

EDXRD Probe for Pharmaceutical Verification



The XT250™ System

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Presentation Organization

1. The **XT250**[™] System Concept
2. **Angle**-Dispersive versus **Energy**-Dispersive **XRD**
3. The **XT250** System Geometry
4. Example Data for Solid State Drugs
5. Verification Method
6. Higher Resolution Measurements
7. Future Performance Improvement





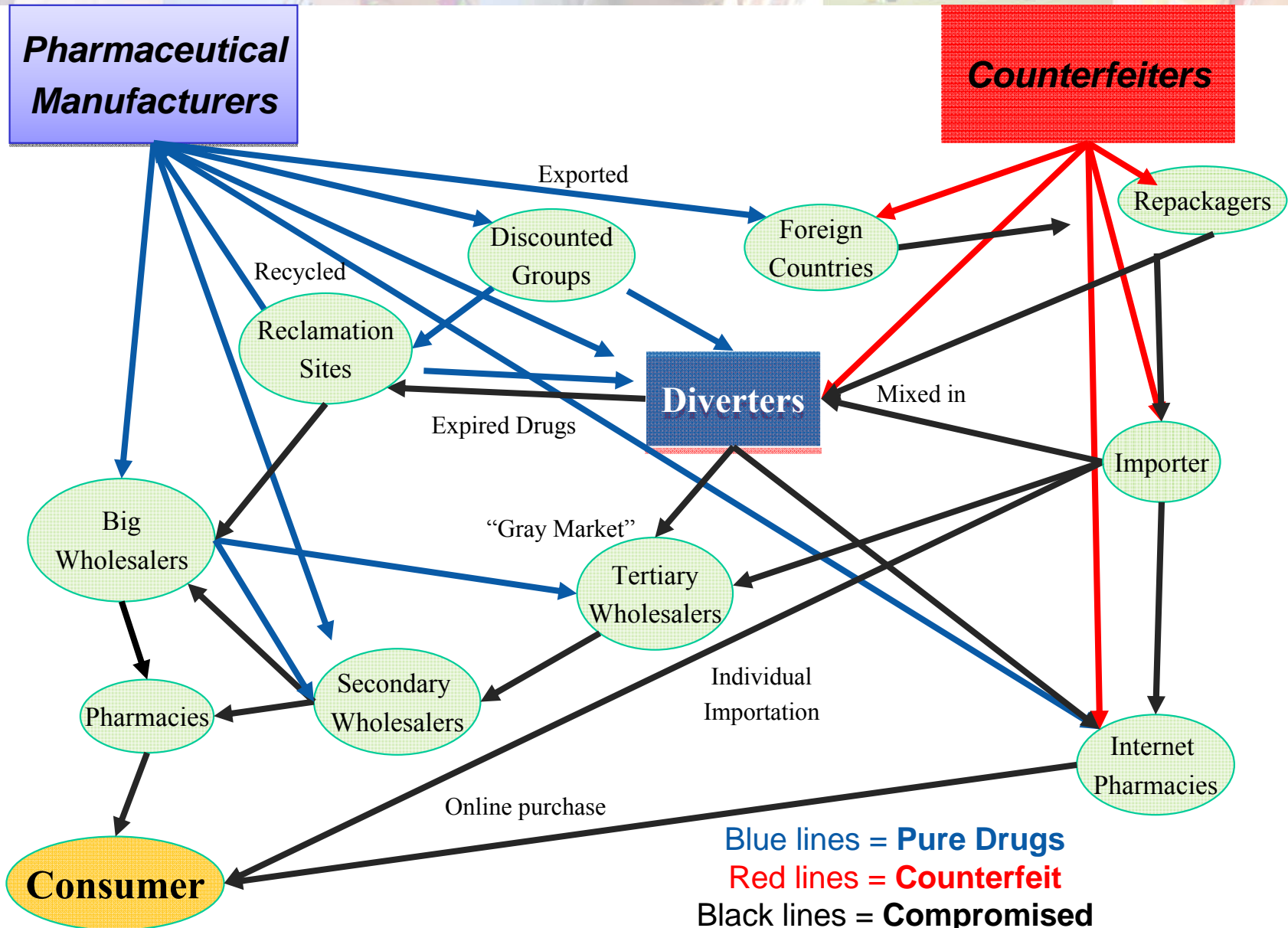
XT250™ System Concept

The **XT250** System is a **qualitative** screening tool to verify solid state drugs in **opaque, sealed** containers. It is based on EDXRD technique.

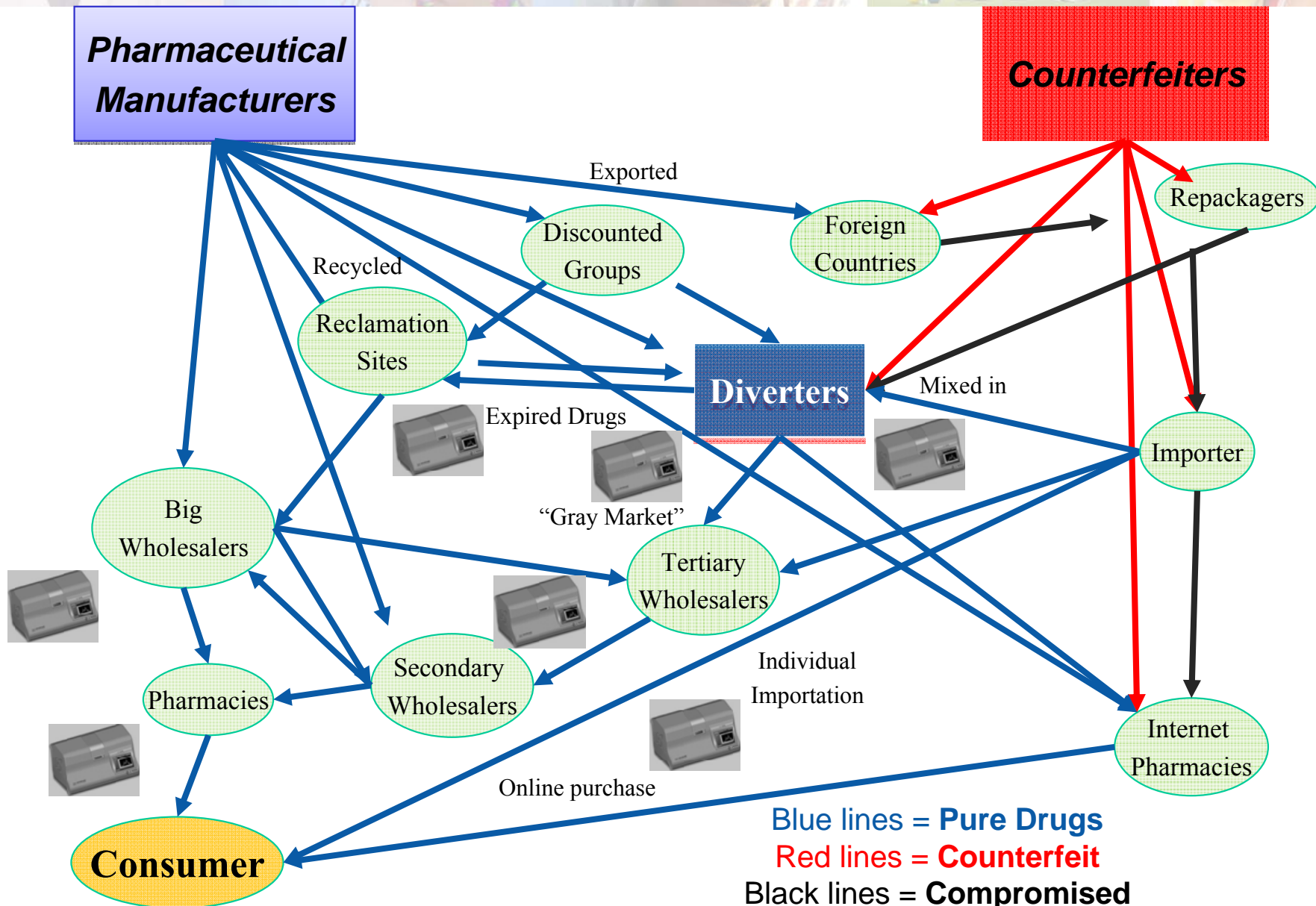
- Accurate
- Fast (*30s to 5min*)
- Trained to recognize drugs
- For non-technical people
- Fits at several points in manufacturing and distribution of pharmaceuticals



Infiltration of US Drug Supply



Protecting the Consumer





Bragg's Law

$$\text{Bragg's Law: } n\lambda = 2d \cdot \sin\theta$$

Where:

n = an integer

λ = wavelength

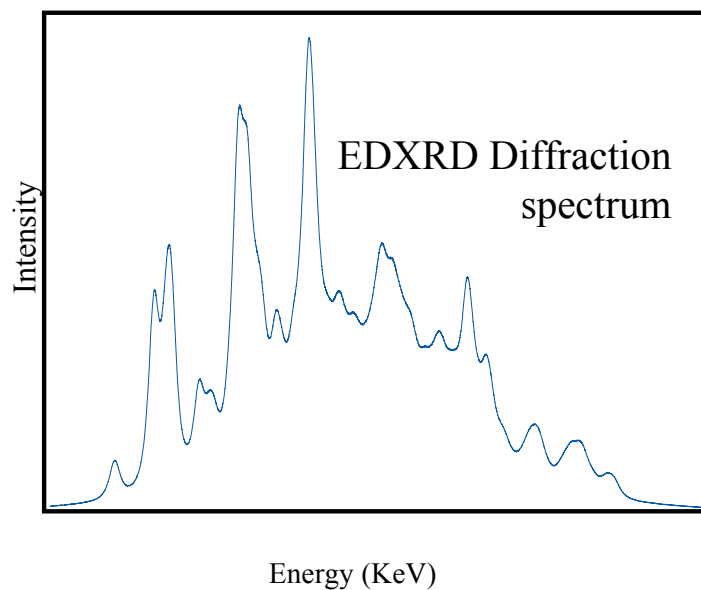
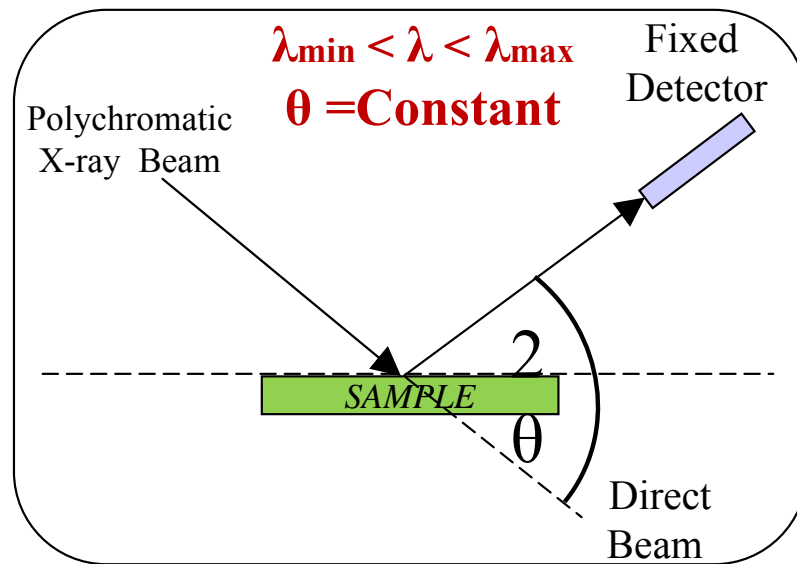
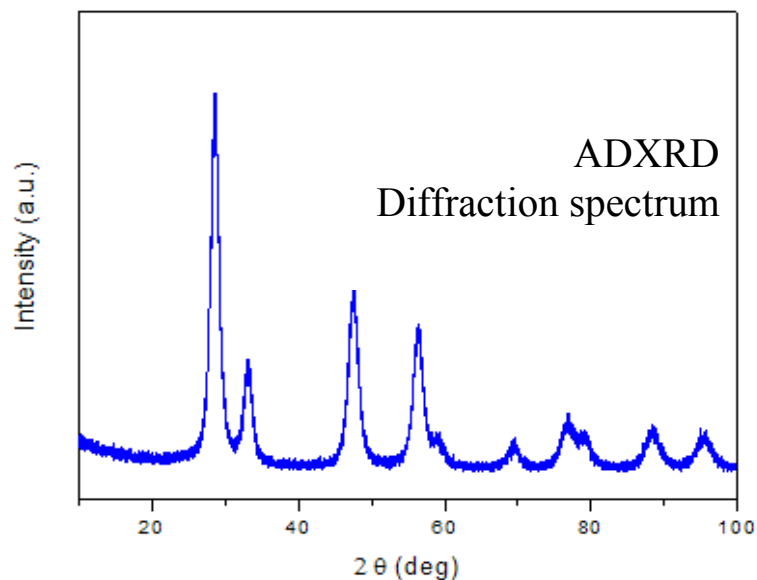
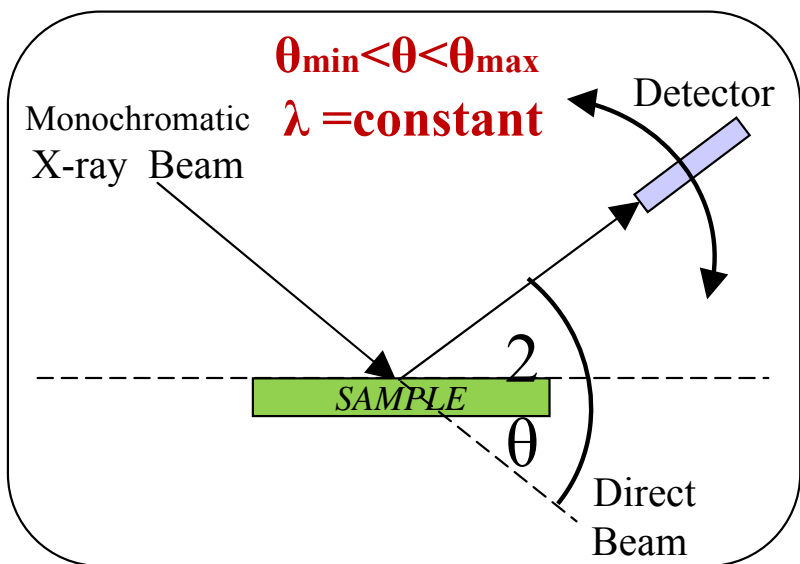
d = d-spacing

θ = diffraction angle

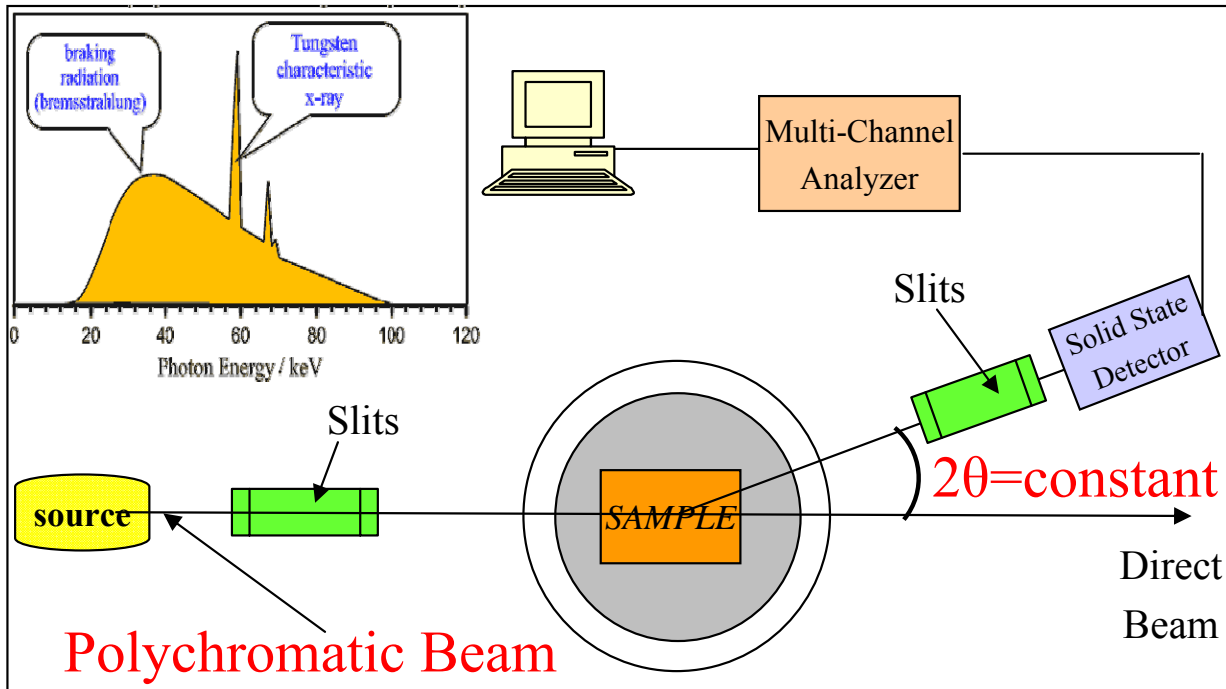


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Angle-Dispersive XRD vs Energy-Dispersive XRD



Traditional EDXRD Experimental Set Up



- Bragg's Law: $\lambda = 2d \cdot \sin\theta$

- In terms of energy:

$$E = h\nu = hc/\lambda = hc/2d \cdot \sin\theta$$

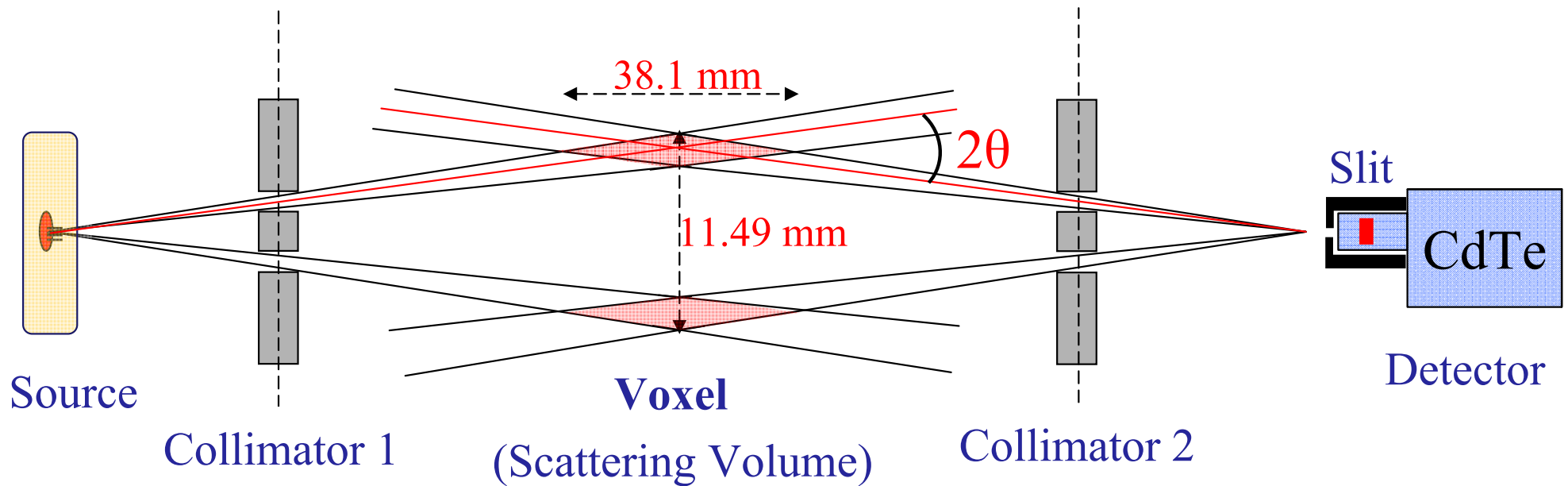
$$E = 6.20/d \cdot \sin\theta$$

- E in KeV, d in Å

- The detector has the capability to resolve diffracted energies.
- Multi-channel analyzer displays the horizontal scale as energy.
- EDXRD is a fast technique and does not require moving any parts.
- Synchrotron radiation are used widely in EDXRD experiments.



The XT250 System Confocal Geometry

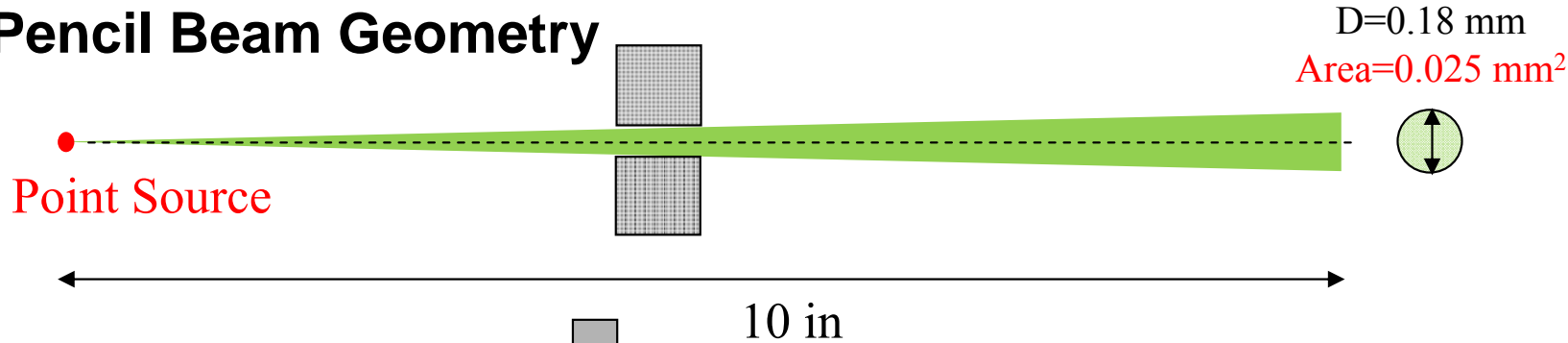


- Confocal geometry requires a source with high flux density
- Air-cooled 40 Watts micro-focused W source: ($\sim 50\mu\text{m}$ focal spot)
- The beam is collimated by circular slit before and after the sample
- CdTe solid state detector thermo-electrically cooled with a resolution $\sim 0.7 \text{ keV}$
- For $\theta=1.28^\circ$ and $0 < E < 80 \text{ keV}$, the d-spacing is $3.39 < d < 27.72 \text{ \AA}$
- Detector slit can vary from 70 mil to 20mil

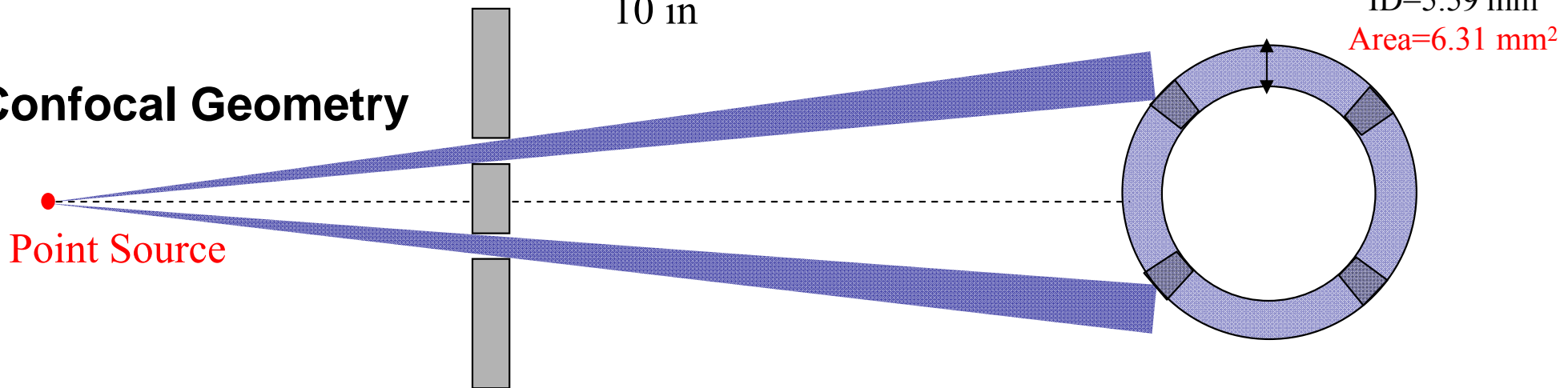


Why Confocal Geometry?

Pencil Beam Geometry



Confocal Geometry

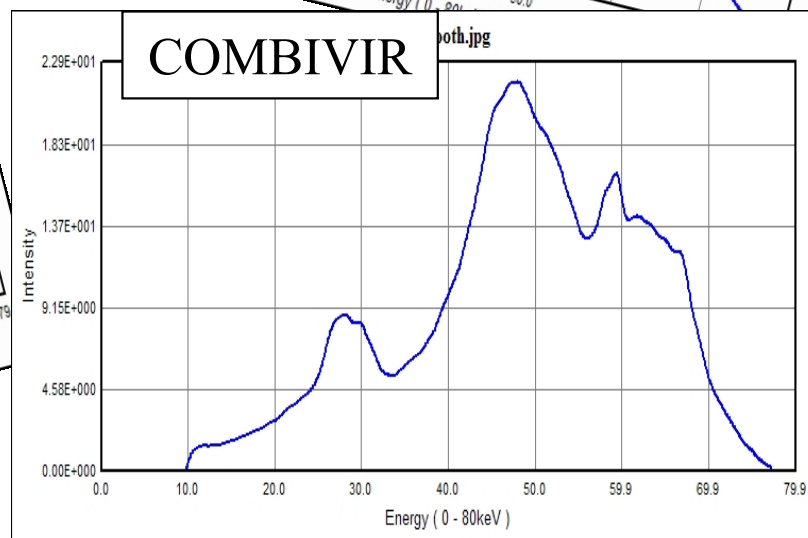
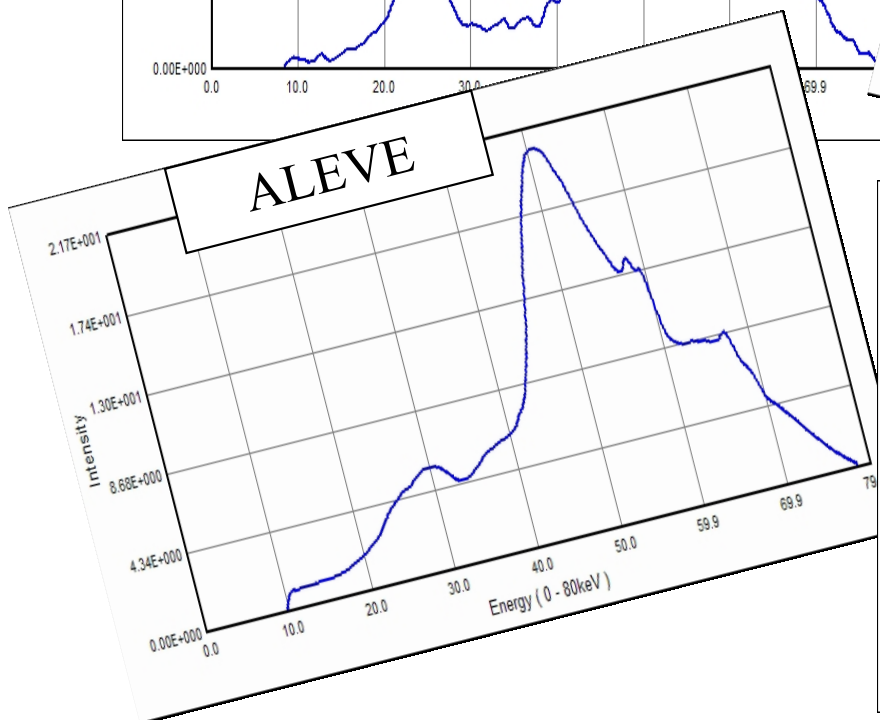
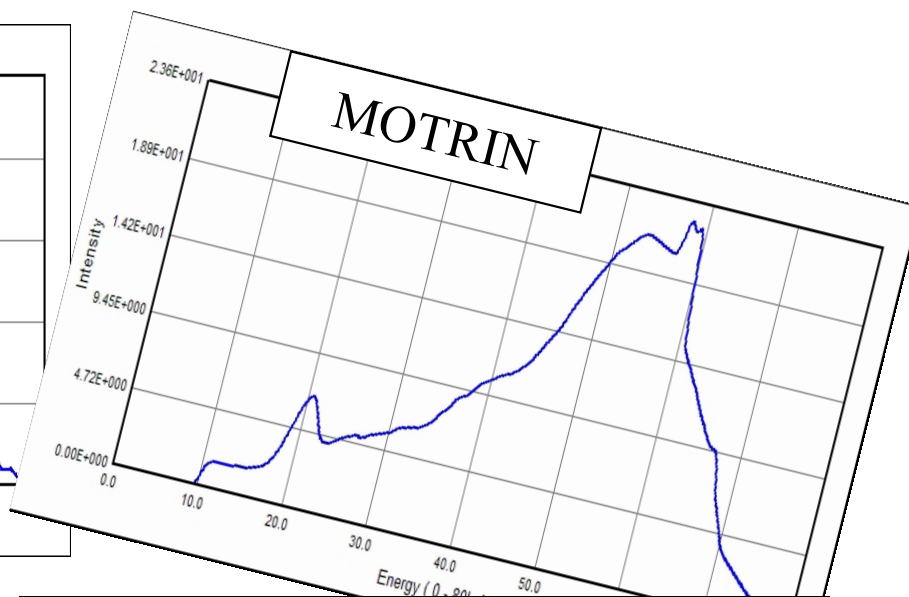
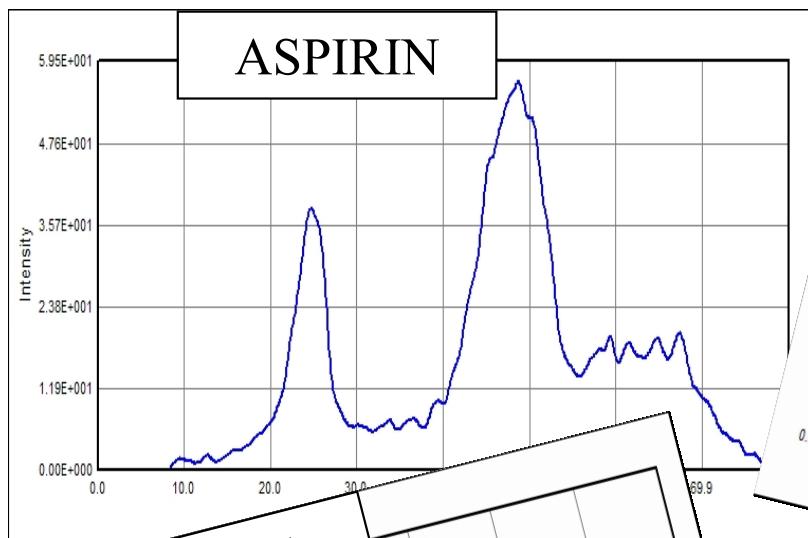


It's important in XRD to have a focused or parallel beam, but it's difficult to do with a white beam having energies above **50 keV**.

Advantages:

- Gain in intensity is **~ 200**.
- The ability to collect signal from a different positions in the specimen.

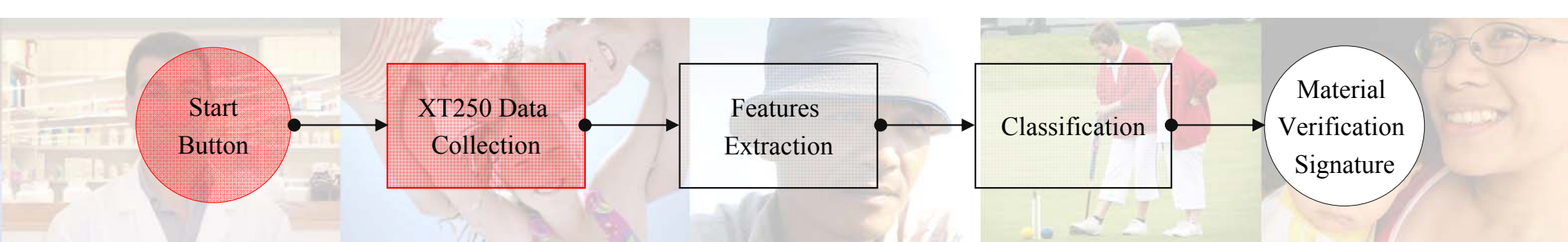
Example Data for Solid Drugs Pills





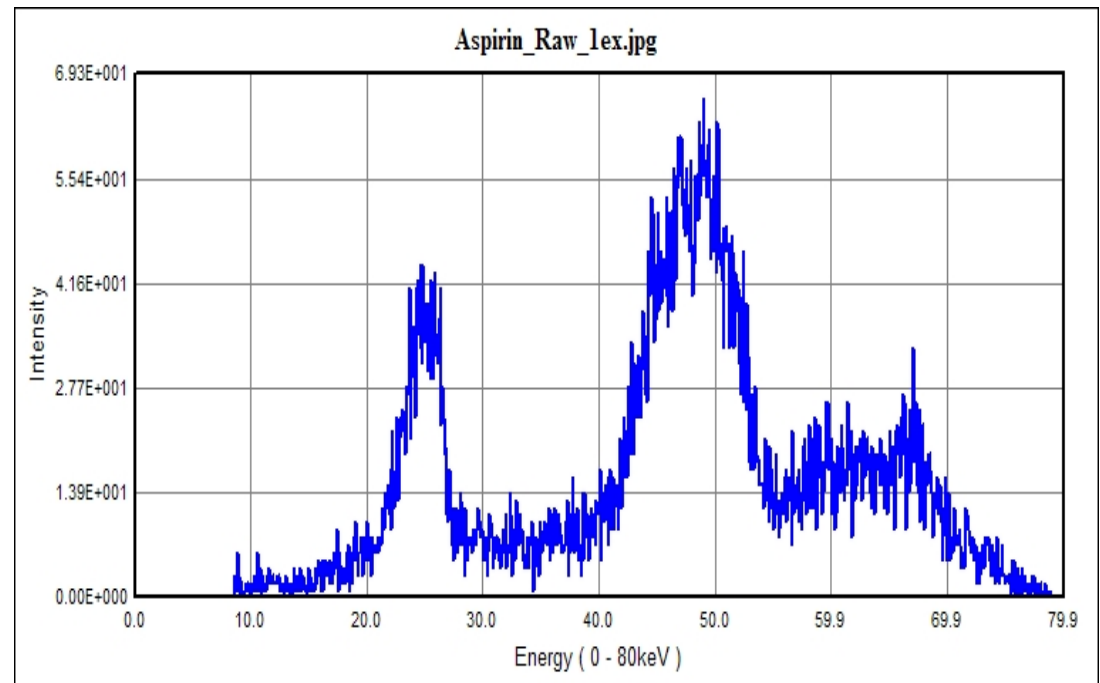
How is a Drug Verified?

- Drugs are verified using **Pattern Recognition** technique.
- Three major steps are required to verify a solid drug:
 - 1.** Data is collected on a drug.
 - 2.** Data is processed and a set of characteristics (i.e., features) are extracted.
 - 3.** A Material Detector uses our proprietary algorithms to check whether these features matches the drug known set of characteristics (features).
- Various Material Detectors can be grouped into custom libraries in our **Material Recognition Software Engine (MRSE)**, which is stored in the machine database.
- The **MRSE** allows automatic and accurate verification of known substances.



1.

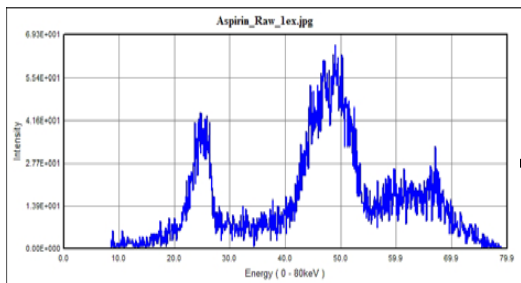
Drug sample is placed in the **XT250 System** / data collected for 5min.



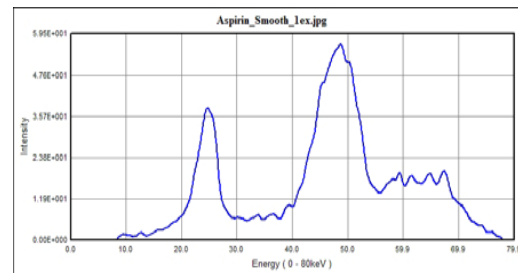
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2.

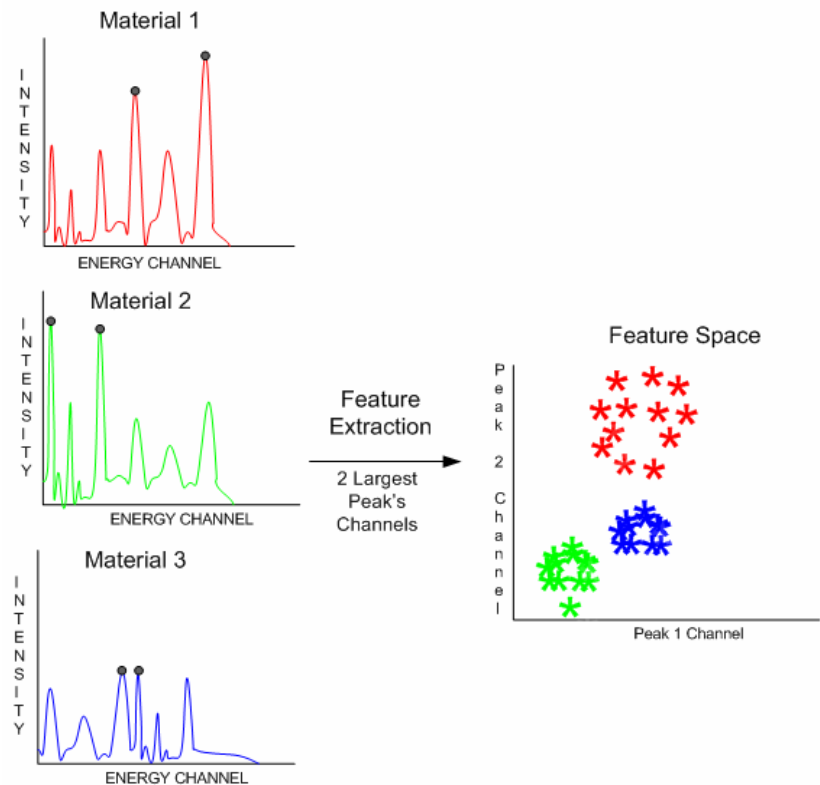
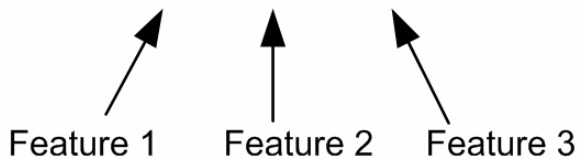


Processing



- Exposure is replaced by a set of features
- Features are selected so that materials can easily be differentiated (peaks position, intensity , FWHM, Area, Background...)
- The number of features can exceed 50 for some samples.

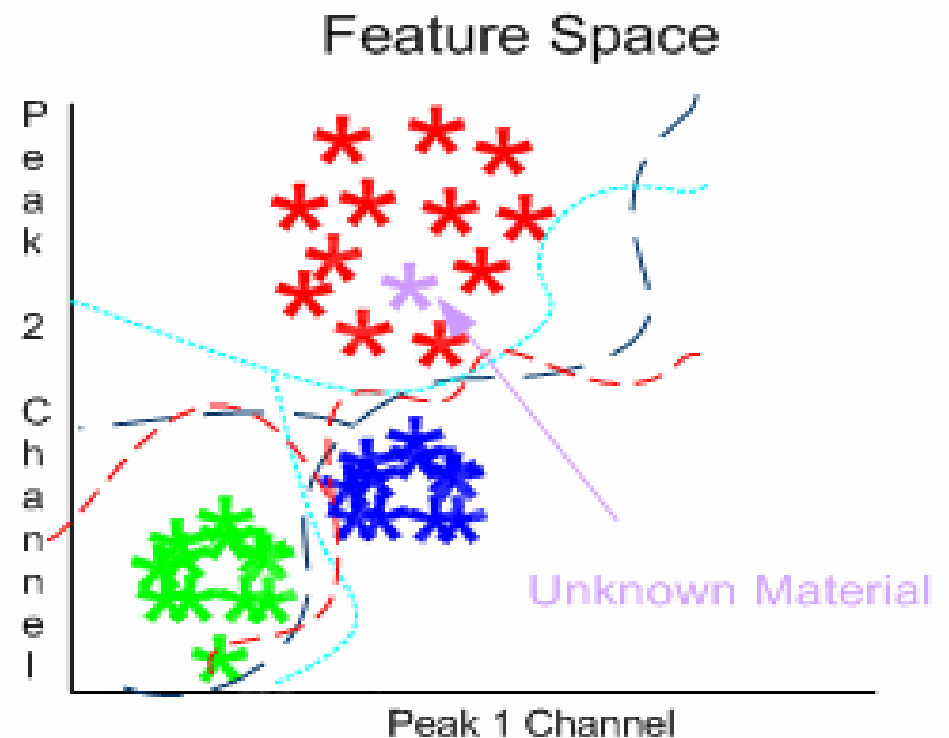
Feature Set: [x1, x2, x3, ...]





3.

- Classifier creates boundaries (decision regions) that separate the materials in the feature space from one another
- Classifiers / Detectors make decisions based on the information they have been trained on
- Many different classification algorithms can be used in this phase



Test Results:

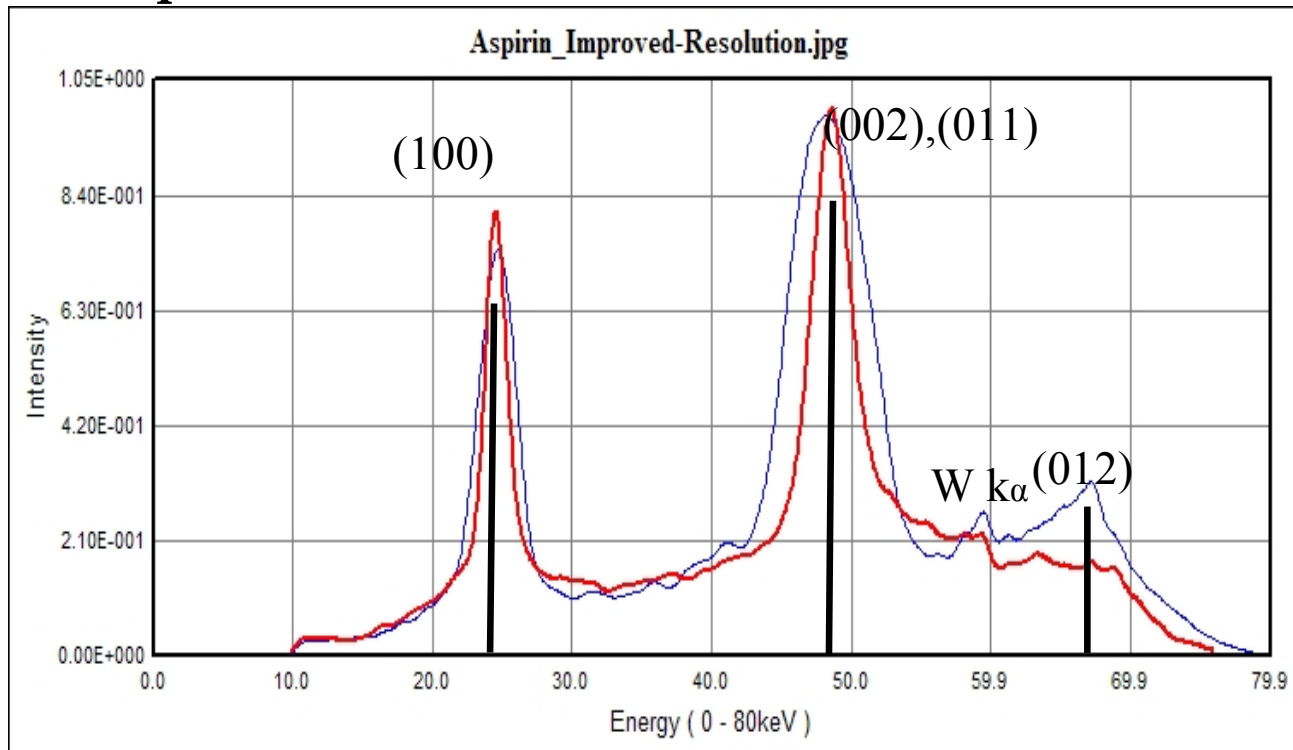
Verification tests have been completed on many drugs,
with MRSE accuracy better than 98%



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Higher Resolution Measurements

Example 1:



FWHM (100)= 1.4keV

FWHM (100)= 3.3keV

Det. Resolution=0.7keV

Red : Detector slit 0.50 mm

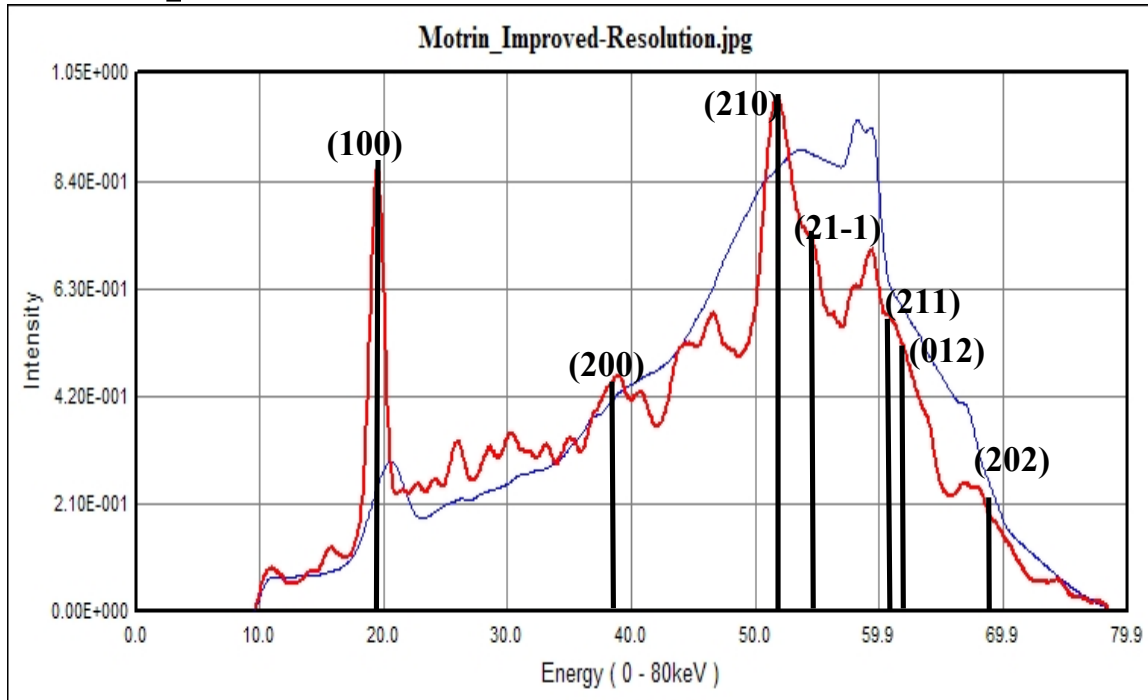
Blue : Detector slit 1.77 mm



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Higher Resolution Measurements

Example 2:



Red : Detector slit 0.50 mm

Blue : Detector slit 1.77 mm

Sample thickness=1/16"

*The black lines represent
Ibuprofen Bragg reflections.*

There are several ways to improve the resolution of the XT250 System:

- 1.Reduce the size of detector slit.
- 2.Use flat samples (~ 1/16" thick).
- 3.Change the collimators size and positions.

Trade-off is between **speed** and **resolution**:

If Resolution
Collection time





Future Performance Improvement

- Increase power
- Address blister packs
(difficult to scan a single pill using the Confocal geometry)
- Robotics for production line use
- Bulk inspection of boxes containing many containers
- Analytical EDXRD applications

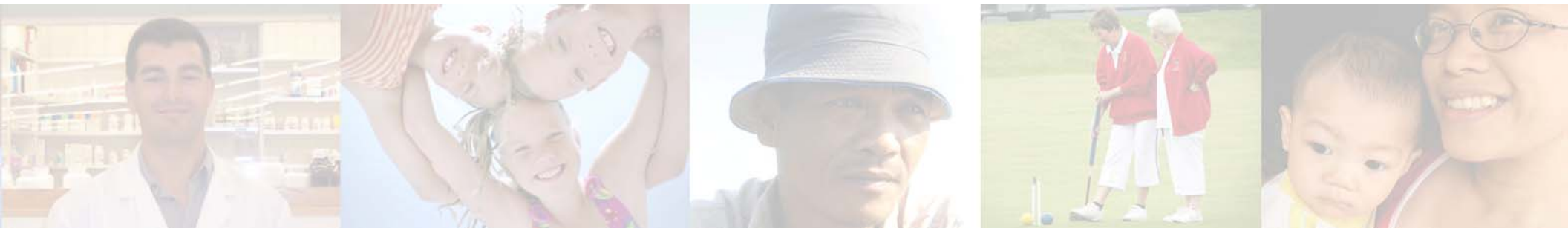




SUMMARY

1. Confocal EDXRD geometry combined with the power of our pattern recognition software (**MRSE**) have proven to **verify** drugs effectively in a short time.
2. High detection; **accuracy** is more than **98%**.
3. Higher instrument resolution can be achieved, but data collection time will increase.
4. The **XT250** System is ideally suited for use in the first line of protection against counterfeit drugs.
5. This technique is used only as a **qualitative** measurement at this present time.





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