The number of international standards relating to Foreign Particulate Matter (FPM) continues to grow steadily, reflecting an increasing awareness of the importance of FPM in numerous industries. Products as diverse as hydraulic fluids and pharmaceutical inhalers are now covered by regulations that adopt or refer to such standards.

This article presents data from an automated image analysis method (Morphologi G3, Malvern Instruments, Figure 1) for the fast, accurate, and highly repeatable measurement of FPM contamination on filters. By automating analysis, removing operator subjectivity and enabling the rapid classification of particles into specified size brackets, image analysis delivers significant methodological improvements over conventional manual microscopy.

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Automated Detection of Foreign Particulate Matter on Filters

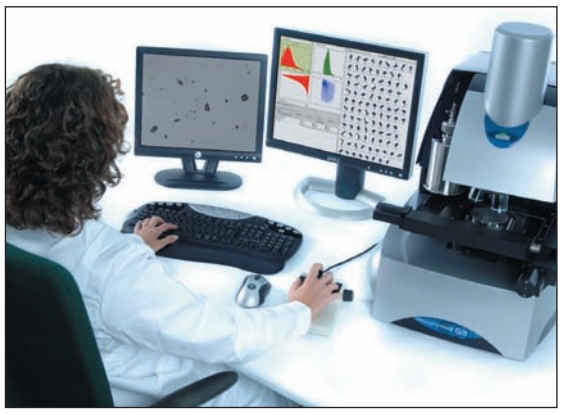

Figure 1. The Morphologi G3 automated particle characterisation system combines light microscopy and image analysis

DEFINING FPM

The term FPM describes extraneous contaminant particles such as glass, transparent synthetic fibres, stainless steel, rubber, aluminium and plastic that can be introduced at any stage in a manufacturing process or during operation. Such contamination potentially has serious implications. The direct health consequences of particulate contaminants in injectable drugs, for example, include blockage of blood vessels and inflammatory or allergenic reactions. How much impact particulate contamination has in any situation depends on a variety of factors, including the chemical composition of the particles, their size, number and rate of introduction.

PARTICULATE STANDARDS

Standards and regulations that have been established to address the issue of FPM contamination are there to ensure quality and safety, and to provide an internationally recognised universal reference system for manufacturers and users. This allows comparison of particulate contamination data and the exact specification of required levels of cleanliness.

HYDRAULIC FLUIDS

In hydraulic systems, power is transmitted and controlled through a liquid under pressure that acts both as a lubricant and power transmitting medium. Particulate contamination in the liquid can interfere with its ability to lubricate and is often the primary cause of wear-related damage, ultimately leading to machine failure and downtime. The most widely used international standards for industrial fluid power systems are: ISO 4407, which specifies how optical microscopy should be used to analyse the fluids; and ISO 4406 which is the standard for coding the level of particles larger than 5µm and those greater than 15µm allowed in a 1ml fluid sample. Another standard, ISO 11218, also relates to the cleanliness classification of hydraulic fluids but applies to aerospace applications.

Figure 2. A glassless sample carrier allows two filters to be mounted at once, for successive analyses without manual intervention (Morphologi G3)

AUTOMOTIVE COMPONENTS

Modern automotive fluid components and systems are highly sensitive to the presence of residual particles from manufacturing and assembly processes. Such particles increase wear rates and enhance the likelihood of system failure, and their strict measurement and control falls within the ISO 16232 series of standards. These enable a company to verify that automotive components meet specific levels of cleanliness.

Compliance with ISO 16232 requires manufacturers to enumerate and record particles 5µm or larger. Again, optical microscopy is identified as being an efficient and accurate method for particle analysis. Analysis of the component cleanliness in fluid circuits is described also in the VDA 19 directive, which establishes a process for quantifying contamination arising during manufacture. It applies to automotive components used in a variety of fluid systems and the directive specifies methods for both particle extraction and subsequent analysis.

PHARMACEUTICALS

The presence of FPM is especially a concern in the pharmaceutical industry where extremely rigorous checks are required. Standards published by the United States Pharmacopeia (USP) include USP 788 that specifies acceptable levels of FPM in injectables, and USP 789, which defines limits for ophthalmics. The US Food and Drug Administration requests that FPM in a wide range of pharmaceutical inhalation devices is subject to quality control limits in defined size ranges. The International Pharmaceutical Aerosol Consortium on Regulations and Science has also discussed the testing for FPM in orally inhaled and nasal drug products.

MEASURING FPM

Conventionally, FPM analysis for compliance with ISO and other standards has relied on the use of manual light microscopy to count contaminant particles collected on filters. However, the many limitations associated with this method mean that it is less than ideal. In particular, it is prone to human error and operator subjectivity, especially given the considerable length of time required to manually count sufficient particles.

Now, however, advances in image analysis techniques are making it possible to automatically classify particulate contaminants in fluids such as hydraulic transmission and fuel injection systems. Automated imaging systems for particle characterisation offer a user-independent solution that combines light microscopy and image analysis with new levels of speed and objectivity. Importantly, there are now systems that allow the analysis of FPM directly on the filter used to collect it.

Automation unquestionably overcomes the drawbacks of conventional manual microscopy: automated systems measure hundreds of thousands of particles within minutes, providing statistically relevant data; operator bias and human subjectivity are eliminated; and the use of Standard Operating Procedures (SOP) gives complete transferability of analysis methods - from the research laboratory to the QC department for example. In addition, the high-resolution images generated allow advanced particle characterisation in terms of the size and morphology of individual particles. Such information allows detailed investigation and effective troubleshooting.

AUTOMATION SOLUTION

Given the advantages, it is unsurprising that there is a trend away from manual measurement of contamination levels towards automated inspection of filters. Fully automated imaging systems do however need suitable hardware and software in order to perform the specialised task of measuring FPM on filters.

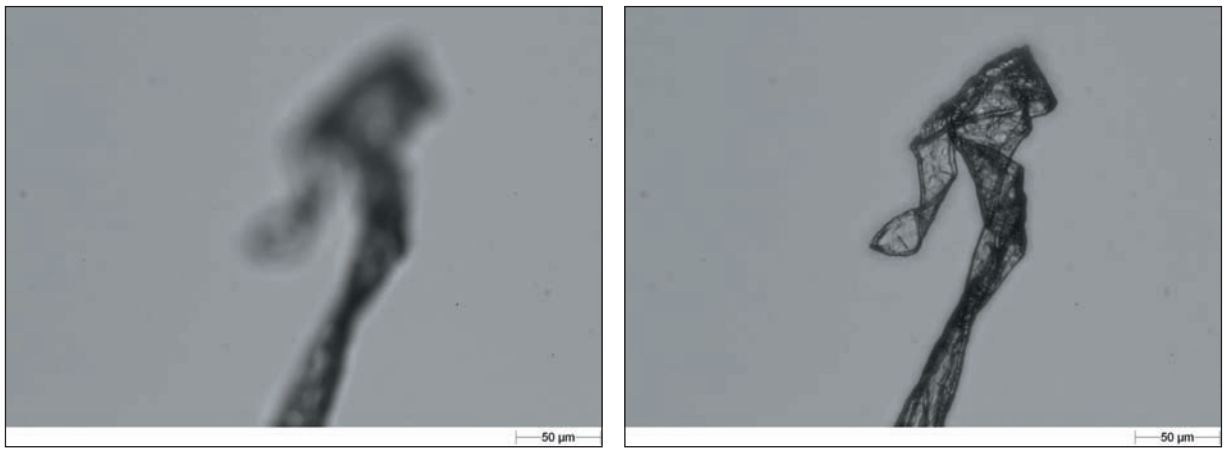

Figure 3. Sections of a field of view frame without (left) and with (right) z-stacking

The first requirement is to hold the filter papers flat, something that can be achieved with a glassless sample carrier plate that stretches prepared filters with a magnetic clamping mechanism *(Figure 2)*.

High resolution is also essential for the successful measurement of particles down to 2µm in size. A combination of high quality microscope objectives and scientific grade cameras is required to ensure that even at such small sizes images contain enough pixels to confidently identify genuine particles.

Where particles cross two or more frames, as is typical for fibrous materials, the image analyser must be able to identify when this occurs. Frames must then be 'stitched' together before the whole edge-stitched particle is extracted from the background. Another valuable function is z-stacking, which allows images taken at different focal points to be combined before the particles are separated from the background. Large particles remain in focus, while small ones located in the well of the filter paper are also included in the measurement. *Figure 3* shows a section of a frame containing a fibrous particle, with and without z-stacking.

A further necessary capacity is detection of both bright and dark particles. Without the ability to discriminate between the two, single particles with both bright and dark areas (often the case for metals) may be identified as separate particles rather than single entities.

At the end of each analysis the generation of a composite image of the whole scanned area verifies both that the filter was in focus and there were no faults in the paper. In the Morphologi G3 for example, the combination of composite image and X-Y scatter plot allows visualisation of the position of particles on a filter, and assessment of the filtration quality. The composite image also *(Figure 4)* provides a permanent electronic record that demonstrates to the regulatory authorities exactly what was measured.

EXAMPLE FPM ENUMERATION

A standard operating procedure (SOP) was set up in the instrument software to analyse filter papers, and to detect and count particles in specific size classes according to the regulations governing the development and quality control of inhaled products. The area for analysis was 10mm in diameter and a circular scan of the whole area took approximately 20 minutes including z-stacking. *Figure 5* shows a report generated after the measurement.

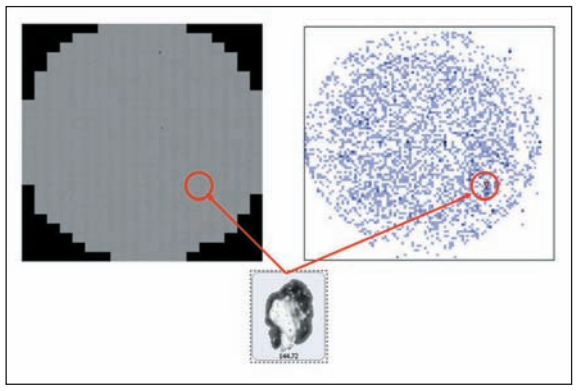

Figure 4. Composite image and X position vs Y position scattergram which show the position of particle of interest on the filter

CONCLUSION

The enumeration of FPM on filters is now a necessity in many industries to ensure compliance with a host of universally acknowledged standards and regulations. While manual microscopy techniques have traditionally been used for this purpose, automation provides a user-independent solution that delivers much-improved statistical sampling. Furthermore, SOP-driven analysis facilitates complete transferability of measurement programs.

Results obtained using the Morphologi G3 demonstrate that automated imaging systems for particle characterisation offer a powerful solution for FPM measurement on filters. Within minutes, highly detailed, reproducible and repeatable particle data was generated and automatically classified into user-definable size ranges.

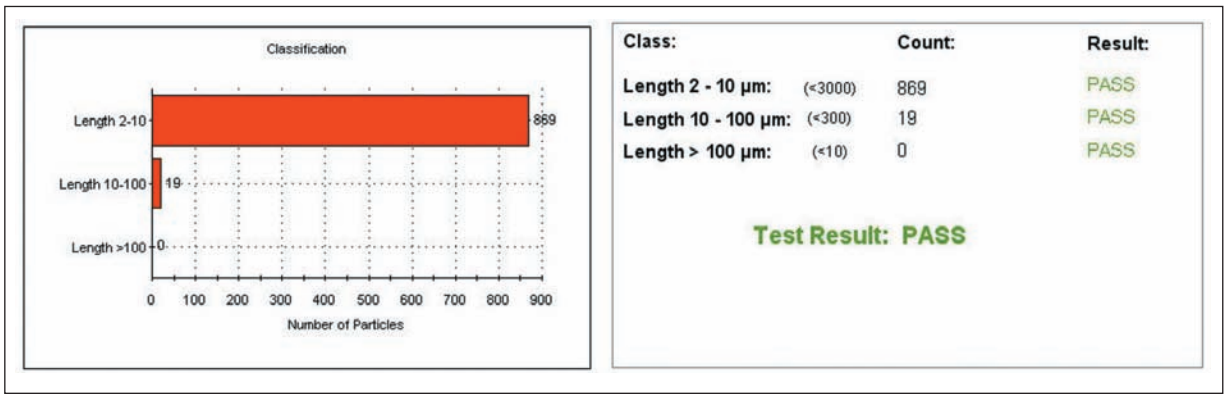

Figure 5. A typical report summarising the data from the analyses.

New Work Describes Characterisation of Mineral-Based Make-Up

A new application note from **Malvern Instruments** outlines research and methodology for measuring the size, shape and intensity of particles in mineral-based powder make-up, using the Morphologi G3 image analysis based particle characterisation system. The freely downloadable publication 'Morphologi G3: Understanding Mineral-based Make-up using Size, Shape and Intensity Measurements', demonstrates how to capture and analyse data for use in optimising the brilliance and coverage of powder makeup.

The Morphologi G3 combines high quality, automated imaging with statistically significant particle shape and particle size measurements delivering more reliable characterisation than is typically obtained with manual microscopy. Images of every particle analysed are retained by the system and can be used to visually inspect the products, thereby providing a qualitative analysis of the sample.

An increasingly popular consumer care product, mineral-based powder make-up is made by blending particles of specific size and shape to obtain a product designed to perfectly hide the fact that it is actually made of discrete particles. The size and shape of constituent particles affect their light dispersing properties, and, in doing so, highly influence final product performance. Overly large particles appear powdery on the skin while those that are too small deliver an insufficient masking effect. Particle shape is equally important. For example, plate-like crystals create a pearlescent effect whereas the size of the plates determines the level of sparkle: Small plates give a more opaque smooth finish, while larger plates add a brilliant spark.

Particle imaging is a discipline that was once labour-intensive and highly subjective because it had to be performed manually. The development of automated particle imaging instruments equipped with integrated computer-controlled dispersion, advanced image processing and statistical analysis tools, such as the Morphologi G3, have taken this informative technique to a new level.

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