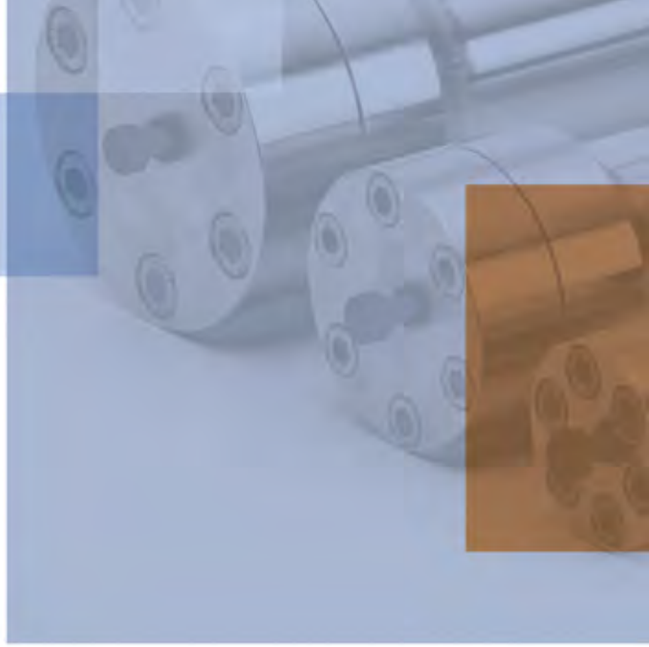


CATALOG

PRODUCTS AND SERVICES

CHIRAL
TECHNOLOGIES INC

SUBSIDIARY OF DAICEL CHEMICAL INDUSTRIES, LTD.

CHIRAL
TECHNOLOGIES INC

SUBSIDIARY OF DAICEL CHEMICAL INDUSTRIES, LTD.

Table of Contents

CHIRAL TECHNOLOGIES, INC.

Innovation Begins Here

CHIRAL TECHNOLOGIES is the leading supplier of enantioselective chromatography products and custom separation services. Coated polysaccharide chiral stationary phases (CSPs) were developed in the early 1980s and became the CSPs of choice for chiral recognition of racemic molecules.

Due to broad selectivity, superior durability and high loading capacity, Chiral Technologies' CSPs have become the most widely used enantioselective chromatography products in the world. The CSPs are available in bulk quantity and are used in columns for High-Performance Liquid Chromatography (HPLC) and Supercritical Fluid Chromatography (SFC). Equipped with more than 20 years of experience and knowledge, as a trusted **IND Enabler** we offer a complete range of products and services for the separation of racemic mixtures:

- Advanced method development
- Custom separation services for isolation and purification of enantiomers in quantities ranging from milligrams to metric tons
- Technical support
- Technology transfer for commercial development of drug candidates

Chiral Technologies, Inc. (West Chester, Pa.) serves North and Latin America and is a subsidiary of Daicel Chemical Industries, Ltd. Chiral Technologies, Inc. is part of Daicel's global marketing network, Chiral Technologies Worldwide, which also includes the following operations:

- Chiral Technologies Europe
- Daicel Chiral Technologies India
- Daicel Chiral Technologies China
- Daicel Chiral Pharmaceutical Ingredients (CPI) Japan

Commitment to Quality

Backed by the unequaled reputation of Daicel, we ensure your success in enantiomeric separations. All of our products are held to an excellent standard of performance and batch-to-batch reproducibility. Each column is individually tested and shipped with its test chromatogram, guaranteeing performance every time.

Chromatographic Experts

A team of expert chromatographers identifies separation methods, develops new applications and provides unparalleled technical support. **We find the solution that allows you to analyze and isolate your chiral compound.**

Immobilized Polysaccharide CSPs and Columns

CHIRALPAK® IA™, CHIRALPAK IB™ and CHIRALPAK IC™

Robustness and solvent compatibility

These unique CSPs consist of a spherical high-quality silica support, onto which the polymeric chiral selectors (polysaccharide derivatives) are immobilized. The **CHIRALPAK IA** chiral selector is the *tris* (3,5-dimethylphenylcarbamate) derivative of amylose, the **CHIRALPAK IB** chiral selector is the *tris* (3,5-dimethylphenylcarbamate) derivative of cellulose, and the **CHIRALPAK IC** chiral selector is the *tris* (3,5-dichlorophenylcarbamate) derivative of cellulose. These CSPs are used in analytical, semi-preparative and preparative columns and are ideal for HPLC and SFC* applications. Immobilizing the polysaccharide derivatives creates a matrix that provides universal organic solvent compatibility, along with:

- Ability to process low-solubility compounds
- High selectivity
- Extended durability
- Excellent column efficiency
- Cost-effective route to scale-up

Our laboratory evaluation of immobilized chiral phases shows that these CSPs are ideal for analytical method development, including reversed-phase (RP) chromatographic conditions.

CHIRALPAK immobilized CSPs are available in 3- and 5-µm particle sizes. For large-scale separations, these CSPs can be obtained in 20-µm particle size.

* Analytical HPLC columns are perfectly safe to use in SFC mode. Preparative HPLC columns (1 cm i.d. and higher) are not to be used for SFC. All semi-preparative and preparative columns for SFC utilize special SFC hardware.

Coated Polysaccharide CSPs and Columns

CHIRALPAK AD®, CHIRALPAK AS®, CHIRALCEL® OD® and CHIRALCEL OJ®

Wide range of applicability

The predecessors to the novel immobilized CSPs, CHIRALPAK and CHIRALCEL coated polysaccharide CSPs are made with a spherical high-quality silica support, onto which the polymeric chiral selectors (amylose or cellulose derivatives) are physically coated. These CSPs are notable for their broad range of applications and outstanding loading capacity, in addition to:

- Excellent resolution of racemates
- Fast, easy method development
- Long lifetime
- Smooth transition from laboratory development to large-scale production

CHIRALPAK AD and **AS**, and **CHIRALCEL OD** and **OJ** are available in 3-, 5- and 10-µm particle sizes. These CSPs are used in analytical, semi-preparative and preparative columns and are ideal for HPLC and SFC applications. Columns are available in a variety of diameters and lengths to meet all your application needs. For large-scale separations, the CSPs are also available in 20-µm particle size. Due to the coated nature of these chiral supports, solvents should be carefully selected.

In addition, Chiral Technologies offers several complementary CSPs and columns (CHIRALCEL OB™, OC™ OF™, OG™ and OK™). Please contact us for more information concerning these products.

New Coated Polysaccharide CSPs and Columns

CHIRALPAK AY™, CHIRALPAK AZ™ and CHIRALCEL OZ™

Novel chiral recognition

These coated CSPs are phases that have been manufactured for several years by Daicel and are now commercially available. Since the chiral selectors are significantly different from those listed above, they enable novel separations to be developed.

CHIRALPAK AY, **CHIRALPAK AZ** and **CHIRALCEL OZ** are available in 3- and 5-µm particle sizes. For large-scale separations, these CSPs can be obtained in 20-µm particle size.

1980s
Professor Yoshio Okamoto of Nagoya University (Japan) invents polysaccharide-based chiral stationary phases (CSPs).

1980s, cont.
Daicel Chemical Industries (Japan) develops polysaccharide-based columns as commercial products.

Reversed-Phase Coated Polysaccharide CSPs and Columns

CHIRALPAK AD, CHIRALPAK AS, CHIRALPAK AY, CHIRALPAK AZ, CHIRALCEL OD, CHIRALCEL OJ and CHIRALCEL OZ

Aqueous-organic mobile phase applications

Analytical reversed-phase (RP) CSPs were developed specifically for the separation of samples present in aqueous media, for example, biological samples. They are also suited for applications where modification of mobile phase pH can affect the quality of separation. In addition, a number of LCMS-compatible applications have been developed using these columns.

The chiral selectors are coated onto a hydrophobic high-quality silica support and are used in analytical, semi-preparative and preparative columns. However, extreme pH values must be avoided as they may damage the silica gel.

Columns are available in 3- and 5-µm particle sizes as indicated by the designations 3R and RH, respectively. The columns are offered in a variety of diameters and lengths to meet your application needs. CHIRALCEL OD columns are also available in 10-µm particle size.

1986
Daicel Chemical Industries introduces chiral columns to the USA.

1990
Chiral Technologies is incorporated in the United States on November 7, 1990.

Chiral Selectors for Special Applications

CHIRALPAK QD-AX, CHIRALPAK QN-AX, CROWNPAK® CR®(+ and -), CHIRALPAK WH and CHIRALPAK MA(+)

Enantioselective HPLC

Anion Exchange Columns

CHIRALPAK QD-AX and **CHIRALPAK QN-AX** contain enantioselective weak anion exchange (AX) chiral selectors. Developed by Professor Wolfgang Lindner's group at the University of Vienna, they are specially designed for enantioselective separations of chiral acids. The CSPs possess exceptional separation capabilities for acidic chiral compounds containing carboxylic, phosphonic, phosphinic, phosphoric or sulfonic groups.

CHIRALPAK QD-AX and CHIRALPAK QN-AX are based on two complementary stereoisomeric derivatives: quinidine (QD) and quinine (QN) derivatives. Due to their pseudo-enantiomeric character, they typically display reversed elution order.

These columns can also be used in reversed-phase and polar organic modes and are compatible with all common HPLC solvents. They can be used in a wide pH range – from pH 2 to 8.

Crown Ether Columns

CROWNPAK CR(+) and **CROWNPAK CR(-)** contain a chiral crown ether as a chiral selector, which is coated onto a 5-µm support. Acidic mobile phases, such as perchloric acid pH 1 to 2, are used to operate these columns. To shorten the retention time of hydrophobic samples, the addition of methanol (15% v/v maximum) has been effective.

CROWNPAK columns are mainly used for the separation of α-amino acids and other small molecules with primary amine groups.

Ligand Exchange Columns

CHIRALPAK WH and **CHIRALPAK MA(+)** contain amino acids and their derivatives as chiral selectors. These columns are ligand exchange type columns and are employed with an aqueous solution of copper sulfate (0.1 to 10 mM) as the mobile phase. The columns can tolerate use of organic modifiers such as methanol and acetonitrile to effect the separation.

Bulk Stationary Phases for Preparative Separations

20-µm CHIRALPAK and CHIRALCEL CSPs

Large-scale enantiomer separations

Chiral Technologies' 20-µm bulk stationary phases are well known for high loading capacities and for excellent batch-to-batch reproducibility. They are particularly well adapted for separations scaled from gram to metric-ton quantities.

Immobilized Bulk Stationary Phases

Immobilization of polysaccharide derivatives increases universal solvent compatibility and greatly improves solubility characteristics of chiral compounds, thus affording high loading column capacities.

- **CHIRALPAK IA** and **CHIRALPAK IC** are compatible with all miscible organic solvents and are ideal for large-scale HPLC and SFC separations. Note: CHIRALPAK IC contains an innovative chiral selector, cellulose *tris* (3,5-dichlorophenylcarbamate), immobilized on silica using proprietary techniques. This selector provides a novel chiral molecular recognition mechanism previously unavailable.

- **CHIRALCEL OD-I** bulk stationary phase consists of a 20-µm silica support, onto which the polymeric chiral selector, cellulose *tris* (3,5-dimethylphenylcarbamate), has been immobilized.

Coated Bulk Stationary Phases

Chiral Technologies' 20-µm bulk stationary phases are also available in coated amylose and coated cellulose matrices for a variety of applications. These phases include, but are not limited to:

- CHIRALPAK AD
- CHIRALPAK AS
- CHIRALPAK AY
- CHIRALPAK AZ
- CHIRALCEL OD
- CHIRALCEL OF
- CHIRALCEL OJ
- CHIRALCEL OZ

Columns

To support specific requirements of your preparative method development, we can pack analytical columns of various lengths using 20-µm CSPs. These columns can be used for developing and optimizing methods for large-scale separations. The loading data obtained from analytical columns packed with 20-µm material can provide direct method transfer from analytical- to preparative-scale separations.

1995
European office founded in France and established as Chiral Technologies Europe.

2004
New facility opens in West Chester, Pa., featuring a business center and laboratories equipped with state-of-the-art chromatography systems.

Protein-Based Columns

CHIRAL-AGP, CHIRAL-CBH and CHIRAL-HSA

Enantiomeric separations and purity analysis

CHIRAL-AGP, **CHIRAL-CBH** and **CHIRAL-HSA** function entirely in the reversed-phase chromatographic mode, using buffers with low organic modifier content and moderate pH values.

A vast variety of chiral compounds can be separated using protein-based columns.

CHIRAL-AGP

The chiral selector of this stationary phase is α_1-acid glycoprotein (AGP) immobilized onto 5-µm spherical silica particles. CHIRAL-AGP has extremely broad applicability for separating a wide range of compounds.

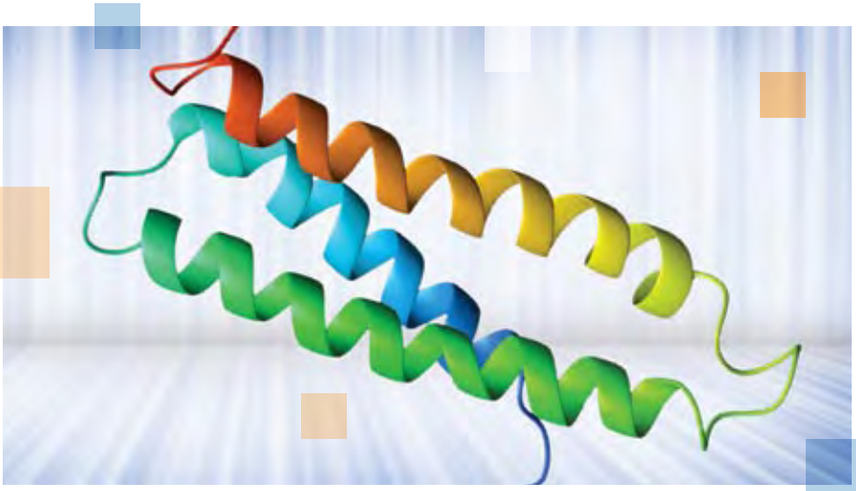
- Amines (primary, secondary and tertiary)
- Acids (strong and weak)
- Nonprotolytes (amides, esters and alcohols)

CHIRAL-CBH

The chiral selector of this stationary phase is cellobiohydrolase (CBH), which is a stable enzyme immobilized onto 5-µm spherical silica particles. It is well suited for separation of primary, secondary and tertiary amines and amino alcohols.

CHIRAL-HSA

The chiral selector of this stationary phase is human serum albumin (HSA), which is immobilized onto 5-µm spherical silica particles. A CHIRAL-HSA column can resolve enantiomers of weak and strong acids and non-protolytic compounds. **Of note, CHIRAL-HSA can separate both chiral acids and amino acids directly without derivatization.**



2004
CHIRALPAK IA bulk CSPs and columns are introduced as the first in a line of new immobilized-phase products.

2005
CHIRALPAK IB bulk CSPs and columns are introduced to the line of new immobilized-phase products.

Column Selection Service

Not sure which column is right for you? Our column selection service is specifically designed to help you find a column that meets your project needs.

As the original developer of polysaccharide chiral stationary phases (CSPs), we have the largest selection of columns available, which includes those packed with our proprietary immobilized CSPs. Our columns can be used in normal-, polar- and reversed-phase chromatography modes.

Our technical expertise, together with our extensive product portfolio, enables us to offer two types of service: Sample Screening and Method Development/Optimization.

Sample Screening

We screen your sample, free of charge, to expediently identify a column/mobile phase combination for the separation of your molecule. Several mobile phase components are varied to cover non-polar and polar solvents. Upon completing the screening you will receive our column recommendation and pertinent chromatography parameters to help you start your separation project.

Method Development/Optimization

Facing a challenging separation? We are confident that we will find the chromatographic method best suited for resolving your racemic mixture. We screen your compound and optimize the separation for you by employing our vast selection of chiral phases with all possible mobile phase combinations, thereby identifying the best chromatographic protocol.

LCMS-compatible mobile phases are included in the column selection service if requested.

The column selection service is performed under strict confidentiality with a Confidential Disclosure Agreement (CDA) being executed, when necessary, prior to the commencement of the project.

2005
Lindner ion-exchange columns are introduced for separations of chiral acids.

2007
Expanding the immobilized-phase product line, Chiral Technologies introduces CHIRALPAK IC bulk CSPs and columns.

Custom Separation Services

Rapid access to pure enantiomers

Enantioselective chromatography is recognized as the quickest route for advancement of small-molecule drug candidates for preclinical and clinical trials.

Our chromatography specialists are fully prepared for any separation project – from supporting medicinal chemists in their quest for active enantiomers to enabling process development chemists in their preparation for clinical studies and cGMP separations for Phase 1 and Phase 2 trials.

Our facilities are equipped with preparative HPLC, SFC and SMB systems to provide high-quality resolutions of single enantiomers in quantities ranging from milligram to multi-kilogram. We deliver purified enantiomers, meeting specifications of ≥98% enantiomeric excess and ≥85% yield. Our separation processes can be conducted under current good manufacturing practices (cGMP) if required.

As with our Column Selection Service, this work is performed under strict confidentiality with a CDA being executed, when necessary, prior to the commencement of the project.

Small Scale: mg to g

For small-scale separations, we screen (via HPLC and SFC) your compound free of charge. Once an appropriate method is identified, we conduct the enantioseparation of your racemate. We deliver purified enantiomers, meeting required specifications, within ten to fifteen days.

Do you need quick delivery of a small amount (milligram quantities) of separated material? We have the solution! Our *FastTrac* program is designed to rapidly separate your racemate and return the pure products to you within five (5) working days. We designed the process with speed in mind!

Pathway of a *FastTrac* Separation

2007
Chiral Technologies partners with South American distributors.

2008
Chiral Technologies introduces *FastTrac* to acceleratedrug development processes.

Custom Separation Services, cont.

Medium Scale: g to kg

For medium-scale separations, we screen, free of charge, using all available CSPs with all possible mobile phase compositions to establish the best protocol for separating your racemic mixture. Once the separation is optimized, we carry out a loading study to determine the production rate and a stability study to ensure complete recovery of the purified enantiomers. We use these studies to estimate project costs. Depending on the scale of your separation, we employ preparative HPLC or SFC to conduct the separation at the required scale and deliver the purified enantiomers.

Large Scale: multi-kg

For large-scale projects we discover the best separation method possible which is then utilized in batch HPLC or SMB operations. We perform, at our facility, SMB separations of racemates in quantities of up to 200 kg. We also offer an SMB method development service, in which we screen a sample for potential large-scale production across our proprietary library of CSPs to determine the optimum conditions for SMB separations. From this data we run a computer simulation to obtain an initial cost estimate to determine if the SMB process is economical. Following the simulation, our scientists confirm the cost estimate with a bench-top SMB unit. The results of this testing are then used to establish the parameters for a production-scale SMB process.

Commercial Scale: metric-ton

For companies preparing for Phase III clinical trials and the commercialization of enantiomerically pure drugs, Chiral Technologies and Daicel can assist in complete outsourcing of drug manufacturing processes. Our facility at the Daicel Arai, Japan, plant is equipped to perform upstream or downstream chemical synthesis, in addition to conducting metric-ton scale separations.

2009
Chiral Technologies introduces 3-micron immobilized columns.

2009
Protein-based columns are introduced for enantiomeric separations.

2009
Chiral Technologies launches Academic Donation Program.

Quality Control and cGMP

Exceeding quality standards

Chiral Technologies and Daicel take extreme care to adhere to updated good laboratory practices (GLP) and comply with cGMP for custom separations. The products of every custom separation project are accompanied by a certificate of analysis.

Our customers can depend on Chiral Technologies as their trusted partner in the development of drug candidates.

Technical Support

Products and services backed by an experienced support team

At Chiral Technologies, we stand behind our products and services by providing comprehensive technical support.

Our technical support team is always available to guide you in the effective use of our chiral analytical columns and bulk CSPs. The team can also assist you on the scope and availability of our custom separation services.

To obtain fast and accurate technical support:

- Visit the Frequently Asked Questions (FAQs) section on our website, www.chiraltech.com. The FAQs are regularly updated to reflect customers' most common inquiries.
- Send an email to questions@chiraltech.com for a rapid response from our team of experts in all areas of enantioselective chromatography.
- Call our toll-free number 1-800-6CHIRAL.

Application Guide

Searchable database of 1200 applications

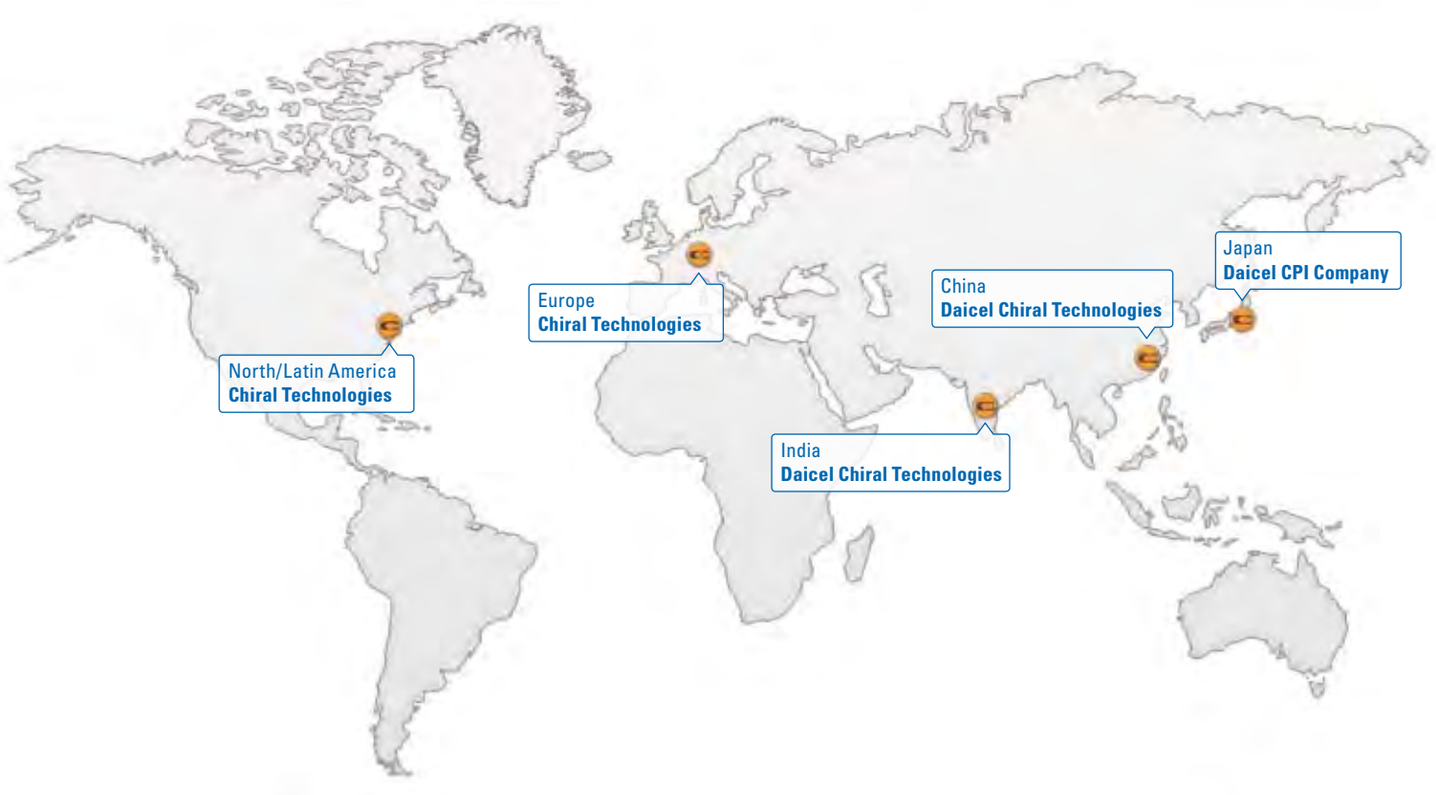
To assist you in finding the best column for your enantiomer separation, Chiral Technologies offers a free application guide on CD-ROM. To obtain this CD, please visit our website at www.chiraltech.com and proceed to the Chiral Columns section where you will find a request form. This application guide is intuitive, straightforward and easy to use.

2009
Chiral Technologies expands column distribution to Canada and Mexico.

2010
Chiral Technologies Worldwide global marketing team formed.

2010
Chiral Technologies celebrates 20 years of business.

Locations



North/Latin America

Chiral Technologies, Inc.
800 North Five Points Road
West Chester, PA 19380
USA
Tel. : +1-610-594-2100
Fax : +1-610-594-2325
www.chiraltech.com
chiral@chiraltech.com

Europe

Chiral Technologies Europe
Parc d'Innovation
Bd Gonthier d'Andernach
67400 Illkirch Cedex, France
Tel. : +33-388-795-200
Fax : +33-388-667-166
www.chiral.fr
cte@chiral.fr

India

Daicel Chiral Technologies Pvt. Ltd.
Lab No. 4A, Phase III
ICICI Knowledge Park
Genome Valley, Turkapally,
Shameerpet, Ranga Reddy Dist.
Hyderabad-500 078, A.P, India
Tel. : +91-40-23480103
: +91-40-23480134
Fax : +91-40-23480104
www.chiral.daicel.com
chiral@chiral.daicel.com

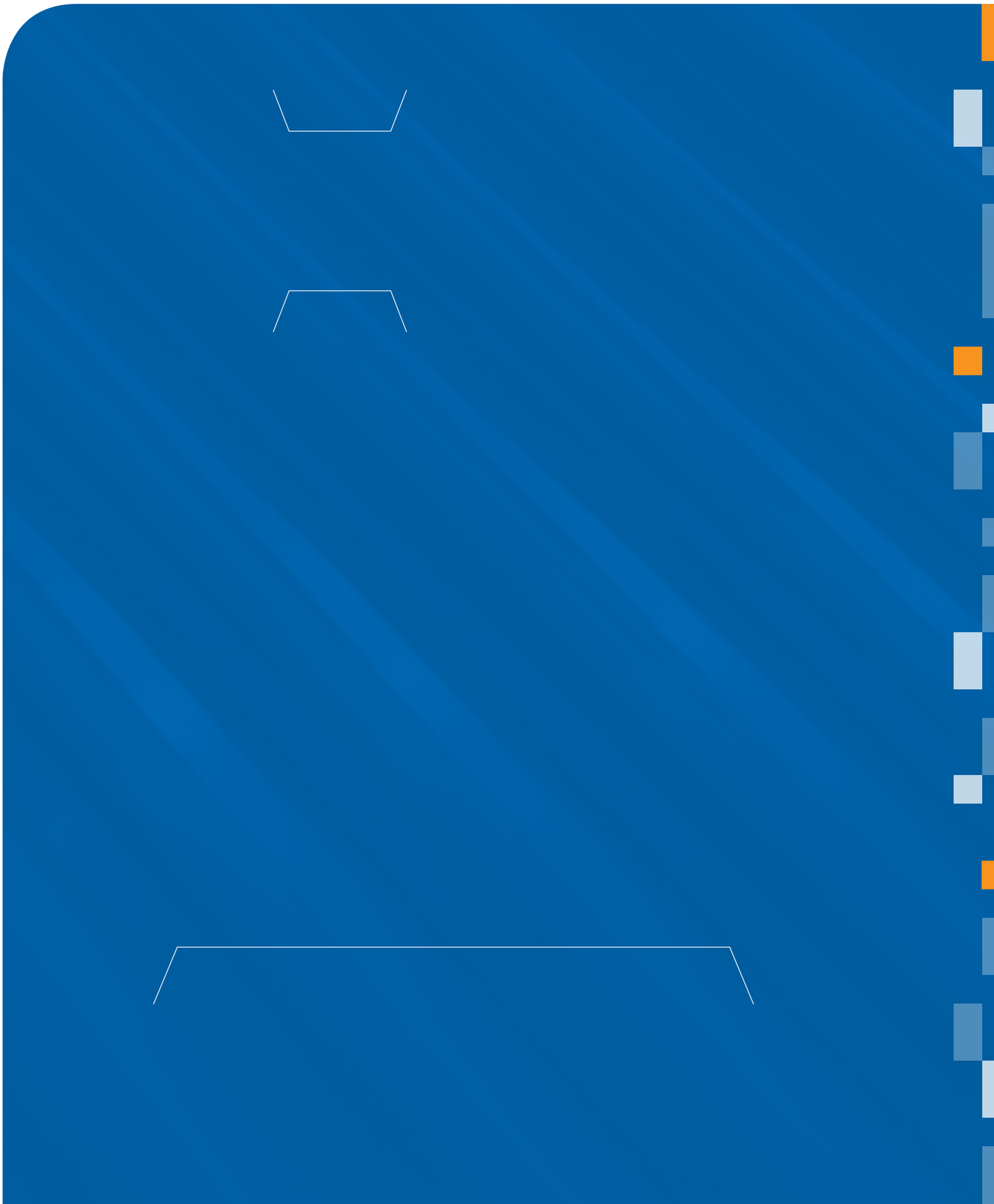
China

Daicel Chiral Technologies Co., Ltd.
Part C, FL5, No.16
Xiya Road No. 69
Waigaoqiao Free Trade Zone
Shanghai, 200131, China
Tel. : +86-21-50460086
Fax : +86-21-50462321
www.daicelchiraltech.cn
chiral@daicelchiraltech.cn

Japan

Daicel Chemical Industries, Ltd.
CPI Company
JR Shinagawa East Bldg., 2-18-1
Konan, Minato-ku
Tokyo 108-8230, Japan
Tel. : +81-3-6711-8222
Fax : +81-3-6711-8228
www.daicel.co.jp
chiral@daicel.co.jp

To learn more about Chiral Technologies' products and services, visit www.chiraltechworldwide.com.



CHIRAL
TECHNOLOGIES INC

SUBSIDIARY OF DAICEL CHEMICAL INDUSTRIES, LTD.

Chiral Technologies, Inc.

800 North Five Points Road
West Chester, PA 19380
USA
Tel. : +1-610-594-2100
Fax : +1-610-594-2325
www.chiraltech.com
chiral@chiraltech.com

www.chiraltech.com