





How investing in Malvern Instruments helped KBI Biopharma find a clear commercial advantage

Dr. Amber Fradkin, KBI Biopharma

-  CHEMICAL IDENTIFICATION
-  PARTICLE SHAPE
-  PARTICLE SIZE
-  PROTEIN AGGREGATION
-  PROTEIN STABILITY

About KBI Biopharma

Dr. Amber Fradkin manages the Particle Characterization Core Facility at KBI Biopharma in Boulder, Colorado. KBI is a biopharmaceutical contract development and manufacturing organization (CDMO) headquartered in Durham, North Carolina, which specializes in accelerating the development of biological therapeutics. KBI's Particle Core provides specialist particle characterization which is tailored for the (bio)pharmaceutical industry, and includes profiling of particles post IV-infusion, investigation of the kinetics of particle formation, particle identification for forensics applications, API characterization, profiling of particles in drug products for biosimilarity and biocomparability, and assessment of formulation stability, amongst other services.

Analytical Challenges

The range of samples analyzed and types of studies undertaken by Amber's team is broad, ranging from parenteral biologics to small molecule topicals, inhalable powders and drug-device compatibility. Differing sample matrices and presentation can create various challenges, not least for KBI's technology platforms, which often require specialized methods and application experts in order to optimize the quality of the data they collect. KBI is fortunate in that their Particle Core team comprises true experts in their field, with more than 10 years' experience in developing and perfecting methods for their instruments. Amber says, "This has been very rewarding for us, knowing that we are supplying our clients with the most optimized methods which produce high quality data that helps them better understand their product." Better product knowledge and understanding leads to better, safer drugs being brought to market much more quickly and cost-efficiently, whilst satisfying all requirements from the FDA and other regulatory agencies.

As our understanding and awareness of the importance and impact of particles in drug products increases, their characterization becomes ever more necessary, both from a perspective of ensuring drug stability, safety and efficacy, and also from the standpoint of meeting regulatory expectations. To support this requirement, analytical instrumentation has advanced significantly over the past decade. "The challenge has been what to do with all of the data these new instruments produce, how to interpret it, how to store it, how to present it in

regulatory filings, and so on. With the installation of routine MFI, we started to learn more about the particles in products, and what they look like”, says Amber. “But with this additional information came more questions: ‘Why do these particles look different to those ones? What are they?’”

In the past, Amber’s team generally tried to chemically ID visible particle contaminants solely by methods such as FTIR. But she acknowledges that this was essentially only worrying about the problem when it was already ‘too late’. “Characterizing nanoparticles and subvisible particles early on allows for a much greater understanding of product particle profiles, which can help prevent visible particle formation related to inherent or intrinsic materials. I think of it as being proactive, rather than reactive,” she explains.

Solution-state analysis for particle characterization

The KBI Particle Core team needed a tool to help them complete their in-house characterization service by providing an answer to the question: “What is it?” for particles they detected in the subvisible and visible size range. They also required a technology which was easy-to-use, with a range of options for analyzing the different samples they handle. Amber explains, “For instance, we wanted to analyze the particles in solution whenever possible, to ensure that our analysis was as close as possible to *in situ* particle characterization. When you are forced to filter particles out of solution, it always leaves concerns such as, ‘were the particles we found formed by the act of filtration itself?’. Malvern was the first company to help us achieve a solution-state analysis for particle characterization by Morphologically-Directed Raman Spectroscopy (MDRS). They took our request and developed a ‘solution’ for us (no pun intended) with their wet cell for the Morphologi G3-ID.”

KBI demoed several systems available from various manufacturers. “We prefer to demo instruments prior to purchasing,” Amber says. “Some instrument manufacturers require you to send samples to them for analysis, and they provide you with the data produced. But that doesn’t work so well for us - we need to have hands-on experience with instruments to know we trust the data they are producing and to evaluate if we will be able to bring a system in-house and have our analysts up to speed on the instrument operation in a timely manner.”

Choosing a Malvern Instrument

Following a thorough investigation of a range of systems, KBI’s Particle Core team decided that Malvern’s Morphologi G3-ID best met their requirements. Amber states, “We found that the Morphologi G3-ID system had the best ease-of-use and also the most versatility, when compared with alternative solutions. With Morphologi G3-ID, we can handle such a diverse range of samples: powders, creams, oils, aqueous solutions, solids, and so on. But also, Malvern’s customer service is outstanding. The Malvern team is very responsive to our requirements. They continuously ask for our feedback and provide rapid solutions to our requests.”

The Malvern portfolio at KBI Biopharma

KBI now owns seven different Malvern instruments: Morphologi G3-ID, Archimedes, NanoSight NS300, Zetasizer Helix, MicroCal VP-Capillary DSC, Zetasizer ZS and Viscosizer, which together form a comprehensive analytical suite. Amber states, "The Morphologi G3-ID has truly been invaluable to our particle characterization core facility. This instrument is the one instrument that provided the answer to 'what is it?' when characterizing particles. I have worked with the Morphologi G3-ID for over 4 years now - it is so versatile, and whether we are using it to develop a method for determining particle size distributions of multi-API topical drug products or isolating subvisible particles from biologics for forensic identification, MDRS proves time and time again to be a powerful technique that gives us the answers we need."

Amber continues, "All of our Malvern instruments have been integral to the KBI Particle Core. Each instrument provides a unique dataset to characterize particles. Applying the right combination of techniques allows us to characterize the full particle profile, spanning from nanometers to millimeters in diameter. Our suite of Malvern particle techniques has provided us with a unique advantage when clients are seeking help with particle characterization."

Malvern as a collaborator

Amber jokes that some days she feels she talks to the Malvern team more than her own colleagues, "They are all such wonderful folks to work with and always make you feel as though you are their most important customer. They are also very technical and know their instruments and software inside and out."

"Malvern has been a very good company to work with. Over the years, I have worked with dozens of Malvern employees, from various areas of the company, including sales, service, technical specialists and product development. Malvern has always been interested in the continuous improvement of their systems. Our team works closely with Malvern to provide feedback on how to improve their systems for our industrial applications and needs. I have watched all of their instruments (Morphologi G3-ID, Archimedes, NanoSight, and so on) evolve over the past few years and I am very satisfied with the response of Malvern in the development of these technologies. I can't wait to see how they will continue to improve their particle characterization solutions. The KBI Particle Core loves to stay on the leading edge of the industry with our technology and Malvern has helped us do that."



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