CHIRAL
TECHNOLOGIES EUROPE

SUBSIDIARY OF DAICEL CHEMICAL INDUSTRIES, LTD.

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Chirality in the Natural Sciences

Pharmaceuticals

Agrochemicals

Flavour
and
Fragrance

Rules and Regulations

Control of Chirality in Pharmaceuticals After Thalidomide by FDA

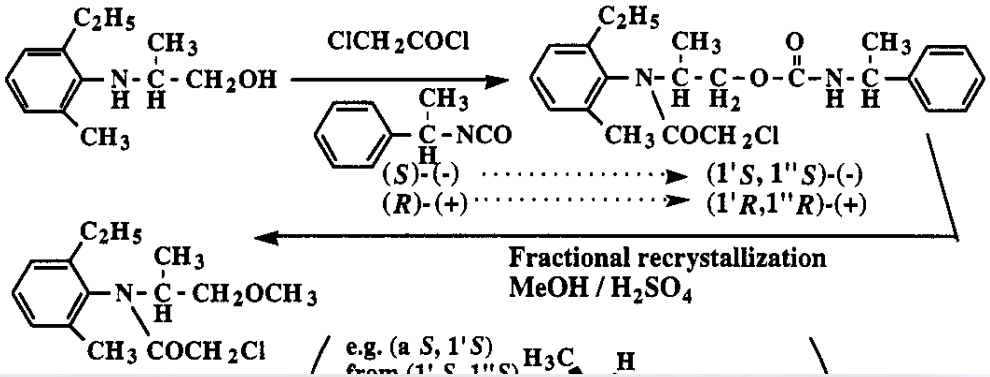
Control of Food Additives by FDA

Control of Chirality in Agrochemicals In Eu and Beyond.

[2]Sumitomo Chemical Co. Ltd., Osaka 541, Japan
[3]US Department of Agriculture, ARS, Fargo, ND 58105, USA
[4]BASF AG, Agricultural Research Station, D-67114 Limburgerhof, F.R. Germany
[5]ZENECA Agrochemicals, Jealotts Hill, Bracknell, Berks, RG42 6EY, UK
[6]Pesticide Research Center, Michigan State University, East Lansing, MI 48824, USA
[7]State Institute for Quality Control of Agric. Products, RIKULT-DLO Wageningen, Netherlands

*Membership of the Commission during the preparation of this report (1993–95) was as follows:

Chairman: 1989–95 E. Dorn (FRG); 1995–97 K. D. Racke (USA); *Secretary:* 1989–97 P. T. Holland (New Zealand): *Titular Members:* S. Z. Cohen (USA; 1991–95); D. J. Hamilton (Australia; 1994–97); A. W. Klein (FRG; 1994–97); N. Kurihara (Japan; 1989–95); G. D. Paulson (USA; 1989–95); R. D. Wauchope (USA; 1991–97); *Associate Members:* M. Akerblom (Sweden; 1995–97); G. C. de Baptista



What is Required

Chiral Analysis
& Separation of:

Isomers
Metabolites
Degradants
Impurities

For

- Research
- Development
- Manufacture

Global Manufacture

Need for reliable and robust chiral analysis anywhere in the world

Daicel Corporation

DAICEL Corporation.

Established as DAI nippon CEL luloid Co. Ltd.,
through a merger of eight celluloid producers in 1919.

Incorporated	Sept. 8, 1919
Employees	ca. 7,900
Head Office	Tokyo
Consolidated Sales	US$ 4.4 billion

Chiral Technologies

Local Support for Chiral Chromatography

- Daicel Japan
- Chiral Technologies Inc.
- Chiral Technologies Europe
- Chiral Technologies China
- Chiral Technologies India

Global Chromatography

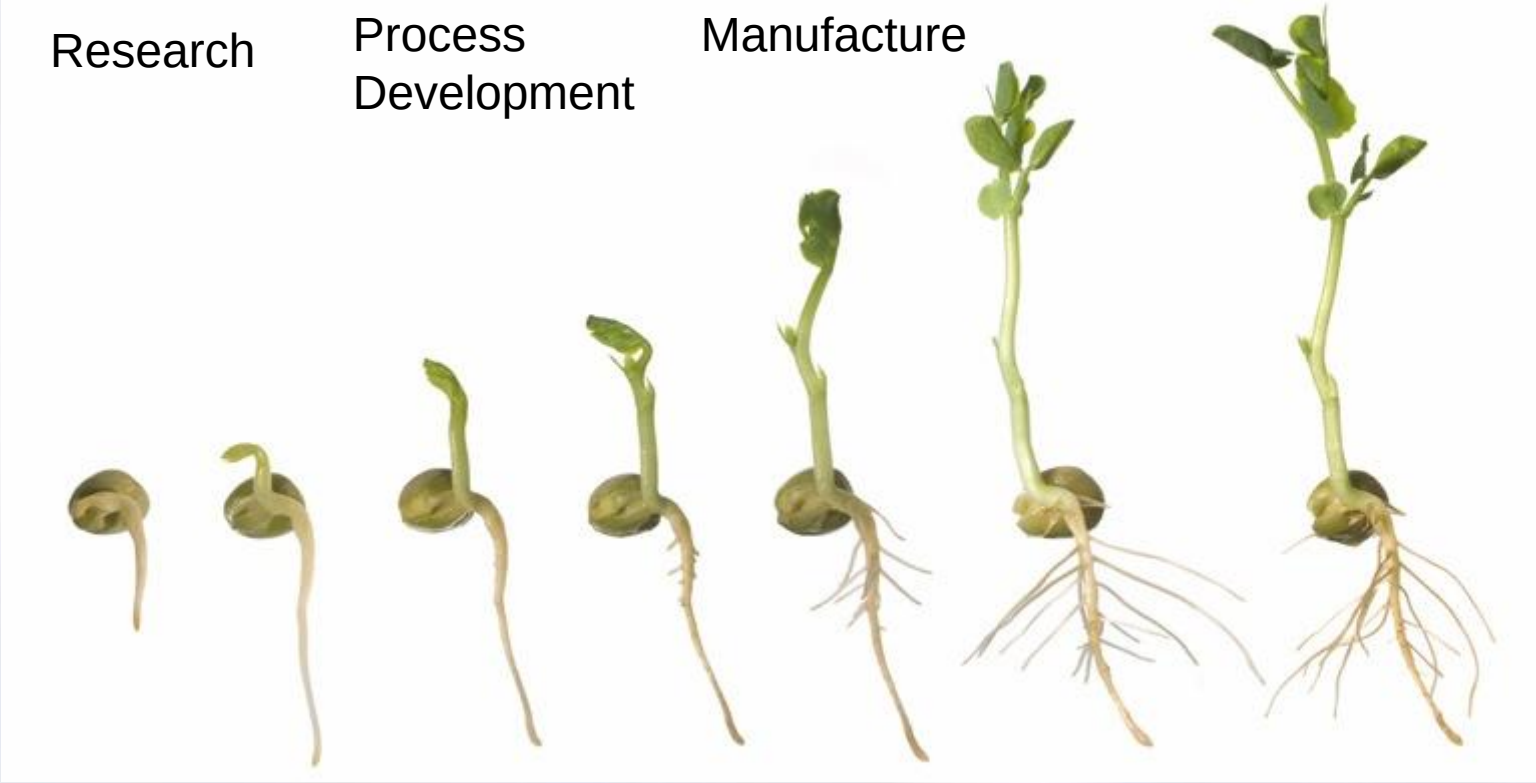
- By Offering
  - Supply of Daicel Columns
  - Local Technical Support
  - Contract Chiral Separations
  - Supply of Bulk Phase

At all stages

Research

Process Development

Manufacture

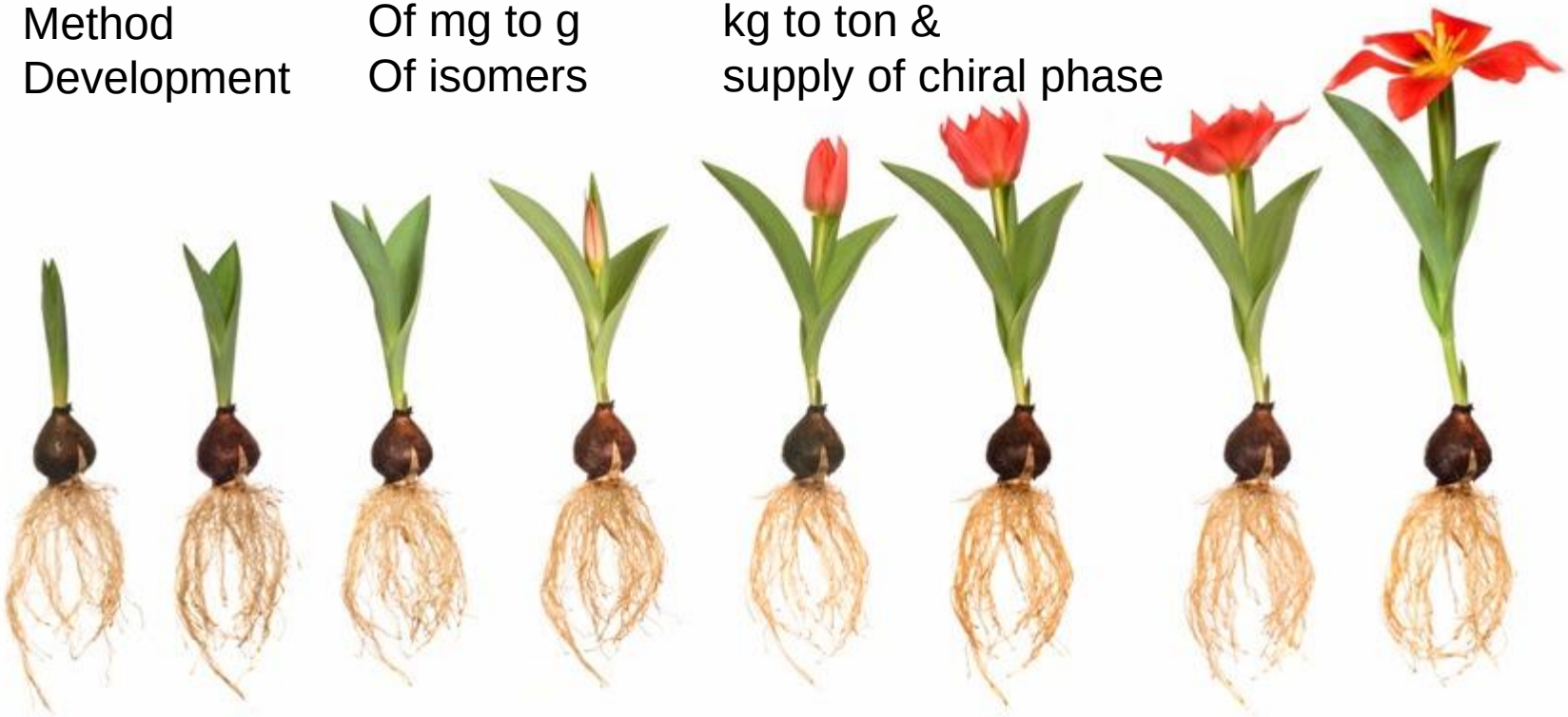


Support Available

Analytical Method Development

Separation Of mg to g Of isomers

Separation of kg to ton & supply of chiral phase



Analytical Method Development

Chiral Analysis

Separation of 2 or more isomers

Robust Methods

Transferrable to 3rd Parties

- HPLC
- UPLC
- SFC

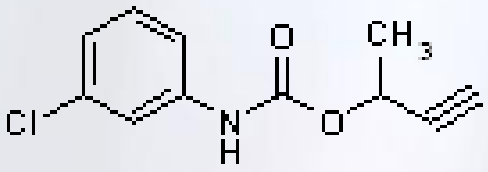
Water Compatible Methods

MS Compatible Methods

Chiral separation of herbicides by HPLC

CHIRALPAK IE

Hexane/EtOH 80/20

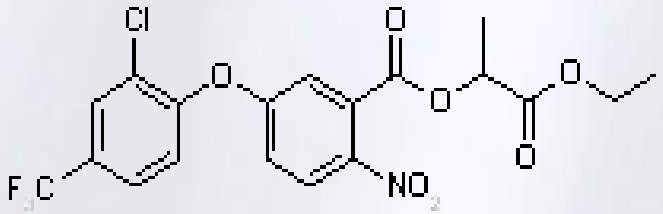


Chlorbufam

Chiral separation of herbicides by HPLC

CHIRALPAK IF

EtOH 100%



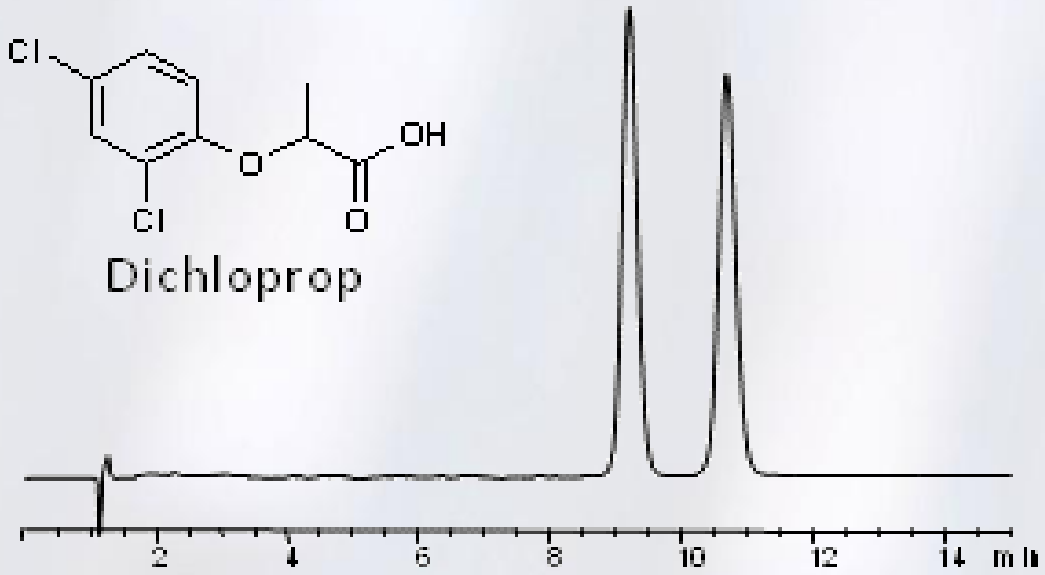
Lactofen

Chiral separation of herbicides by SFC

CHIRALPAK QN-AX

CO_2/ Modifier 55:45

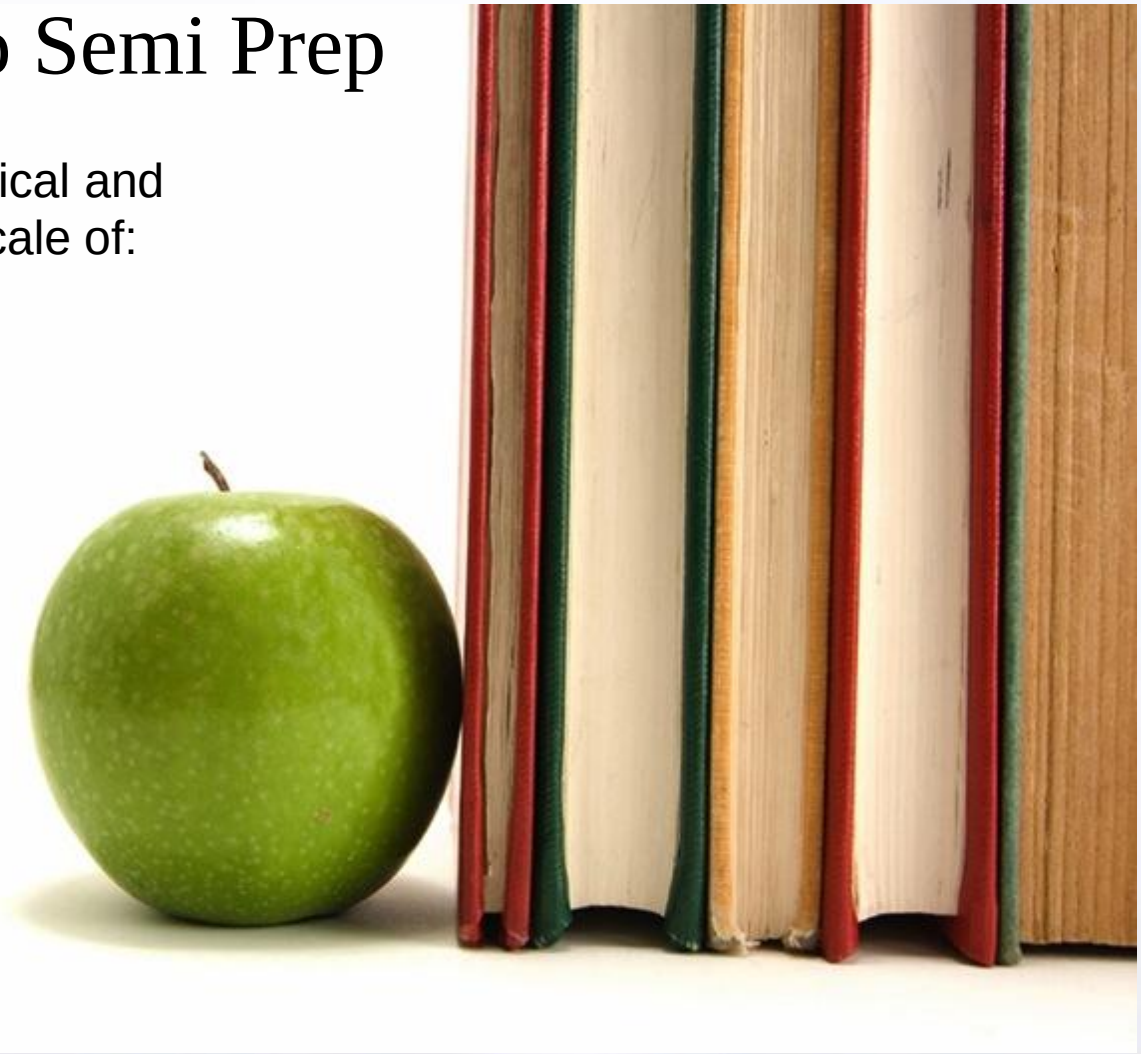
Modifier: MeOH/FA/NH4OOCH 100/0.40/0.35 v/v/m



Analytical to Semi Prep

Separation at Analytical and Semi Preparative Scale of:

- Metabolites
- Standards
- Impurities
- Degradants
- Etc.



Small Scale Separations

Need for 10 mg to 10 g for initial studies

Racemisation and Chemical Stability Tested

Isomers at High Yield (> 85%)

Isomers at High Specification (> 98% e.e.)

Fast, Reliable Service (1 week)

Good Communication

Right Price

Free Method Development

Medium Scale Separations

Isomers needed at 10 g to 2 kg scale

Fast availability of Isomers

High Yield (85 – 90%)

High Specification (> 98% e.e.)

Method scalable to multi kg.

Manufacturing Scale

SMB and Prep HPLC

Equipment within DAICEL

OR

Support at CRM Worldwide

CSP long Life

Environmentally Sound

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New Developments
in
Chiral Chromatography

New Immobilised Chiral Phases

Derivatised polysaccharide phases developed >> 20 years ago.

- Compatible with alkanes, alcohol and acetonitrile.
- High casualty rate due to use of wrong solvent.

New immobilised phases give

- Robust analytical methods
- Improved solubility of samples
- Higher productivity of methods

Injection of Complex Mixtures

Chiral Phase Portfolio

20 Coated Polysaccharide Phases

6 Immobilised Polysaccharide Phases

2 Anion Exchange Phases

2 Zwitterionic Exchange Phases

7 Protein Phases

Phases manufactured in
3 µm 5µm 10µm 20µm

> 120 Library Phases

Screening and Separation

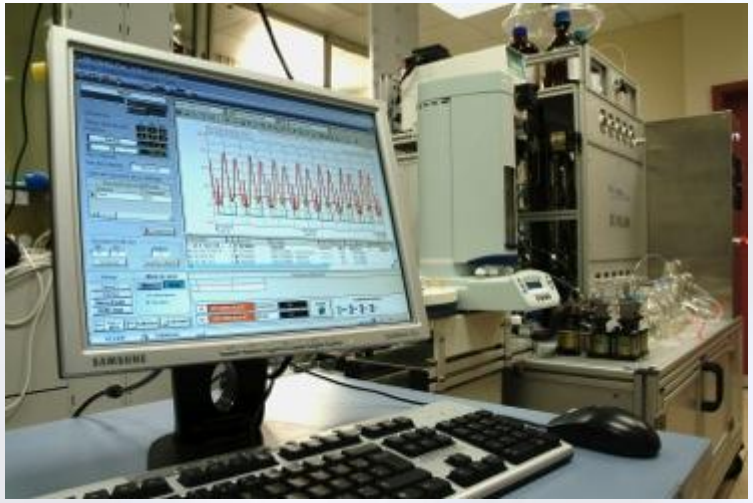
Equipment
SFC and HPLC

Comprehensive Screening
Widest Portfolio of Phases
New Immobilised Phases

Best Method
> 20 years experience
RP, NP and MS

Technical Support
Method Development
Loan Columns

Contract Separations



Chiral Stationary Phase

> 30 Commercial Chiral Phases

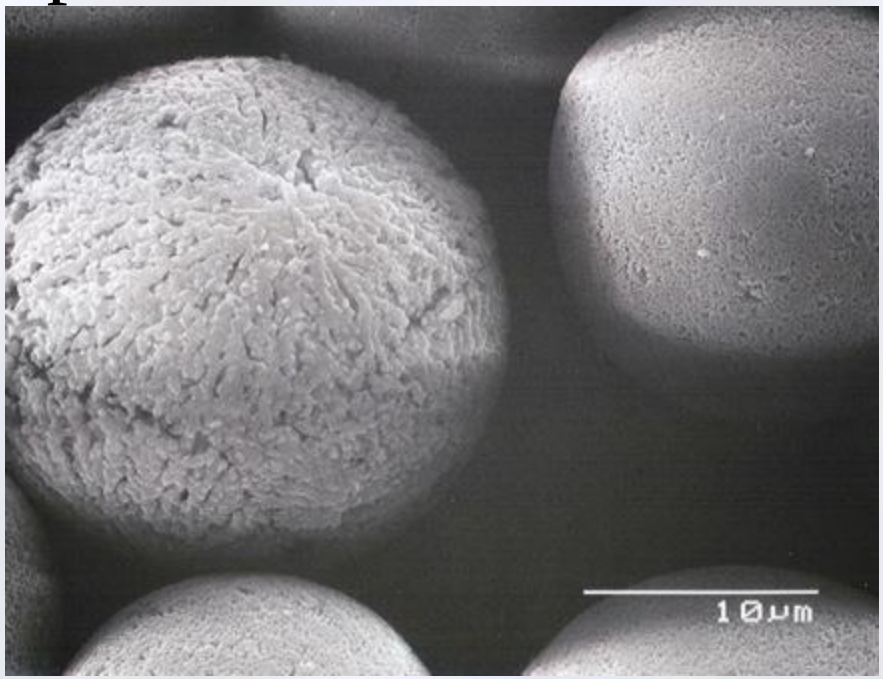
>120 Library Chiral Phases

New Column Development

- 6 in 2012
- 5 in 2011
-10 in 2010

Currently

6 Immobilised Phases



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Technical Support

Problem Solving

Method Development Service
- •Analytical
- •Semi Preparative
- •Preparative

Technical Support
- **•Training**
- •New Phase Introduction
- •Application Guides

Library Screening
- •>120 Chiral Phases
- •Screening for Manufacture

Chromatography Equipment

milligram to gram
gram to kg
kg to ton

SFC
HPLC
Batch and SMB

Outsource Chromatography

Global support

- Daicel Japan
- Chiral Technologies Inc.
- Chiral Technologies Europe
- Chiral Technologies China
- Chiral Technologies India

Capacity added to match demand!

Daicel Separation Facilities

	Europe 10 mg to 5 kg	India 10 mg to 50g	China 10 mg to 200	Japan 1g to 1000 kg	USA 10 mg to 10 kg
HPLC	🗐	🗐	🗐	🗐	🗐
SFC	🗐	🗐	🗐	🗐	🗐
HPLC Prep	🗐		🗐	🗐	🗐
SMB			🗐	🗐	
Production				🗐	

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Thank You