

REQUEST FOR PROPOSAL

**Pilot-Plant Photochemical Reactor**

May 4, 2022

Enabling Technologies Consortium™

Request for Proposals

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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 Proposals

Publication of this Request for Proposals (RFP) is the first step by ETC to solicit interest in collaborating on the project titled “**Pilot-Plant Photochemical Reactor.”** The information collected during this process along with subsequent interviews will be used for evaluation purposes.

## Disclaimer

The contents and information provided in this RFP are meant to provide general information to parties interested in developing the project **“Pilot-Plant Photochemical Reactor.”** 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 RFP, please note the following:

* This RFP is not an offer or a contract
* Responses submitted in response to this RFP become the property of ETC
* Respondents will not be compensated or reimbursed for any costs incurred as part of the RFP process
* If ETC receives and responds to questions from RFP 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 RFPs 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 RFP responses but agrees not to publicly distribute RFP responses outside of ETC or share RFP responses with other respondents.
* ETC is not obligated to contract for any of the products or services described in this RFP
* 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 RFP at any time

## RFP 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 RFP May 4, 2022

Questions on RFP due Jun 1, 2022

ETC responds to any RFP questions Jun 15, 2022

Responses from potential collaborators due Jul 18, 2022

Invitations sent to respondents for presentation Jul 19 - Aug 1, 2022

Presentation to ETC by respondents Aug 2022

*\*Dates subject to change without notice*

***Please submit your response electronically to the above address. Responses received after July 18*** ***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, Boehringer Ingelheim, Bristol Myers Squibb, Merck, Zoetis  |

## Description

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| Photochemistry employs the use of light as a means to carry out a desired chemical transformation. This can be achieved in a number of ways, including direct photoexcitation of the substrate by light, or by photoexcitation of a photocatalyst or sensitizer which allows for the subsequent desired transformation to take place. The use photochemistry has been extensively reported in academic settings, with many elegant uses in synthetic work over the past decades. A distinguishing feature of photochemistry is that it allows for transformations that i.) are not achievable by other means (e.g., photocyclization reactions) or ii.) use difficult or undesirable conditions utilizing traditional methods employing chemical reagents. As such, it would be expected that the use of photochemical transformations would be utilized quite often in the pharmaceutical industry given its ability to install unique functionality within molecules and potentially generate less waste by reducing the amount of chemical reagents needed in processes. Only recently, due to the development of high-intensity LEDs covering UVA to blue wavelengths and an expanded reaction scope, has it become practical to explore the application of photochemistry as a scalable technology in the pharmaceutical industry.One key factor for limiting the implementation of photochemistry in a pharmaceutical manufacturing setting is the limited commercially available equipment options for use in a scale up/pilot plant facility. Oftentimes, to support internal development work, a fit-for-purpose photochemical reactor is constructed\* that can be utilized for a particular manufacturing process but is not intended to be broadly reproduced for other processes. Likewise, when transferring processes to external partners, they may have limited photochemistry equipment/experience and the design of a custom reactor for their facility creates risk for a technology transfer. In both cases this leads to an increase in project cycle time, creates a significant barrier when looking to incorporate photochemistry in a manufacturing setting, and adds noteworthy challenges to commercialization of processes using photochemistry.Additionally, due to constraints of light penetration through large volumes, effective irradiation of the photoreactors has been historically challenging. Because of the decay in light intensity with reaction depth, the performance of photochemical reactions are highly light source and reactor geometry dependent. In addition to the reactor geometry and light source considerations such as intensity and wavelength, factors including material of construction, throughput capacity, and temperature control all play important roles in ensuring a process can be executed successfully. There is currently a lack of commercially available and GMP qualified scale-up photochemical reactors that meet the needs of organic photochemistry, which has led to the proliferation of custom, one-off reactors across this industry. In addition to the significant individual efforts expended by many companies to develop scale-up photoreactors, this approach has limited the widespread uptake of photochemistry as a scale-up technology as development groups hesitate to explore this complex technology landscape. To address this issue, ETC proposes development of a commercially available scale-up reactor that meets the needs of the pharmaceutical industry. The project involves designing, building, and characterizing a commercially available pilot-plant scale photoreactor. Characterization is expected to include light characterization (photon count and spectral irradiation) and reactor characterization (material of construction, chemical compatibility, pressure rating, mixing, residence time distribution, heat transfer, scaling factor, etc.). The unit is expected to comply with the electrical hazard rating requirements of pharmaceutical manufacturing settings and be suitable for GMP qualification. ETC members are expected to provide feedback on the initial design and may suggest revisions. A collaboration between light manufacturer and reactor manufacturer companies can be considered to meet the needs of the project. *The deliverable from this project is a commercially available pilot-plant scale photoreactor that can be purchased outside the terms of this agreement*\* References Beaver, M.G., *et al.* Development and Execution of a Production-Scale Continuous [2 + 2] Photocycloaddition, *Org. Process Res. Dev.* **2020**, 24, 2139–2146. Bottecchia, C., *et al.* Manufacturing Process Development for Belzutifan, Part 2: A Continuous Flow Visible-Light-Induced Benzylic Bromination, *Org. Process Res. Dev.* **2021**, 10.1021/acs.oprd.1c00240.Corcoran, E. B., *et al.* Photon Equivalents as a Parameter for Scaling Photoredox Reactions in Flow: Translation of Photocatalytic C-N Cross-Coupling from Lab Scale to Multikilogram Scale, *Angew. Chem. Int. Ed.* **2020**, *59*, 11964-11968.Harper K.C., *et al.* A Laser Driven Flow Chemistry Platform for Scaling Photochemical Reactions with Visible Light, *ACS Cent. Sci.* **2019**, 5, 109–115. Lévesque, F., *et al.* Design of a Kilogram Scale, Plug Flow Photoreactor Enabled by High Power LEDs, *Org. Process Res. Dev.* **2020**, *24*, 2935-2940.Robinson, A., *et al.* Development and Scale-Up of a Novel Photochemical C–N Oxidative Coupling, *Org. Process Res. Dev.* **2021**, 25, 10, 2205–2220.Sezen-Edmonds, M., *et al.* Predicting Performance of Photochemical Transformations for Scaling Up in Different Platforms by Combining High-Throughput Experimentation with Computational Modeling, *Org. Process Res. Dev.* **2020**, *24, 2128-2138.* |

## Requirements

### Necessary Hardware and Software Requirements

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| The ETC envisions that a successful prototype photochemical reactor for this proposal would possess the following capabilities:1**. Light Source Requirements**1. The ability to switch/swap between multiple wavelengths (with spectral output characterization for each). 365 nm and 450 nm light sources with narrow wavelength distribution are required. Access to additional wavelengths is desired but not required at this stage.
2. Sufficient number of photons reaching the reaction stream to access desired scales (> 10 kg/day output). For example, minimum 1000 Watts LED power for > 10 kg/day productivity is estimated assuming 24-hour operation and at least 20% of light reaching inside the reactor.
3. The ability to modulate the light intensity
4. The ability to cool the light source independently from the reactor and ensure consistent LED performance with the state-of-the-art technology (for example, at least 9000 hours of runtime with <5% performance loss at the operation temperature.)
5. Is compatible with safety requirements of manufacturing facilities. Electrical design should be compatible for safe handling of processes with flammable materials.
6. Safety control in place for auto shutdown under excursions from operating conditions
7. Light-blocking cover available to minimize occupational exposure during the operation of the unit

2. **Reactor Design Requirements**1. Material of construction compatible with reaction conditions (i.e., common organic reaction solvents and acid/bases)
2. Ability to handle range of temperatures (-20 °C to 80 °C)
3. Minimum 10 kg/day output (assuming pharmaceutically relevant photochemical reactions\*\* with dilution of 10 L/kg, quantum yield of 0.5, and product molecular weight of 350 g/mol)
4. Accommodate on-line temperature and pressure monitoring, on-line PAT equipment, and sampling capability for reaction monitoring
5. Complies with requirements to operate within a GMP environment
6. Ability to GMP qualify the equipment based on customer needs
7. All different reactor modes (batch and flow) will be considered

3. **Software requirements** 1. Ability to monitor, control, and record the light intensity and reactor operation via user interface software
2. System has the capability to communicate to user control system over a variety of communication protocols

For all the proposals above respondents should provide a full plan to complete the work, including an estimated timeline with milestones, cost to ETC in US dollars, and a description of deliverables.\*\* Examples of some pharmaceutically relevant photochemical reactionsBeaver, M.G., *et al.* Development and Execution of a Production-Scale Continuous [2 + 2] Photocycloaddition, *Org. Process Res. Dev.* **2020**, 24, 2139–2146. Bottecchia, C., *et al.* Photon Equivalents as a Parameter for Scaling Photoredox Reactions in Flow: Translation of Photocatalytic C−N Cross-Coupling from Lab Scale to Multikilogram Scale, *Angew. Chem. Int. Ed.* **2020**, 59, 11964–11968.Duvadie, R., *et al.* Photoredox Iridium–Nickel Dual Catalyzed Cross-Electrophile Coupling: From a Batch to a Continuous Stirred-Tank Reactor via an Automated Segmented Flow Reactor, *Org. Process Res. Dev*. **2021**, 25, 10, 2323–2330.Howie, R.A., *et al.* Integrated Multistep Photochemical and Thermal Continuous Flow Reactions: Production of Bicyclic Lactones with Kilogram Productivity, *Org. Process Res. Dev.* **2021**, 25, 2052−2059.Hsieh, H.-W., *et al.* Photoredox Iridium–Nickel Dual-Catalyzed Decarboxylative Arylation Cross-Coupling: From Batch to Continuous Flow via Self-Optimizing Segmented Flow Reactor, *Org. Process Res. Dev.* **2018**, 22, 4, 542–550.Graham, M.A., *et al.* Development and Proof of Concept for a Large-Scale Photoredox Additive-Free Minisci Reaction, *Org. Process Res. Dev.* **2021**, 25, 57−67 |

### Optional Hardware and Software Features

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| * Ability to run pressurized reactions
* Ability to handle suspensions without clogging or settling of solids
* Ability to handle gas-liquid mixtures with interfacial mixing
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# Criteria for Evaluation

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| The ETC will evaluate the responses to this RFP 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 RFP as evidenced by the RFP 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 “Pilot-Plant Photochemical Reactor.”
* 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 RFP.
* 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 RFP. 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 RFP (*to be completed by RFP 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 |
| --- | --- | --- | --- |
| **Light Source** | The ability to switch/swap between multiple wavelengths (with spectral output characterization for each). 365 nm and 450 nm light sources with narrow wavelength distribution are required. Access to additional wavelengths is desired but not required at this stage. |  |  |
| **Light Source** | Sufficient number of photons reaching the reaction stream to access desired scales (> 10 kg/day output). For example, minimum 1000 Watts LED power for > 10 kg/day productivity is estimated assuming 24-hour operation and at least 20% of light reaching inside the reactor |  |  |
| **Light Source** | The ability to modulate the light intensity |  |  |
| **Light Source** | The ability to cool the light source independently from the reactor and ensure consistent LED performance with the state-of-the-art technology (for example, at least 9000 hours of runtime with <5% performance loss at the operation temperature.) |  |  |
| **Light Source** | Is compatible with safety requirements of manufacturing facilities. Electrical design should be compatible for safe handling of processes with flammable materials. |  |  |
| **Light Source** | Safety control in place for auto shutdown under excursions from operating conditions |  |  |
| **Light Source** | Light-blocking cover available to minimize occupational exposure during the operation of the unit |  |  |
|  |  |  |  |
| **Reactor Design** | Material of construction compatible with reaction conditions (i.e., common organic reaction solvents and acid/bases) |  |  |
| **Reactor Design** | Ability to handle range of temperatures (-20 °C to 80 °C) |  |  |
| **Reactor Design** | Minimum 10 kg/day output (assuming pharmaceutically relevant photochemical reactions with dilution of 10 L/kg, quantum yield of 0.5, and product molecular weight of 350 g/mol) |  |  |
| **Reactor Design** | Accommodate on-line temperature and pressure monitoring, on-line PAT equipment, and sampling capability for reaction monitoring |  |  |
| **Reactor Design** | Complies with requirements to operate within a GMP environment |  |  |
| **Reactor Design** | Ability to GMP qualify the equipment based on customer needs |  |  |
| **Reactor Design** | All different reactor modes (batch and flow) will be considered |  |  |
| **Software** | Ability to monitor, control, and record the light intensity and reactor operation via user interface software |  |  |
| **Software** | System has the capability to communicate to user control system over a variety of communication protocols |  |  |
| **Optional** | Ability to run pressurized reactions |  |  |
| **Optional** | Ability to handle suspensions without clogging or settling of solids |  |  |
| **Optional** | Ability to handle gas-liquid mixtures with interfacial mixing |  |  |

## 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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