

REQUEST FOR INFORMATION

*2D-LC-SFC Instrumentation**Test*

November 18, 2019

Enabling Technologies Consortium™

Request for Information

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# Introduction

## About Enabling Technologies Consortium™ (ETC)

The Enabling Technologies Consortium™ (ETC) is comprised of pharmaceutical and biotechnology companies collaborating on issues related to pharmaceutical chemistry, manufacturing, and control with the goal of identifying, evaluating, developing, and improving scientific tools and techniques that support the efficient development, and manufacturing of pharmaceuticals. The purpose of this consortium is to identify pro-actively high-value opportunities to deliver innovative technologies where the business case is compelling and collaboration with the broader external community is required.

## Request for Information

Publication of this Request for Information (RFI) is the first step by ETC to solicit interest in collaborating together on a vendor-supported 2D-LC-SFC instrument. The information collected during the RFI process along with subsequent interviews will be used for evaluation purposes. Depending on the responses received ETC may choose to select a collaborator solely based on their response to the RFI or may choose to refine project requirements and subsequently release a Request for Proposals (RFP) to aid in the collaborator selection process.

The goal of this collaborative project is the creation of a prototype to evaluate the feasibility for commercial production and implementation in the future.

## Disclaimer

The contents and information provided in this RFI are meant to provide general information to parties interested in developing the 2D-LC-SFC instrument. The successful respondent selected by ETC at either the RFI stage or RFP stage (if applicable) will be required to execute an Agreement that will govern the terms of the project. When responding to this RFI, please note the following:

* This RFI is not an offer or a contract
* Responses submitted in response to this RFI become the property of ETC
* Respondents will not be compensated or reimbursed for any costs incurred as part of the RFI process
* If ETC receives and responds to questions from RFI respondents, ETC reserves the right to anonymize the questions and make the questions and ETC’s responses available to all respondents via our website
* Responses to RFIs should contain only high-level discussions of product development efforts and should not contain trade secrets or confidential information. ETC does not make any confidentiality commitments with respect to RFI submissions but agrees not to publicly distribute the RFI responses outside the consortium or share RFI responses with other respondents.
* ETC is not obligated to contract for any of the products or services described in this RFI
* ETC reserves the right to:
  + Accept or reject any or all proposals
  + Waive any anomalies in proposals
  + Negotiate with any or all bidders
  + Modify or cancel this RFI at any time

## RFI Contact Information

All questions and inquiries regarding this RFI should be directed to:

Ms. Alexis Myers

ETC Secretariat

c/o Drinker Biddle & Reath, LLP

1500 K St NW

Washington DC, 20005-1209

(202) 842-8800

[info@etconsortium.org](mailto:info@etconsortium.org)

<http://www.etconsortium.org/>

## Anticipated Time Frames for Evaluation and Selection Process

Issue RFI November 18, 2019

Questions on RFI due December 16, 2019

Responses to RFI due January 21, 2020

Invitations sent to respondents for presentation February 2020

Presentation to ETC by respondents Feb. – Mar. 2020

Select Finalists for RFP Mar. – Apr. 2020

***Please submit your response electronically to the above address. Responses received after January 21, 2020*** ***will not benefit from full consideration and may be excluded from the selection process.***

# Project Information

## Possible Project Sponsors

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| Amgen, AstraZeneca, Eli Lilly, Genentech, Merck, Pfizer |

## Description

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| Two-dimensional (2D) chromatographic techniques have become very popular in the past decade for analyzing simple, yet challenging problems to complex samples. Compared to one-dimensional (1D) chromatography, 2D chromatographic techniques have higher selectivity and resolving power assuming the retention mechanisms are complementary. If the retention mechanisms are complementary, the theoretical peak capacity of the system will be the product of the individual peak capacities. Such systems will have immense applications in pharmaceutical and other industries.  One of the major challenges encountered in multi-dimensional separations is the incompatibility of solvents used in the two dimensions that can result in severe band dispersion or broadening and peak deterioration limiting most two-dimensional separations to reverse phase in both dimensions. Since the retention mechanisms in a reversed phase – reversed phase (RP-RP) separation are driven primarily by the hydrophobic nature of the analytes in both dimensions, the separation is not fully orthogonal and the effective peak capacity is much smaller than the theoretical peak capacity, resulting from an inability to access the full chromatographic space. Alternatively, coupling “reversed phase” to “normal phase” will offer the most complementary, useful separation due to differences in the retention mechanisms. As addressed earlier, designing such a system would be challenging if not impractical. Supercritical fluid chromatography (SFC), a form of “normal phase” liquid chromatography (NPLC), can address the incompatibility issues between dimensions. SFC is superior to NPLC due to its versatility, improved efficiency, higher throughput, and faster analysis times. Supercritical fluids have low viscosity and high diffusivity (similar to gases) to allow higher flow rates, faster re-equilibration times and have a high density (similar to liquids) to provide a high solvating power. This technique would have wider applications in pharmaceutical and other industries ranging from peak purity assessment to simultaneous achiral-achiral/chiral separations to high-throughput analysis. Also, this technique would be quite powerful compared to current RP-RP separations. Additionally, the resolved fractions can be isolated from non-polar supercritical CO2 mobile phase if desired.  The proof of concept (design) and applications of a fully automated 2D-LC-SFC system in achiral-chiral analysis of pharmaceutical compounds with multiple chiral centers, including the analysis of residual chiral metabolite in complex plasma sample, has been demonstrated. The key component of the system is the low-volume high-capacity interface between the dimensions enabling selective retention of primary column eluent and its reinjection to the secondary SFC for further separation.  The objective of this “request for information” is towards the development and demonstration of a commercially-feasible 2D-LC-SFC system that can meet the current and future analytical needs.  The ETC is seeking companies interested in supplying a viable commercial 2D-LC-SFC system. The complementary retention mechanisms of the proposed system offer unique advantages over the current RP-RP LC separation for a wide range of applications that are not amenable by 2D-LC.  The sections below detail the system requirements as identified by a working group within the Enabling Technologies Consortium (ETC). ETC is interested in entertaining proposals from vendors regarding technologies that might be amenable to collaborative development. |

## 2D-LC-SFC Instrument Requirements

### Necessary Hardware and Software Requirements

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| Hardware Requirements   * **LC and SFC:**   The LC and SFC instruments constituting the 2D-LC-SFC system should operate as standalone units to maximize its use when not used in hyphenated mode. Preferably, the instrumentation should offer flexibility in terms of pumps (binary/quaternary), detectors (Diode Array Dectector – DAD or Variable Wavelength Detector – VWD), column compartment with column switching capabilities and independent temperature control for the two dimensions, pressure limits to support the use of sub2 micron columns.   * **MS:**   MS should be able to operate in a time-sharing and or bypass mode enabling it to monitor the primary and or secondary column separation.   * **2D-LC-SFC Interface:**   The 2D-LC-SFC interface must effectively trap primary column eluent and re-inject them into the secondary column without significant loss in primary column fractions. The interface should have the capability to trap and simultaneously retain multiple components emerging from primary column to support multiple heart-cutting to selective to comprehensive 2D-LC-SFC separation if practical.  Note: The specifications (e.g. pump pressure limits and flow rates, column compartment temperature range, detection wavelength range, interface capability, MS mass range) and performance (e.g. resolution, sensitivity, analysis time) of all the analytical instruments should be comparable to and or better than the current state of the art benchtop instruments.  Software Requirements   * The software should be intuitive, user friendly enabling non-specialists to operate the instrument with training. Control through conventional chromatography data systems is strongly desired. * The software should offer capability to perform repetitive solvent gradients in the secondary dimension assuming multiple fractions are sampled and transferred from the primary to secondary column, with the ability to leverage progressively stronger gradients in the secondary dimension to compensate for increase in sample hydrophobicity of later eluting components. * The software should effectively track each secondary chromatogram to its associated primary column fractions, display data either as a contour plot or format easy to visualize, interpret, and minimize the use of 3rd party software for necessary data processing. * Setup to enable a sequence of analyses (e.g. sampling interval, method parameters, number of samples, etc.) should be available in a user-friendly fashion that requires minimal training or special expertise.   Other System Requirements   * Vendor-provided IQ/OQ (Installation Qualification/Operational Qualification) process. * The ability to stack sequential analyses during real-time operation for visualization process evolution is desired, as is the capability of plotting individual species as a function of time (trend plots). * Operation with an autosampler (vendor-supplied) to enable standard bench-top measurements and troubleshooting would be useful. |

### Availability Requirements

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| * Commercially available instrument, in the form of a dual standalone LC and SFC systems to maximize its use when not used in hyphenated mode. * Vendor-provided, hardware and software support for instrument setup, operation and data processing expected for the reasonable life of the product. * Hardware, software, and firmware updates should be available at reasonable cost following launch of the commercial technology. |

### Licensing Requirements for Commercialized Product

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| 1. Software will be licensed to ETC participants at no cost during (i) development and (ii) a mutually agreed beta testing period at zero cost. 2. Thereafter, software will be available for licensing on a perpetual basis and subscription basis at the option of ETC participants. The company shall make available industry standard support. 3. Software shall be available for self-hosting by (or on behalf of) the ETC participants. 4. Ownership of data generated on system resides with customer. |

# Criteria for Evaluation

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| The ETC will evaluate the responses to this RFI based on the vendor’s ability to:   * Provide responses reflecting a desire to participate in collaboration. * Meet the functional, performance, and technical requirements described in this RFI as evidenced by the RFI response and presentations made to ETC. * Provide a cost-effective solution that is compatible with the goals of the project. * Demonstrate domain expertise and an ability to work collaboratively with the ETC in development of the 2D-LC-SFC Instrument. * Provide a superior level of customer service and technical support, both pre-installation and post-installation to clients. * Discuss potential partnerships and current development efforts that show similarities to this request. * Provide any additional capabilities that may differentiate them from other potential collaborators.   The ETC will not provide individual feedback directly to RFI respondents beyond the status of their response to this RFI. |

# Respondent Profile *(to be completed by RFI respondent)*

Please provide information to the following:

## Company/Organization Information

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| --- | --- |
| Company/Organization Name |  |
| Address |  |
| City |  |
| State |  |
| Country |  |
| Zip Code |  |
| Website |  |

## Primary Contact Person

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| --- | --- |
| Name |  |
| Title |  |
| Email address |  |
| Phone Number |  |

## Company/Organization Overview

Provide a brief overview of your company/organization including number of years in business, number of employees, nature of business, description of clients, and related products developed and commercialized to date.

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## Parent Corporation and/or Subsidiaries

Identify any parent corporation and/or subsidiaries, if appropriate.

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## Summary of Expertise

Give a brief description of your company/organization’s expertise in the area/field related to this RFI. Include any experience working on projects with Consortia/Associations.

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## Standards Certifications

List any certifications currently held, including date received, duration, and renewal date.

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## Goals and Strategic Vision

Provide a summary of your company/organization’s short term and long-term goals and strategic vision.

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## Miscellaneous

Please enter your response to each requirement using the guidelines provided in the tables below. If additional documentation or schematics are required to respond to a particular question, please answer the question as succinctly and accurately as possible and reference supplemental attachments.

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# Company/Organization Response to RFI (*to be completed by RFI respondent)*

## Proposal

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## Functional Requirements & Specifications

Refer to the following Functional Requirements and Specifications checklist which summarizes the collective requirements and specifications by the member companies participating in the project.

Based upon your proposed approach to deliver a solution, provide a response to each checklist item along with comments and assign one of the following Codes to each item:

|  |  |
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| A | Current capability of existing product |
| B | Able to add capability as requested |
| C | Able to add capability with modification to ETC request |
| D | Unable to add capability |

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| --- | --- | --- | --- |
| Feature | Requirement | Code | Vendor Comments |
| LC and SFC | The LC and SFC instruments constituting the 2D-LC-SFC system should operate as standalone units to maximize its use when not used in hyphenated mode. Preferably, the instrumentation should offer flexibility in terms of pumps (binary/quaternary), detectors (Diode Array Dectector – DAD or Variable Wavelength Detector – VWD), column compartment with column switching capabilities and independent temperature control for the two dimensions, pressure limits to support the use of sub2 micron columns. |  |  |
| MS | MS should be able to operate in a time-sharing and or bypass mode enabling it to monitor the primary and or secondary column separation. |  |  |
| 2D-LC-SFC Interface | The 2D-LC-SFC interface must effectively trap primary column eluent and re-inject them into the secondary column without significant loss in primary column fractions. The interface should have the capability to trap and simultaneously retain multiple components emerging from primary column to support multiple heart-cutting to selective to comprehensive 2D-LC-SFC separation if practical. |  |  |
| Specifications | The specifications (e.g. pump pressure limits and flow rates, column compartment temperature range, detection wavelength range, interface capability, MS mass range) and performance (e.g. resolution, sensitivity, analysis time) of all the analytical instruments should be comparable to and or better than the current state of the art benchtop instruments. |  |  |
| Software | The software should be intuitive, user friendly enabling non-specialists to operate the instrument with training. Control through conventional chromatography data systems is strongly desired. |  |  |
| Software | Offer capability to perform repetitive solvent gradients in the secondary dimension assuming multiple fractions are sampled and transferred from the primary to secondary column, with the ability to leverage progressively stronger gradients in the secondary dimension to compensate for increase in sample hydrophobicity of later eluting components. |  |  |
| Software | Effectively track each secondary chromatogram to its associated primary column fractions, display data either as a contour plot or format easy to visualize, interpret, and minimize the use of 3rd party software for necessary data processing. |  |  |
| Software | Setup to enable a sequence of analyses (e.g. sampling interval, method parameters, number of samples, etc.) should be available in a user-friendly fashion that requires minimal training or special expertise. |  |  |
| Other | Vendor-provided IQ/OQ (Installation Qualification/Operational Qualification) process. |  |  |
| Other | The ability to stack sequential analyses during real-time operation for visualization process evolution is desired, as is the capability of plotting individual species as a function of time (trend plots). |  |  |
| Other | Operation with an autosampler (vendor-supplied) to enable standard bench-top measurements and troubleshooting would be useful. |  |  |

## Estimated Timeline

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## Estimated Project Cost

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