Liquid Particle Explorer® Application Note

Identification of Foreign Particles in Dry Powder Inhaler Product

Sample Description

rap.ID test sample: Powder from 10 dry powder inhaler (DPI) capsules.

Purpose of Analysis

A number of different regulatory authorities demand the evaluation of foreign particles in all types of respiratory drugs. The described test is useful for detection of foreign particulate matter and large particles and agglomerates of the drug substance as well. It can define morphology of drug substances and carrier 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

The primary package of the product is opened and its content is sucked through an area with a diameter of 4 mm of the patented membrane filter.

The particle-loaded area is then automatically analyzed with the Liquid Particle Explorer®. Each particle larger than 2 µm is identified by the system.

The system works highly automated. Only three parameters had to be set: **1.** Size of the particle loaded area of the membrane. This was 4 mm. **2.** Only particles larger than 2 µm where evaluated by the system. **3.** Each particle was exposed to the laserbeam and measured for a time of 30 s. The Raman spectrum was interpreted automatically by the comparison with an internal Raman database.

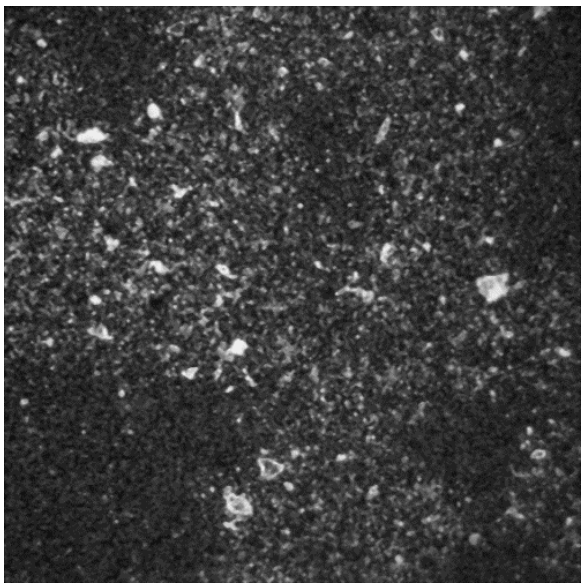

Figure 1: Dark field picture of on automatically generated microscopic image (500 µm x 500 µm).

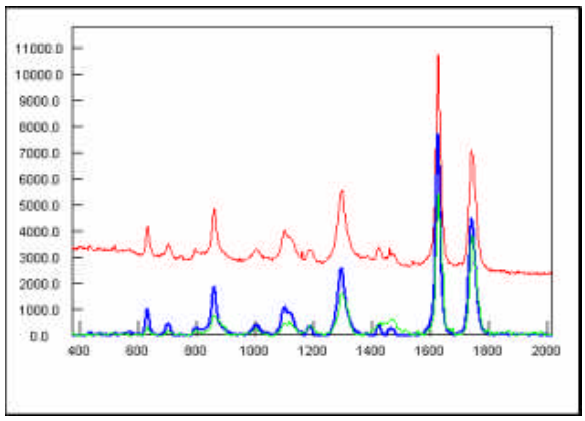

Figure 2: Original spectra of one particle (red), proceeding spectra (blue) from the automated database search of the major contamination: Polyester.

Results Summary

Substance	Nr.	Size			
-	-	2-5	5-10	10-25	≥25
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
Total	**514**	**422**	**58**	**28**	**6**

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

514 particles where investigated by Raman spectroscopy leading to high quality spectra, which were analyzed by the APSys - Identifier® database. The major product contaminations (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. Other contaminants were only found in lower numbers and totaled 95 particles for 9 different species.

Benefits

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

The results obtained with the Liquid Particle Explorer® enable statistically relevant and reliable conclusions about the chemical composition of the particles in a short time period. The main contamination sources can be detected.

Phone: +49 (0)30 6576 3440 Email: LPE@rap-ID.com Web: www.rap-ID.com