

## Raw Materials Verification without Opening the Container



Regulatory authorities often mandate 100% inspection of pharmaceutical incoming goods verification. This is a significant challenge for quality control and a drain on resources, particularly when the container must be opened, as expensive sample handling facilities are required. This note demonstrates a new approach where material verification is performed in the warehouse without opening the container.

### The Packaging Problem

Incoming goods must be verified before they can be used in pharmaceutical manufacture and the most convenient place to do this is in the warehouse shortly after unloading. Techniques based on spectroscopic methods, particularly Raman spectroscopy, are successful in performing this function and their use is growing. However, use of spectroscopy is often limited because the container is not transparent. This means that a wide range of products have to be tested by opening the packaging in a controlled area – typically a powder sampling booth. For most manufacturing plants this is a significant task requiring large amounts of resource and expense.



Cobalt's RapID Instrument

Non-transparent packaging requires the container to be cut open and either a NIR probe inserted or a sample taken for wet testing or IR analysis. The container must be resealed using an approved sealing tag. The powder sampling booth must then be thoroughly cleaned before the next batch can be tested. The total process can add hours or days on to the release of an incoming batch of materials and may risk sample contamination.



Powder sampling booth

### RapID

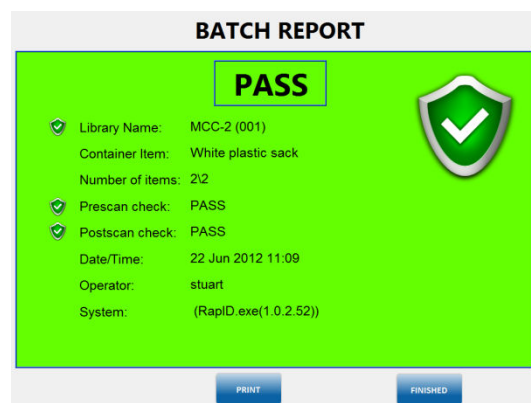
Raman spectroscopy is a powerful tool for identification of materials and is widely used on opened or transparent containers. RapID uses a new variant called Spatially Offset Raman Spectroscopy (SORS) to quickly probe through many common containers to identify the contents. RapID is compatible with plastic and multi-layer paper sacks, as well as plastic and glass bottles.

## RapID in Use

RapID uses SORS to obtain a spectrum through the container and then identifies the material using a library database. RapID is not supplied with a spectral library as the container and contents need to be modelled together. Typically this takes a few hours per container and is a one-time process completed by the user using a software wizard.

## Examples of Materials Verification

To examine the application to the typical flow of goods into a solid oral dosage manufacturing plant a series of containers and their corresponding packaging were analysed. Models were built for each of the materials and verified by cross-checking against the other containers of materials. The analysis should a) unambiguously identify the contents through the packaging and b) not mistake one material for another in the database.



The seven container/contents pairs are listed in the table below and were chosen to be a good representation of typical pharmaceutical raw materials. The model-building and testing were performed under mixed lighting conditions that included strong direct fluorescent light and sunlight. Each model was tested on each of the seven materials between 10 and 30 times and each result recorded. Where RapID positively matched the material 100% of the time a correlation was recorded (green in the matrix) and where a positive match was made 0% of the time it was recorded as a negative match (red in the matrix).

## Conclusion

RapID was successfully used to identifying the contents of a range of common materials in their respective packaging with no false positives. The time taken was 5-20 seconds and the models were robust to cross-validation meaning that RapID can be successfully deployed for all of the test materials.

#	Material	Container Type	ID	Time (s)
1	Avicel (MCC)	White PE sack	✓	13
2	Acetaminophen	White HDPE bottle	✓	5
3	Magnesium stearate	White paper (1 layer)	✓	10
4	Lactose monohydrate	Brown paper (2 layers)	✓	20
5	Lactose (anhydrous)	Brown paper (2 layers)	✓	20
6	Flavonoids	FIBC Container	✓	8
7	Propanol	Brown glass bottle	✓	8

#	1	2	3	4	5	6	7
1	Green	Red	Red	Red	Red	Red	Red
2	Red	Green	Red	Red	Red	Red	Red
3	Red	Red	Green	Red	Red	Red	Red
4	Red	Red	Red	Green	Red	Red	Red
5	Red	Red	Red	Red	Green	Red	Red
6	Red	Red	Red	Red	Red	Green	Red
7	Red	Red	Red	Red	Red	Red	Green

Goods analysed and their containers (left). ID correlation matrix (right) where green is 100% probability of identification and red is 0% probability of identification.