PARTICULATE CONTAMINATION ANALYSIS AND CONTROL

Particle contamination analysis helping to eliminate risk in industry.

Extraneous matter such as particulate contamination in products such as pharmaceuticals, medical devices, specialty chemicals and others can impact production efficiency, product quality control and brand integrity. Consequently, it is critical to identify and mitigate the risk of particulate contamination in your product, operation or supply chain.

Particulate contamination
One of the most serious problems facing industry today is particulate contamination. Usually, contaminants are present as microscopic particles however these can become a significant issue if they carry a toxicological risk, become large enough to be visible to the naked eye or otherwise make their presence known by being a “performance detractor” with respect to the specific product concerned.

Particulate contamination investigations encompass the identification of microscopic particles, the isolation of different particulate phases of in-homogeneous production deposits and determination of the source(s) of the various contaminants. The aim of these steps is to deliver the insight required to facilitate decision making and so mitigate the negative impact of particulate contamination on product quality (and safety) or production efficiency. The impact of particles finding their way into valuable samples, such as pharmaceuticals and medical devices (for example) is wide-reaching; it can mean manufacturing processes inefficiencies, compromised product quality and delays in the delivery of product to patients. However, once the source of contamination is known, action can be taken to control and prevent any future occurrence.

A forensic, step-wise approach to particulate contamination analysis starts with good communication between the investigator and client to understand the manufacturing process, the nature of the product itself and how the extraneous material has impacted the process or product.

In terms of particle analysis, chemists in the 21st Century have a huge range of analytical techniques available to them for the solution of chemical problems. However, in the case of particulate contamination, preliminary microscopical examination assists in ensuring recognition of the issue at hand, isolation of particles critical to the investigation and a more focused choice of subsequent instrumentation with which to solve the problem. Without microscopy at the forefront of particle analysis, many of today’s particulate contamination issues would go unsolved. The reason microscopy forms a firm foundation for particle analysis is that the unaided human eye & brain are capable of recognizing thousands of objects – this natural skill being transferred to microscopic particles through the use of the light or polarizing microscope.

Following microscopic investigation, other analytical techniques can be more sensibly applied with their selection based on knowledge generated through microscopy.
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Particulate contamination can occur unexpectedly at multiple points along the supply chain and can typically involve:

- Extraneous particulates or fibers
- Residuals from cleaning and maintenance
- Particles observed upon dissolution
- Metal abrasion and corrosion
- Particles stemming from process equipment (e.g., PTFE particles from filters, joints or gaskets)
- Glass fragments caused by glass delamination or breakage
- Biological matter of microbiological origin
- Mineral particles where the manufacturing or geographic origin is important
- Rubber, silicone or other polymeric particles

Our strategic approach
Our experts apply their knowledge and world experience to identify contaminants and locate their source, driving greater knowledge about supply chains, processes and products while working closely with our clients to implement necessary contamination control actions or validate legal action.

We adopt a strategic approach to identifying contaminants which includes expertise in sampling and sample preparation, visual / physical examination, chemical identification and root cause analysis. Using microscopy techniques, contaminant particles are digitally imaged to provide forensic traceability. Following the initial microscopical assessment, analysis can be performed using Energy-Dispersive X-Ray Spectroscopy (EDX) on isolated particles using Scanning Electron Microscopy (SEM) or vibrational spectroscopy (Infra-Red or Raman), as appropriate.

To characterise the size or shape of contaminating particles, photomicrography, image analysis and particle sizing are used to assess and quantify so that comparisons with “latent” or “suspect” contaminants can be made to increase the weight of evidence relating to potential sources.

Intertek offers both standardized and rapid deployment services for the identification and characterization of particulate contaminants and impurities using the following techniques:

- Molecular Spectroscopy: including Nuclear Magnetic Resonance Spectroscopy (NMR) and Pyrolysis Mass Spectroscopy.
- Surface analysis: X-ray photoelectron spectroscopy (XPS)
- Thermal analysis e.g. Differential scanning calorimetry (DSC)

Sampling and sample preparation
Whether your contamination is embedded in a solid, gel or liquid, is present in a homogeneous or heterogeneous environment, is of organic or inorganic nature or appears as fibers or crystallites, our experts apply the most suitable preparation method for your samples. Sampling of particles is rarely straightforward and cross-contamination has to be avoided. We can advise on proper sample collection and can suggest appropriate sample packing or can provide suitable packaging material. Alternatively, our experts can visit your site and take care of sample collection and transport.

Visual characterization
Microscopy techniques play an important role and, in the hands of an experienced scientist, can reveal information regarding particle size, morphology, consistency, shape, color, unique features and whether the sample is either of organic or inorganic nature. Light microscopy can be used for low magnification viewing, typically an essential first step on the road to identification as it offers a rapid assessment of some of the distinguishing features which can be used to direct the investigation and make progress towards identification. Our multidisciplinary team of experts carefully document (using digital media) the visual appearance of foreign particulate matter.

Chemical identification
Our scientists deploy microscope based techniques such as SEM with EDX which can provide valuable elemental information about particulate chemical composition. We also apply spectroscopy techniques such as infra-red (ATR-FIR), FTIR Imaging, Raman imaging and confocal Raman microscopy often with supporting techniques such as TDS-CCAMS, GC/MS, LC/MS, NMR, MALDI-MS to expertly characterise “unknown” particulate matter. Raman spectroscopy, in particular, can be yielded valuable information whilst being non-destructive. It allows analysis of materials in glass vials, polymer containers both in water and other transparent solvents. Orientation information can be obtained using polarization of the light signal with good spatial resolution. The technique complements infrared microscopy in terms of the chemical information obtained.

Contamination root cause analysis and control
We have the capability to fully review analytical results and assess the findings of analytical studies focused on contamination incidents associated with production, engineering and the supply chain.

Our Total Quality Assurance expertise is deployed accurately and rapidly, enabling you to identify and mitigate the intrinsic risk in your operations, supply chains and products. We go beyond just “testing” to look at the underlying elements that have contributed to the contamination. Our experts provide the tailored assurance solutions you need to define both corrective and preventive measures.

CASE STUDY: MANUFACTURING CONTAMINANT PARTICLE ISOLATED ON A SWAB

In a production sample, multiple particulates of metallic matter were observed exiting a certain processing vessel. The vessel was swabbed and the particulates were isolated from the swab fabric followed by rapid deployment of instrumental analysis at Intertek.

Our Solution
Images were obtained by SEM Philips XL30 SFEG SEM in backscatter electron detection mode (BSE) for effective differentiation between atomic number. The particles <10 microns were imaged and separately probed for elemental composition using EDAX. Particle 1A is a particle consistent with stainless steel swarf and Particle 1B is consistent with Alumina (Figure 1).

Benefit delivered to our client
This nondestructive approach allowed qualitative information to identify the nature of the particulate contamination. In this case, the production vessel integrity had been found to be compromised through the use of an abrasive cleaning material.
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**CASE STUDY: GLASS PARTICULATE FROM PACKAGING**

Glass vial packaging was investigated for compatibility with a drug formulation and stored at extreme conditions as part of an “accelerated” stability study. Flakes were observed in multiple vials by the naked eye after stability-storage.

**Our Solution**
The solutions were filtered and the isolated flakes were examined by SEM. The photograph (below) shows an SEM image of what appear to be glass flakes on the filter media. The corresponding EDX spectra recorded from the flake with detected elements (B, Na, Al, Si) identifies the particle as glass released due to exfoliation from the glass vials inner surface.

**Benefit delivered to our client**
This study allowed the client to screen vials from several different manufacturers to determine the compatibility of the glass packaging with the formulation. Particles and delamination were apparent in several types of vials and so the client was able to select the most compatible with the drug product at an early stage of development and so avoid costly scrap and rework at a later stage of development.

**CASE STUDY: FIBRE CONTAMINANT IN CONSUMER HEALTHCARE**

Fibres can be a common cause of contamination on production sites and can potentially originate from many sources such as the use of wipes, brushes and/or clothing or other domestic sources. In this case, a batch of consumer healthcare products was observed to contain fibers at quality control inspection. The batch was not released for commercial market but was investigated in order to determine the source of the contamination.

**Our solution**
The samples were examined, and the fibers were isolated with the aid of Polarized Light Microscopy. Optical microscopy was used to explore fiber color, diameter and longitudinal morphology. Cross sections were also made, and the fibers surface characteristics and chemical information was obtained. The fibers were also compared to a range of potential sources including, clothing and several items used in the cleaning process.

**Benefit delivered to the client**
The investigation revealed that the brushes using in the cleaning process were degrading and losing minute particles of the brush hair. As a result, the client was able to reassess the cleaning tools and cleaning protocol to avoid this in future batches.