

REQUEST FOR INFORMATION

Automation, Robotics, and AI-Enabled High Throughput Screening Platform for Wet Granulation*Test*

January 7, 2020

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 a Wet Granulation project. 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 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 Automation, Robotics, and AI-Enabled High Throughput Screening Platform for Wet Granulation. 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 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. 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 January 7, 2020

Questions on RFI due January 21, 2020

Responses to RFI due February 18, 2020

Invitations sent to respondents for presentation March 2020

Presentation to ETC by respondents March – April 2020

Inform respondents of next steps May 2020

***Please submit your response electronically to the above address. Responses received after February 18, 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, Biogen, Bristol-Myers Squibb, Eli Lilly, Genentech, Takeda |

## Description

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| High shear wet granulation (HSWG) is an established pharmaceutical technology that is currently carried out in one batch at a time which creates the following limitations: (a) Very limited number of batches can be manufactured during product development because of containment requirements for relatively high powder loads and time required for processing. This leads to:1. High API, development time, and FTE requirements, which are opposed to current industrial trends to try to minimize API and time consumption in early drug development.
2. Low resolution Design of Experiment (DoE) studies and inability to test process and formulation variables to identify the critical parameters/factors.
3. Statistical significance interpretation in the DoE studies is based on variability at one point of the DoE design – typically center point. The random variation is likely different at different points in the DoE space and an ability to run replicates at different points would provide greater scientific and statistical confidence in the DoE results.

(b) Difficulty in assessing the impact of bulk powder parameters to process scale-up in the context of process analytical technologies (PAT) that can be applied to larger scale manufacturing equipment. Miniaturized granulator might allow measurement of: (1) Torque using a calibrated shaft. (2) Powder wettability and flow parameters. (3) Rapid assessment of technology options for enabling new chemical entities and newer modalities of drugs through wet granulation routes in early stages of drug development.A miniaturized, high throughput, multi-container granulator is proposed to address current limitations in the industrial practice of wet granulation (WG). |

## Wet Granulation Requirements

### Necessary Hardware and Software Requirements

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| Carry out wet granulation process in its entirety.Dispense powders [(including fillers (1-4), binders (1-3), disintegrants (1-3), other excipients (1-3), and API (1-2)]. Numbers in parenthesis indicate number of powders that the system should be able to dispense.Accuracy ± 2% by weight.Weight range 10 mg to 2 g for each.Some excipients may be hygroscopic.The requirement for number of powders to be dispensed would vary by project. For scouting experiments, being able to use a variety of excipients would be helpful. For someone designing this system, it might be helpful to design for the high end of number of powders that may be used.Range of batch sizesThe above dispensed quantity estimations are designed to be able to support small batch sizes. When making a 2 g batch with 1% disintegrant, the quantity would be 20 mg. While the ETC project team has listed 10 mg here, the team is willing to consider equipment capabilities . Larger batch sizes will be viewed favorably depending on API availability. Thus, being able to support a range of batch sizes would be of value.Blade mixingBe able to mix at different tunable speeds.Liquid addition during mixingAccuracy ± 2% by weight.Flow rate 0.10 mL to 1.00 mL per minute.Liquid addition method could be syringe injection or an alternative that can allow control with respect to drop size, e.g. the Litster dimensionless spray flux, or otherwise ability to distribute better within the powder bed. Be able to manufacture at different tunable pressure/shear forces acting on the powder mixture. Possible options may include:Impeller speed to simulate lab/pilot/large scale.Impeller blade design can be a variable if interchangeable blades with different imparted shear can be used.Variable load on the enclosed vessel that contains powder.Adjustable volume of the enclosed vessel that contains powder (essentially generating pressure after powder is loaded).Being able to measure pressure is important.The liquid addition or distribution process should not be hindered.PAT. Continuous inline monitoring, storage, and retrievability of information including:Impeller torquePower consumptionFlow force of the granulesNeeds integration of the Drag Force Flow (DFF) sensorDrying the granules after processing. Options to enable this may include:Use of vacuum with or without heat and mixing of the impeller after processing.Drying powder material, removing powder material into a separate container, washing and drying of the granulating vessel, followed by next cycle of operation with the same vessel in place should be possible with this option.Transfer of the contents to another vessel for drying, the other vessel being customized and enabled separately to effect drying by the use of vacuum, fluidized air bed, or tray drying.Change of granulating vessel to a fresh one to enable processing of the next batch, while the old vessel is transferred to a drying setup.Preferred approach instead of powder transfer to avoid material loss due to adhesion to vessel. On a percentage basis, this loss could be a significant amount at these very low batch sizes.Adaptive DoE* Utilization of AI, machine learning, and/or computer algorithms to enable design of a series of experiments in a succession, feeding off of the data from previous experimental runs, that can be carried out in an automated fashion using robotics without human intervention.

Intuitive, graphic user interface with real time data graphics. These data can include, for example, below parameters as a function of time:Impeller torqueImpeller power consumptionImpeller speedDrag force signal (DFF sensor)Absolute value and percentage of liquid addedProgrammable execution of multiple batches Automated profiling of desired response space with computer-generated input variable options * These variables may include qualitative and quantitative composition, and process ranges within the boundaries specified by the user and technical equipment capability.

Mixing dynamics can be monitored using colored particles and video camera.Assessment of quality of granules and conformance with expected patterns of changes to input variables. Attributes to be measured include the following. These attributes are to be measured in dry granules as off-line test for verification that the system is performing as expected.Granule sizePorosityDensityInput variables that may be changed include:Liquid amountLiquid addition rateBinder amountOther offline assessments of granules may include:Tablet compaction (including friability and hardness testing)* Tablet disintegration and dissolution testing
 |

### Optional Hardware and Software Requirements

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| The dispensed liquid can be a viscous binder solution instead of water.Viscosity should be less than 20 cP.The dispensed liquid can be ethanol instead of water. Multiple vessel processing at a time or one vessel processing at a time. |

### Availability Requirements

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| During the project ETC anticipates the creation and availability of prototype(s) for evaluation to aid in the design of the instrument. Upon conclusion of the project, it is expected that a commercial version of the instrument will be available within approximately 2 years following project completion.  |

### 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 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 Automation, Robotics, and AI-Enabled High Throughput Screening Platform for Wet Granulation.
* 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 them 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 |
| Wet Granulation Process | Dispense powders [(including fillers (1-4), binders (1-3), disintegrants (1-3), other excipients (1-3), and API (1-2)]. Numbers in parenthesis indicate number of powders that the system should be able to dispense.Accuracy ± 2% by weight.Weight range 10 mg to 2 g for each.Some excipients may be hygroscopic.The requirement for number of powders to be dispensed would vary by project. For scouting experiments, being able to use a variety of excipients would be helpful. For someone designing this system, it might be helpful to design for the high end of number of powders that may be used.Range of batch sizes* The above dispensed quantity estimations are designed to be able to support small batch sizes. When making a 2 g batch with 1% disintegrant, the quantity would be 20 mg. While the ETC project team has listed 10 mg here, the team is willing to consider equipment capabilities . Larger batch sizes will be viewed favorably depending on API availability. Thus, being able to support a range of batch sizes would be of value.
 |  |  |
| Blade mixing | Be able to mix at different tunable speeds. |  |  |
| Liquid addition during mixing | Accuracy ± 2% by weight.Flow rate 0.10 mL to 1.00 mL per minute.* Liquid addition method could be syringe injection or an alternative that can allow control with respect to drop size, e.g. the Litster dimensionless spray flux, or otherwise ability to distribute better within the powder bed.
 |  |  |
| Manufacture at different tunable pressure/shear forces acting on the powder mixture | Possible options may include:Impeller speed to simulate lab/pilot/large scale.Impeller blade design can be a variable if interchangeable blades with different imparted shear can be used.Variable load on the enclosed vessel that contains powder.Adjustable volume of the enclosed vessel that contains powder (essentially generating pressure after powder is loaded).Being able to measure pressure is important.The liquid addition or distribution process should not be hindered. |  |  |
| PAT | Continuous inline monitoring, storage, and retrievability of information including:Impeller torquePower consumptionFlow force of the granulesNeeds integration of the Drag Force Flow (DFF) sensor |  |  |
| Drying the granules after processing | Options to enable this may include:Use of vacuum with or without heat and mixing of the impeller after processing.Drying powder material, removing powder material into a separate container, washing and drying of the granulating vessel, followed by next cycle of operation with the same vessel in place should be possible with this option.Transfer of the contents to another vessel for drying, the other vessel being customized and enabled separately to effect drying by the use of vacuum, fluidized air bed, or tray drying.Change of granulating vessel to a fresh one to enable processing of the next batch, while the old vessel is transferred to a drying setup.Preferred approach instead of powder transfer to avoid material loss due to adhesion to vessel. On a percentage basis, this loss could be a significant amount at these very low batch sizes. |  |  |
|  | Adaptive DoE |  |  |
| AI, Machine Learning, and/or Computer Algorithms | Utilization of AI, machine learning, and/or computer algorithms to enable design of a series of experiments in a succession, feeding off of the data from previous experimental runs, that can be carried out in an automated fashion using robotics without human intervention. |  |  |
| Intuitive, graphic user interface with real time data graphics | These data can include, for example, below parameters as a function of time:Impeller torqueImpeller power consumptionImpeller speedDrag force signal (DFF sensor)Absolute value and percentage of liquid added |  |  |
|  | Programmable execution of multiple batches  |  |  |
|  | Automated profiling of desired response space with computer-generated input variable options  |  |  |
|  | These variables may include qualitative and quantitative composition, and process ranges within the boundaries specified by the user and technical equipment capability. |  |  |
|  | Mixing dynamics can be monitored using colored particles and video camera. |  |  |
| Assessment of quality of granules and conformance with expected patterns of changes to input variables. | Attributes to be measured include the following. These attributes are to be measured in dry granules as off-line test for verification that the system is performing as expected.Granule sizePorosityDensityInput variables that may be changed include:Liquid amountLiquid addition rateBinder amountOther offline assessments of granules may include:Tablet compaction (including friability and hardness testing) |  |  |
|  | Tablet disintegration and dissolution testing |  |  |
| Optional | The dispensed liquid can be a viscous binder solution instead of water.Viscosity should be less than 20 cP. |  |  |
| Optional | The dispensed liquid can be ethanol instead of water. Multiple vessel processing at a time or one vessel processing at a time. |  |  |

## Estimated Timeline

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## Estimated Project Cost

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