rap.ID Single Particle Explorer® Application Note

Measuring Silicone Oil Interaction with Formulation through Particle ID

Silicone oil in biopharmaceuticals can induce particle formation

Many biopharmaceutical actives are lipophilic. So they are prone to strong interactions with the silicone oil used in prefillable syringes or vials. This can result in the aggregation and formation of visible rejects after storage time, or simply in the loss of product potency. Information about this behaviour on a sub-micron level is very valuable for biopharmaceutical drug development.

Isolation and identification with the Single Particle Explorer

A biopharmaceutical formulation was filtered through a 5 µm filtr.AID membrane, rap.ID. The sample was washed 3x with 10 ml particle free (0.45 µm syringe filter) WFI.

This membrane was evaluated by means of the qualified automated 532 nm Raman system, the Single Particle Explorer (SPE), rap.ID. Integrated dark field illumination and image analysis is able to pick up sub micrometer layers on the membrane and count them as particles.

The SPE was set up to measure an Effective Filtration Area (EFA) of 5.6 x 5.6 mm. From the image information the entire Particle Size Distribution was available in 3 minutes.

The 2068 largest particles were chosen for the automated Raman Spectroscopy with an integration time of 5s each. After only 3 hours the result (images, spectra and interpretation) was stored in a 21 CFR Part 11 compliant report file.

Results from the automated imaging analysis and Raman measurement

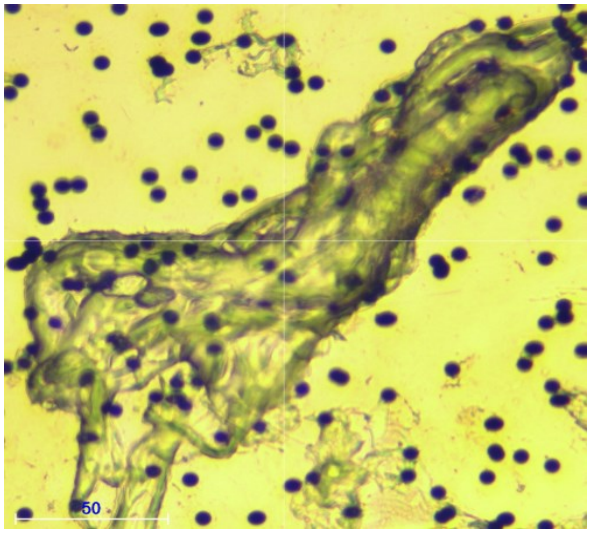

Fig.1: dark field image of a 335 µm particle

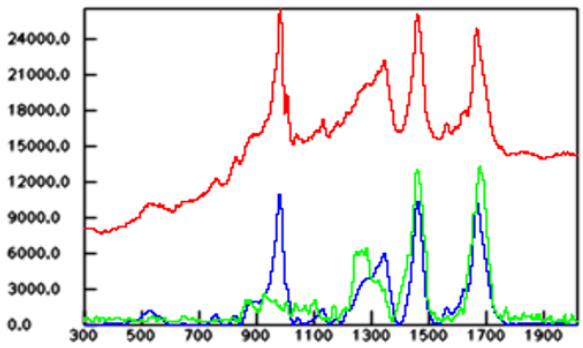

Fig.2: Raman Spectra of the API (protein) (red original, blue optimized, green database)

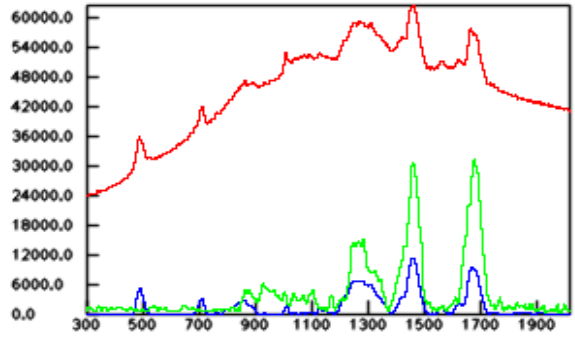

Fig. 3: Raman Spectra of silicone oil and mixed Protein

The amount of particles consisting of pure protein and those of silicone and of intermediates are documented displayed in a condensed table format.

Tab. 1: particle size and compound distribution

Particle Size Distribution						
Total	2-5µm	5-10 µm	10-25 µm	25-50 µm	50-100µm	>=100
Silicone	380	54	18	5	0	0
Glass	143	24	3	1	0	0
Stopper	53	12	8	3	0	0
Silicone + API	1278	678	287	153	73	15
Protein API	167	76	32	6	0	0
TWEEN 80	45	13	4	1	0	0
Cellulose	2	19	13	5	1	0
Identified	2068	876	365	174	74	15
Particle Count	2480	876	365	174	74	15

Meaningful stability data within 3 hours

In combination with the filtr.AID membrane, SPE gives fast, easy access to determine the possibility of protein-related particle formation @ 2 µm. In total 2068 particles were identified by means of 532 nm Raman Spectroscopy with the SPE in only 1 hour.

This allows the monitoring of particle formation due to silicone oil interaction within the biopharmaceutical formulation on a statistically meaningful basis.

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