

REQUEST FOR INFORMATION

Crystal Morphology Prediction

December 2, 2019Test

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 Crystal Morphology Prediction Tool. 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 upon 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.

## Disclaimer

The contents and information provided in this RFI are meant to provide general information to parties interested in developing the Crystal Morphology Prediction Tool. 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

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

## Anticipated Time Frames for Evaluation and Selection Process

Issue RFI December 2, 2019

Questions on RFI due December 31, 2019

Responses to RFI due January 31, 2020

Invitations sent to respondents for presentation February 2020

Presentation to ETC by respondents March 2020

Select Finalists for RFP April 2020

***Please submit your response electronically to the above address. Responses received after January 31, 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, Amgen, AstraZeneca, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, Genentech, GlaxoSmithKline, Merck, Pfizer, Takeda |

## Description

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| The shape of isolated API particles has a large impact on their downstream performance. To improve downstream processing of powders, a novel software package is required to predict the steady-state shape of API particles through the estimation of the relative growth rates of crystal faces. The predictive models implemented in the software package shall capture the effect of operating conditions on the relative growth rates of crystal faces. The software package shall enable comparison of the predicted morphology with experimental results as well as enable comparison of crystal morphologies predicted at different operating conditions.The current software packages either (1) predict the steady-state shape by applying the attachment energy model or the Bravais model, both of which rely solely on crystal properties; or (2) predict the steady-state in the spiral growth regime as a function of operating conditions. In addition, academic groups have had success in predicting the crystal shape through molecular dynamics simulations.The limitation of current morphology prediction tools are summarized below:

|  |  |  |
| --- | --- | --- |
| **Morphology Prediction Model** | **Commercial Software Available**  | **Limitations** |
| BFDH | Yes | Cannot account for effect of solvent, impurities, additives, supersaturation and temperature. |
| Attachment Energy or Modified Attachment Energy | Yes | Can model solvent(s) effect, but with poor accuracy.Cannot account for effect of supersaturation and temperature. |
| Growth Kinetics based models | Yes | Prediction in single solvent, accounts for effect of supersaturation and temperature.Cannot predict morphology in solvent mixtures.Cannot model salts, cocrystals, hydrates and solvates.Validation and commercialization is needed. |
| Monte-Carlo or Molecular Dynamics based models | No | Difficult to learn and use.Computationally demanding. |

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## Crystal Morphology Prediction Tool Requirements

### Necessary Hardware and Software Requirements

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| The developed software package should have the ability to: 1. Predict the steady-state morphology of free forms (Z’=1, 2 and more), solvates, hydrates with centrosymmetric and non-centrosymmetric growth units from the crystal structure.
	* The minimal requirement is a qualitative prediction of the steady-state shape (e.g. needle, platelet, cube)
	* The Wulff construction featuring all crystal faces present in the steady-state shape is preferred.
2. Capture effect of supersaturation, temperature, solvent composition (single solvent as well as binary or ternary solvent mixtures) and impurities/additives on steady-state shape.
3. Compare between crystal morphologies.
	* The software package should allow an easy comparison of morphologies predicted at different conditions and allow comparison between experimental and predicted crystal morphologies.
	* The tool should allow for a qualitative (or visual) comparison between predicted and experimental morphology by enabling import of microscopic or SEM images.
	* The tools should calculate key descriptors such as e.g. the particle’s aspect ratio or the March-Dollace parameter to ease comparison between predicted morphologies.
	* The tools should also allow overlay of the predicted morphology with the 3D graphical representation of the crystal obtained from single crystal analysis, defined by the Miller Indices of the prevailing crystal faces and their distances from the origin.

The development of a user-friendly interface is desirable. The guarantee of long-term support will be considered favorably. |

### Optional Hardware and Software Requirements

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| --- |
| As optional requirements, the developed software package should result in the ability to: * Predict the time trajectory of the shape from the shape/size of seeds.
* Capture effect of pH on the steady-state shape.
* Predict morphology of salts and co-crystals.
* Seamlessly integrate with commonly used programming frameworks (e.g., C, C++, Matlab, Python, Material Studio, COSMO-RS, etc.)
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### Availability Requirements

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| The expected output is a commercially available software package to provide crystal morphology prediction capabilities as specified in section 2.3.1.Timing for development and availability can be negotiated, but proposals that can deliver a prototype for evaluation within one (1) year of project start and a commercial software within two (2) years will be considered favorably. The vendor must be open to feedback on the roadmap to product delivery. |

### 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.
2. Thereafter, software will be available for licensing on a perpetual basis **[and subscription basis at the option of ETC participants]**. The vendor 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 vendor elects to make a software as a service (SaaS) alternative available.
4. 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 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 Crystal Morphology Prediction Tool.
* 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 the vendor from other potential collaborators.

The ETC will not provide individual feedback directly to RFI respondents beyond the status of their response to this 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 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 |

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| --- | --- | --- | --- |
| Feature | Requirement | Code | Vendor Comments |
| Software | Predict the steady-state morphology of free forms (Z’=1, 2 and more), solvates, hydrates with centrosymmetric and non-centrosymmetric growth units from the crystal structure. The minimal requirement is a qualitative prediction of the steady-state shape (e.g. needle, platelet, cube) The Wulff construction featuring all crystal faces present in the steady-state shape is preferred. |  |  |
| Software | Capture effect of supersaturation, temperature, solvent composition (single solvent as well as binary or ternary solvent mixtures) and impurities/additives on steady-state shape. |  |  |
| Compare between Crystal Morphologies |
| Software | The software package should allow an easy comparison of morphologies predicted at different conditions and allow comparison between experimental and predicted crystal morphologies.  |  |  |
| Software | The tool should allow for a qualitative (or visual) comparison between predicted and experimental morphology by enabling import of microscopic or SEM images.  |  |  |
| Software | The tools should calculate key descriptors such as e.g. the particle’s aspect ratio or the March-Dollace parameter to ease comparison between predicted morphologies. |  |  |
| Software | The tools should also allow overlay of the predicted morphology with the 3D graphical representation of the crystal obtained from single crystal analysis, defined by the Miller Indices of the prevailing crystal faces and their distances from the origin.  |  |  |
| General | The development of a user-friendly interface is desirable. |  |  |
| General | The guarantee of long-term support will be considered favorably. |  |  |
| Software - Optional | Predict the time trajectory of the shape from the shape/size of seeds. |  |  |
| Software - Optional | Capture effect of pH on the steady-state shape. |  |  |
| Software - Optional | Predict morphology of salts and co-crystals. |  |  |
| Software - Optional | Seamlessly integrate with commonly used programming frameworks (e.g., C, C++, Matlab, Python, Material Studio, COSMO-RS, etc.) |  |  |

## Estimated Timeline

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## Estimated Project Cost

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