

Pharmaceutical Solutions



W. R. Grace & Co.'s history of exceeding customer expectations is built upon our unyielding commitment to innovation and advancement of technical expertise, which is reflected throughout the drug development process.



Grace's Portfolio for Pharmaceutical Solutions Includes:

Fine chemicals synthesis expertise

- Decades of experience in organic chemical synthesis at our three fully integrated North American sites

Unique multifunctional excipients

- SYLOID® multifunctional excipients
- SILSOL® silica active ingredient delivery technology

Highly efficient chromatography resins

- DAVISIL® silica, VYDAC® chromatography resins, and VYKING™ superparamagnetic silica

Custom Engineered Silica

By tailoring raw materials and processing aids precisely to your specifications, Grace's multifunctional excipients and chromatography resins offer unmatched quality and reproducibility.

- Improve efficiency and reproducibility from small-scale discovery and clinical trials to mass production
- Develop differentiated formulations that assist with the delivery of desired health or medical benefits
- Accelerate speed to market and stay ahead of the competition

A Leading CDMO in North America

Grace's Fine Chemical Manufacturing Services (FCMS) is a leading North American contract development and manufacturing organization (CDMO), known for our extensive expertise and ability to provide integrated solutions for the pharmaceutical, nutraceutical, and other fine chemical industries.

Our fine chemicals capabilities enable Grace to be your fully integrated US-based partner for the development and production of custom active pharmaceutical ingredients (APIs), regulatory/registered starting materials (RSMs), and intermediates. We can partner with you from the lab to commercial production while providing quality leadership throughout the process and meeting regulatory compliance.

Grace's Quality and Regulatory Standards:

- ISO 9001 2015 certification
- EXCiPACT® 2017 certification
- Compliant with current good manufacturing practices (cGMP) for pharmaceutical grades, fine chemicals, and VYDAC® chromatographic resins
- Halal and Kosher certifications
- OSHA VPP Star Participant
- EcoVadis platinum corporate social responsibility (CSR) rating

Fine Chemicals

Grace's FCMS is a premier CDMO that provides integrated pharmaceutical services through its network of North American facilities. We offer a full range of solutions for product development, analytical method development and validation, project management, scale-up expertise, and other areas of custom chemical synthesis.

Grace's FCMS supports companies throughout the small molecule development cycle, from pre-clinical stages to full-scale commercial manufacturing in our kilo lab (16-30 liters) and production reactors up to 16,000 liters.

Supply Chain Risk Mitigation

Organizations are quickly realizing the extent to which they underestimated the risks of manufacturing overseas. Hence, supply chain strategies have shifted in recent years towards reshoring to reduce tariffs and mitigate disruptive global events. With three integrated US facilities, Grace's FCMS is a stable and reliable partner in fine chemicals production, ranging from RSMs to custom APIs while providing end-to-end domestic project management relationship.



Our fine chemicals capabilities include:

- Custom API development and commercial manufacturing in cGMP-compliant facilities
- API development including Quality by Design (QbD) to support validation of processes
- Chemistry Manufacturing and Controls (CMC) support
- Supply chain risk mitigation
- Custom ingredients for food or dietary supplement development and manufacturing
- RSMs and registered intermediates synthesized on scales up to 100MT per year
- US-manufactured generic API portfolio
- Expertise with chiral molecules, custom boronic acids, custom amino acids, and protecting groups, solution-phase peptide synthesis, aminations, alkylation, and homogeneous catalysis via Suzuki coupling
- World-class analytical capabilities
- Cryogenic chemistry
- Ultra-low vacuum distillation

Grace's fine chemical facilities are strategically located in Pennsylvania, Michigan, and Oregon, and designed to meet customers' quality, regulatory, and confidentiality expectations.

Capabilities include:

- Audited and qualified cGMP environments
- Kilos-to-tonnes custom manufacturing
- Scale-up expertise and technology
- Extensive research and development (R&D) capabilities

Excipients

Excipients have a variety of functions within formulations: lubricant, glidant, filler/diluent, binder, preservative, coating material, surfactant, and thickener. Optimized excipients can help address solubility and bioavailability challenges that more than 50% of small-molecule drug candidates face.

Grace's mesoporous silica excipients can be used to formulate both solid and semi-solid finished dosage forms. In solid dosage forms, mesoporous silica-based excipients can also act as a glidant, an inert carrier, and provide moisture protection. In semi-solid dosage forms, mesoporous silica can act as a thickening agent, provide a dry feel (oil-absorbing effect) and in some cases, allow for a more uniform distribution of the drug substance.

With increased regulatory and consumer attention on excipients, the need for approved alternatives has become integral. Grace's mesoporous silica excipients meet ICH guidelines on elemental impurities, comply with the monographs of the US Pharmacopoeia-National Formulary (USP-NF) for Silicon Dioxide, and the European

Pharmacopoeia (Ph. Eur.) for Colloidal Hydrated Silica. SYLOID® mesoporous silicas are also listed on the FDA's inactive ingredient database and are manufactured under GMP quality standards certified by EXCiPACT®.

SYLOID® Mesoporous Silicas

Grace's SYLOID® mesoporous silicas are versatile drug development materials used to improve formulations, enhancing solubility and bioavailability. SYLOID® mesoporous silica particles have a unique combination of properties, where parameters such as pore volume, pore diameter, pore size distribution, and internal surface area can be fine-tuned, and the functionality can be modified to meet your exact requirements.

SYLOID® mesoporous silicas are used in a wide range of applications, including:







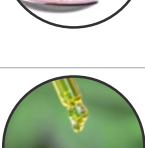


- Moisture protection
- Improved flow through the reduction of electrostatic charging
- Moisture-Assisted Dry Granulation (MADG)
- Liquisolid formulations
- Oil absorption in lipid-based technologies (Self-emulsifying drug delivery systems, SEDDS)



SYLOID® FP Silica



Fumed Silica

	Product Name	Application Description	SYLOID® 244 FP Silica	SYLOID® 72FP Silica	SYLOID® AL-1 FP Silica	SYLOID® XDP Silicas	SILSOL® 6035 Silica
	Glidant	<ul style="list-style-type: none"> • Improve flow to make free-flowing powders • Reduce short range adhesive forces • Reduce effect of capillary water bridges between particles 	●	●			
	Anti-caking	<ul style="list-style-type: none"> • Prevent moisture uptake by the other components of the powder formulation 	●	●			
	Anti-electrostatic charging	<ul style="list-style-type: none"> • Avoid electrostatic charging of powder formulations during manufacturing • Reduce the loss of the API by minimizing the need for sieving prior to use 	●				
	Moisture protection	<ul style="list-style-type: none"> • Control trace amounts of moisture and moisture transfer • Improve stability of the API • Reduce sticking and picking during the tableting process 	●		●		
	Tablet hardness	<ul style="list-style-type: none"> • Improve tablet hardness at lower compression forces • Decrease friability • Reduce the tendency of capping and lamination 	●				
	Suspension aid and anti-tacking in tablet coatings	<ul style="list-style-type: none"> • Improve suspension stability and prevent blockage of valves and spraying nozzles • Reduce interaction between coated tablets with a formed micro-structured surface • Reduce or eliminate the use of talc in coating formulations 	●				
	Flavor absorption and stabilization	<ul style="list-style-type: none"> • Absorb flavors while improving oxidation stability • Retain the formulated flavor and mask the bitter taste of APIs 	●				
	Carrier for Oils and SEDDS	<ul style="list-style-type: none"> • Convert oily APIs and SEDDS into free-flowing powders • Ease of processing solid dosage forms such as tablets and capsules 	●			●	
	Drug delivery: Improve solubility and bioavailability	<ul style="list-style-type: none"> • Increase bioavailability of water-insoluble new chemical entities (NCE) • Stabilize the API in its amorphous form • Prevent re-crystallization with optimized diameter of pores 					●

Chromatography

Leveraging Grace's 100-year history of silica expertise, our broad portfolio of chromatography resins offers a wide range of pore diameters, particle sizes, and chromatography phases. Our engineering capabilities allow particle properties to be fine-tuned to meet your specific requirements, as well as batch-to-batch consistency and reproducibility.

Our team develops resins that can be used from analytical lab scale through to commercial scale and are certified according to the ISO 9001 standard.

Grace brands include:

DAVISIL® silica products

Available in granular form, in a wide range of particle and pore sizes, and in many phases from small to multi-ton quantities

DAVISIL® sphere silica

Designed to be robust with a narrow particle size distribution, resulting in highly reproducible, superior chromatographic performance leading to improved separation

DAVISIL® Extra Wide Pore (XWP) silica

Offers enhanced mechanical stability and large pore sizes with narrow pore size distribution, making it ideal for separations of large biological molecules

VYDAC® spheroidal silicas

Well-defined, highly pure, and fully porous separation resins, with excellent selectivity and reproducibility for biopurification

VYKING™ superparamagnetic silica

Features a novel particle design that clads a superparamagnetic core with silica to eliminate the need for the chromatography, centrifugation, or vacuum filtration steps

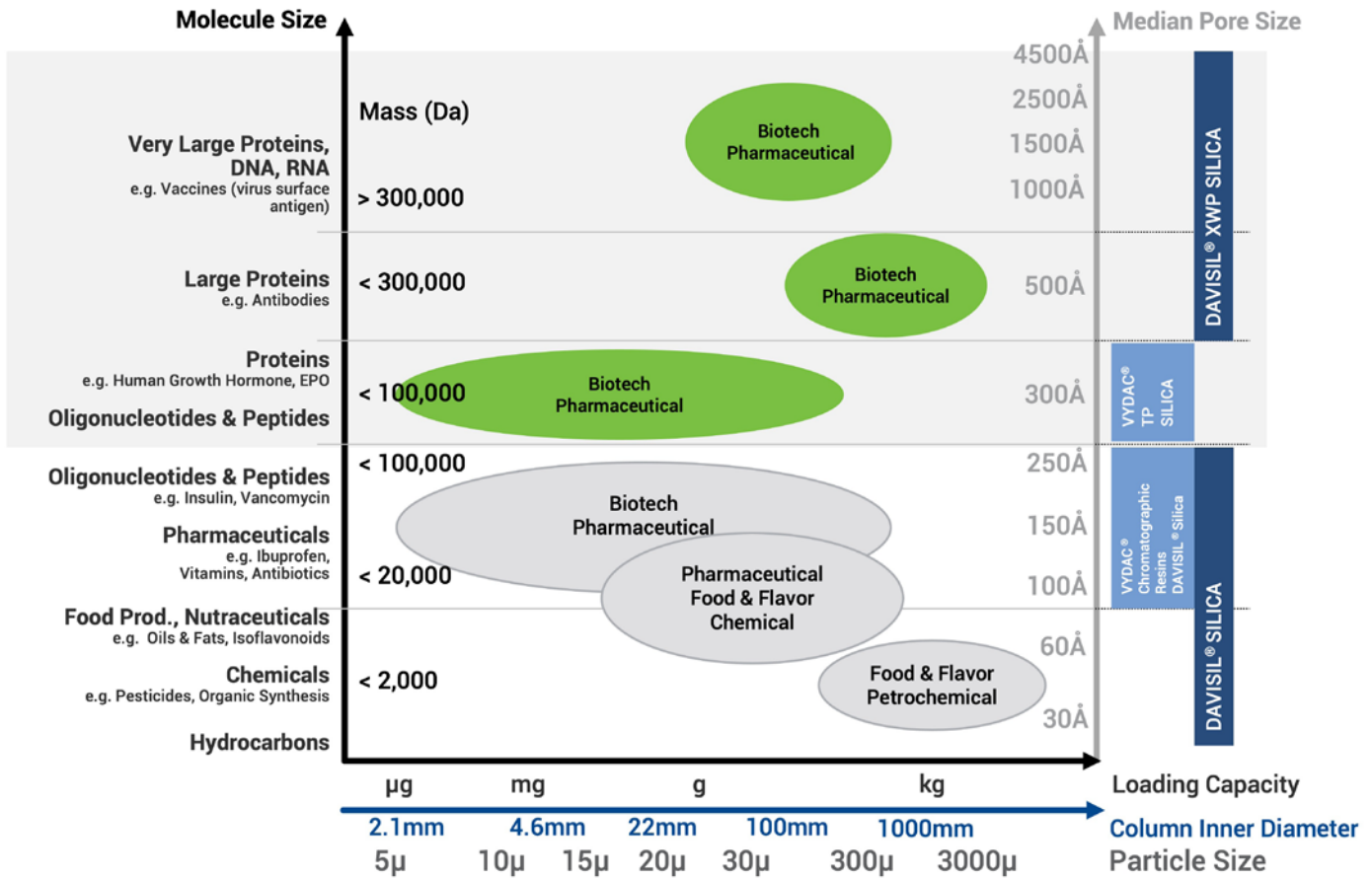
For specialized applications, Grace can develop customized products to suit your specific needs, including custom bonding of chromatography resins.

Custom bonding capabilities:

Grace is the world's largest manufacturer of specialty silicas, with 100 years of silica manufacturing expertise and more than 45 years of chromatography experience. Grace has extensive experience in bonding different resins. With our expertise, we can offer:

- Custom bonding of Grace's silica (30Å-4500Å; 5µm to 200µm) or other resins
- Different reversed and normal phase (C1, C2, C4, C8, C18, Phenyl, Amino, Diol, Cyano), ion exchange, and other chemistries
- Batch-to-batch reproducibility
- Scalability: Small micron ($\leq 10\mu\text{m}$) bonding from 50g to 5kg batch size; large micron bonding from 50g to 200kg batch size
- GMP compliant management system that meets the stringent requirements of the pharmaceuticals industry

Chromatography Applications and Industries



Phase	Silica	Custom Bonding	C18	C8	C4	Phenyl	Amino	Cyano	Diol
VYDAC® Chromatographic Resins Oligonucleotides, Peptides, Proteins	●	●	●	●	●	●			
VYKING™ Superparamagnetic Silica Nucleic Acids, Proteins	●	●							
DAVISIL® Silica Small Molecules, Peptides, Oligonucleotides	●	●	●	●	●	●	●	●	●
DAVISIL® Extra Wide Pore (XWP) Silica Large Molecules	●	●							

For more information about Grace Pharmaceutical Solutions, visit grace.com/pharma



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