

Foreign Particles Method Development and Identification in Inhalable Drug Products with Single Particle Explorer in the QbD Paradigm

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Dedicated Approach for Foreign Particles



filtr.AID



Sample Preparation

The special filtration and sample preparation equipment and the controlled filtr.AID filters minimized the amount of time for cleaning of the equipment and resulted in the quick establishment of a low blank value.



Single Particle Explorer



Database

Enumeration

Substance	All particles	Size distribution (µm)						
		2-5	5-10	10-25	25-50	50-100	100-200	
All particles	4516	2368	1976	459	846	660	207	



ID Raman

Use of the LPE streamlined method development, directly verifying ideal active and carrier dissolution parameters with integrated Raman



Substance	All particles	Size distribution (µm)						
		2-5	5-10	10-25	25-50	50-100	100-200	
Polysorbate	230	58	34	20	0	20	20	
Polysorbate	154	29	2	56	0	59	4	
Polysorbate	59	146	22	12	34	7	7	
Talcom	26	17	7	9	21	18	0	
Proline	221	97	0	27	24	44	14	
Analysed	800	347	65	124	79	140	45	
All particles	8516	2368	1976	459	846	660	207	

ID Result for Lactose

Identifying Control Points of a Dry Powder Inhaler Formulation



Process Environment

As an example, several parts of a dry powder inhaler formulation were measured separately. For each part, an FP assessment method was developed and validated. In the validation step the linearity, robustness, repeatability and intermediate precision were tested according to the ICH parameters.



Formulation

Active 1

Active 2

Lactose



Delivery Device

For three of the major components of the inhaler, different methods of particle extraction were established. This was also

Part A

Part B

Part C



Delivered Dose

Particle Counting Results after Method Development Qualification of Components and Parts of a Dry Powder Formulation and the

Substance	Amount (mg)	Size Distribution (µm)						
		All particles	>=2	>=5	>=10	>=25	>=50	>=100
Active 1	33	2264	1550	345	267	81	17	4
Active 2	39	1999	1634	224	89	48	4	0
Lactose	507	6516	3524	1475	978	357	174	8
Part A	1 Piece	1668	988	415	197	48	17	3
Part B	1 Piece	13521	6345	4215	1987	635	287	52
Part C	1 Piece	15958	7865	4486	2450	784	325	48
Delivered Dose	7 Actuations	678	485	117	52	19	4	1

The Analytical Method leads to the right Decision

In the development of the Design Space for enumeration and identification of foreign particulate matter, possible factors affecting measurement results must first be considered.

Design Space

Enumeration Development Batches

Stability Trend

No

Control Space

Specification for NDA

Enumeration

OOS/ OOT

No

Yes

Development

Routine QC

LPE High Throughput Raman spectroscopy enables quick root cause and the elimination of source of foreign particles directly after enumeration without further sample preparation.

Root Cause