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Effective Solutions for Material Characterization

WHITEPAPER

FACILITATING VALIDATION OF GAS ADSORPTION SYSTEMS USING NEW TRACEABLE REFERENCE MATERIALS

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Measuring the surface area of a material is an essential task, as the surface area of a solid determines how it interacts with its surroundings. For example, the surface area of a pharmaceutical oral dosage form, such as a tablet, determines how quickly the drug's active pharmaceutical ingredient enters a patient's bloodstream, which has a significant impact on its safety and efficacy. The ideal method for measuring surface area is gas adsorption analysis, which relies predominantly on relatively simple measurements of temperature, pressure, and volume.

To ensure a gas adsorption system is functioning properly and thereby delivering consistent, reproducible results, manufacturers are responsible for conducting periodic testing on their analytical instruments. Equipment that is not working properly could deliver out of specification (OOS) data later, leading to investigations that slow progress or even compromise a regulatory submission. For a commercialized product, it could mean a product recall. The investigation and implications of an OOS result are associated with high costs and, potentially, damage to a company's reputation. Therefore, safeguarding the integrity of analytical data is paramount.

Testing instrument performance requires the use of a reference material of known surface area with well-characterized properties. Government agencies, such as the National Institute of Standards and Technology (NIST) and Germany's Federal Institute for Materials Research and Testing (also known as BAM), produce, certify, and sell these reference materials. A manufacturer that purchases these materials can then compare the results from their system with that of the data for the NIST or BAM materials. If they match within the provided tolerances, it is confirmation for the manufacturer that the instrument is functioning as expected. However, these materials are expensive, and there is often a limited supply of them. Overcoming these challenges requires materials that are not only accessible and affordable but also suitable for analysis in highly regulated industries, such as pharmaceutical manufacturing.

Increased Access To Traceable Reference Materials

Delivering a product with the highest level of quality and fit for its intended use is a top priority in any industry. Yet, the stakes become much higher with pharmaceuticals, as product quality has a direct link to clinical performance and patient safety. As the industry has evolved and grown over the last couple of decades, the FDA has encouraged the adoption of Quality by Design (QbD), which is a systematic approach to drug development. QbD emphasizes product and process understanding and process control by using factors, such as critical quality attributes (CQA), to design formulations and manufacturing processes that achieve a predefined level of quality.

The surface area of an API and its excipients is a CQA that must be understood and controlled to ensure that a drug product functions as it is intended. That is why regulatory agencies, such as the U.S. Pharmacopeia, require the measurement of surface area and encourage the use of traceable reference materials when testing analytical equipment. NIST and BAM materials are available in limited quantities and costly, so manufacturers typically do not have a large amount of stock available for testing over long periods of time.

Micromeritics recognized the need for increased access to reference materials and committed to addressing it through a significant investment in the development and supply of its own materials, which are developed from commercially available materials produced in large quantities. Micromeritics has verified the measurement systems and methods used to characterize the new materials by applying them

to relevant certified reference materials from NIST or BAM and ensuring that the results are traceable to NIST and BAM standards. Micromeritic's materials are valid for 10 years, with each individual bottle expiring one year from the date it is opened.

Using Reference Materials In An Analytical Instrument

Micromeritics offers four traceable reference materials that work on Micromeritics instruments as well as those of its competitors. One of the materials is available for purchase now, two are in testing and expected to be available in early 2020, and the fourth is expected soon after.

The materials span a surface area range of 1 to 175 material per unit of mass (m2/g), which is how Micromeritics, as well as other instrument companies, measure the total amount of surface area in the sample holder. The specific surface area in m2/g is calculated from the measured total surface by dividing the user-entered sample mass. There is a perception that it is necessary to have a reference material that has the same, or nearly the same, specific surface area as their material under test (in m2/g).

Available Reference Materials:

- Alumina reference material
  - with an approximate surface area of 5.2 m2/g
  - 0.25 m2 /g, 15 g; for krypton analysis
- Carbon Black, 24.1 m²/g
- Silica-alumina pellets, surface area approx. 198 m²/g, 10 g

However, what is actually needed is to use a mass of a traceable material that provides the desired total amount of surface area of the material in the sample holder. The surface area analyzer software will then divide what is measured by the user-entered sample mass to give what is called specific surface area. This is important because another analysis of the same sample may be performed using a different amount of material, or the amount in the pharmaceutical preparation that you take may be different than what was analyzed, and it is the surface area of what is in your body that matters. For example, if 1 gram of a material with 10 m2/g specific surface area is analyzed, then there is 10 m2 of total surface area under test. If 2 grams of a second material is analyzed with a specific surface area of 5 m2/g, there will be 10 m2 of surface in the sample tube again, essentially testing the instrument in the same operational range as when 1 gram of the first material was analyzed. And so, by selecting different amounts of one reference material, the performance of the instrument can be tested over different ranges of total surface area. There should also be a range of materials available to facilitate achieving total surface area amounts near the amounts generally analyzed for a material. However, the analytical balance for the masses of the material under test will need to be validated separately.

It is also important to keep in mind that it is not critical to use a reference material that matches the product. The results from the analytical instrument are not dependent on the chemistry of the material being tested as long as it is stable under analysis conditions. The most important factor that differentiates one material from another is how it has to be treated to remove any elements, such as water, oxygen, or carbon dioxide, that are brought in from the environment, which could potentially damage the instrument. These are removed using a process called degassing.

Overall, reliable instrument operation facilitated by the analysis of traceable reference materials is vital. Micromeritics' new reference materials, which are suitable for any gas adsorption apparatus, have been developed and tested by leaders in gas adsorption technology and are underwritten by a long-term commitment to their provision. Available for many years to come, they offer an affordable and accessible alternative that can help promote consistency and reproducibility in surface area measurement and ensure the highest level of quality assurance in gas adsorption measurement.

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About Micromeritics Instrument Corporation

Micromeritics Instrument Corporation is a global provider of solutions for material characterization with best-in-class instrumentation and application expertise in five core areas: density; surface area and porosity; particle size and shape; powder characterization; and catalyst characterization and process development.

The company is headquartered in Norcross, GA, U.S.A. and has more than 400 employees worldwide. With a fully integrated operation that extends from a world-class scientific knowledge base through to in-house manufacture, Micromeritics delivers an extensive range of high-performance products for oil processing, petrochemicals and catalysts, to food and pharmaceuticals, and works at the forefront of characterization technology for next-generation materials such as graphene, metal-organic-frameworks, nanocatalysts, and zeolites. Under its premium brand Particulate Systems, Micromeritics discovers and commercializes innovative material characterization technologies that are complementary to core product lines. Cost-efficient contract testing is offered via its laboratory Particle Testing Authority (PTA).

The strategic acquisitions of Freeman Technology Ltd. and Process Integral Development S.L. (PID Eng & Tech) reflect an ongoing commitment to optimized, integrated solutions in the industrially vital areas of powders and catalysis.

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