

REQUEST FOR PROPOSAL

***Improving IVIVC of Immediate Release Oral Drug Products by new PBPK/PBBM Approaches***

November 6, 2023

Enabling Technologies Consortium™

Request for Proposal

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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 Proposal

Publication of this Request for Proposal (RFP) is the first step by ETC to solicit interest in collaborating on the project titled “Improving IVIVC of Immediate Release Drug Products by new PBPK/PBBM Approaches.” 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 RFP 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 RFP are meant to provide general information to parties interested in developing the project “Improving IVIVC of Immediate Release Drug Products by new PBPK/PBBM Approaches.” 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 RFP 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 Nov 6, 2023

Questions on RFP due (via email) Nov 30, 2023

RFP Responses Due to ETC Dec 22, 2023

*\*Dates subject to change without notice*

***Please submit your response electronically to the above address. Responses received after Dec 22, 2023*** ***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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| Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Genentech, Merck & Co., and Zoetis |

## Description

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| For solid oral drug products, the establishment of in vitro in vivo correlation (IVIVC) between in vitro dissolution and in vivo absorption data is highly desirable. However, most IVIVC cases in the literature are for extended release (ER) formulations. It is much more challenging to achieve IVIVC for immediate release (IR) formulations commonly used for oral drug products. Physiologically based pharmacokinetic (PBPK) modeling or physiologically based biopharmaceutics modeling (PBBM) can incorporate many relevant physicochemical properties and physiological factors to simulate/predict in vivo PK profiles. However, often times PBPK/PBBM employs models (e.g. Johnson model) that solely rely on drug substance properties (solubility, permeability, particle size distribution) without any relationship to in vitro dissolution of different formulations or formulation variants. In cases where in vitro dissolution profiles are used as direct input for PBPK/PBBM with a Weibull function, it generally works better for ER formulations than IR formulations. Another approach (z-factor model) that uses in vitro dissolution profiles as input to calculate dissolution rates may work in some cases but not for all.In recent years, there has been a strong interest from pharmaceutical companies and academia to address the gaps described above for IVIVC for IR drug products. Several case studies were published in the literature using drug product specific dissolution profiles as input for PBPK/PBBM modeling with extensive data processing outside the software. Attempts to optimize the z-factor approach were also published. Some companies have developed proprietary software internally, which however is not commercially available for wider use. The ETC is seeking companies interested in supplying vendor-supported, commercially available new in silico PBPK/PBBM approaches in a single, user friendly software product that can be effectively used for IVIVC of IR drug products, which has not been achieved by existing software. The majority of the in vitro data needed for software development would be from existing data in literature or new data that could be generated from commercially available drug products. In addition, the ETC companies may be able to collaborate with the vendor by providing relevant in vitro dissolution profiles as additional input for PBPK/PBBM, and in vivo PK profiles to verify whether IVIVC has been achieved, if possible. The ETC companies may also collaborate with the vendor by participating in beta testing of the developed software. Some of the successfully IVIVC case studies from the collaboration may be publishable. |

## Requirements

### Necessary Software Requirements

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| The new software and PBPK/PBBM approach will 1. take into consideration recent advances in IVIVC for IR drug products by using novel product specific in vitro dissolution input and successful case studies reported in the literature.
2. be able to use relevant in vitro dissolution profiles from different formulations or formulation variants as input to simulate in vivo PK profiles.
3. be universally applicable to different BCS classes of compounds, salts, and commonly used formulations including amorphous solid dispersions (ASD).
4. demonstrate successful IVIVC case studies for various basic, acidic, and neutral compounds, salts, as well as various formulations and formulation/process variants.
5. Include the physiology for canine (small, medium, and large) animal model for use in preclinical applications.
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### Optional Software Requirements

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| Another challenge in PBPK/PBBM modeling of oral drug products is the input of precipitation time in the software. Precipitation of basic compounds observed in in vitro 2-stage dissolution experiments often overestimate the extent of precipitation in vivo. The default precipitation time in currently available PBPK software also tends to overestimate precipitation. A better way to determine the default precipitation time or compound/formulation specific precipitation time would be desirable in the new software.The pH in the stomach under fed conditions is higher than in fasted conditions but decreases over time. There are published case studies that show better food effect predictions by applying a dynamic pH profile for fed conditions in PBPK. In contrast, false negative food effects predicted by PBPK have been known for basic compounds that show reduced dissolution at a fixed, elevated pH for fed conditions. If would be a plus for the new software to address this issue.  |

### Availability Requirements

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| * New commercial software or new version of current commercial software available to customers within one year of project completion.
* Vendor-provided, software support is expected for the reasonable life of the product.
* Software updates should be available at reasonable cost following launch of the commercial software.
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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.
* 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 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 a vendor supported, IVIVC of IR drug products by PBPK 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 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 |
| --- | --- | --- | --- |
| Necessary | Take into consideration recent advances in IVIVC for IR drug products by using novel product specific in vitro dissolution input and successful case studies reported in the literature |  |  |
| Necessary | Be able to use relevant in vitro dissolution profiles from different formulations or formulation variants as input to simulate in vivo PK profiles |  |  |
| Necessary | Be universally applicable to different BCS classes of compounds, salts, and commonly used formulations including amorphous solid dispersions (ASD) |  |  |
| Necessary | Demonstrate successful IVIVC case studies for various basic, acidic, and neutral compounds, salts, as well as various formulations and formulation/process variants |  |  |
| Necessary | Include the physiology for canine (small, medium, and large) animal model for use in preclinical applications. |  |  |
| Optional | A better way to determine the default precipitation time or compound/formulation specific precipitation time would be desirable in the new software |  |  |
| Optional | The pH in the stomach under fed conditions is higher than in fasted conditions but decreases over time. There are published case studies that show better food effect predictions by applying a dynamic pH profile for fed conditions in PBPK. In contrast, false negative food effects predicted by PBPK have been known for basic compounds that show reduced dissolution at a fixed, elevated pH for fed conditions. If would be a plus for the new software to address this issue. |  |  |

## 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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