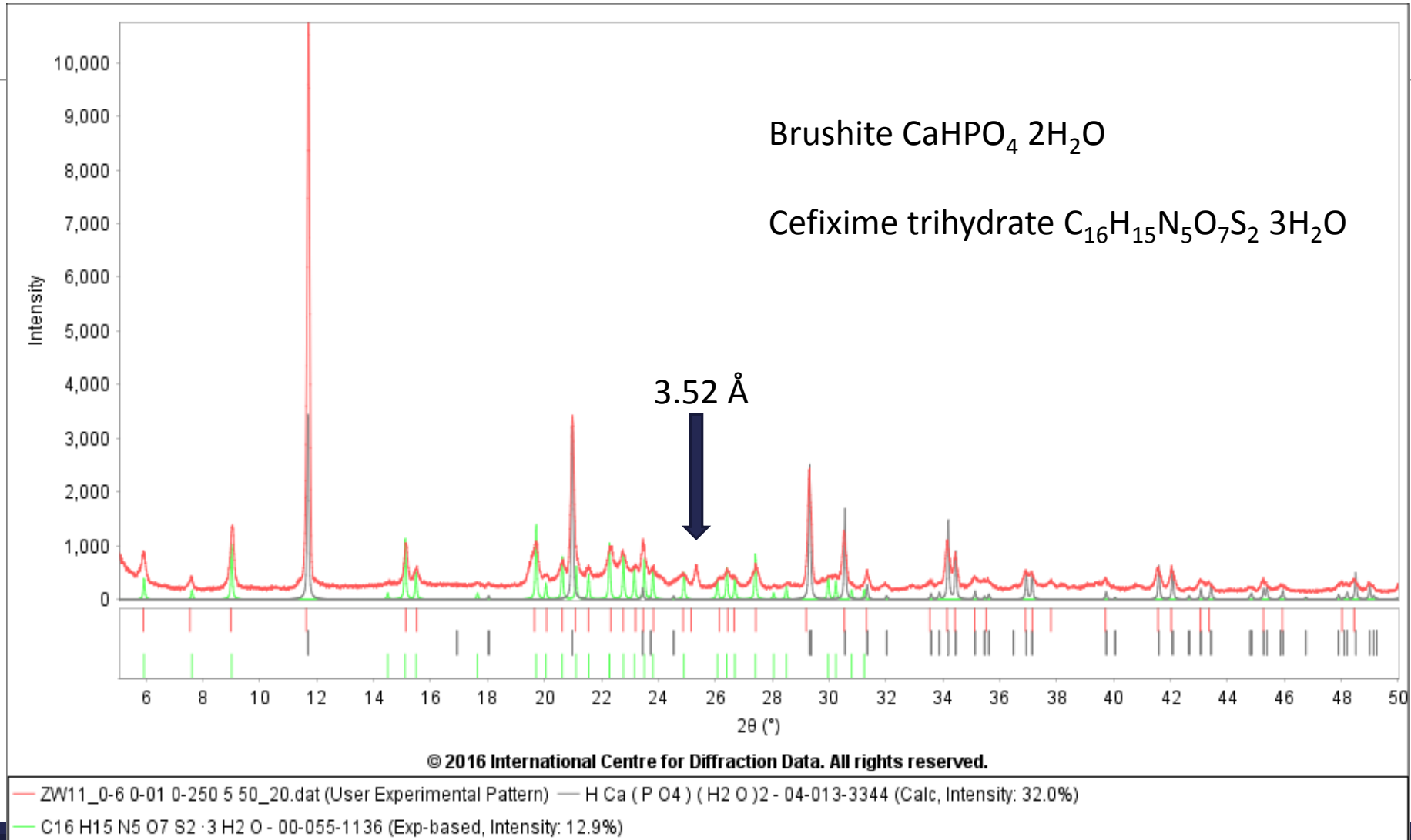
Phases (2)

#	PDF #	QM	Compound Name	Matched	I Ratio	I %	I/Ic	Est Wt %
1	04-013-3344	S	Hydrogen Calcium Phosphate Hydr...	23 of 36	0.320	71.299	1.42	100%
2	00-055-1136	O	Cefixime trihydrate	21 of 28	0.129	28.701		

Diffraction Patterns Lines (40 of 42) Estimated Weight %

#	PDF #	QM	Compound Name	Matched	I Ratio	I %	I/Ic
1	04-013-3344	S	Hydrogen Calcium Phosphate Hydr...	23 of 36	0.320	71.299	1.42
2	00-055-1136	O	Cefixime trihydrate	21 of 28	0.129	28.701	

# Phase identification – Suprax core



# PDF Data Mining

The screenshot displays the ICDD Search interface with the following search criteria highlighted by red circles:

- Subfile:** Pharmaceutical > Excipient
- Strong Line (Å):** 3.52 x 0.05
- Classification:**  D1  D2  D3
- Search Criteria:** [Subfile/Subclass (Pharmaceutical/Excipient)] And [Strong Line = 3.52(0.05) Å] And [Status (Primary, Alternate)]

Other visible search filters include:

- Environment:** Ambient, Press. (Non-ambient), Temp. (Non-ambient), Press. & Temp. (Non-ambient), Atomic Coordinates, Raw Diffraction Data
- Status:**  Primary,  Alternate,  Deleted
- Quality Mark:** Star, Rietveld, Good, Indexed, Calculated, Prototyping, Minimal Acceptable, Blank
- Database:** ICDD (00), ICSD (01), CSD (02), NIST (03), LPF (04), ICDD Crystal Data (05)

# PDF Data Mining

Results - [Subfile/Subclass (Pharmaceutical/Excipient)] And [Strong Line = 3.52(0.05) Å] And [Status (Primary, Alternate)]

File Edit Fields Similarity Index Help

Preferences
  Open PDF Card
  Simulated Profile

Results: 105 of 384,613

ICDD Defaults

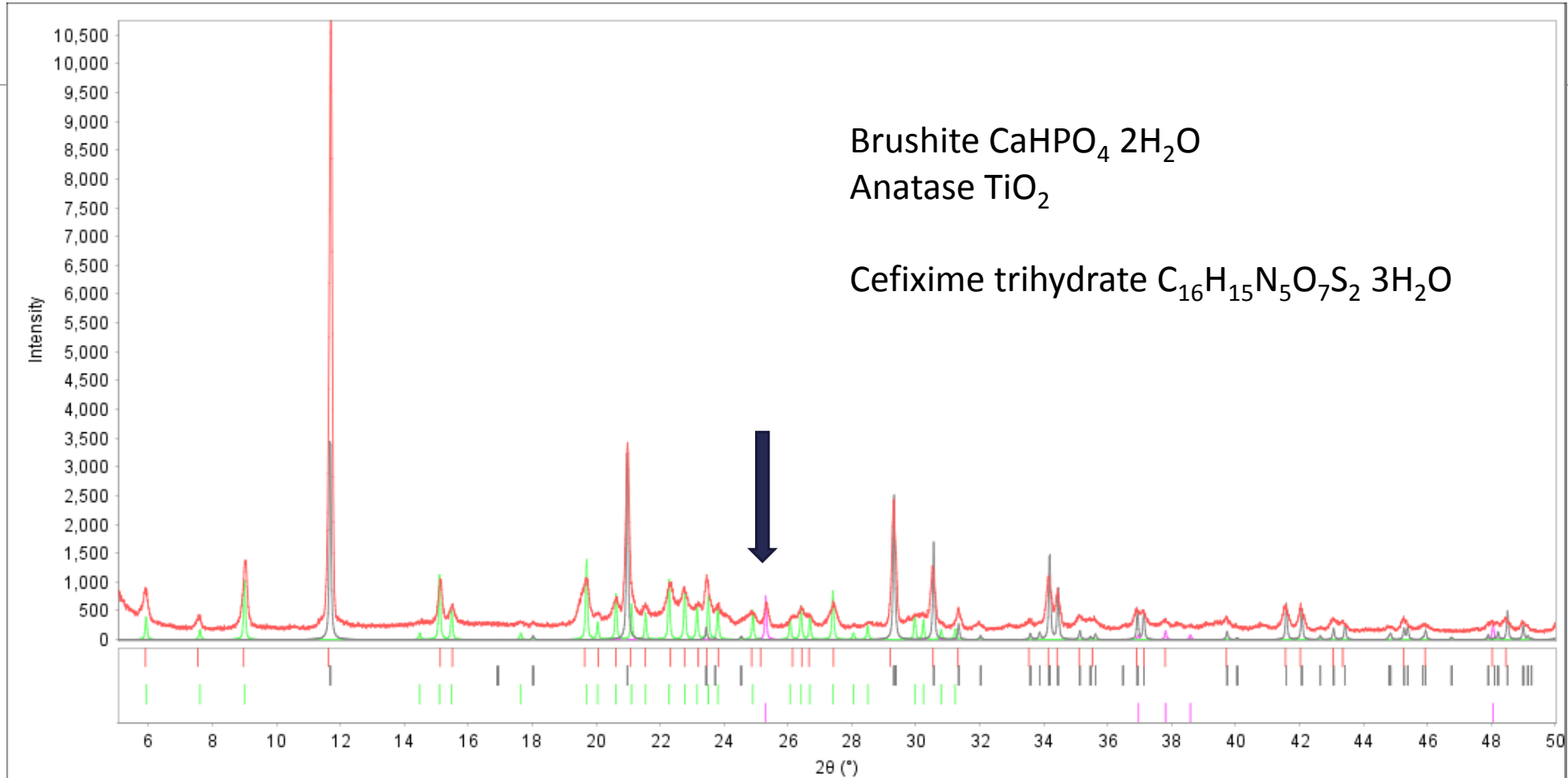
PDF #	QM	Chemical Formula ↑	Compound Name	D1 (Å)	D2 (Å)
00-021-1272	● S	Ti O2	Titanium Oxide	3.520000	1.89200
00-029-1360	● S	Ti O2	Titanium Oxide	3.512000	2.90000
00-035-0088	● I	Ti O2	Titanium Oxide	3.560000	3.11000
★ 00-046-1237	● R	Ti O2	Titanium Oxide	3.568540	5.82368
00-046-1238	● R	Ti O2	Titanium Oxide	3.568640	6.23732
00-064-0863	● S	Ti O2	Titanium oxide	3.516160	1.89268
01-070-6826	● S	Ti O2	Titanium Oxide	3.501410	1.88550
01-070-7348	● S	Ti O2	Titanium Oxide	3.515390	1.89200
01-071-1166	● S	Ti O2	Titanium Oxide	3.516290	1.89210
01-071-1167	● S	Ti O2	Titanium Oxide	3.521430	1.89460
01-071-1168	● S	Ti O2	Titanium Oxide	3.520000	1.89200

Search Description: [Subfile/Subclass (Pharmaceutical/Excipient)] And [Strong Line = 3.52(0.05) Å] And [Status (Primary, Alternate)]

Calculations: Mean: Median: ESD:



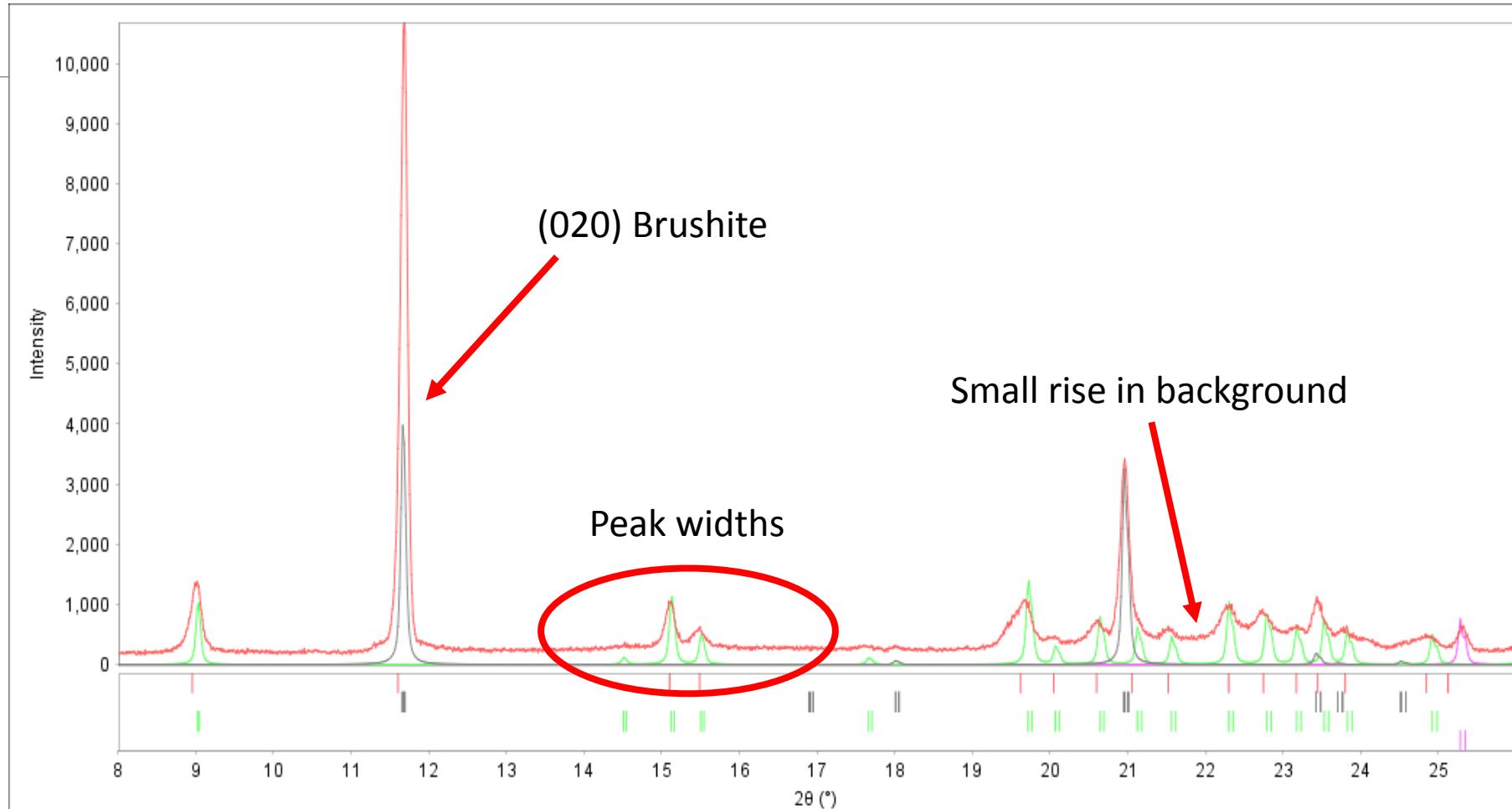
# Phase identification – Suprax core



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— ZW11\_0-6 0-01 0-250 5 50\_20.dat (User Experimental Pattern) — H Ca ( P O 4 ) ( H 2 O ) 2 - 04-013-3344 (Calc, Intensity: 32.0%)  
— C16 H15 N5 O7 S2 · 3 H2 O - 00-055-1136 (Exp-based, Intensity: 12.9%) — Ti O2 - 00-021-1272 (Exp-based, Intensity: 7.0%)

# Phase identification – Suprax core

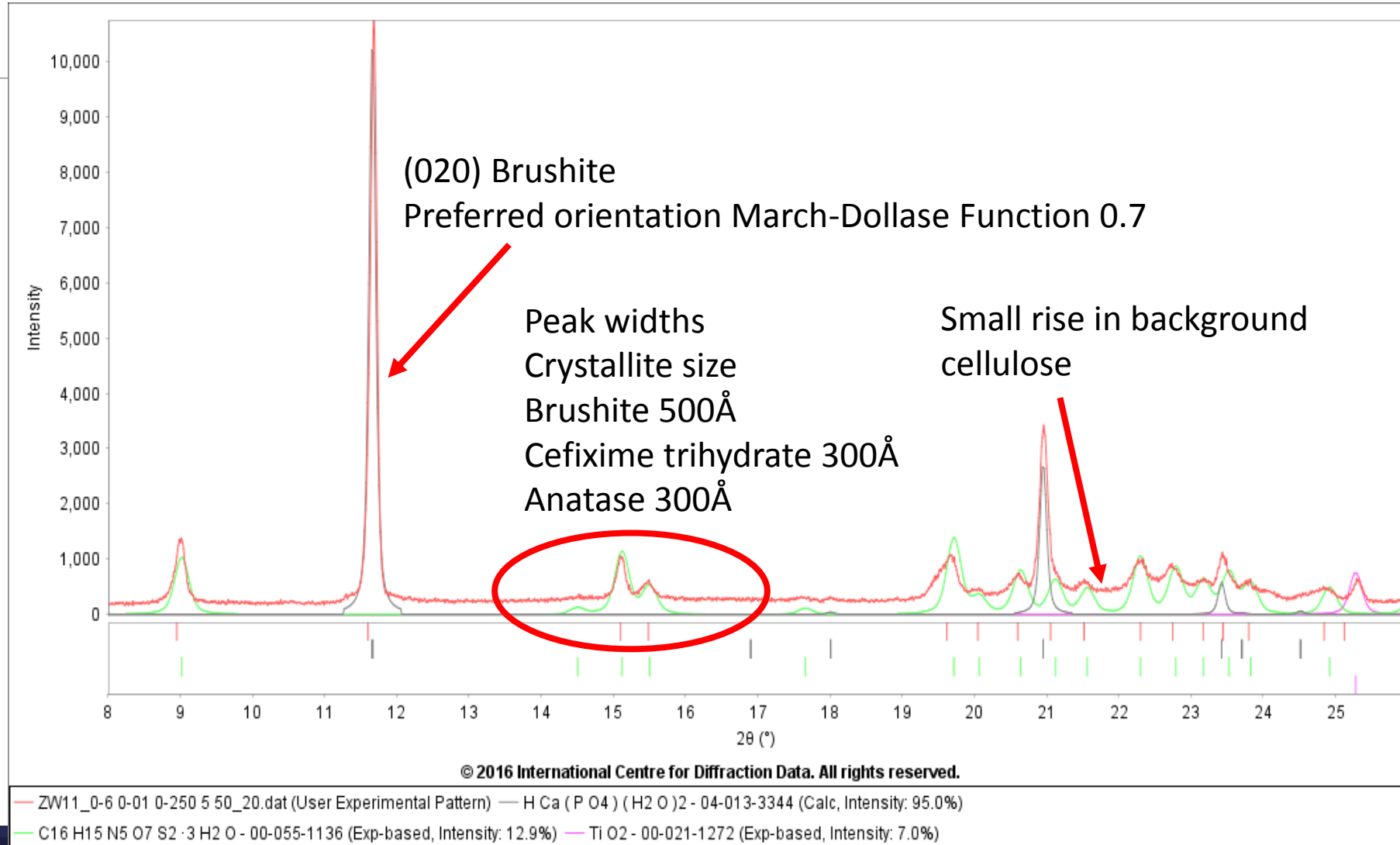


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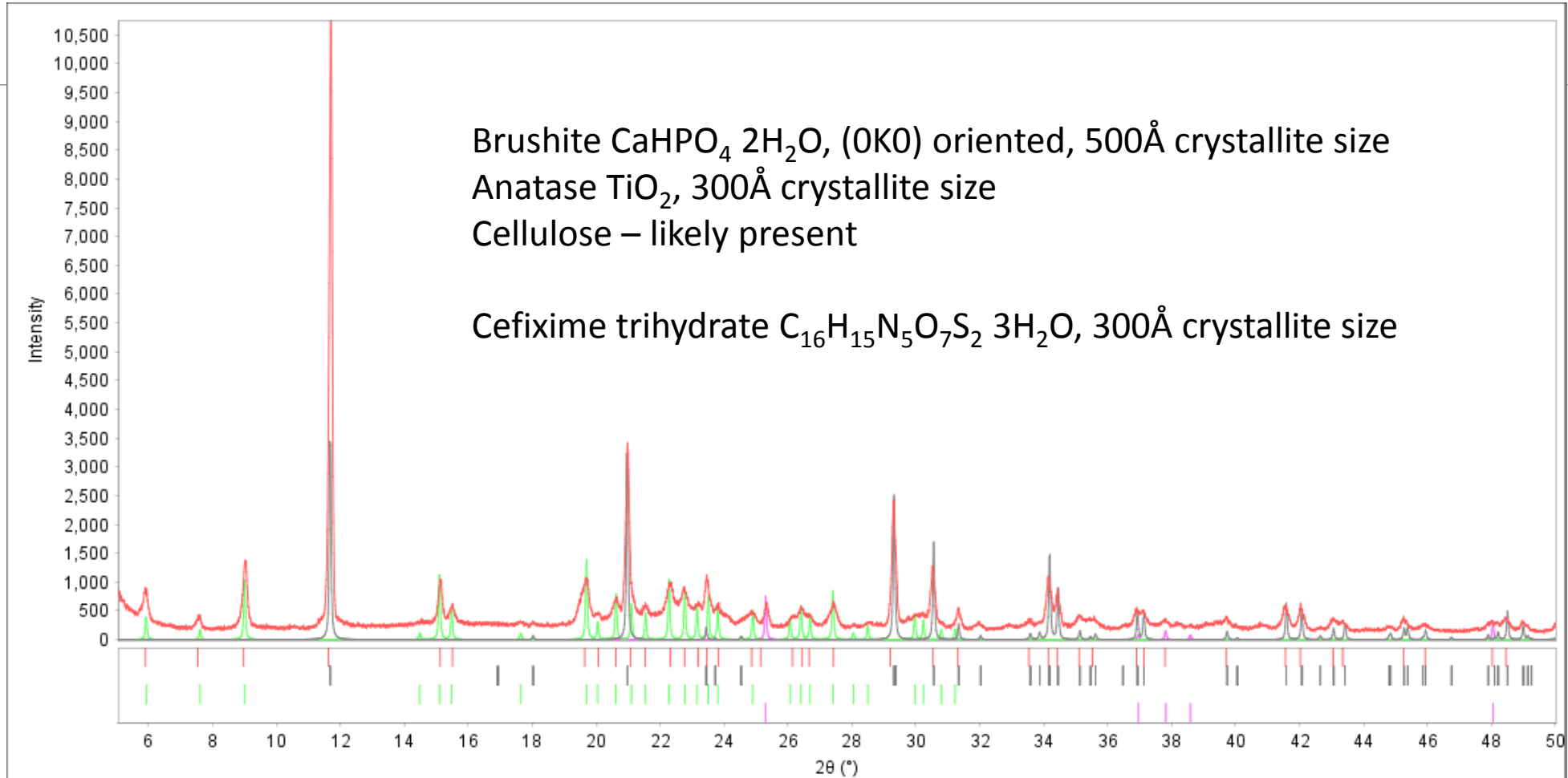
— ZW11\_0-6 0-01 0-250 5 50\_20.dat (User Experimental Pattern) — H Ca ( P O4 ) ( H2 O )2 - 04-013-3344 (Calc, Intensity: 37.0%)  
— C16 H15 N5 O7 S2 · 3 H2 O - 00-055-1136 (Exp-based, Intensity: 12.9%) — Ti O2 - 00-021-1272 (Exp-based, Intensity: 7.0%)



# Phase identification – Suprax core



# Phase identification – Suprax core



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— ZW11\_0-6 0-01 0-250 5 50\_20.dat (User Experimental Pattern) — H Ca ( P O4 ) ( H2 O )2 - 04-013-3344 (Calc, Intensity: 32.0%)  
— C16 H15 N5 O7 S2 · 3 H2 O - 00-055-1136 (Exp-based, Intensity: 12.9%) — Ti O2 - 00-021-1272 (Exp-based, Intensity: 7.0%)

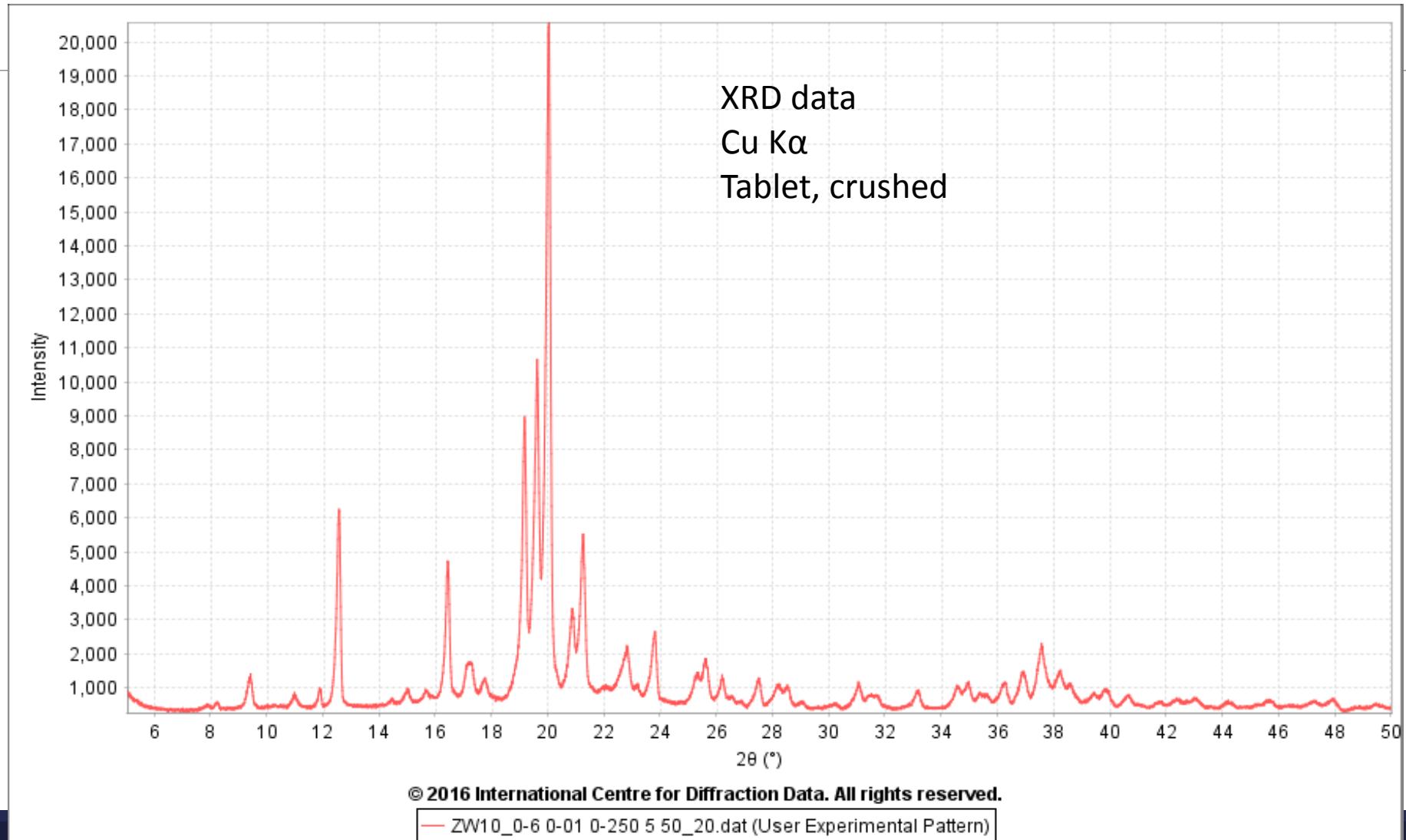
# XRD analysis of Zocor<sup>®</sup> generic

---

Zocor generic (API: Simvastatin) is a statin used to lower blood cholesterol

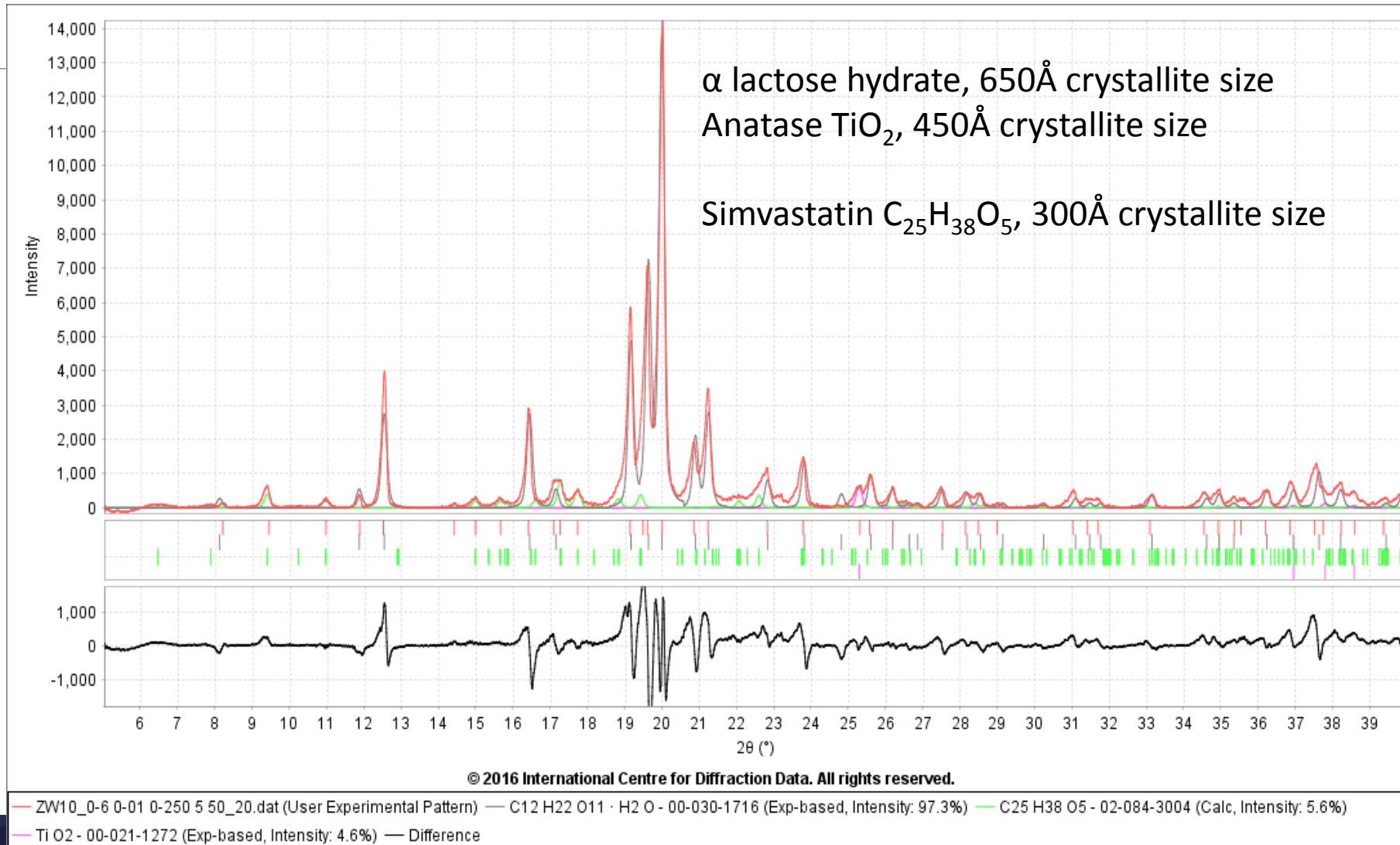


# Phase identification – Zocor generic core





# Phase identification – Zocor<sup>®</sup> generic



# Phase identification – Zocor<sup>®</sup> generic

Slewe+ - ZW10\_0-6 0-01 0-250 5 50\_20.xml

File Edit Matches Phases Help

Import (1D) Import (2D) Open Session Save Session Print Preferences Accept Phase Remove Last Phase

Matches

GOM	PDF #	QM	Status	Coords	I/Ic	Compound Name	Mineral Name	Chemical Formula	D1 (Å)	D2 (Å)	D3 (Å)	D4 (Å)	
<													>

Change Filter... Primary Patterns

Experiment

Search Lines: 4.554315 Å D1 Range: 4.513 Å - 4.596 Å Rotation: All

Preferences

Radiation: X-ray Use Residual Intensities

Wavelength: Cu Kα1 1.54056 Å 2nd Pass Filter

Search Method: Hanawalt Weight d-Spacings

Search Window: 0.18° Lowest Allowable GOM: 2000

Match Window: 0.18°

Phases (3)

#	PDF #	QM	Compound Name	I Ratio	I %	I/Ic	Est Wt %
1	00-030-1716	I	Lactose hydrate	0.973	90.463	1.55	85

Diffraction Patterns Lines (43 of 44) Estimated Weight %

#	PDF #	QM	Compound Name	I Ratio	I %	I/Ic	Est. Wt %
1	00-030-1716	I	Lactose hydrate	0.973	90.463	1.55	85
2	02-084-3004	B	(1S,3R,7S,8S,8aR)-3,7-Dimethyl-8-(...)	0.056	5.234	0.53	14
3	00-021-1272	S	Titanium Oxide	0.046	4.303	*5.0	1

## RIR method for multiphase sample

---

$$\sum_{j=1}^n X_j = 1$$

$$X_{\alpha} = \frac{I_{(hkl)\alpha}}{RIR_{\alpha} I_{(hkl)\alpha}^{rel}} \left[ \frac{1}{\sum_{j=1}^n \left( I_{(hkl)'j} / RIR_j I_{(hkl)'j}^{rel} \right)} \right]$$

# Phase identification – Zocor<sup>®</sup> generic

Sleve+ - ZW10\_0-6 0-01 0-250 5 50\_20.xml

File Edit Matches Phases Help

Import (1D) Import (2D) Open Session Save Session Print Preferences Accept Phase Remove Last Phase

Matches

GOM	PDF #	QM	Status	Coords	I/Ic	Compound Name	Mineral Name	Chemical Formula	D1 (Å)	D2 (Å)	D3 (Å)	D4 (Å)
<input type="text" value="Change Filter..."/> Primary Patterns												

Experiment

Search Lines: 4.554315 Å D1 Range: 4.513 Å - 4.596 Å Rotation: All

Preferences

Radiation: X-ray Use Residual Intensities

Wavelength: Cu Kα1 1.54056 Å 2nd Pass Filter

Search Method: Hanawalt Weight d-Spacings

Search Window: 0.18° Lowest Allowable GOM: 2000

Match Window: 0.18°

Phases (3)

#	PDF #	QM	Compound Name	I Ratio	I %	I/Ic	Est Wt %
1	00-030-1716	I	Lactose hydrate	0.973	90.463	1.55	85
2	02-084-3004	B	(1S,3R,7S,8S,8aR)-3,7-Dimethyl-8-(...)	0.056	5.234	0.53	14
3	00-021-1272	S	Titanium Oxide	0.046	4.303	*5.0	1

Diffraction Patterns Lines (43 of 4) Estimated Weight %

Titanium Oxide - 00-021-1272: 1%

(1S,3R,7S,8S,8aR)-3,7-Dimethyl-8-(2-((2R,4R)-4-hydroxy-6-oxo-3,4,5,6-tetrahydro-2H-pyran-2-yl)ethyl)-1,2,3,7,8,8a-hexahydronaphthalen-1-yl 2,2-dimethylbutanoate - 02-084-3004: 14%

Lactose hydrate - 00-030-1716: 85%

# Atomic coordinates in the PDF-4 databases

C12 H22 O11 - 00-062-0928

File Edit Plots Window Help

Save Print Preferences Temperature Series Toolbox Property Sheet 2D 3D Bonds SAED EBSD Ring Simulated Profile Raw Diffraction Data

Cu Kα1 1.54056 Å  Simulated Profile (Exp-based)

Fixed Slit Intensity  Raw Diffraction Data (PD3)

2θ (°)	d (Å)	I	h	k	l	*
4.4920	19.655000	48	0	1	0	
8.9910	9.827410	24	0	2	0	
12.1580	7.273680	67	1	0	0	
12.3590	7.155830	148	1	-1	0	
13.5480	6.530380	42	1	1	0	
14.0850	6.282590	59	1	-2	0	
16.8820	5.247460	17	1	-3	0	
18.0370	4.913960	191	0	4	0	
18.5660	4.775120	722	0	0	1	

Intensity

2θ (°)

ac's added to PDF entries

PDF

ADP: U Origin: Modulated Data

Crystal (Symmetry Allowed):

- Centrosymmetric
- Non-centrosymmetric
  - Enantiomorphic Pyro / Piezo (p)
  - Optical Activity Piezo (2nd Harm.)

Structure

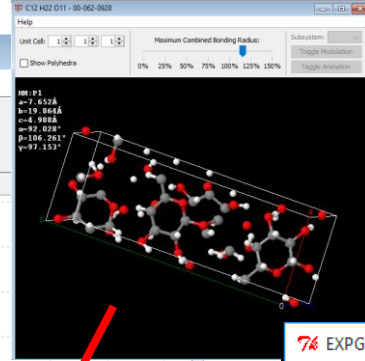
SG Symmetry Operators (1)

Seq	Operator
1	x,y,z

Atomic Coordinates (90)

Atom	Num	Wyckoff	Symmetry	x	y	z	SOF	Uiso	AET
C	1			0.4157	0.5519	0.824	1.0	0.0174	
C	2			0.2271	0.573	0.811	1.0	0.0174	
C	3			0.2221	0.6383	0.663	1.0	0.0174	
C	4			0.391	0.6908	0.783	1.0	0.0174	
C	5			0.5698	0.6604	0.844	1.0	0.0174	
C	6			0.7358	0.7119	0.978	1.0	0.0174	

Anisotropic Displacement Parameters (0)



EXPGUI interface to GSAS: 3PHASE-START.EXP

File Options Powder Xtal Graphs Results Calc Macro Import/Export Help

expnam expdet genes powpref powplot lstview liveplot

LS Controls Phase Powder Scaling Profile Constraints Restraints Rigid Body MD Pref Orient SH Pre

Select Histogram

Last History: EXPGUI 1.75 1.42 (3 changes) -- 10/01/08 16:18:41

Title: CPD

Print Options (0)

Marquardt Damping 1.00

LS matrix bandwidth 0

Reflection Intensity Extraction

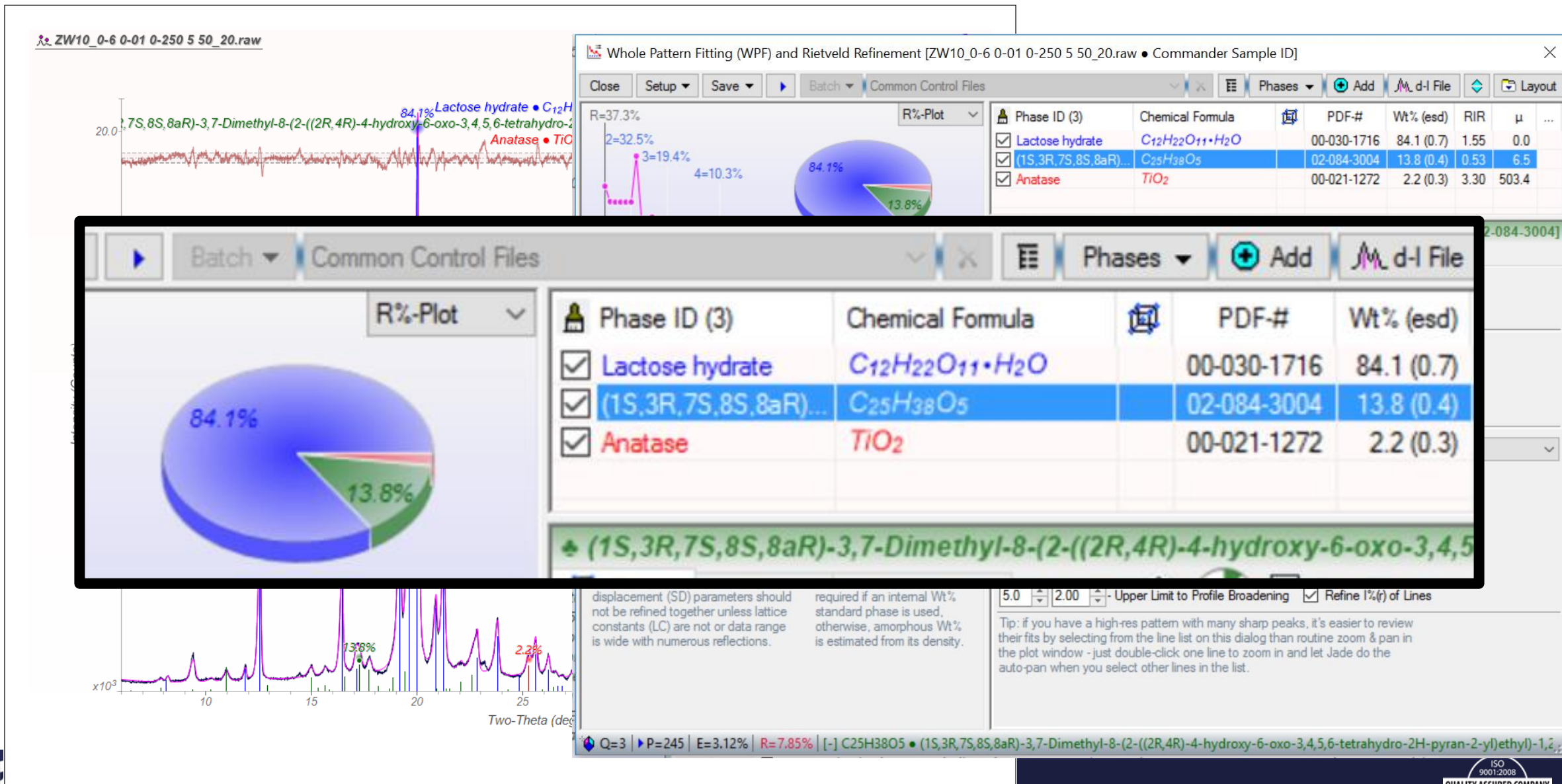
Extraction Method LeBail damping 0 Extract Fobs (Phase #)

Rietveld (Model biased)

F(calc) Weighted (Le Bail method)

Equally Weighted

# Phase identification – Zocor<sup>®</sup> generic



# Phase identification – Zocor<sup>®</sup> generic

---

## PDF-4 SIEVE+ RIR

$\alpha$ lactose hydrate	85 wt.%
Simvastatin C <sub>25</sub> H <sub>38</sub> O <sub>5</sub>	14 wt%
Anatase TiO <sub>2</sub>	1 wt.%

## WPF RIETVELD

$\alpha$ lactose hydrate	84.1(7) wt.%
Simvastatin C <sub>25</sub> H <sub>38</sub> O <sub>5</sub>	13.8(4) wt%
Anatase TiO <sub>2</sub>	2.1(3) wt.%

The RIR method works well when samples are randomly oriented and I/Ic values are known



# Keys to successful excipient phase analysis

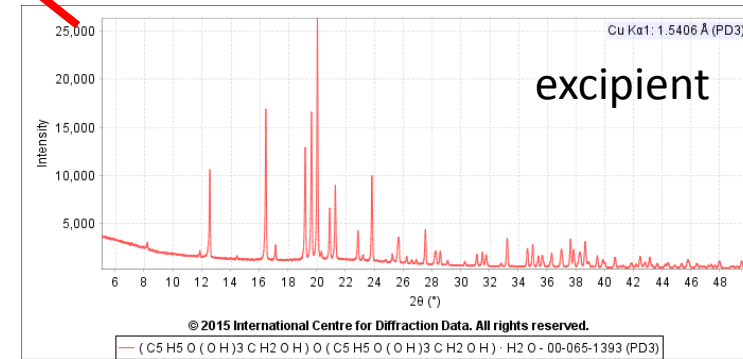
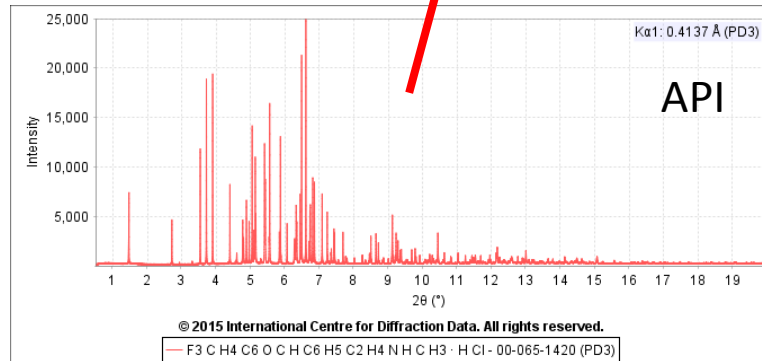
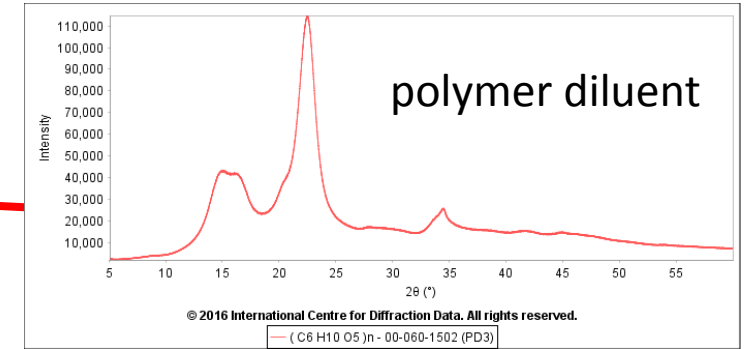
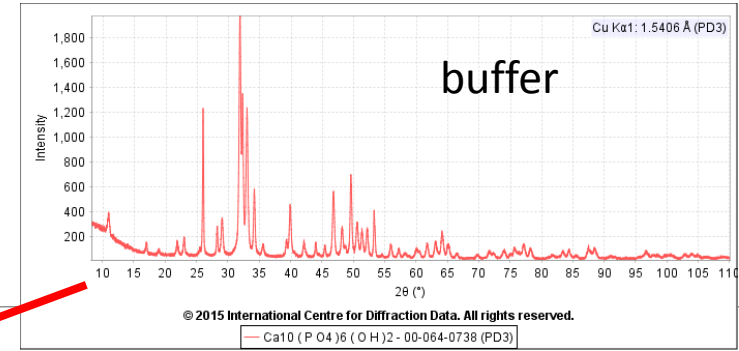
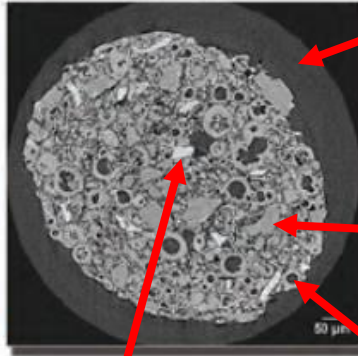
---

- Research the pharmaceutical – understand the drug and formulary being evaluated
- Sample preparation – particle size, sample thickness, specimen displacement
- Instrument alignment – run calibration standards to confirm proper operation
- Data collection – use the proper count time for good counting statistics
- Reference database – must have pharmaceutical and excipient subfiles, editorially reviewed

# The future



3d X-ray tomography  
(courtesy of Rigaku)



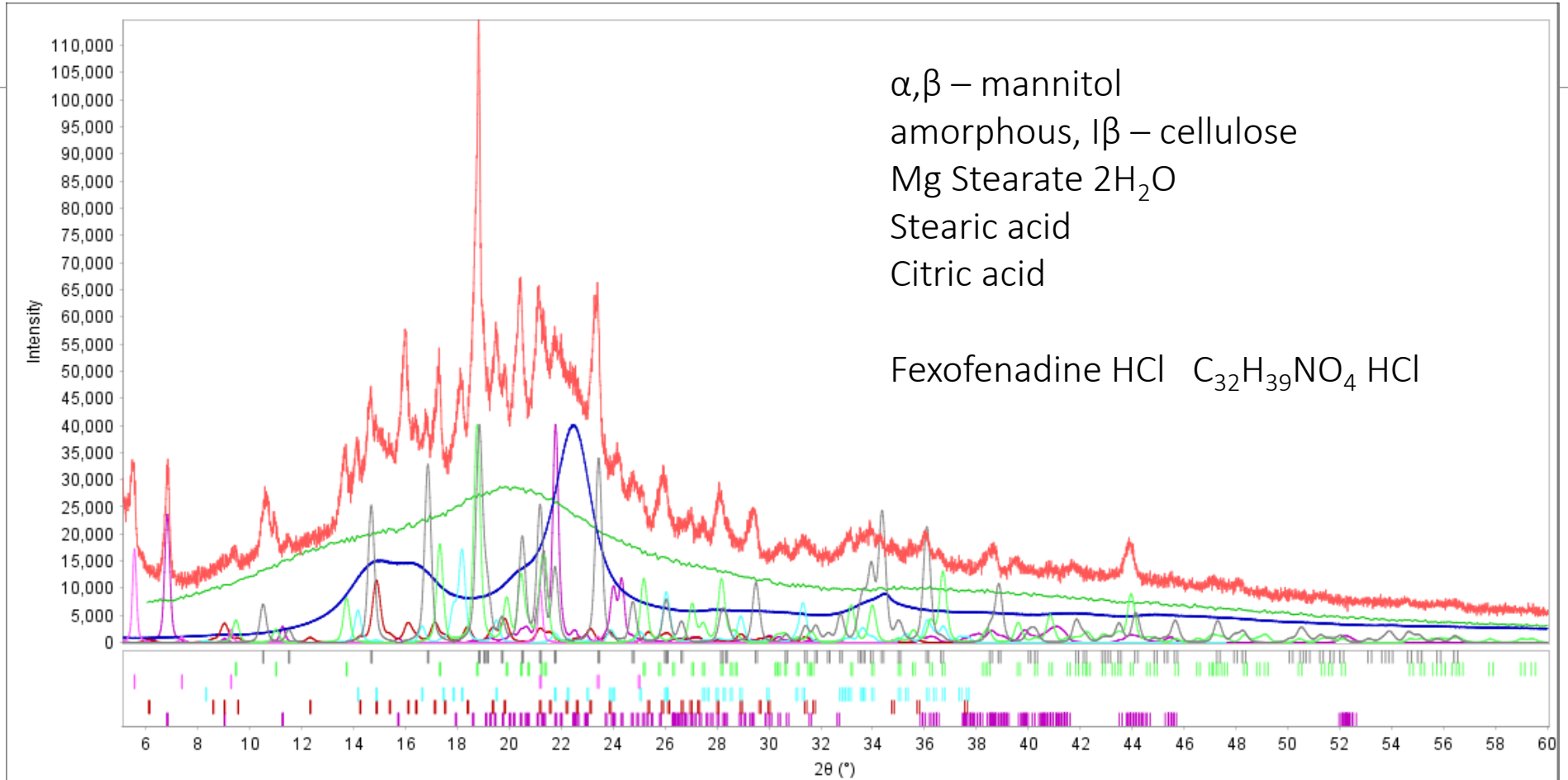
# XRD analysis of Allegra®

---

Allegra (API: Fexofenadine HCl) is an antihistamine used for the treatment of hay fever and related allergy symptoms.



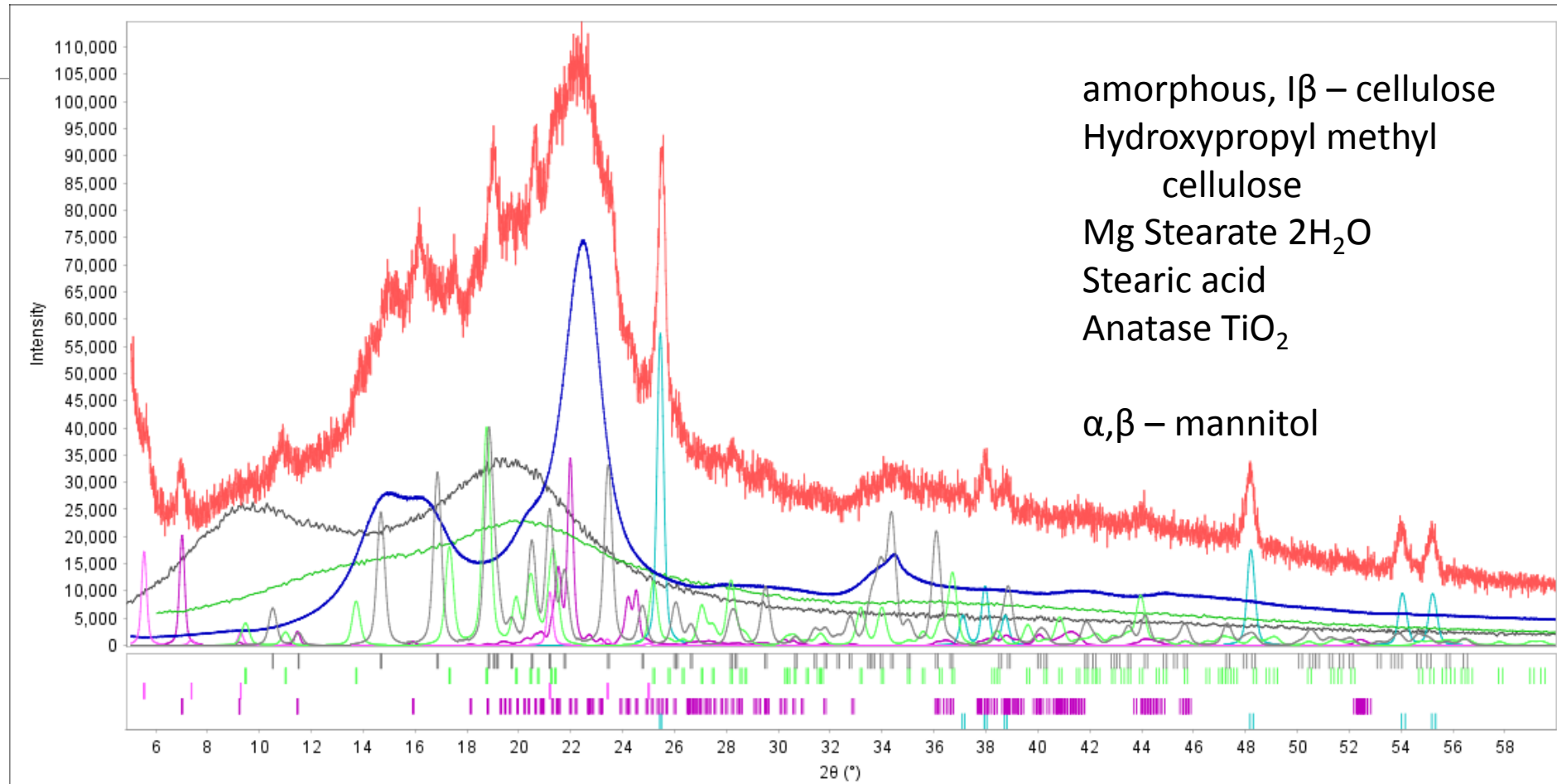
# Phase identification – Allegra<sup>®</sup> core



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— Allegra Core.dat (User Experimental Pattern) — C6 H14 O6 - 00-022-1797 (Exp-based, Intensity: 35.0%) — C6 H14 O6 - 00-022-1793 (Exp-based, Intensity: 35.0%)  
 — C36 H70 Mg O4 · 2 H2 O - 00-054-1973 (Exp-based, Intensity: 15.0%) — C6 H8 O7 - 00-016-1157 (Exp-based, Intensity: 15.0%) — C32 H39 N O4 · H Cl - 00-058-1149 (Exp-based, Intensity: 10.0%)  
 — ( C6 H10 O5 )n - 00-060-1502 (PD3, Intensity: 35.0%) — \*( C6 H10 O5 )n - 00-060-1501 (PD3, Intensity: 25.0%) — C18 H36 O2 - 00-038-1923 (Exp-based)

# Phase identification – Allegra® shell



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- C6 H14 O6 - 00-022-1797 (Exp-based, Intensity: 35.0%)
- C6 H14 O6 - 00-022-1793 (Exp-based, Intensity: 35.0%)
- C36 H70 Mg O4 · 2 H2 O - 00-054-1973 (Exp-based, Intensity: 15.0%)
- (C6 H10 O5)n - 00-060-1502 (PD3, Intensity: 65.0%)
- \*(C6 H10 O5)n - 00-060-1501 (PD3, Intensity: 20.0%)
- C18 H36 O2 - 00-038-1923 (Exp-based, Intensity: 30.0%)
- allegra shell.dat (User Experimental Pattern)
- Ti O2 - 00-021-1272 (Exp-based, Intensity: 50.0%)
- (C36 H70 O19)n - 00-066-1663 (PD3, Intensity: 30.0%)