

REQUEST FOR INFORMATION

***Portable NMR reaction monitoring platform***

28 March 2022

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 on the project titled “Portable NMR reaction monitoring platform.” The information collected during this 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 upon its 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.

## Disclaimer

The contents and information provided in this RFI are meant to provide general information to parties interested in developing the project “Portable NMR reaction monitoring platform.” The successful respondent selected by ETC 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 responses but agrees not to publicly distribute RFI responses outside of ETC 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. Fatou Sarr

ETC Secretariat

c/o Faegre Drinker Biddle & Reath, LLP

1500 K St NW

Washington DC, 20005-1209

202.230.5148

info@etconsortium.org

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

## Anticipated Time Frames for Evaluation and Selection Process\*

Issue RFI March 28, 2022

Questions on RFI due April 11, 2022

ETC responds to any RFI questions April 25, 2022

Responses from potential collaborators due May 9, 2022

Invitations sent to respondents for presentation May 9-23, 2022

Presentation to ETC by respondents May 9-June 6, 2022

*\*Dates subject to change without notice*

***Please submit your response electronically to the above address. Responses received after May 9, 2022*** ***will not benefit from full consideration and may be excluded from the selection process.***

## Project Scoping and Project Execution

ETC project sponsors will work with the selected collaborator to define the project scope and work to finalize a Statement of Work (SOW) for the project which describes project timelines, milestones, budget, deliverables, etc. Depending on the project, the scoping exercise will be conducted via email, web-meetings, and/or an in-person workshop. Following finalization of the SOW, the project will be brought forward to the ETC Board of Directors to authorize moving to execution.

Once authorized by the ETC Board of Directors, the ETC Secretariat will work with the selected collaborator to negotiate and finalize a contract between the two parties, leveraging ETC’s Development Agreement and Non-Disclosure Agreement accelerator templates. In parallel to this negotiation, the Secretariat will also work to finalize and execute our internal project Charter between participating ETC members.

## Intellectual Property

ETC acknowledges that this project, or aspects thereof, may require the use and incorporation of existing intellectual property and/or the development of new intellectual property in order to successfully complete the project.

### Existing Intellectual Property

* ETC as an organization will not engage in negotiations with the owner of any intellectual property on the respondent’s or ETC’s behalf;
* It is the responsibility of the respondent to conduct an intellectual property search and take all necessary steps to ensure their proposed project will not infringe or misappropriate any intellectual property right of a third party and/or obtain all necessary consents, assignments and licenses to provide the solution in the project proposal.

### New Intellectual Property

With most projects conducted with ETC:

* All commercialization rights will reside with the collaborator;
* ETC will not assume ownership of any intellectual property (IP) developed by the collaborator or expect royalties from future commercial sales.

# Project Information

## Possible Project Sponsors

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| AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Eli Lilly, Genentech, GlaxoSmithKline, Janssen, Merck & Co., Pfizer, and Takeda |

## Description

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| Process/reaction monitoring and characterization technologies are very important for the chemical industry, as they enable a comprehensive understanding of the studied reaction and the optimization of reaction conditions in real-time based thereon. Above all, NMR spectroscopy as a monitoring tool allows simultaneous structural and quantitative analysis of chemical substances produced during the reaction. In particular, low-field NMR spectrometers have remarkably high potential, as they are sufficiently compact and portable to be operated even in a fume hood, without the need for cryogens, etc. The usage of benchtop NMR spectroscopy as a PAT tool in the small molecule space has been limited due to several factors, namely, 1) the narrow range of reaction temperatures offered, as accurate kinetic profiles require tight temperature control; 2) the low sensitivity and low signal dispersion that could pose signal overlap and quantification errors; 3) the need of optimized transfer lines & flow cell systems, and 4) lack of user-friendly software designed for easy reaction monitoring data collection and analysis. The ETC is seeking companies interested in supplying a vendor-supported portable benchtop low-field (≥ 60-200 MHz, with a footprint suitable for a standard chemistry lab hood) NMR system that can be effectively deployed for real-time analysis of reaction mixtures in process development settings. The ultimate goal is to provide an end-to-end solution that will encompass sample delivering (transfer lines & flow cell/tubes), hardware and software (acquisition and data analysis) components that will meet the following requirements: 1. Transfer lines & Flow cell/tubes: compact and low dead volume; with high chemical and thermal compatibility and ability to handle biphasic, high pressure, and air-sensitive reactions, etc. Transfer lines might rely on a combination of active heat regulation and passive heat insulation to offer high thermostability during a wide range of temperatures.
2. Hardware: with optimized probe/receiver coil design to achieve high sensitivity and high dynamic range; and very importantly, be able to offer variable sample temperature capability with high thermostability.
3. Software: with built-in automated and user-friendly platforms for data analysis; and very importantly, as a PAT tool, it should provide a user-friendly interface to be able to provide real-time concentration vs time data, to add annotations of different events, and to interface with other software environments for data visualization/fusion, etc.)
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## Requirements

### Necessary Hardware and Software Requirements

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| **I. Transfer lines & Flow cell/tubes**The transfer lines & **flow cell** system needs to meet the following requirements: 1. Compact and lowest dead volume possible (target: <3 mL, ideally 2-3 mL)
2. Transfer lines, connections, pump seals must be chemically resistant to corrosive materials (acids, etc.) and common organic and caustic solvents, it should also possess low gas permeability. The ability to perform experiments at pH ranging from 0 to 12 is desirable.
3. Ability to handle biphasic mixtures (liquid/gas, liquid/solid, liquid/liquid), high pressure and air-sensitive reactions.

And the system will encompass all components needed to connect the NMR analyzer to a reaction vessel / reactor. This includes but is not limited to: 1. Transfer lines capable of moving material in and out of the reaction vessel while keeping the sample at the desired temperature. Similarly, the temperature of the **flow cell/tube** inside the spectrometer should be controllable, via an external VT control unit.
2. Flow pump capable of circulating material through the whole system with accurate control over the flow rate. The flow pump control should be integrated into the NMR analyzer system control. This will allow the design of NMR data collection schemes in continuous and stop-flow modes and real time self-optimization for flow analyses (e. g. to control rate of addition of the reagents).
3. Flow cell / flow tube that enables adequate positioning of the sample inside the NMR spectrometer. The sample in the flow cell must be representative of the mixture in the reactor. The ability to effectively displace the system dead volume and replenish the flow cell between time points is critical.
4. Have a compact filtration system that, a) prevents solids from reaction mixture from entering the line; b) easy to change out; c) provide adequate safety from clogging and backpressure buildup.
5. The materials should be easy to clean-up to avoid cross contamination.
6. Transfer lines are easily replaceable when necessary and commercially available.

**II. Hardware****A. Temperature control** (recycling loop, pump head, magnet). A tight control of the operating temperature throughout the whole sample path is of paramount importance 1. Accurate and consistent temperature control. Required (0 – 90 °C), nice-to-have (-20°C to + 100°C). Sample chamber needs to be insulated to protect magnet.
2. Transfer lines might rely on a combination of active heat regulation and passive heat insulation. The ability to monitor temperature along the sample path using thermocouples is highly desirable.

**B.** Achieve further improvement of **sensitivity** via optimization of the probe/receiver coil design: 1. Sensitivity up to 1H S/N 400-500:1 (or 1 scan of 0.2 M solution gives good impurity understanding).
2. High dynamic range (at min 10K, 100K preferred)
3. High resolution (e.g. <0.4 Hz (50%))

**C.** The NMR spectrometer should be capable of collecting 1D 1H and 19F data. The ability to tune to 31P, 11B, 13C will be nice to have.**D.** Std electrical voltage standard 120V US.**III. Hardware-Software**1. It also should provide a stable, and frequency/nuclei independent shimming, be able to maintain auto shimming in the background. Also, advanced shimming routine algorithm (Convection compensation, gradient shimming, protonated solvents, high temp, etc.) & gradient capabilities required (e.g. presat and multiple frequency suppression).
2. Specifications in terms for signal-to-noise and lineshape should be clearly stated. Ideally, a standard solution of an analyte containing both 1H and 19F will be used for this purpose.

**IV. Software**1. With built-in automated and easy-to-use platforms for data analysis and visualization.
2. Be able to provide a unified and open file format
3. Should allow the addition of more NMR experiments while the reaction is ongoing as well as enable to add experiments with different time intervals.
4. The software should enable easy setup of an array of 1D experiments. Should be easy to queue multiple studies of the same type, allow easy setup of complementary 1D studies in the queue (such as alternate 1H, 19F NMRs). Should allow easy start/pause/stop experiment options.
5. Very importantly, as a PAT tool, it should provide but is not limited to:
* Real time concentration vs time data with the ability to correct in situ any signal drift caused by changes on pH, etc. that might occur during the reaction.
* With the ability of adding annotations
* Be able to interface with other software environments for data visualization/fusion, etc.)

Other considerations: 1. Ideally, both the NMR analyzer and the Automatic Lab Reactor can be placed inside a safety enclosure.
2. User-friendly, engineers and chemist as primary users.

Safety considerations: Equipment must be tested to ensure that no spark or fire will occur |

### Optional Hardware and Software Requirements

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| 1. We understand that this is an extensive list of requirements and the difficulties to deliver on all of them. All proposals that address >50% of the requirements will be considered.
2. Also, considering requests are being made for both hardware and software improvements, collaboration between different vendors to deliver together in a new portable NMR reaction monitoring platform is encouraged.
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### Availability Requirements

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| * Commercial and supported system available to customers within 2 years of project completion
* Any requisite service on the instrument should be available globally.
* Vendor-provided, hardware and software support is expected for the reasonable life of the product.
* Hardware, software, and firmware updates should be field deployable and available at reasonable cost following launch of the commercial technology.
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### Licensing Requirements for Commercialized Product

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| * Software will be licensed to ETC participants at no cost during (i) development and (ii) a mutually agreed beta testing period. Thereafter, software will be available for licensing on a perpetual basis or subscription basis at the option of customer.
* Software shall be available for self-hosting by (or on behalf of) customer even if the collaborator elects to make a SaaS alternative available.
* The collaborator shall make available industry standard support.
* Ownership of data generated on system resides with customer.
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# Criteria for Evaluation

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| The ETC will evaluate the responses to this RFI based on the respondent’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 a vendor supported, portable NMR reaction monitoring platform.
* 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 RFI.
* Provide any additional capabilities that may differentiate them from other potential collaborators.

Please note that due to the volume of responses received, ETC only provides general updates related to the status of the review process and will not provide individualized feedback as to why a particular proposal was not selected by ETC. |

# Respondent Profile

*(To be completed by 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.

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 |
| --- | --- | --- | --- |
| Transfer lines & Flow cell/tubes | Compact and lowest dead volume possible (target: <3 mL, ideally 2-3 mL) |  |  |
| Transfer lines & Flow cell/tubes | Transfer lines, connections, pump seals must be chemically resistant to corrosive materials (acids, etc.) and common organic and caustic solvents, it should also possess low gas permeability. The ability to perform experiments at pH ranging from 0 to 12 is desirable. |  |  |
| Transfer lines & Flow cell/tubes | Ability to handle biphasic mixtures (liquid/gas, liquid/solid, liquid/liquid), high pressure and air-sensitive reactions. |  |  |
| Components needed to connect the NMR analyzer to a reaction vessel / reactor | Transfer lines capable of moving material in and out of the reaction vessel while keeping the sample at the desired temperature. Similarly, the temperature of the flow cell/tube inside the spectrometer should be controllable, via an external VT control unit. |  |  |
| Components needed to connect the NMR analyzer to a reaction vessel / reactor | Flow pump capable of circulating material through the whole system with accurate control over the flow rate. The flow pump control should be integrated into the NMR analyzer system control. This will allow the design of NMR data collection schemes in continuous and stop-flow modes and real time self-optimization for flow analyses (e. g. to control rate of addition of the reagents) |  |  |
| Components needed to connect the NMR analyzer to a reaction vessel / reactor | Flow cell / flow tube that enables adequate positioning of the sample inside the NMR spectrometer. The sample in the flow cell must be representative of the mixture in the reactor. The ability to effectively displace the system dead volume and replenish the flow cell between time points is critical. |  |  |
| Components needed to connect the NMR analyzer to a reaction vessel / reactor | Have a compact filtration system that, a) prevents solids from reaction mixture from entering the line; b) easy to change out; c) provide adequate safety from clogging and backpressure buildup. |  |  |
| Components needed to connect the NMR analyzer to a reaction vessel / reactor | The materials should be easy to clean-up to avoid cross contamination |  |  |
| Components needed to connect the NMR analyzer to a reaction vessel / reactor | Transfer lines are easily replaceable when necessary and commercially available |  |  |
| Temperature Control (recycling loop, pump head, magnet) | Accurate and consistent temperature control. Required (0 – 90 °C), nice-to-have (-20°C to + 100°C). Sample chamber needs to be insulated to protect magnet. |  |  |
| Temperature Control (recycling loop, pump head, magnet) | Transfer lines might rely on a combination of active heat regulation and passive heat insulation. The ability to monitor temperature along the sample path using thermocouples is highly desirable. |  |  |
| Sensititivity via optimization of probe/receiver coil design | Sensitivity up to 1H S/N 400-500:1 (or 1 scan of 0.2 M solution gives good impurity understanding).  |  |  |
| Sensititivity via optimization of probe/receiver coil design | High dynamic range (at min 10K, 100K preferred) |  |  |
| Sensititivity via optimization of probe/receiver coil design | High resolution (e.g. <0.4 Hz (50%)) |  |  |
| Nuclei/Data Types | The NMR spectrometer should be capable of collecting 1D 1H and 19F data. The ability to tune to 31P, 11B, 13C will be nice to have |  |  |
| Voltage | Std electrical voltage standard 120V US |  |  |
| Hardware-Software: Shimming | It also should provide a stable, and frequency/nuclei independent shimming, be able to maintain auto shimming in the background. Also, advanced shimming routine algorithm (Convection compensation, gradient shimming, protonated solvents, high temp, etc.) & gradient capabilities required (e.g. presat and multiple frequency suppression).  |  |  |
| Hardware-Software: SN and Lineshape | Specifications in terms for signal-to-noise and lineshape should be clearly stated. Ideally, a standard solution of an analyte containing both 1H and 19F will be used for this purpose.  |  |  |
| Software: Visualization | With built-in automated and easy-to-use platforms for data analysis and visualization |  |  |
| Software: Data Format | Be able to provide a unified and open file format |  |  |
| Software | Should allow the addition of more NMR experiments while the reaction is ongoing as well as enable to add experiments with different time intervals |  |  |
| Software | The software should enable easy setup of an array of 1D experiments. Should be easy to queue multiple studies of the same type, allow easy setup of complementary 1D studies in the queue (such as alternate 1H, 19F NMRs). Should allow easy start/pause/stop experiment options. |  |  |
| Software | Very importantly, as a PAT tool, it should provide but is not limited to:* Real time concentration vs time data with the ability to correct in situ any signal drift caused by changes on pH, etc. that might occur during the reaction.
* With the ability of adding annotations
* Be able to interface with other software environments for data visualization/fusion, etc.)
 |  |  |
| Other | Ideally, both the NMR analyzer and the Automatic Lab Reactor can be placed inside a safety enclosure. |  |  |
| Other | User-friendly, engineers and chemist as primary users |  |  |
| Safety | Equipment must be tested to ensure that no spark or fire will occur |  |  |

## Estimated Timeline

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## Estimated Project Cost

The overarching goal of ETC is to help bring innovative technologies to the commercial marketplace in partnership with third parties.  Aligned with that goal, participating ETC members will provide resources in the form of funding and subject matter expertise to support the development of this project.  While ETC will entertain all proposals received, regarding funding from ETC, please consider the following:

* Proposed budgets should be provided as **fixed-costs in US Dollars;**
* When partnering with a commercial vendor, any monetary resources provided by ETC should be viewed as seed funding to supplement the total development costs with the collaborator investing as well;
* When partnering with an academic or non-profit organization, any monetary contributions requested from ETC should be for the total project costs, inclusive of indirect costs (i.e., proposed costs should be inclusive of any indirect or other hidden costs);
* Include a payment schedule, based upon time from project start and/or milestones.

Please describe below project costs, including not only the total project costs but also costs to be paid by ETC and any costs borne by your organization.

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## Commercialization and Support

The overarching goal of ETC is to help bring innovative technologies to the commercial marketplace in partnership with third parties.  Aligned with that goal ETC looks to collaborate on projects which will result in products that are commercially available and supported in the marketplace.

* With most projects, all commercialization rights will reside with the collaborator;
* ETC will not assume ownership of any intellectual property (IP) developed by the collaborator or expect royalties from future commercial sales.

Please describe your organization’s plans for commercialization and support of this technology following the successful conclusion of this project.  If your organization is not a commercial entity (e.g., academic or non-profit), please describe any plans related to the availability of the technology following the successful conclusion of the project. Note that for projects where there isn’t an expectation of a commercial product or service offering, (e.g., research and development project, services-only project) it is expected that each ETC member participating in this project will be provided a non-exclusive, royalty-free license to the output of the project and any new Project IP developed under this project for commercial purposes.

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