

REQUEST FOR INFORMATION

*Online Sampling UHPLC Instrument**Test*

December 1, 2016

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, portable online UHPLC, with robust, probe-based sampling. The information collected during the RFI process along with subsequent interviews will be used for evaluation purposes, refinement of the subsequent Request for Proposals (RFP), and selection of respondent(s) who will be invited to submit a proposal to the future online UHPLC RFP. The goal of this collaborative project is the creation of a prototype with the hope it will become a commercial product in the future.

## Disclaimer

The contents and information provided in this RFI are meant to provide general information to parties interested in developing the UHPLC RFP. The successful respondent 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
* Proposals submitted in response to this RFI become property of ETC
* Respondents will not be compensated or reimbursed for any costs incurred as part of the RFI process
* Any questions received will be anonymized and made available to all respondents via our website
* All proposals received will remain confidential within ETC and not shared with other respondents
* ETC is not obligated to contract for any of the products and 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

Project Coordinator

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 December 1, 2016

Questions on RFI due December 8, 2016

Responses to RFI due December 23, 2016

Invitations sent to respondents for presentation January 13, 2017

Presentation to ETC by respondents January 23 – 27, 2017

Select Finalists for RFP February 3, 2017

***Please submit your response electronically to the above address. Responses received after December 23, 2016* *will not benefit from full consideration and may be excluded from the selection process.***

# Project Information

## Possible Project Sponsors

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| Merck, Pfizer, AbbVie, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly |

## Description

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| Online HPLC analysis is becoming increasingly important for studying the kinetic profiles of chemical reactions, from which valuable mechanistic information can be obtained. Historically, online sample collection was performed *via* either flow of the reaction medium through a sample loop, followed by injection, or by metered withdrawal of a defined volume flowing via a sampling tube or capillary. Both of these approaches work well for homogeneous solutions, but are not well suited to the investigation of heterogeneous reactions where solids are present or where active precipitation or crystallization is taking place. The recently introduced Mettler Toledo EasySampler 1210 addresses this limitation, allowing for reliable sampling of heterogeneous reactions using a mechanically actuated, 20 µL fixed-pocket based sampling mechanism. However, this tool is limited to the collection of a carrousel of 12 samples, limiting the utility for detailed kinetic profiling with frequent, and extending sampling needs, especially when there is poor sample stability of the diluted solution.  The ETC is seeking companies interested in supplying a vendor supported online sampling system with integrated liquid chromatographic (LC) analysis employing a low volume, probe-based sampling system capable of repeated automated sampling with the ability to perform direct sample injection for LC analysis for any desired number of reaction time points. Automated sampling is expected to accommodate both homogeneous and heterogeneous (solid/liquid) reaction mixtures, and in the case of heterogeneous mixtures, the sampler is expected to perform representative sampling of both the solid and liquid components. Also, a cart-mounted system to allow flexibility and portability in the laboratory environment is required. Lastly, a fully integrated data management and data visualization environment is also deemed critical, enabling seamless collation of sampling specifics and chromatographic results for further analysis. |

## Online Sampling UHPLC Instrument Requirements

### Necessary Hardware and Software Requirements

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| Sampler:   * Ability to reliably sample from both homogeneous and heterogeneous reactions and/or reactions undergoing active precipitation or crystallization * Representative sampling of the solid and liquid components of slurries * Ability to take reproducible samples 25µL or smaller in volume, from a wide variety of reactor types * Ability to quench reaction aliquots by addition of quench solution, ideally at reaction temperature, in near real-time. * ability to accurately dilute quenched reaction aliquots across a broad dilution range (i.e. 10-1000x dilution) prior to chromatographic analysis * direct injection into UHPLC system * Maximum sampling frequency of less than 4 minutes * Material of construction of wetted parts is compatible with a wide variety of solutions and solvents   UHPLC Requirements   * Sensitive, accurate and reliable UHPLC performance consistent with state of the art in 2016 * Ability to easily integrate MS detection, in addition to UV and other traditional LC detection modalities including universal detector options * Ability to incorporate High-Dynamic Range detection modalities, enabling error-free automated peak integration, of both main components and low level impurities simultaneously * Cart mounted, enabling portability throughout a typical laboratory environment * Enables rapid LC runs comparable to the maximum sampling rate of the sampler   Control Software Requirements – User Interface   * Plug and play ability for non-specialist to use equipment and run experiments * Convenient setup of sampling interval, dilution ratio, number of samples, duration of sampling run, etc. in a user friendly fashion that requires minimal training or special expertise. * Ability to adjust sampling parameters after a run has been started (e.g. to prolong a run or change sampling frequency and/or dilution) * Ability to ‘sleep and wake’ during a prolonged run, to allow for sampling over long intervals without requiring the instrument to run continuously * Seamless integration of reaction sampler specifics (reaction ID, sample time, dilution ratio etc.) and chromatographic results (Peak Retention times, Peak area, Peak Area percent etc.)a single data management environment * Ability to display data using waterfall plots, or via monitoring of peak height or peak area of up to 20 or more selected peaks * Ability to utilize MS detection data, including extracted ion chromatograms for up to 20 or more different masses simultaneously   Other System Requirements   * Vendor specified IQ/OQ and PM/PV packages * ER/ES compliance to facilitate GMP use |

### Optional Hardware and Software Requirements

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| --- |
| * Ability to perform multiple draws/injections within a single chromatographic run * A variety of probe formats to accommodate reactors of varied geometry * Ability to sample only the liquid phase of a heterogeneous solid/liquid mixture * Maximum sampling frequency of under 1 minute * Elementary kinetic profiling/curve fitting capability to help to assist in interpretation of kinetic trends * Multiplexed probe format with up to 4 probes for parallel reaction monitoring * Fraction collection capabilities to enable offline testing post-experiment * Probe may be autoclaved to enable sampling of biological reactions * Sampling interface for continuous flow reactors such as tubular plug flow reactors |

### Availability Requirements

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| * Commercially available instrument, ideal as a single unit, vs. multiple complementary instruments * The price-point of the product should be competitive with current online HPLC offerings * Service availability for the instrument should allow rapid repair throughout main global market laboratories * Vendor-provided, hardware and software support for both the chromatographic and sampling system is expected for the reasonable life of the product * A performance guarantee for 5-7 years is desirable |

### Licensing Requirements for Commercialized Product

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| * Software licenses are expected to be perpetual based upon software version. Customers who choose to upgrade to a new software version may be subject to new software fees, depending on vendor’s typical license structure * Ownership of data generated by the online UHPLC 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 response with 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 Online Sampling UHPLC 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. |

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

Please provide information to the following:

## Company/Organization Information

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

## Primary Contact Person

|  |  |
| --- | --- |
| 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.

Note, **required** (vs. desired) functional requirements are highlighted in **bold.**

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:

|  |  |
| --- | --- |
| 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 |
| **Sampler** | |  |  |
| Sampling Format | **Probe based sampler with a maximum o.d. of 9.5 mm.** |  |  |
| Sample Size | **<25 µL** |  |  |
| Sample Quench | **Local, at reaction temperature and pressure** |  |  |
| Minimum Dilution | **10 – 50x** |  |  |
| Maximum Dilution | **500 – 1000x** |  |  |
| Heterogeneous Mixture sampling: | **Representative sampling of the solid and liquid phases** |  |  |
|  | Sampling of the liquid phase only |  |  |
| Sampling frequency | **<4 minute** |  |  |
|  | <1 minute |  |  |
| Sample carry over | **Efficient washing of sampling device to minimize sample carryover** |  |  |
| Multiplex capabilities | 2-4 probe options |  |  |
|  |  |  |  |
| **Chromatographic system** | |  |  |
| Portability | **Cart based system for lab environments** |  |  |
| Detection modes: | **UV detection** |  |  |
|  | Universal detection |  |  |
|  | Other detector options |  |  |
|  | **MS detection** |  |  |
|  | High Dynamic Range detector option |  |  |
|  |  |  |  |
| **User Interface** | |  |  |
| User type | **Intuitive for a non-specialist** |  |  |
| Integrated Sampling Setup: | **Sample interval/Scheduling** |  |  |
|  | **Sample Dilution** |  |  |
|  | Wake and Sleep for solvent conservation |  |  |
| Integrated data visualization: | **Waterfall plots** |  |  |
|  | **Peak profiling** |  |  |
|  | **Automated integration of main components and low-level impurities** |  |  |
|  | Kinetic profiling/curve fitting tools |  |  |
|  | Statistical process control plots |  |  |
| Data Output: | **Reaction ID**  **Reaction Time**  **Peak Retention Time**  **Peak ID**  **Peak Area**  **Peak Area %**  **m/z and count info** |  |  |
| Data Export: | **Easily transferrable to other environments** |  |  |

## Estimated Timeline

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## Estimated Project Cost

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