Liquid Particle Explorer® Application Note

IPC – Root Cause Search in Clean Production Processes

Particle Reduction

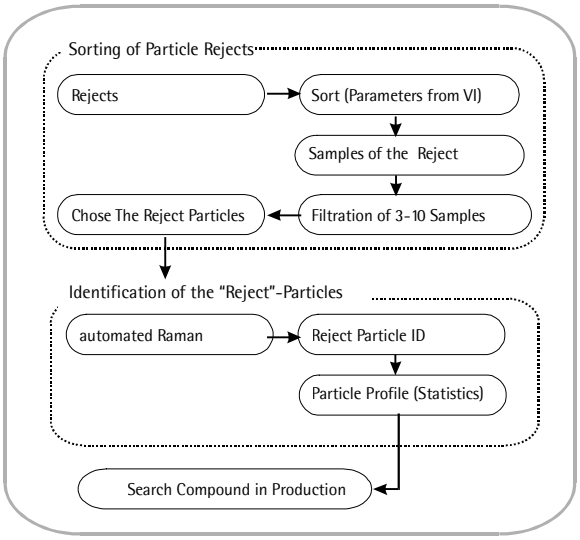
Root cause search is necessary when a known process does not conform to its specification. If the reason is a high load of unwanted particles or visual particle contamination, it is necessary to search and eliminate the source of these contaminations.

First, the particles which are responsible for the out of specification (OOS) situation have to be identified, the so-called Reject Particle. After the isolation of those Reject Particles on the APSys-membrane® the automated Raman spectroscopy is performed. After obtaining spectra of the Reject Particles a sample of the suspected material can be taken in production to verify the finding.

Identification of the Reject Particle

Very often different types of particles are categorized through visual inspection. In most of the cases "fibers" or "black particles" are recognized. The result of this selection is used for further determination of the particles.

After this procedure the samples are filtered on the membrane and investigated as described in [1].



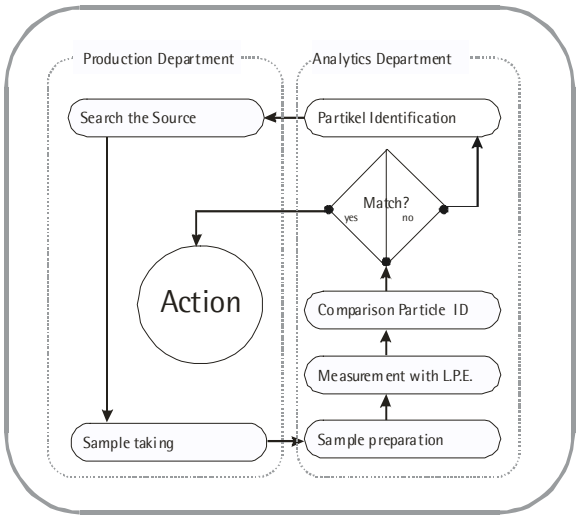
The automated database search usually gives reliable results. The finding is ranked and the automated system only gives a result if the spectrum fits better than 85% to the stored spectrum. The integrated database consists of more than 600 spectra of real life samples of pharmaceutical production and is customized for each customer with not more than 100 product specific spectra. Our experience with identifying of some 500 parenterals shows that regularly 95% of the particles where identified, at least the material class.

The search of the specific particle source in the production can than started directly and purposeful. For example the finding of polyethylene (PE) with a consistency of 86% leads to a search for different sources of PE. If the exact match e.g. high-density polyethylene (HDPE) of a specific cap is found the consistency rises up to 98%.

At less good match of the spectra itself points at the class of the material. If, for example, an Ester Raman bands show up, some more trial samples have to be collected and measured. With the standardized procedure and the APSys Identifier® software it is easy for everyone to compare the samples with the spectra of the Reject Particle. Rap.ID supports its customers by offering external database searches. Customers use this service simply by sending a spectrum via Email to obtain the result within minutes.

Allocation of the materials to the process

Often a major contamination can be identified [1] by performing statistical measurements. The following figure shows a scheme that describes the iterative approach and the intensive cooperation between the departments of production and analytical/quality assurance.



After the identification of the material with the automated Raman spectroscopy it is very important for final verification of the result to track down the assumed source of the contamination in the production process and to obtain its spectrum, too. After successful allocation the new spectra from the material sample will be added to the database with a mouse click. These additional data will be the best possible basis of the future supervision.

Benefits

The identification of contamination and the allocation of its source within hours in the production process safes cost: The reject rate is lowered significantly and the danger of batch loss is minimized.

[1] rap.ID Application Note: Identification of Foreign Particles in Small Volume Parenterals.

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