

REQUEST FOR PROPOSALS

Cohesive Powder Feeding Modelling

October 7, 2020

Enabling Technologies Consortium™

Request for Proposals

Table of Contents

1 Introduction 3

[1.1 About Enabling Technologies Consortium™ (ETC) 3](#_Toc52978828)

[1.2 Request for Proposal 3](#_Toc52978829)

[1.3 Disclaimer 3](#_Toc52978830)

[1.4 RFP Contact Information 4](#_Toc52978831)

[1.5 Anticipated Time Frames for Evaluation and Selection Process 4](#_Toc52978832)

[2 Project Information 5](#_Toc52978833)

[2.1 Possible ETC Project Sponsors 5](#_Toc52978834)

[2.2 Description 5](#_Toc52978835)

[2.3 Cohesive Powder Feeding Model Requirements 8](#_Toc52978836)

[2.3.1 Necessary Requirements 8](#_Toc52978837)

[2.3.2 Optional Hardware and Software Requirements 9](#_Toc52978838)

[2.3.3 Software Availability Requirements 9](#_Toc52978839)

[2.3.4 Software Licensing Requirements 9](#_Toc52978840)

[3 Criteria for Evaluation 10](#_Toc52978841)

[4 Respondent Profile *(to be completed by RFP respondent)* 11](#_Toc52978842)

[4.1 Company/Organization Information 11](#_Toc52978843)

[4.2 Primary Contact Person 11](#_Toc52978844)

[4.3 Company/Organization Overview 11](#_Toc52978845)

[4.4 Parent Corporation and/or Subsidiaries 12](#_Toc52978846)

[4.5 Summary of Expertise 12](#_Toc52978847)

[4.6 Standards Certifications 12](#_Toc52978848)

[4.7 Goals and Strategic Vision 12](#_Toc52978849)

[4.8 Miscellaneous 13](#_Toc52978850)

[5 Company/Organization Response to RFP (*to be completed by RFP respondent)* 14](#_Toc52978851)

[5.1 Proposal 14](#_Toc52978852)

[5.2 Functional Requirements & Specifications 14](#_Toc52978853)

[5.3 Estimated Timeline 15](#_Toc52978854)

[5.4 Estimated Project Cost 15](#_Toc52978855)

[5.5 Software Availability and Support 16](#_Toc52978856)

# 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 Proposals (RFP) is intended to solicit interest in collaborating together on Cohesive Powder Feeding Model. The information collected during the RFP process along with subsequent interviews will be used for evaluation purposes, refinement of project plans, and selection of respondent(s) for collaboration. The goal of this collaborative project is the creation of a publicly available open source model.

## Disclaimer

The contents and information provided in this RFP are meant to provide general information to parties interested in developing the Cohesive Powder Feeding Model. The successful respondent 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 submissions but agrees not to publicly distribute the RFP responses outside the consortium 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](about:blank)

[http://www.etconsortium.org/](about:blank)

## Anticipated Time Frames for Evaluation and Selection Process

Issue RFP October 7, 2020

Questions on RFP due October 23, 2020

Responses to RFP due November 13, 2020

Invitations sent to respondents for presentation Nov – Dec 2020

Presentation to ETC by respondents December 2020

Select collaborator for project Dec 2020 – Jan 2021

***Please submit your response electronically to the above address. Responses received after November 13, 2020*** ***will not benefit from full consideration and may be excluded from the selection process.***

# Project Information

## Possible ETC Project Sponsors

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| Merck, Astra Zeneca, Genentech, Biogen, Eli Lilly, Bristol Myers Squibb, Pfizer, AbbVie, Takeda |

## Description

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| Continuous manufacturing is emerging as a reliable, robust, and even preferred means to produce oral solid dosage forms. As dosage unit potency is determined by the relative flowrates of the solid components, precise control of powder feed rates and levels of variability is essential to adequate control of product quality. Material is typically introduced into a continuous process by loss-in-weight (LIW) feeders. LIW feeders consist of a reservoir hopper filled with powder sitting above horizontal screws that rotate at a controlled speed. The entire assembly sits atop a scale and change in mass is recorded over time as the screws rotate and pull material from the hopper and dispense at the end of the screw. Screw design and speed can be altered to achieve a wide range of flow rates for a given material. However, consistent feed rates can be difficult to achieve due to the cohesive nature of materials in pharmaceutical formulations, most notably the active pharmaceutical ingredient (API). The API is typically in the micron particle size range where interparticle forces are similar to the gravitational force per particle. High feed rate variability might result in high unit dosage variability, which may pose challenges to continuously manufacture some oral formulations. In addition, as multiple kilograms of material are necessary to fill the reservoir hopper to relevant fill levels, proper evaluation for feasibility of continuous manufacturing may have to be delayed until later in process development. At this point switching to continuous processing from typical batch processing (or the reverse if the evaluation is unsuccessful) can be costly and delay development and filing timelines. Therefore, the objective of this proposal is to seek a partner to develop a model that scientists, operators, and engineers can use to predict feeding performance (flow rate and associated variability) of a granular material based on a short list of material properties, which can be measured on a small sample of material. Such a model can provide appropriate estimates of probabilities of success for continuous manufacturing early on during development.  This working group (WG) was formed as a sub-team of the Drug Product Working Group of the Enabling Technologies Consortium (ETC) to tackle an emerging issue relevant to the potential partners listed above. These partners aligned on the potential benefits of developing an industrially implementable model to reduce experimental work and material consumption required to predict feeding performance of cohesive powders. In addition, the partners request a tool to deploy the model to answer questions encountered during development. Such a tool should be simple to use in both collecting and providing the input parameters, as well as generating a usable result, which is based on a strong theoretical understanding of the physics determining the flow of cohesive powders.  The WG is sensitive to suggesting a specific design and unintentionally limiting ideas and/or responses to this RFP. However, for the purpose of stimulating responses to a technology space that is still emerging, the WG shares below a brief survey of potential solutions. The applicant is encouraged to consider these approaches, combinations of these approaches, and others that may have potentially been overlooked.   |  |  |  | | --- | --- | --- | | **Approach** | **Brief Description** | **Example Reference(s)** | | Semi-mechanistic | Predict feeder performance based on stress on the feed hoppers and mass balance around the entire system | [Link](https://www.web-tech.com.au/wp-content/uploads/Design-efficient-feeders.pdf)  [Link](https://pubs.acs.org/doi/abs/10.1021/acs.iecr.0c00420) | | Computational | Numerical simulations to fully develop the flow of powders with a range of properties through a given geometry | [Link](https://doi.org/10.1016/j.powtec.2014.01.062) | | Empirical | Calibrate feed profiles for a range of materials and fit feeding coefficients to the profiles based on material properties | [Link](https://rucore.libraries.rutgers.edu/rutgers-lib/57542/)  [Link](https://link.springer.com/article/10.1007%2Fs12247-010-9086-y) |   Each of the approaches has its benefits and limitations. For example, computational-only approaches require enormous computing resources and yet still cannot completely replicate the complicated multi-phase flow behavior of cohesive powders. Such computing resources may not exist at all partner companies and the expense and expertise to support and run these types of models may be prohibitive. Similarly, purely empirical approaches require large datasets following carefully planned and executed experimental protocols. Such experimental plans are often too difficult to execute with limited resources and tight development timelines. Semi-mechanistic approaches are of particular interest to the WG, as they can leverage strengths of each approach within suffering from most of the limitations. For example, a reduced order model calibrated via DEM simulations capable of accurately predicting average mass flow rate and variability from a limited set of material properties that can be measured from a powder sample of 50 g or less would be an attractive proposal.  The ETC will provide the following:   * A list of preferred physical property measurement techniques based on commonality across the industrial members, method robustness, and relevance of method for screw feeding application. * Typical ranges of material properties for powders of interest. * Context will be provided related to downstream manufacture. * A list of common materials to evaluate in order to properly span the range of cohesive powders. * Suggestions for typical data collection and analysis approaches. * Preference for model output and interface to increase usability at the member companies.   The vendor will develop the model and methodology to deploy the model and use it to assess the risk of feeding a cohesive material, delivering the following:   * A list of inputs and detailed methods to determine those inputs on a relatively small sample of powder. * Typical input values for the provided list of common materials. * Videos of feeding performance. * Data collection methodologies, including material conditioning, equipment setup, and method execution. * Model equations predicting average feed rate and expected variability, and calculated feed factor for given geometric configurations. * Strong preference for an open source tool along with source code to deploy the model to predict the performance of a system and material of interest.   It is expected that the vendor selected will have access to laboratory facilities with the following capabilities to generate testing data in order to develop the model:   * Commercial powder characterization equipment needed for the model input, such as powder flowability, density, particle size distribution, permeability, internal friction and wall friction coefficients, among others. * Commercial feeder equipment with standard screw designs and integrated LIW system. * Laboratory space for safe powder handling, including ventilated balance enclosures, scales, and cameras. * The developed model will be applicable to polydisperse, cohesive materials for feeding trials spanning a flow function coefficient (ffc) range from 1-4, such as micronized lactose, magnesium stearate, cohesive microcrystalline cellulose, micronized acetaminophen, spray dried polymer, and calcium carbonate, or the mixtures thereof. |

## Cohesive Powder Feeding Model Requirements

### Necessary Requirements

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| Necessary software   * Appropriate software with minimal access requirements or license management, for example open source downloadable code in Python, Matlab, or Excel, or a web-based portal for user access control and model execution. The source code for the tool must be easy to work on and maintain on a variety of operating systems and security protocols.   Data to be recorded   * For each material, a library of relevant material parameters is to be collected for model input, including proper documentation of environmental conditions. Material properties to consider include but are not limited to particle size, flowability, density, permeability, friction, and compressability. * For each experiment, mass dispensed with time is to be recorded across a range of processing conditions and equipment setup variations. This includes the period of hopper refill which is typically governed under volumetric control.   Data analysis   * This data is to be analyzed to yield an average powder flow rate, a calculated feed factor, and quantification of the level of variability.   Develop the model   * A model supplementing that available in the existing literature is to be developed and equations shared publicly with the scientific community for peer review and comment.   Build the tool   * Build, validate, and deliver a tool and a detailed workflow consisting of instructions to properly determine the input parameters from material characterization tests, execute the calculation, and draw conclusions from the results. Member companies request access to a prototype tool during development, with full access to the source code at the completion of the project period.   Model validation   * The model is not expected to be used to support manufacturing of product, thus validation refers to mathematical accuracy of the code and ability to adequately predict feeding performance. * Depending on modeling approach, the experimental data may need to be split into a calibration/training data set and a validation data set. * A series of round robin testing by the ETC Members may be executed to confirm the applicability of the methodology and model approach utilized on ETC member equipment with ETC member materials.   Model publication   * At the conclusion of the collaboration, the model will be published in a peer reviewed journal and/or scientific conference proceedings. * As part of the open source request, source code will be shared via a code repository. |

### Optional Hardware and Software Requirements

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| None |

### Software Availability Requirements

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| * Software will be distributed as an “open-source” package, available at no cost and hosted on a public repository. Preference will be given to a distribution strategy that allows for continued development by the scientific community. * Ownership of data generated on system resides with the customer. * 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 final software package within two (2) years of project start will be considered favorably. The vendor must be open to feedback on the roadmap to product delivery, including the approach to model testing and demonstration. |

### Software Licensing Requirements

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| The open-source software should be subject to one of the commonly used open-source licenses available with minimal restrictions and no copyleft provisions (e.g., Apache License 2.0, MIT License, the Unlicense). |

# Criteria for Evaluation

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| The ETC will prioritize a model that is simple to execute and maintain. The ETC encourages a range of approaches, including semi-mechanistic, computational, and empirical models as well as any other models that would meet the requirements.  Proposals can include collaborations between equipment producers, academic labs and other third parties. Data generated as part of this collaboration will be made available to all parties for use at their discretion. ETC members can also support modeling and experimental efforts. If such support is needed, the proposals should describe the scope of support needed.  The ETC will evaluate the responses to this RFP 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 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 the Cohesive Powder Feeding Model. * Show genuine interest in developing a tool that contributes to the scientific understanding and the improvement of prediction of cohesive powder feeding. * Support member companies in the local implementation of the tool. * 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. * Provide a list of the experimental equipment planned for use. * Support installation and deployment at the member companies.   Please note that ETC will not be able to provide individual feedback to RFP respondents on why their proposal was not selected. |

# Respondent Profile *(to be completed by RFP respondent)*

Please provide information to the following:

## Company/Organization Information

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| Company/Organization Name |  |
| Address |  |
| City |  |
| State |  |
| Country |  |
| Zip Code |  |
| Website |  |

## Primary Contact Person

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| --- | --- |
| 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

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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. 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.

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:

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| 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 |
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## 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.

For academic or non-profit partnerships, any monetary contributions by ETC should be considered “Direct Cost Only” awards.  Any indirect costs by the third party are subject to negotiation and not guaranteed.

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 (if applicable).  All projects awarded by ETC are fixed cost engagements paid in U.S. Dollars.

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## Software Availability 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 with ETC not assuming ownership of any intellectual property (IP) developed by the collaborator nor expecting 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.

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