

REQUEST FOR INFORMATION

Development of a robust in-line monitoring system for continuous manufacturing of low-dosed drug product

November 4, 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 development of a robust in-line monitoring system for continuous manufacturing of low-dosed drug product. 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 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 a robust in-line monitoring system for continuous manufacturing of low-dosed drug product. 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 4, 2019

Questions on RFI due December 31, 2019

Responses to RFI due January 31, 2020

Invitations sent to respondents for presentation March 1, 2020

Presentation to ETC by respondents April 2020

Select Finalists for RFP May 31, 2020

***Please submit your response electronically to the above address. Responses received after 31st January 2020* *will not benefit from full consideration and may be excluded from the selection process.***

# Project Information

## Possible Project Sponsors

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| AbbVie, Biogen, Eli Lilly, GlaxoSmithKline, Merck, Pfizer |

## Description

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| Since the issue of Process Analytical Technology (PAT) guidelines by FDA in 2004, a variety of in-line non-invasive sensors have been introduced and implemented on pharmaceutical manufacturing processes to provide real-time process monitoring and control. Most process analytical technologies have been developed for the manufacture of formulations with high drug loads. However, there is a lack of sensitive and robust analytical tools to provide real-time monitoring for low-dose drug formulations (<1%, w/w). Pharmaceutical scientists have used techniques such as light-induced fluorescence (LIF), x-ray fluorescence (XRF) and laser-induced breakdown spectroscopy (LIBS) for real-time monitoring of low-dose formulations with limited success in both development and manufacturing. Given the popularity of continuous manufacturing for drug substance and drug product, and the criticality for real-time analytics for control of these processes, there is a need for a process analytics tool providing an ability to monitor sub-percent drug levels in pharmaceutical liquid and solid formulations.ETC formed a discussion group focused on the use of a wide array of real-time analytical tools in a unique PAT monitoring location in tablet presses, i.e., feed frame. The discussion group was joined by 2018 Pharmaceutical Process Analytical Roundtable (PPAR) audiences and generated a list of user requirements for next generation instrumentation development on measuring API content in low-drug loaded formulations. This cross-companies effort intends to leverage ETC to locate a capable instrumentation vendor to deliver a sensitive and robust in-line monitoring system that matches user requirements based upon past industry experience using LIF, XRF, and LIBS. |

## User Requirements

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| The user requirements are divided into three parts: (1) general requirements, (2) requirements on analytical figures of merit, and (3) other considerations. The preferred requirements are what pharmaceutical researchers ultimately want the next generation in-line instrumentation to be. Understanding that preferred requirements may be out of reach at the current point in time, minimum requirements are also tabulated below to serve as basic deliverables for the intended purposes, such as real-time monitoring of low-dose formulations in continuous manufacturing processes for drug products. |

### General Requirements

|  |  |  |
| --- | --- | --- |
| **Objectives** | **Minimum requirements** | **Preferred requirements** |
| Spectroscopy versus non-spectroscopy | Non-applicable | Non-applicable |
| Analysis turn-around time | <5 minutes (including sample handling) | Fraction of seconds to 2 minutes (including sample handling) |
| Sampling interface | At-line / on-line | In-line |
| Sample destructive versus non-destructive | Destructive (such as LIBS) | Non-destructive |
| The physical dimension of the instrument | Non-applicable | For powder measurement, it needs to fit in manufacturing equipment |
| Cleanability | Cleanable | IP65 |
| Sample preparation | Limited amount of sample preparation | In-line |
| Packaging of the instruments/explosion proof | General purpose | ATEX rating |
| Software | Seamlessly communicate with the instrument to allow normal operation | Adaptable to PAT data warehousing package and CFR211 compliant |

### Requirements on Analytical Figures of Merit

|  |  |  |
| --- | --- | --- |
| **Objectives** | **Minimum requirements** | **Preferred requirements** |
| Instrument performance (reliability, robustness) across long term usage | No drift within the length of single reference measurement (stable operation within a work shift or 8 hours) | No drift for relative length of measurements (hours to days) |
| Dynamic API concentration range sensitive by the instrument | Sub-percent (<1%) | Sub-percent (500-1000ppm) |
| Sample size | >10% of unit dose within the analysis turnaround time | Unit dose (typically 50-500mg) within the analysis turnaround time |
| Single-digit instrument precision (excluding sampling error) | <1% RSD for 100% label claim | <1% RSD for 100% label claim |
| Sensitivity in a matrix environment | See accuracy requirement | See accuracy requirement |
| Accuracy in a matrix environment | Equivalent to reference methods (HPLC) | Equivalent to reference methods (HPLC) |
| Specificity | Specific/chemically sound | Specific/chemically sound |

### Other Considerations

|  |  |  |
| --- | --- | --- |
| **Objectives** | **Minimum requirements** | **Preferred requirements** |
| Product contact versus non-contact | Contact | Non-contact |
| Tablet vs powder | Tablet | Powder |
| Benchtop versus probe-based instrument | Benchtop | Probe |
| Sample throughput | See analysis turn-around time | See analysis turn-around time |
| Operational complexity | Require SME to operate | Can be run autonomously on the manufacturing floor, connectivity to PAT warehousing package |

### 2.3.4 Availability Requirements

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| 1. Vendor-provided hardware and software support for both analyzer and sampling interface is expected for the reasonable life of the product. 2. A performance guarantee around 10 years is desirable. |

### 2.3.5 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 even if the company elects to make a SaaS alternative available. 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 project. * 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 the RFI. |

# 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 Functional Requirements and Specifications checklist below, 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:

|  |  |
| --- | --- |
| 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 |

|  |  |  |  |
| --- | --- | --- | --- |
| Feature | Requirement | Code | Vendor Comments |
| General | Spectroscopy versus non-spectroscopy |  |  |
| General | Analysis turn-around time |  |  |
| General | Sampling interface |  |  |
| General | Sample destructive versus non-destructive |  |  |
| General | The physical dimension of the instrument |  |  |
| General | Cleanability |  |  |
| General | Sample preparation |  |  |
| General | Packaging of the instruments/explosion proof |  |  |
| General | Software |  |  |
| Analytical Figures of Merit | Instrument performance (reliability, robustness) across long term usage |  |  |
| Analytical Figures of Merit | Dynamic API concentration range sensitive by the instrument |  |  |
| Analytical Figures of Merit | Sample size |  |  |
| Analytical Figures of Merit | Single-digit instrument precision (excluding sampling error) |  |  |
| Analytical Figures of Merit | Sensitivity in a matrix environment |  |  |
| Analytical Figures of Merit | Accuracy in a matrix environment |  |  |
| Analytical Figures of Merit | Specificity |  |  |
| Other Considerations | Product contact versus non-contact |  |  |
| Other Considerations | Tablet vs powder |  |  |
| Other Considerations | Benchtop versus probe-based instrument |  |  |
| Other Considerations | Sample throughput |  |  |
| Other Considerations | Operational complexity |  |  |

## Estimated Timeline

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## Estimated Project Cost

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