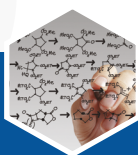


R&D SERVICES





Founded in 1995, SiliCycle is specialized in the development, manufacturing and commercialization of high value silica gels and specialty products for chromatography, purification and synthesis.

R&D Services

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SiliCycle R&D Services

- We listen. We understand. We work with you.
- We are flexible, committed, reliable, and innovative.
- Our objective: reinvesting our experts' talent in your very own expertise.
- Wide range of services offered.

One Partner: SiliCycle

SiliCycle is devoted to serving its customers and constantly focuses on quality.

SiliCycle offers turnkey solutions based on its long expertise. Our main priority is to ensure you real innovation, tangible ROI, quality assurance and intellectual property within your tight timeframes. Our programs focus on issues of strategic importance for your venture: a unique value proposition to deliver results of high impacts.

Our flexible approach for each project brings added value to our services to match each client's requirements.

Our business models:

- Full Time Equivalent (FTE)
- Fee for Service (FFS)
- Milestone Based



Facility and Lab Infrastructure

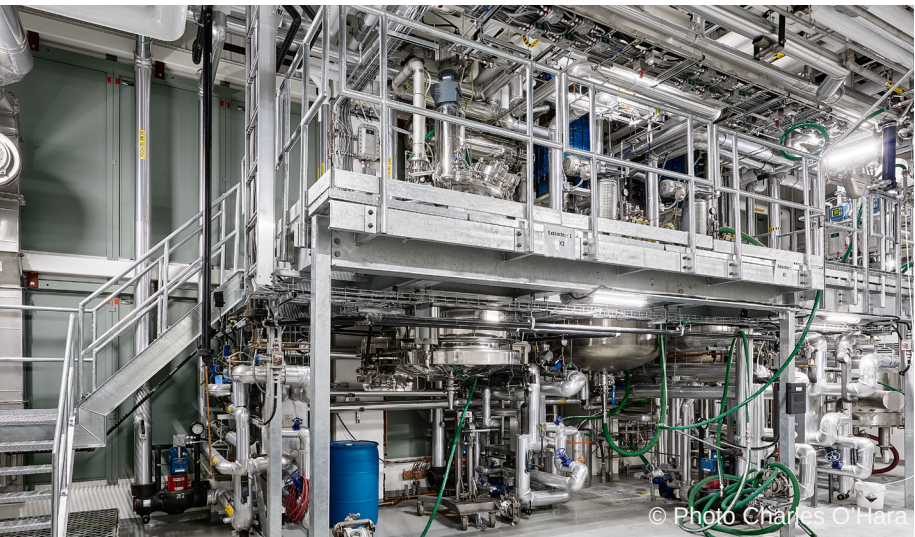
SiliCycle Headquarters is a new cutting-edge plant with a multi-ton scale manufacturing capability. With state-of-the-art instrumentation park in the areas of chromatography, spectroscopy, and manufacturing combined to an application support laboratory, we are devoted to extend your R&D and make your project a success.



As a certified ISO 9001:2015 company, we have a rigorous quality system: all procedures and employees are in place to assure you ultimate quality and an unbeatable customer service.



Enjoy a virtual tour of SiliCycle's facility



R&D Services Portfolio

Our R&D Services are categorized into 8 streams, and you can learn more about them throughout the next pages.

Material Science Services

- Customized Products
- Optimization of Grafted Catalysts

Metal and Organic Scavenging Screening Services

- Screening Conditions Evaluation
- Process Scaling-Up and Transfer to Production

Organic Synthesis Services

- Designing optimal synthetic routes from milligrams to hundred-grams scale

Catalysis Services

- Setting up catalytic reactions
- Designing tailor-made silica-supported catalysts

Process Services

Chromatography and Purification Services

- Compound Extraction and Sample Preparation
- Impurity Isolation and Structure Elucidation
- Method Development, Optimization and Transfer

Method Development, Optimization and Transfer

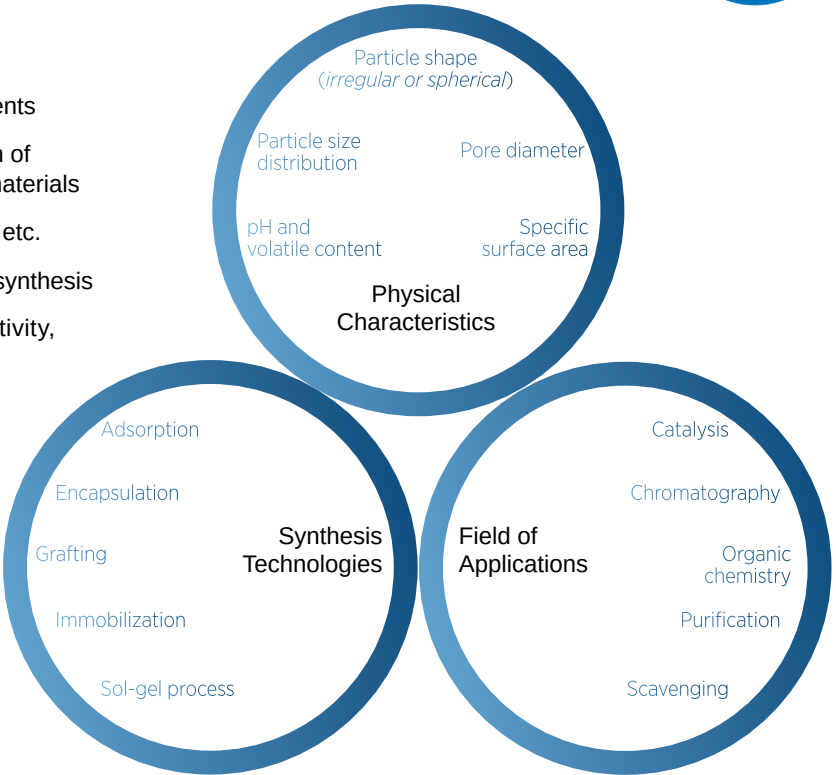
Analytical Laboratory Services

Material Science Services

We have close to three decades of experience working with silica and we can work closely with you to design and manufacture customized products that will meet your requirements. Our experienced chemists can graft demanding organic or inorganic molecules on many matrices to meet your needs.

Most Popular Material Science Services

- Custom material synthesis based on your requirements
- Immobilisation, grafting, encapsulation or adsorption of organic and inorganic molecules on silica or other materials
- Customized particle size distribution, water content, etc.
- Catalyst support, mixed-oxides or organic moieties synthesis
- Improvements of your own catalysts to enhance activity, selectivity, etc.



Metal and Organic Scavenging Screening Services

Our scavenging screening services provide solutions to quickly develop the most efficient metal scavenging process providing both time and cost savings. Confidentiality is assured and we will be working with you, in function of your needs



Screening and Optimization Services

Batch: Lab and Process Development

Step 1: Screening

- Different SiliaCarb activated carbons and SiliaMetS metal scavengers will be tested on the crude product at two different temperatures.
- Influence of contact time will also be evaluated.

Step 2: Optimization

- After this initial screening, we will select the most efficient carbon and scavenger to optimize the ratio vs the API.
- Pairwise combinations of metal scavengers could also be tested, if satisfactory results are not obtained. Scavenging yields as well as recoveries will be evaluated.

Step 3: Scale-up Confirmation and Optimization

- A new amount of crude product will then be treated with SiliaCarb (if relevant), using the best obtained conditions to get enough product to work on the next step.
- Finally, we will test the best conditions on the API solubilized in two other solvent systems (depending on API solubility and customer's requirement). Scavenging yields as well as recoveries will be evaluated.
- Best conditions will be transposed on larger scale (to be determined based on the remaining crude product).

Batch to E-PAK: Including E-PAK Process Development

Includes all points performed with "batch" service plus the following:

- SiliaCarb and SiliaMetS best conditions will be transferred to E-PAK radial flow cartridges.
- Contact time's effect can be evaluated as well as parameter's optimization on E-PAK for both SiliaCarb and SiliaMetS.
- Scalability study based on customer final equipment can be performed if enough crude is available.

→ Main objective is to **accelerate research, optimize production costs**, while remaining fully in compliance with **new regulations and environmental challenges**

→ Scavenging strategies imply **lower volumes of solvent and higher yields** by minimizing loss of product via classical purification processes

Two Plans for R&D Services		
Includes	BATCH Scavenger Screening	BATCH TO E-PAK Scavenger Screening
SiliaCarb and SiliaMetS screening in bulk	✓	✓
Optimization in different solvents	✓	✓
Metal concentration tracked by ICP-MS or ICP-OES	✓	✓
Scale-up confirmation and optimization*	✓	✓
Transfer of the optimized conditions to E-PAK radial flow cartridge		✓
Evaluation of contact time in E-PAK radial flow cartridge		✓
Scalability based on customer final equipment can be performed if enough product is available		✓
Complete report provided	✓	✓
Expected screening service delay after reception of customer's sample Typical crude quantity needed*	3 - 4 weeks 50 to 200 g of crude	4 - 6 weeks 100 to 200 g of crude

* Will need to be confirmed by our researchers.

Organic Synthesis Services

SiliCycle has a wide experience in the design and synthesis of new organic molecules and the development of novel methodology for their preparation. In especially challenging synthetic pathways, we can help you with your most difficult reactions, using cutting-edge technology to develop cost-effective solutions.



Available Technologies

- Flow chemistry
- High-pressure chemistry
- Solid-supported chemistry
- Microwave-assisted reaction
- Parallel synthesis and purification

Areas of Chemical Expertise Include Synthesis of

- Analytical standards
- API's, impurities, and metabolites
- Building blocks and complex intermediates
- Chiral molecules
- Derivatives of lead compounds
- Natural products

Typical Organic Chemistry Reactions

- Oxidation and reduction
- Reductive amination
- Couplings (*Suzuki, Sonogashira, Stille, Negishi, etc.*)

Most Popular Organic Synthesis Services

- Project evaluation and literature searches
- Synthesis of active compounds, building blocks and intermediates from mg to hundred-grams scale
- Synthetic route design, realization, and optimization
- Scale-up of existing or new reactions
- Transfer of homogeneous process to heterogeneous
- Scavenging of residual metal catalyst

→ We **accelerate drug development** by setting up and optimizing crucial steps using an **innovative silica-based technology** in a matter of weeks

→ We develop safer and cleaner processes leading to **atom economy** and **further cost reduction**

Catalysis Services

Our approach combines a broad scope of expertise which can accelerate your catalyst's screening, optimize an existing catalytic process, test the feasibility of a new one or understand metal-catalyzed reaction.

As a catalyst manufacturer with multiple patents, our skilled and competent catalysis group can investigate any reaction parameter (*catalyst loading, solvent, ligand, base / additive nature, concentration, temperature, time, etc.*) to maximize yields and purity as well as to reduce wastes and costs.



Typical Catalysis Reactions

- Couplings such as:
 - Borylation
 - Heck
 - Kumada
 - Negishi
 - Suzuki
 - Sonogashira
 - Stille, etc.
- Hydrosilylation
- Selective Debenzylation and Hydrogenation
- Selective Reduction of Nitroarenes

Most Popular Catalysis Services

Setting up catalytic reactions with SiliaCat

- Designing a catalytic step from scratch
- Taking a homogeneous process and transferring it to heterogeneous (*supported*) catalysis in batch
- Scaling up a heterogeneous process to kg scale
- Transferring a batch, heterogenous process into a flow process (*on gram scale*)

Designing tailor-made silica-supported catalysts

- If we don't have an existing silica-based catalyst, we can develop one
- or
- Tweaking an existing catalyst to enhance activity, selectivity, physical parameters (*particle size*), etc.

Process Services

SiliCycle understands the importance of having a robust and cost-effective synthesis when it comes to process development and manufacturing. We offer flexible process services based on a structured approach to increase yields and purities at reduced costs. We can help you make your project a success story and work with you on process improvements.



Typical Process Improvements Parameters

For each process service, these parameters can be further refined upon request:

- Safety
- Reproducibility
- Cost optimization
- Yield and purity improvement
- Time constraints (*productivity*)
- Solvent substitution (*greener, safer or cheaper*)
- Volume constraints
- Robustness

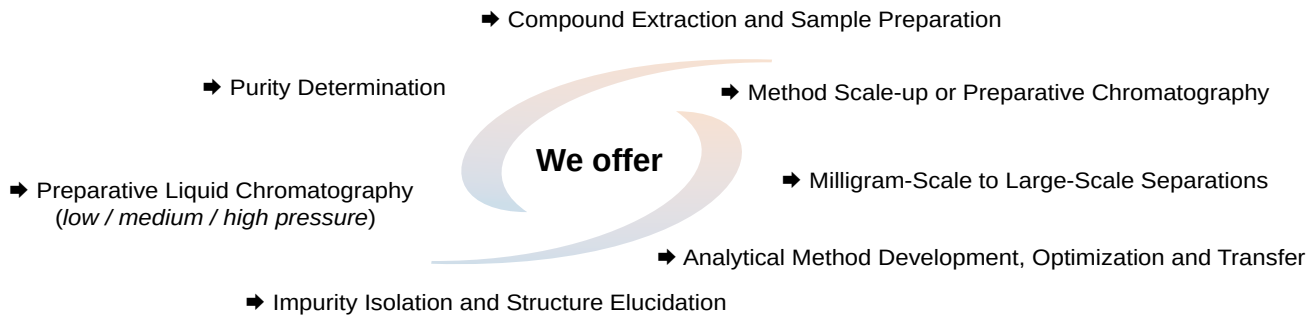
Most Popular Process Services

- Identification of safety issues and synthetic opportunities
- Route scouting and feasibility
- Yield and purity optimization
- Resolution of challenging bottleneck steps
- Process scale-up from laboratory to kilo-lab synthesis
- Scavenging of residual metal catalyst



Chromatography and Purification Services

For decades, SiliCycle has been dedicated to silica gel manufacturing and has built a strong skilled team in this field. You can now benefit from years of experience in chromatography, purification and method development. Our expertise covers a wide spectrum of applications on various purification scales.



Compound Extraction and Sample Preparation

Looking to extract a specific product from a complex matrix? Let our experts develop a process for you. We can screen various methods and determine the most efficient ones to extract any value-added product from biomass or solution. Some typical molecules we have worked with include polyphenols and phytonutrients, omega-3 and omega-6, fatty acids, pesticides, vitamins, dioxins, pollutants, and conjugate polymers.

Furthermore, we can optimize your sample preparation processes using SPE cartridges, well plates, or liquid-liquid extraction to maximize recovery and reduce interferences.

Our generic approach for method extraction will decrease development time and costs.

→ We enable scientists to quickly separate mixtures, isolate molecules or elucidate structures for **rapid commercialization onto global markets**

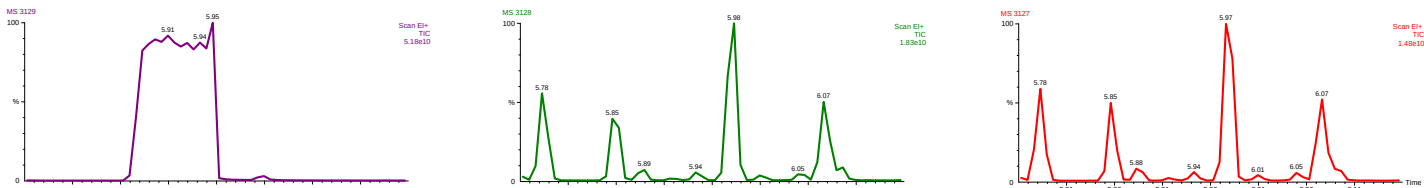
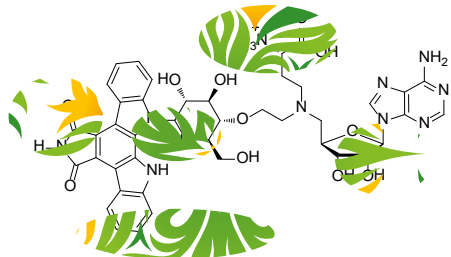
→ We help ensure that compounds fall into FDA's and Pharmacopeia's **stringent regulations**

→ We ensure quick, reliable, efficient **transfer of complex chemistry to timely scale-up** for early stage clinical API

Impurity Isolation or Removal and Structure Elucidation

We can help you identify, isolate and characterize impurities present in the final product or potential contamination source from a specific synthesis pathway. Our unique approach using state-of-the-art techniques and strategies allows the detection of a wide range of products even at low concentration. Based on your project requirements, many type of services are available:

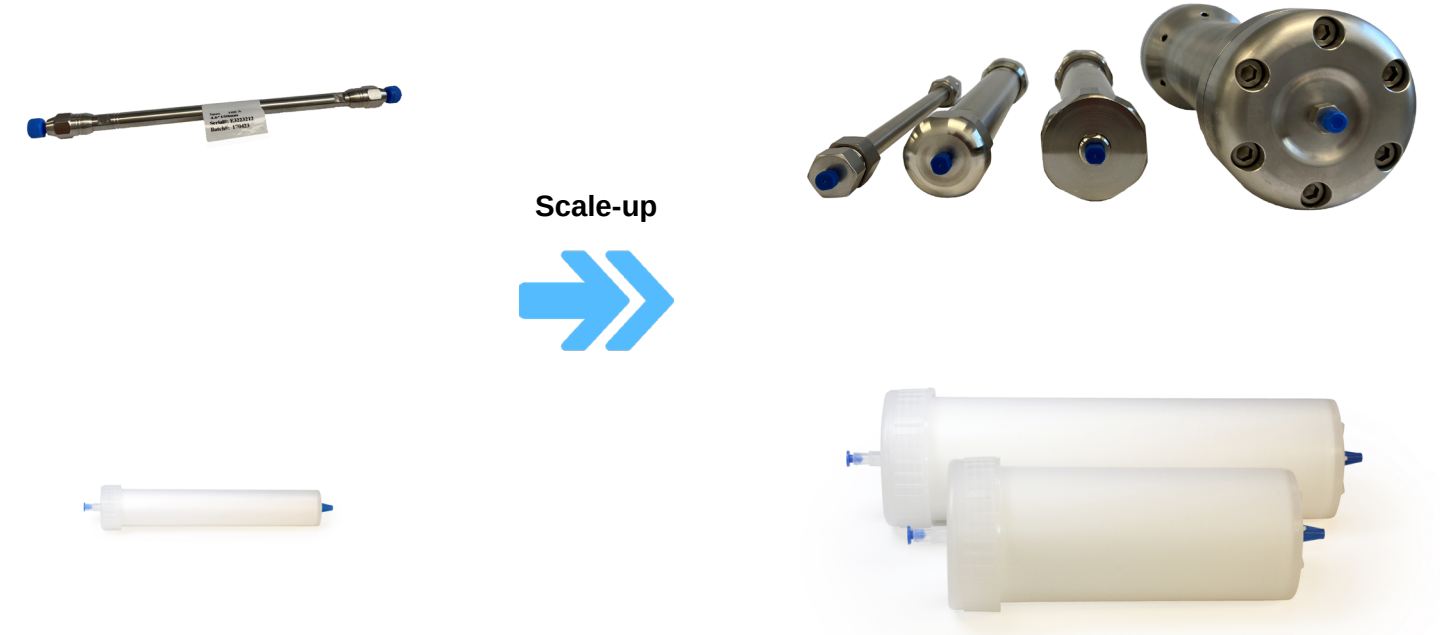
- Structure elucidation of unknown degradation or by-products
- Preparative isolation of contaminants from the final product
- Targeted synthesis of the impurity, followed by its analytical qualification (*reference standard*) for higher concentration compared to the specified accepted limit value
- Detection in trace range (*ppb*) of genotoxic impurities
- Stability studies of final product



Chromatographic Method Scale-up

Scale-up strategies are based on initial separation from an analytical column to a preparative one or a small cartridge to a multi-kilogram one using the same packing material. This is the most important aspect of scalability. SiliCycle recognizes this fact and offers the same sorbent in both analytical and preparative columns. This allows easy scale-ups with constant performance which guarantees optimal results throughout your purification process.

SiliCycle can provide turnkey solutions to your purification problems by performing your scale-up process or your purification with our expert staff in our laboratories.



Analytical Method Development, Optimization and Transfer



Our experts in method development, optimization and transfer can help you with your projects. You will benefit from our highly experienced team dedicated to develop or optimize methods in different matrices (*biological, food, beverages, water, etc.*) and for a wide range of molecules (*small to large*).

Our approach is flexible and can be customized to support your product development timeline. We work with you to establish the scope of the project and determine the most suitable factors to consider for the method development.

Method Development Considerations

- **Molecular Structure:** functional groups, polarity, pKa, chirality, etc.
- **Synthetic Route:** raw materials used, intermediates, possible by-products, isomers, etc.
- **Sample Availability:** can be purchased, API, generated, etc.
- **Separation Modes:** reversed-phases (*first mode screened*), normal, and hilic phases
- **Detection Modes:** MS, ELSD, UV, Fluorescence, etc.
- **Purity Assessment Methods:** HPLC, GC, NMR, etc.

With the availability of different HPLC column formats (*ID from 4.6 to 50 mm*) combined to various particle sizes (*3, 5, and 10 µm*) and phases (*RP, NP, HILIC, and specialized phases*), we can achieve selective and reproducible chromatographic separations for your analysis. All experiments are performed in-house with our analytical instrumentation and based on your requirements. At the end of the project, we deliver a comprehensive report including the method development for an efficient and easy method transfer.

Analytical Laboratory Services

SiliCycle's analytical testing laboratory operates under stringent ISO 9001:2015 procedures and therefore always focus on quality and customer satisfaction. All procedures and employees are in line to assure you ultimate quality work at extremely competitive pricing.

SiliCycle has earned its international reputation through our commitment to high quality standards. Now everyone can take benefit of our state-of-the-art instrumentation park and expertise in analytical chemistry to guarantee the quality of your products.

→ We provide a strong assistance in **defining a QA / QC program** that meets the full scope of your requirements

→ We handle **development and QC release testing** for individual methods or complete release packages

Available Instrumentation

SiliCycle possesses several synthesis, chromatography, and analytical equipments to help you achieve your project goals. Please see the following tables for a quick overview of our instrumentation park.

Available Instrumentation		
Analysis and Apparatus		Typical Applications
Chromatography	Dynamic Axial Compression (DAC) Technology <ul style="list-style-type: none">Agilent, Load and Lock Column (DAC) 500 mm x 25 mmAgilent, Load and Lock Column (DAC) 500 mm x 50 mmAgilent, Load and Lock Hydraulic Packing Station	Packing system for process preparative LC. Packing capacities for applications ranging from development (<i>multigrams</i>) to production (<i>multi-kilo</i>) of pharmaceutical compounds, peptides and natural products with unique fluid / sample distribution system to maximize productivity.
	Flash Chromatography <ul style="list-style-type: none">Gilson®, Flash Chromatography System, Spot Prep IIBüchi®, Flash Chromatography system, SepacoreSantaï, Sepabean Machine LSantaï, Sepabean Machine T	Integrated purification system with gradient solvent delivery, sample detection and fraction collection UV-directed. Designed for easy and straightforward flash purification.
	High Performance Liquid Chromatography <ul style="list-style-type: none">Applied Biosystems / MDS Sciex®, LC-MS/MS, API 3000Sciex Exion AD UHPLC, LC-MS/MS, QTRAP 6500+Gilson®, Preparative LC-MS systems , Flexar SQ 300MSShimadzu®, Prominence®, Preparative Liquid ChromatographThermo, HPLC with Photodiode Array Detector, Surveyor Plus®Thermo Finnigan®, HPLC, Surveyor®	Analytical tools for method development. Reaction mixtures and purified products analysis. Structural information based on the MS/MS fragmentation and liquid chromatographic separation. Optical purity determination (<i>diastereomeric and enantiomeric excess</i>). Stereoisomers separation & isolation.
Synthesis	Parallel Evaporation <ul style="list-style-type: none">Büchi®, Syncore® Polyvap	Parallel evaporation of multiple samples for increased productivity in parallel and multistage synthesis.
	Microwave Synthesis <ul style="list-style-type: none">CEM®, Discover®, Microwave Synthesizer	Energy transfer from electric field to molecules through dipole rotation and ionic conduction.
	Flow Chemistry <ul style="list-style-type: none">Syrris Asia®, 220 Flow Chemistry	Great variety of chemical reactions, with wide ranges of temperatures, pressures and reaction times on scales from mg to kg.
	Parallel Synthesis <ul style="list-style-type: none">SiliCycle MiniBlock® and MiniBlock XT®	Specially designed for carrying multiple reactions simultaneously, with refluxing and inerting capabilities. Compatible with solution & solid-phase synthesis.
	Automated Sample Preparation <ul style="list-style-type: none">Gilson®, Solid Phase Extraction, GX-274 ASPEC	Automated sample preparation system for sample prep and run: positive pressure extractions and filtrations. SPE process performed in either batch or sequential mode.
	Freeze Drying <ul style="list-style-type: none">Labconco, Lyophilizer, FreeZone™ Bulk Tray Dryers	Product drying following HPLC purification.

Available Instrumentation			
Analysis & Apparatus		Resolution & Detection Specifications	Typical Applications
Analysis Technologies	Elemental Analysis • PerkinElmer®, 2400 Series II CHNS/O Analyzer	3 modes: CHN, CHNS, and Oxygen Temperature range: 100 - 1,000°C	Rapid determination of carbon, hydrogen, nitrogen, sulfur and oxygen content in organic and other types of materials.
	Tap Density • Electrolab, Tap Density Tester, ETD-1020	Two-stations tester USP I, USP II, ASTM test methods Min. sample required: 25 g	Tapped density measurements of powders, granules, pellets, flakes and other bulk substances.
	Sieve Shaking • Gilson®, Tapping Sieve Shakers, SS-8R	Particle range: 20 - 4,000 µm Agitation mode: tapping Min. sample required: 10 g	Consistent and repeatable particle size testing over a broad range of irregular particle sizes and material types.
	Particle Size Analysis by Laser Diffraction • Malvern Instruments™, Mastersizer 2000™, Hydro 2000S	Particle range: 0.01 - 3,000 µm Min. sample required: 0.5 - 1 g	Metal powder particle size distribution measurement. Optical diffusion of laser light on particle in suspension.
	pH Measurement • VWR®, pH meter, SympHony SB70P®	Min. sample required: 5 mL (<i>liquids</i>) or 5 g (<i>solids</i>)	Acidity or alkalinity measurement.
	Water Content Determination • Mettler Toledo®, Karl Fischer, Coulometric KF Titrator C20 • Mettler Toledo®, Karl Fischer, Volumetric KF Titrator V20 • Sartorius®, Moisture Balance, MA30	Min. sample required: 10 mg 200 mg	Simple, secure water determination by electrolysis or chemical titration.
	Surface Area and Porosity Analysis • Micromeritics®, BET, TriStar • Micromeritics®, BET, TriStar II	Range: From 20 to 250 Å Hg porosimetry available for sizes above 250 Å Min. sample required: 1 g	Surface area and porosity analysis, determined by physical adsorption of a gas (<i>N₂</i>) on surface of the solid (<i>amount of adsorbate gas vs monomolecular layer on surface</i>). Amount of gas adsorbed can be measured by volumetric or continuous flow procedure.
	Inductively Coupled Plasma (ICP) Analysis • PerkinElmer®, Optima™ 2100 DV ICP-OES • Thermo Scientific, XSERIES 2 ICP-MS	Specifications of analysis, detections limits dependent on substrate, element, interferences, initial concentration, dilution solvent etc.	Identification and concentration measurement of up to 70 elements simultaneously (<i>mostly metals</i>). Solid samples must be digested prior to analysis.
GC	Gas Chromatography (GC) • PerkinElmer®, GC/FID, GC, Clarus 400® • PerkinElmer®, GC/MS, GC, Clarus 600®, MS, Clarus 600C	Min. sample required: 1,000 µL Molecular ions up to m/z 500	Separation and analysis of compounds that can be vaporized without decomposition, for purity testing, components separation and relative amounts.
Spectroscopy	Spectrophotometry • Agilent, Spectrophotometer, Cary 60	λ range: 190 - 1,100 nm	Transmission and reflection (<i>diffuse and specular</i>) color, concentration (<i>solution</i>).
	Infrared Spectroscopy • PerkinElmer®, FT-IR Spectrometer, Spectrum 100®	Min. sample required: 1 mL (<i>liquids</i>) or 1 g (<i>solids</i>)	High spectral resolution data collection over a wide spectral range, for structural analysis or non-destructive measurement applications.
Thermal Analysis	Thermogravimetric Analysis (TGA and TGA-MS) • TA Instruments®, TGA 2950 • TA Instruments®, TGA Q500 • Pfeiffer Vacuum, ThermoStar™ GSD 301 T	Mass: 0.1 mg Temperature: ~0.1°C MS: 0 - 300 amu	Mass change vs time and temperature, identification of volatile degradation components.

DISCOVER AND DOWNLOAD OUR BROCHURES

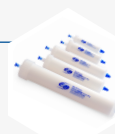
METAL AND ORGANIC SCAVENGING

SiliaMetS® – Metal Scavengers
SiliaBond® – Organic Scavengers
E-PAK® – Fixed Bed Flow-Through Purification Cartridges



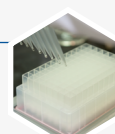
CHROMATOGRAPHY AND PURIFICATION

SiliaFlash® – Irregular Silica Gels | **SiliaSphere™ PC** – Spherical Silica Gels
SiliaBond® – Chromatographic Phases
SiliaSep™ – Flash Cartridges | **SiliaPlate™** – TLC Plates



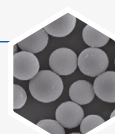
SAMPLE PREPARATION

SiliaPrep™ – Silica-based SPE Cartridges and Well Plates
SiliaPrepX™ – Polymeric SPE Cartridges and Well Plates



ANALYTICAL AND PREPARATIVE CHROMATOGRAPHY

SiliaSphere™ – Spherical Silica Gels
SiliaChrom® – HPLC Columns



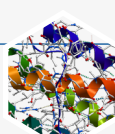
ORGANIC SYNTHESIS

SiliaBond® – Reagents and Oxidants
SiliaCat® – Heterogeneous Catalysts



PEPTIDE SYNTHESIS

Peptide Synthesis and Purification Solutions
Amine Free Basing and TFA Removal



R&D SERVICES

Metal and Organic Scavenging Screenings | Organic Synthesis
Chromatography and Purification | Material Science
Method Development, Optimization, and Transfer



Technical Support

At SiliCycle, we are committed to providing the best technical support possible.

Our worldwide Technical Support Group of highly qualified M. Sc., Ph. D. Chemists and Engineers will answer your questions and provide solutions to your most advanced chemistry and purification needs. Contact us at support@silicycle.com or call us.



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