

## Purpose of Analysis

A number of different regulatory authorities demand the evaluation of foreign particulate matter in all types of respiratory drugs. The described test detects inhalable foreign particulate matter (2-10 µm) and larger particles. Furthermore, the type, origin and profile of foreign particulates, including fine particulates, can be directly identified, and the source in the production process can be located and eliminated subsequently.

## Procedure

3 acutations of a dry powder inhaler are collected on a clean bench in a foreign particulate sampling tube, FPST. The powder is dissolved in 150 ml of solvent (Ethanol, Water 30/70). The so prepared suspension is filtered through a 0.8 µm pore size gold coated polycarbonate membrane (filtr.AID, rap.ID)

The particle-loaded area is then automatically analysed with the Single Particle Explorer®. A statistical significant amount of particles (500) larger than 2 µm are identified by the system.

All particles of the samples are counted from 2 µm and up. The system selects after a morphologic analysis of the particles 500 particles for the chemical identification by means of Raman spectroscopic analysis. The collected spectra are automatically compared with previously recorded spectra in a database (see Fig. 2).

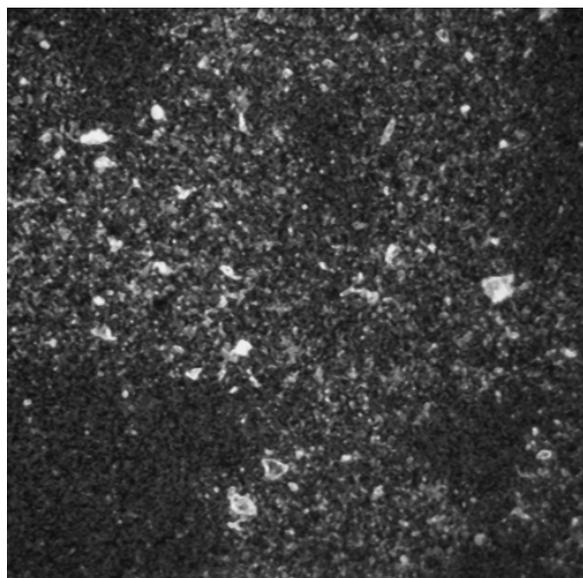


Figure 1: Dark field image of single field of view.

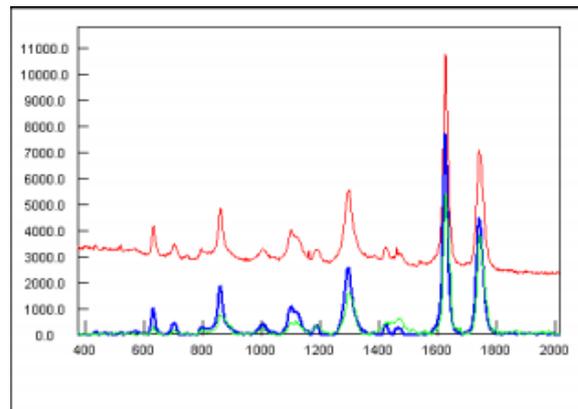


Figure 2: Original spectra in red, proceeding spectra (blue) from the automated database search of the major contamination: Polyester.

## Results Summary

Substance	Nr.	Size			
		2-5	5-10	10-25	≥25
-	-	60	12	5	
Others (9 different species)	77	60	12	5	
Cellulose Acetate	41	32	6	3	
Polyamide	95	78	12	5	
Carbon	141	120	11	8	2
Polyester	160	132	17	7	4
<b>Total</b>	<b>514</b>	<b>422</b>	<b>58</b>	<b>28</b>	<b>6</b>

Table 1: Identified Particle > 2 µm from the capsule powder after dissolving the actives and excipients.

Single Particle Explorer identified 514 particles. Major product contaminants (160 of 514 particles) could be assigned to Polyester and Carbon (141 particles.) Particles larger than 25 µm were found for both substances. Polyamide and Cellulose Acetate were identified as two additional impurities.

## Benefits

With the patented filtr.AID technology, quick collection of samples and low background counts are ensured.

The fully automated identification of foreign particles from the DPI sample is a big advantage, and helps to determine contamination sources in primary package materials as well as in production processes.

The results obtained with the Single Particle Explorer® enable statistically relevant and reliable conclusions about particle chemical composition in a short time period. This enables for the main contamination sources to be detected.