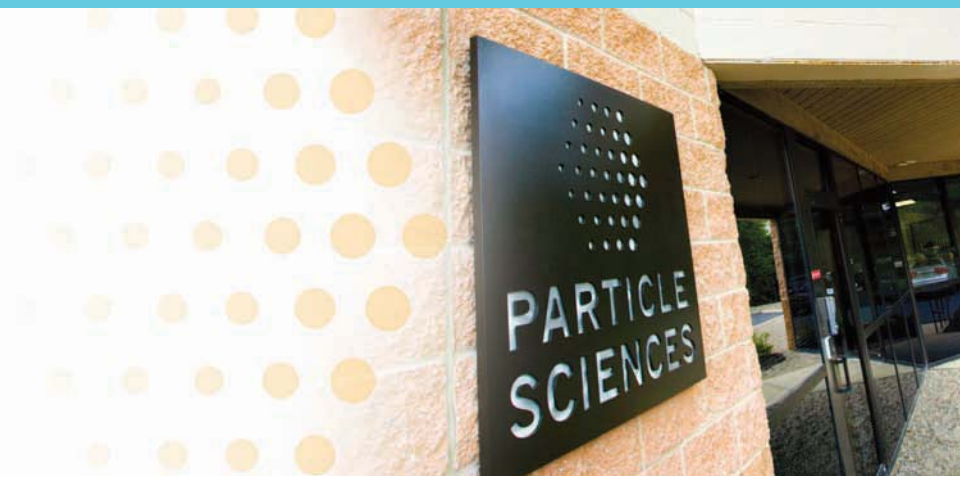
A Lubrizol Company
PARTICLE® SCIENCES
DRUG DEVELOPMENT SERVICES



OVERVIEW

The majority of drug products being developed today face one or more technical challenges. Whether dealing with a new chemical entity or reformulating an existing active pharmaceutical ingredient (API), the product's scientific and commercial success will pivot around the choice of the right drug delivery system. On top of this increasingly difficult technical burden, the pharmaceutical industry is moving towards a business model that embraces lower fixed costs, greater efficiency and an increased use of outsourcing.

This is where Particle Sciences comes in. We are strategically positioned to serve our pharmaceutical clients as a cost efficient integrated part of their drug development program. We work with a range of clients from small venture backed firms to not-for-profits to the world's largest pharmaceutical and biotech companies. Established in 1991, Particle Sciences is the leading specialty drug development CDMO with a scientific staff of 50+ and 40,000 ft^2 of development and manufacturing space.

Our focus is drug product formulation for small and large molecules. We support this with full analytical, bioanalytical and manufacturing services

Our focus is drug product development from post-discovery through manufacturing. We design your program around identifying the right drug delivery system for your specific API and indication. Using our DOSE® platform, Particle Sciences methodically and efficiently arrives at the dosage form that best meets your clinical, regulatory and business goals.

- **FDA registered**
- **DEA licensed**
- **cGMP / cGLP compliant**
- **Highly potent compound handling**
- **Biologics and small molecules**
- **Sterile and non-sterile manufacturing**

Our core expertise is in drug delivery. We have assembled an unparalleled array of technologies designed to meet today's most prevalent challenges. The combination of our unique understanding of solubility, industry leading array of formulation approaches and our extensively equipped cGMP facilities sets Particle Sciences apart from the pack.

At Particle Sciences we are expert in maximizing and controlling the solubility and bioavailability of difficult-to-formulate API's. Common approaches at Particle Sciences include micro-/nano-particulates, solid solutions (spray drying and hot melt extrusion), semi-solids such as emulsions, dispersions and unique solvent systems. Additionally, we are the leading CDMO for combination products (drug-eluting devices).

As an integrated CDMO, we provide a seamless drug development program by combining our extensive formulation and physical characterization capabilities with industry leading state-of-the-art analytical, bioanalytical, and manufacturing services.

At Particle Sciences, We Deliver®, taking your API from concept to clinic. Contact us at 610.861.4701 to see how we can help.

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MICRO / NANO TECHNOLOGY

There are many reasons to choose a particulate based formulation including solubility, stability, convenience and tissue targeting to name a few. By far, the most common is to increase bioavailability due to solubility issues, or more precisely, lack of solubility. For moderately to virtually insoluble compounds, maximizing surface area is a tried and true approach to increasing bioavailability and this is most often done using nanoparticles. The incorporation of an API into a particle can take many forms. Possibilities range from an emulsion droplet to any number of encapsulation systems to a nanoparticle of the API itself. These various formats cover a range of sizes from tens of microns down to several nanometers, each providing their own utility with respect to a given API.

Particle Sciences is a world leader in micro- and nano-based pharmaceutical formulation development for both small and large molecules

At Particle Sciences, our goal is to find the most practical solution for your application. Particle Sciences has been at the forefront of fine-particle and nanotechnology since the early 1990s and we provide a wide range of particle fabrication and preparation services. Our efforts have resulted in commercial products scaled to as much as half a million kg per year. Whether it's Particle Sciences' proprietary technology or conventional systems, our staff has the know-how to apply these tools to meet your needs.

Particle Sciences is outfitted with a comprehensive array of production equipment and characterization instrumentation. This provides our clients with a broad choice of technologies assuring that the best solution is achieved. Our expertise in fine-particle and nanotechnology includes milling (wet and dry), spray drying, emulsions, solid lipid nanoparticles, liposomes, drip casting, suspensions, solid dispersions, solid solutions and encapsulated systems, allowing us to work with even the most difficult to solubilize API's.

Micro and nanoparticle fabrication under cGMPs for both sterile and non-sterile products including highly potent compounds

Using fine-particle and nanotechnology approaches can help address a number of issues in drug development. They include:

- Incorporation of difficult to solubilize API's
- Controlling bioavailability
- Controlling drug /excipent interactions
- Improving API stability
- Targeted delivery
- Controlling content uniformity
- Enhancing vaccine efficacy
- Drug /antibody complexation

Particle Sciences' staff has designed and scaled many fine-particle and nanotechnology systems. By engaging Particle Sciences you are benefiting from our decades of experience. Our micro/nano development labs are extremely well equipped and are supported by in-house cGMP/cGLP analytical facilities and ICH stability programs. We have worked with small molecules, oligonucleotides, peptides, proteins and carbohydrates. We are registered with the DEA and can work with controlled substances. In conjunction with our clients, we design the optimum program to achieve the desired goal.

When ready, Particle Sciences can scale particle production to clinical and production levels. With processing equipment ranging from high shear emulsifiers to spray dryers to ball mills, Particle Sciences is the best equipped CDMO to rapidly advance your project.

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FORMULATION / DRUG DELIVERY

Increasingly, drug product innovation is centered on formulation. Most new API's present solubility, stability and/or delivery hurdles and life cycle management of existing API's requires performance enhancements that can only come from formulation technologies. Biologics benefit from formulation through increased stability, altered pK and targeting strategies. At Particle Sciences, we have methodically assembled a series of approaches to address these challenges. Our technologies include particle engineering, emulsions, solutions, suspensions, solid solutions and antibody/drug complexes. In addition we are the leading combination (drug-eluting devices) product developer and clinical trial material manufacturer. Although broad in scope, all these technologies are aimed at matching the physical state of the drug with the clinical application. At Particle Sciences, our approach is not centered on a particular dosage form but is instead organized around the physicochemical properties of your API and a set of complimentary tools designed to optimize bioavailability.

We can scale and produce clinical trial materials under cGMP's in our state-of-the-art clean rooms, sterile, non-sterile and high potency. We are FDA registered and DEA licensed for all schedules

The formulation process starts by clearly defining the client's goals regarding API performance. Next, API characteristics are evaluated through a thorough preformulation program and mapped against the desired performance. From this, a clear picture emerges as to what the entire delivery system needs to accomplish, enabling Particle Sciences to design a crisp program incorporating timelines, milestones and performance testing.

Particle Sciences is a world leader in formulation innovation. Through rational vehicle design we maximize the solubility and bioavailability of your API

Preformulation studies are the foundation of any efficient drug product development effort. Particle Sciences has developed DOSE®, our proprietary preformulation approach based on empirically obtained data collated and interpreted through customized solubility and stability software. This powerful approach of combining hands-on measurements with predictive software provides PSI's clients with a competitive advantage by decreasing the time and money necessary to make informed decisions early on in the formulation process. The result is increased efficiency and a more data-driven and rational approach to product development. This reduces the amount of time and resources used in developing formulations by providing insight into the physicochemical behavior of the API's and narrowing the region of excipient space that needs to be evaluated during product design. Our formulation development labs are extremely well equipped and are supported by in-house cGMP/cGLP analytical facilities and ICH stability programs. Particle Sciences has worked with small molecules, oligonucleotides, peptides, proteins and carbohydrates. We are registered with the DEA and can work with all controlled substances. In concert with our clients, we design the optimum program to achieve the desired output.

From nanoparticles to spray drying to drug/device combinations, Particle Sciences has the tools to address your needs.

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PARTIAL EQUIPMENT LIST:

- Class 100 - 10,000 cleanrooms
- Sterile laminar flow hoods
- Silverson L4RT-A homogenizer
- Ad-mix Benchmix OPLB-300 Rotosolver
- Three Ultrasonic 500W dispersers/homogenizers with in-line capability
- Netzsch and DynoMill media mills
- Two Premier PLM-1.5 liter jacketed double planetary mixer with vacuum
- Two Buchi B-290 mini-spray dryers with solvent capability
- Multiple Sturtevant micronizers
- Roller mills
- Semi-automatic film production
- Four lyophilizers, including pilot scale
- WaterSep tangential flow filtration unit
- Multiple high energy mixers
- 22-ton injection molder
- 3-ton bench scale injection molder
- Multiple single and twin screw extruders
- USP water treatment system
- Multiple stability chambers
- Drip casting
- Multiple induction welders
- Two M-110EH-30 BioPharma and LV-1 Microfluidizers

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cGMP SCALE UP & MANUFACTURING

Efficient drug development can only be accomplished if there is a smooth transition between preclinical activities and clinical trial material production. These capabilities are integrated at Particle Sciences. With a robust Quality System and on-site clean rooms, Particle Sciences seamlessly takes your product from the bench into production.

Particle Sciences is FDA registered and DEA licensed for all schedules. Our manufacturing areas include sterile and dedicated highly potent suites.

With 4,000 square feet of cGMP manufacturing space and highly potent compound containment systems in place, Particle Sciences can fully develop even the most challenging drug products

Our manufacturing suites range from class 100 to class 100,000 and are supported by 4,000 ft^2 of cGMP storage. We have dedicated suites for highly potent compounds and custom built containment systems. We are FDA registered and can work with all controlled substances.

At Particle Sciences, the formulation staff is directly responsible for the transfer from bench to production. This ensures continuity and the most efficient process. Manufacturing is supported by our own experienced Analytical Services group. Running under full cGMPs, appropriate anaylytical methods are developed in-house and advanced according to the stage of development. The same analytical team will follow a project from concept-to-clinic and final validation. This, too, is designed to minimize the risk associated with scale up and technology transfer.

Particle Sciences equipment list is extensive including, among others, several varieties of dry and wet mills, spray dryers, twin-screw extruders, co-extrusion kit, injection molders, high and low shear mixers, high pressure systems (Microfuluidizer®), tangential flow filtration, ultrasonics, lyophilizers, drip casting and recrystallization systems. Together, these enable the design and manufacture of a wide variety of dosage forms including powders, semi-solids, devices, solutions and suspensions. Using these approaches Particle Sciences has developed hundreds of dosage forms ranging from IV nanoparticles to nasal solutions to vaginal rings to IM semisolids and many more. We regularly support these projects through clinical testing and, when appropriate, will establish commercial production for our clients.

Complete manufacturing capabilities ranging from nanoparticles, to solids, to semi-solids to drug-eluting devices

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DRUG / DEVICE COMBINATION PRODUCTS

Drug-eluting devices have now become one of the go to approaches for long term drug delivery. From NCE's to 505(b)(2) applications, implanted polymeric devices are a tried and true technology and Particle Sciences is the leading developer in this rapidly growing space. Since 2003, Particle Sciences has been working with clients designing ground-breaking combination products. Our hot-melt extrusion and injection molding capabilities are supported by our industry leading analytical and physical characterization groups.

Particle Sciences is FDA registered and DEA licensed and has the containment infrastructure in place to work with highly potent compounds

Combination products offer a unique approach to drug delivery. With a properly designed drug/device combination, one can impact any number of properties including bioavailability, stability and of course pharmacokinetics. Additionally, combination products afford a variety of potential intellectual property and life-cycle management opportunities.

Whether zero or first order release kinetics are desired, Particle Sciences can help. We work with a variety of polymers including both thermoplastic and thermoset systems. In addition to the requisite technical competence, we have put in place strategic supply agreements with the world's leading polymer suppliers to ensure an efficient development process.

Particle Sciences is the world leader in combination product development and is continually expanding production capabilities

Using DOSE® (our proprietary preformulation approach) and our extensive database of previous formulations, the compatibility, solubility and expected release kinetics of a client's API with a variety of polymers is quickly assessed. From there, products are rapidly prototyped and testing begins, often within weeks after commencing a project.

Particle Sciences' staff has designed and scaled multiple combination products ranging from vaginal rings, to intracranial implants. By engaging Particle Sciences you are leveraging our extensive experience. Our combination product development labs are extremely well equipped and are supported by in-house cGMP/cGLP analytical facilities and ICH stability programs. We have worked with small molecules, oligonucleotides, peptides, proteins and carbohydrates. We are FDA registered and DEA licensed for all controlled substances. In conjunction with our clients, we design the optimum program to achieve the desired output.

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PHYSICAL & SOLID STATE CHARACTERIZATION SERVICES

With many, if not most, drug product development projects now focusing on API's with variable solid states and/or solubility issues, physical characterization is critical to efficient formulation and regulatory support. Particle Sciences offers world-class physical characterization capabilities both as part of our development programs and as a standalone service.

The physical characteristics of an API and the formulation will largely dictate, among other things, stability, bioavailability and ultimately, performance. As API's move further away from small, highly soluble highly permeable molecules, these issues have increasing importance.

Particle Sciences is the leading CDMO when it comes to micro- and nano-particulate drug delivery systems

With growing frequency, as part of the overall QbD trend, regulators are requiring in depth characterization and tight control over physical parameters such as polymorphic state, particle or droplet size, viscoelastic properties and the quantification of the relationship of such parameters to drug release and product performance. Particle Sciences is uniquely positioned to meet this challenge. Our facility is comprehensively equipped and our staff has been at the cutting edge of fine-particle, nanoparticle and solid state characterization for decades. This expertise is a true competitive advantage for Particle Sciences' clients. We are FDA registered and DEA licensed. Additionally, Particle Sciences has invested in the infrastructure necessary to handle high potency compounds, such as chemotherapeutics and hormones.

Particle Sciences has one of the most complete suites of characterization tools on the East Coast

In addition to our advanced in-house characterization and analytical capabilities, our scientists can help you qualify suppliers, identify critical parameters for excipients and active substances and examine interactions between them, and develop and validate characterization methods, reducing variations in raw materials that can affect performance.

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OUR FACILITIES INCLUDE:

- Particle Size via Dynamic Light Scattering
- Particle Size via Laser Diffraction
- Particle Size via X-Ray Disc Centrifuge
- Particle Size and Morphology via Dynamic Image Analysis
- Surface Area via Flowing Gas Adsorption
- Particle Charge (Zeta Potential) by Electrophoretic Light Scattering
- Particle Charge (Zeta Potential) by Phase Analysis Light Scattering
- Rotational Rheometry
- Squeeze Flow Rheometry
- Tensile and Tack Testing
- Dynamic Contact Angle
- Surface Tension
- Turbidity
- Osmolality
- Differential Scanning Calorimetry
- Thermal Gravimetric Analysis
- Turbiscan Sedimentation-Stability Analyzer
- HPLC with Ultraviolet, Photo Diode Array, Refractive Index Evaporative Light Scattering Detectors
- UV/VIS Spectrometer
- ICH Temp/Humidity Stability Chambers
- ICH Photostability Chambers
- LC/MS Ion Trap
- LC/MS Triple Quad
- FTIR
- Microscopic Image Analysis
- Fluorophotometer
- Multiple Dissolution Apparatuses
- Percutaneous Absorption (IVRT)
- Karl Fischer Titration
- Total Organic Carbon Analyzer
- Horiba Raman/Particle Analysis

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ANALYTICAL SERVICES: SMALL MOLECULE AND BIOLOGICS

Analytical method development, validation, and execution are key to efficient drug product development, especially in an environment of increasing regulatory demands. Particle Sciences offers world-class analytical capabilities both as part of our development programs and as a standalone service.

Our services encompass a broad range of analytical, cell based, protein and bioanalytical techniques and our in-depth industry experience will help you in data interpretation and analysis. Particle Sciences' cGMP/cGLP facilities are equipped with a wide range of state-of-the-art instrumentation and experienced technical staff to assist you in method development, characterization, and routine and specialized testing. Our facility also offers exceptional capabilities in solid state and physical property characterization. We are registered with the DEA and can work with controlled substances. Additionally, Particle Sciences has invested in the infrastructure necessary to handle high potency compounds.

To complement our biologics formulation our biologics testing includes cell culture, cell based assays, ELISA, protein quantification, PAGE, SDS-PAGE and Western blotting with image analysis

Starting with forced degradation studies and method development, through commercial validation to long-term stability testing, the analytical group works hand-in-hand with formulation and manufacturing. This insures the most efficient path forward up to and including providing process development support, equipment cleaning validation and verification, and quality control testing.

Drug-eluting devices present special analytical challenges. Particle Sciences is the leader in method development for such products

To support formulation development and the establishment of release specifications, Particle Sciences offers drug-release testing appropriate to the intended dosage form. This includes USP solid-dose dissolution testing, an IVRT program using vertical diffusion (Franz cells) for semi-solids, and long term elution testing for combination products. The choice of collection medium, and conditions, membrane and interpretation of data all takes experience. At Particle Sciences, our staff has that experience. We regularly work with synthetic, biomimetic and tissue membranes and biologic simulant fluids. We routinely design and validate performance-indicating drug release test protocols for both product development and regulatory purposes.

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PARTIAL INSTRUMENTATION LIST:

- HPLC, UPLC
- LC/MS Ion Trap
- LC/MS Triple Quad
- NMR by Third Parties
- UV/Vis Spectrometer
- FTIR
- Differential Scanning Calorimetry
- Optical Microscopy/Image Analysis
- Fluorophotometer
- USP Dissolution Testing I, II, IV
- Percutaneous Absorption (IVRT)
- Cell Culture
- ELISA
- Gel Electrophoresis Particle Size via Dynamic Light Scattering
- Particle Size via Laser Diffraction
- Particle Size via Disk Centrifuge
- Particle Size via Light Absorption Disk Centrifugation
- Particle Charge (Zeta Potential)
- Oscillatory Rheometry
- Squeeze Flow Rheometry
- Tensile and Tack Testing
- Dynamic Contact Angle
- Surface Tension
- Turbidity
- Osmolality
- Thermogravimetric Analysis
- Contact Angle/Surface Energy
- Sedimentation-stability Analyzer
- Refractometry
- Surface Area Analysis
- Particle Size Analysis
- HPLC with Ultraviolet, Photo Diode Array, Fluorescence, Refractive Index, and Evaporative Light Scattering Detectors
- ICH Temperature/Humidity-Controlled Stability Chambers/Refrigerators
- ICH Photostability Chambers
- Horiba Raman Particle Characterization System