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The science & business of drug development in specialty pharma, biotechnology, and drug delivery

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Robert Lee, PhD
Vice President, Pharmaceutical Development Particle Sciences, Inc.

Particle Sciences & Horiba Instruments: Providing Clients a Total Solution

Particle Sciences, Inc. (PSI), located in Bethlehem, PA, is a full-service CRO specializing in nano-based and rational solubility systems design approaches to formulation. PSI brings this skill set to bear on all dosage forms ranging from oral to parenteral to topical and drug/device combinations. In addition to industry-leading formulation capabilities, PSI has GLP/GMP analytic, bioanalytic, and characterization labs and class 100 clean room facilities. Providing an integrated suite of services aimed at minimizing the time and risks of drug development, PSI is expert in fine-particle and nanotechnology approaches and regularly deals with challenging APIs, high-potency compounds, and controlled substances. They work with a variety of APIs, including small molecules, peptides, proteins, and oligos. The company brings 2 decades of expertise providing an expansive suite of preformulation, formulation, analytic, and GLP/GMP manufacturing services - including sterile products. A responsive and collaborative approach ensures the objectives of all clients, large and small, are successfully met on-time and on-budget with the highest degree of quality.

The HORIBA Group of worldwide companies provides an extensive array of instruments and systems for applications ranging from automotive R&D, process and environmental monitoring, in vitro medical diagnostics, semiconductor manufacturing, and metrology, to a broad range of scientific R&D and QC measurements. Proven quality and trustworthy performance have established widespread confidence in the HORIBA Brand. HORIBA's current R&D efforts are directed toward nanotechnology instrumentation and its application to the field of Life Sciences. From Microscopic Raman Imaging to Fluorescence Spectroscopic mapping to miniaturized Water Quality measurements, the analysis of small, biological materials is a key focus. In the area of Particle Characterization products, a number of new technologies have been introduced to support industrial R&D initiatives. One recent example would be Dynamic Light Scattering (DLS) for the determination of size and Zeta Potential for small particles in dilute systems. Acoustic spectroscopy is also offered for similar types of measurements in more concentrated samples. Both Static and Dynamic Image Analysis has been developed to provide size and shape information for small particles in wet and dry systems. This provides a nice arsenal of weapons to characterize particles that are of major concern to the Life Sciences Industry.

Specialty Pharma recently spoke with Robert Lee, PhD, Vice President of Pharmaceuticals and Quality, Particle Sciences, and Michael C. Pohl, PhD, Vice President, Horiba Instruments, Inc. to discuss their recent strategic alliance to provide their clients with the most up-to-date physical characterization tools with operational expertise in a fully GLP/GMP-compliant setting.

Q: ***For the benefit of our readers who are not familiar with HORIBA, what does HORIBA bring to the Pharmaceutical Industry?***

Dr. Pohl: HORIBA Instruments is an analytical instruments company headquartered in Kyoto, Japan, with its US operations situated in Irvine, CA, and Edison, NJ. The company has a number of core competencies that range from X-ray Fluorescence to Raman Spectroscopy to Atomic Emission Spectroscopy. While all of these are of great interest to the Pharmaceutical Industry, our collaboration with Particle Sciences currently focuses on our Spectroscopic and Particle Characterization Products. These products focus on Microscopic Raman Imaging, Particle Sizing, Surface Area Determination, Zeta Potential Measurement, and Particle Shape Characterization. While these instruments are provided by a few other suppliers, HORIBA offers some unique accessories, algorithms, and applications to meet the needs of this industry.

Q: ***What is unique about Particle Sciences and their capabilities?***

Dr. Lee: PSI differs from many CROs in that our genesis was as a formulation group and that remains our core competency. We continue to grow deeper and deeper in our core skill set and are intentionally not trying to be all things to all people. This is one of the drivers to form an alliance with HORIBA. Increasingly, the regulatory characterization burden placed on drug developers is becoming gating. Solutions often require deep understanding of the techniques and devices used in establishing specifications. Particle Sciences is a leading expert in physical characterization and by establishing this close relationship with HORIBA, a scientific instrumentation company that will listen and use our feedback to improve their equipment, our clients will ultimately reap the benefits. Our goal is to solve our clients' problems, and we are not wed to any given drug delivery technology or characterization methodology. To that end, we have designed or acquired multiple drug delivery technologies so that we can best serve our clients. We view ourselves as technology consolidators, and our role is to offer our clients a complete solution. This includes both the actual drug delivery techniques as well as the analytic and characterization components.

As our name implies, we have special expertise in particulate-based systems. This encompasses both microparticles and nanoparticles. We are well versed in several technologies, including encapsulation, particle size reduction - both top down (including high energy milling and high pressure homogenizers, such as Microfluidizers®) and bottom-up (solvent/antisolvent precipitation, including Microfluidics PureNano Continuous Crystallizer) approaches, and particle engineering. In addition, we have developed a proprietary approach, termed DOSE™, to maximize the solubilities of the APIs we work with. These techniques are all employed as appropriate for a client's specific delivery goal, independent of dosage form, and PSI has worked on most routes of administration, including non-sterile, sterile, oral, vaginal, topical, ophthalmic, inhalation, injectables, etc. Additionally, and unique to PSI, is our capability to develop combination drug-eluting devices, which flows naturally from our sweet spot in particulates and solubilization techniques. Our focus on particulate-based and unique solvent systems differentiates PSI from other CROs, and we believe this better serves our clients, and it seems like this is in sync with a vast majority of our clients' requirements. Not to be minimized and a key aspect of our business strategy is our initial interaction with our clients. Early in our discussions, we strive to understand exactly what our clients' goals are - we want to

make sure we hear and understand their needs and design our programs to satisfy these goals. For example, an early question is whether our clients are interested in a formulation approach using proprietary intellectual property (IP). In some cases, our clients have strong IP surrounding their new chemical entity or use for their molecule and are interested in a straight line to some value-inflection milestone, such as in vivo evaluation or human proof-of-concept. In these cases, PSI will employ, whenever possible, a non-proprietary drug delivery approach. We remain agnostic when it comes to using either our existing proprietary or non-proprietary drug delivery technology - it is based on our clients' requirements and often, a simple emulsion or non-proprietary nanoparticulate approach fulfills our clients' requirements. In other cases, our clients may be seeking to reposition a marketed drug or may have mediocre or no IP protection for their product concept or may be seeking life cycle management for one of their currently marketed products. In these cases, PSI can draw upon our existing IP or create new IP to better protect our clients' products. As you can see, it is critical to understand our clients' needs, and PSI is uniquely positioned to support their development strategies - both from a technical and business perspective.

Q: ***What will the recent collaboration between HORIBA and Particle Sciences provide that is new to the industry?***

Dr. Lee: What this collaboration provides to PSI's clients is access to state-of-the-art equipment and, because of the close relationship between PSI and HORIBA, the ability to fully leverage today's best technology to most efficiently get to a clinic-ready product. This also provides a seamless path, from a product characterization perspective, from research to preclinical to clinical and ultimately, into commercial production. We offer full cGLP and cGMP development services, not only bioanalytical and manufacturing, but also analytical and physicochemical characterization. We can fully develop and validate methods plus conduct testing in support of regulatory filings, such as INDs and NDAs.

Dr. Pohl: As previously mentioned, HORIBA has instruments with unique features widely applicable to Pharmaceutical R&D. A great example of this is our LA-950, which offers a versatile Auto Sampler, a temperature-controlled measurement cell, a paste cell, and a variety of other accessories. Due to our corporate headquarters being located on the West Coast, it is challenging for us to make this technology accessible to the major Pharmaceutical companies headquartered on the East Coast. The ideal location of Particle Sciences makes this much more available to our core customers.

What this collaboration provides to potential HORIBA customers is access to HORIBA instrumentation so they can evaluate it in a lab setting before committing to purchase of the equipment. Additionally, PSI is expert in the use of the HORIBA equipment they currently own and will become expert in those they will acquire through the collaboration. This will provide HORIBA clients with a valuable resource for method development and validation. Additionally, if our clients desire to use our equipment strictly for research and not to support cGLP and cGMP studies, then PSI can also provide this service.

Q: ***What new services do HORIBA and PSI see the industry needing?***

Dr. Pohl: The tough times in the Pharmaceutical Industry are far from over. Patent expiration, healthcare reform charges, limited new drug pipelines, and other headwinds are not likely

to dissipate in the near future. Faced with these challenges, the industry will be faced with more rounds of cost cutting and retrenchment. A major area for cost containment is surely capital spending for analytical instrumentation in R&D, production, and Q&C. HORIBA's goal is to provide application-specific equipment to the Pharmaceutical Industry at cost-effective pricing.

HORIBA believes it has been doing this for the industry for many years now. Our collaboration with Particle Sciences now provides a ready means for the industry to test their application on this equipment. This can be done safely and confidentially with a group of industry experts in a very convenient geographic location. Particle Sciences will further elaborate on the capabilities that are available in Bethlehem, PA.

Dr. Lee: Pharmaceutical development is highly regulated and is getting more stringent on a continuing basis. This translates into Pharma and BioPharma having to adopt higher standards for characterizing their formulations. One potential example is the integration of optical microscopic image analysis coupled with spectroscopic analyses in order to identify particles using Raman spectroscopy in a semisolid formulation. PSI is working with HORIBA on just such a project and sees the value of this to our clients - the ability to not only determine morphology and particle size of discrete particles, but to then couple that to the generation of the associated Raman fingerprint for that specific particle amongst a sea of particles in a formulation. This will allow the client to see which particles are growing as a function of storage condition or formulation.

Q: *What are some of the challenges facing the Pharmaceutical Industry?*

Dr. Lee: Recent challenges have been imposed by the downsizing experienced across the Pharmaceutical Industry; resources have evaporated, companies are getting leaner, and talent is reshuffled or lost. Still work has to get done to support product development. Some of the gap has been filled by outsourcing. There is pressure, which will continue to grow across the industry to more accurately characterize products. This stems from both safety and efficacy perspectives. The question is a how to balance doing the appropriate level of testing and managing a shrinking budget. Hopefully, as better analytical tools become accessible, there will not be any question of compromising.

Q: *Where does HORIBA see the industry heading?*

Dr. Pohl: The Pharmaceutical Industry has proven throughout the years to be very resourceful when it comes to developing new delivery systems for drugs. Measuring the properties of these systems in order to predict performance has proven to be a serious challenge for the analytical instruments industry. HORIBA has always been striving to develop new instruments and accessories to meet these challenges. As the industry moves forward, HORIBA will be attempting to keep pace with instruments to properly characterize them. It may range from the development of totally new techniques to increasing the capabilities of current instruments to designing new accessories for older instruments. HORIBA will continue to strive to provide the Particle Characterization solutions required by this very innovative industry ■