

REQUEST FOR INFORMATION

Sticking Assessment Tool

October 20, 2022

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 sticking assessment 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 sticking assessment 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. 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 RFI October 20, 2022

Questions on RFI due November 7, 2022

Responses from potential collaborators due December 15, 2022

*\*Dates subject to change without notice*

***Please submit your response electronically to the above address. Responses received after December 15, 2022*** ***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, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly, Genentech, GSK, Merck, Novartis, Pfizer, Takeda, Zoetis |

## Description

### Background

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| Sticking during tablet compaction is a phenomenon that results in the adherence of material onto the punch faces and die wall. The initial adherence of material onto the punch faces can appear as a light dusting of fine powder or as a fine film coating. The quantity of adhered material on the punch faces can accumulate with successive compression cycles. The occurrence of this phenomenon during tablet manufacture can decrease tablet quality, bring manufacturing campaigns to a halt and result in expensive mitigation strategies. Sticking is a multi-faceted phenomenon because there are numerous factors that can simultaneously contribute to the issue. Sticking has been shown to be affected by several factors including compression speed, compression force, lubricant, powder processing conditions, punch surface chemistry, punch surface roughness, punch geometry, humidity, moisture, temperature, melting point and particle size (1,2).During early-stage drug development, the quantity of active drug substance is limited, resulting in only a few dozen tablets being produced to support development activities. Sticking is usually not observed during this stage and product development progresses to identify the formulation components, powder processing conditions and compaction parameters to produce tablets. Typically, it is not until a large-scale manufacturing campaign involving the production of several thousand tablets during which sticking is visually observed on the punch tip. During this stage of development, there is little room to adjust formulation composition or instrument parameters to mitigate sticking.Over the past decade, several methods to assess sticking were employed by various research groups. In general, these methods can be categorized as either directly or indirectly measuring sticking. Methods that directly attempt to measure sticking, do so by making measurements directly on the material stuck to the punch tip. Indirect methods are correlative and attempt to estimate or predict the severity of sticking based on measurements of other paraments that are related to sticking. To date, there has not been an indirect method that demonstrates the ability to estimate or predict sticking with high reliability. This lack of reliability with indirect methods is largely due to the multi-faceted complexity of the phenomenon of sticking as alluded to earlier. Due to this reason, many researchers use the direct assessment methods on the adhered material after sticking had occurred. A review of the direct and indirect methods are discussed by Tsosie et all (3). Although direct methods in general are more reliable, they also exhibit various disadvantages.In general, direct methods can be categorized by the timing of the sticking assessment. The timing can be live, mid-production or post-production. Live methods do not require stopping the tablet press and can make non-destructive live measurements of sticking during tablet production. The adhesion punch (4) that measures the force of punch-tablet detachment and the laser sensor (5) that measures the changes to punch reflectivity are examples of such methods. In contrast, mid-production methods require stopping the press intermittently to non-destructively assess sticking before continuing tablet production. Such methods may not properly capture time-related phenomena associated with sticking such as heat. Perhaps the most popular technique in this category is the removable punch tip method that allows for the measurement of weight of material adhered to the punch tip. The simplicity and reliability of this method is attractive; however, it typically requires several grams of powder in order to accumulate a weighable quantity of adhered material. In contrast, post-production methods are usually destructive to the adhered material and do not allow the continuation of sticking assessment with further compression cycles. Some direct methods such as microscopic analyses of area coverage by an optical (6) or Scanning Electron Microscope (SEM) (3), content quantification by High Performance Liquid Chromatography (HPLC) (7) or assessment of punch reflectivity by laser (5) can offer greater sensitivity but present disadvantages in other areas.

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| **Method** | **Live/mid/post Prod.** | **Destructive** | **Remarks** |
| Optical | Mid-production | Maybe | Requires press stoppage |
| SEM | Post-production | Likely | Complex technique |
| HPLC | Post-production | Yes | Destructive to adhered material |
| Removable tip | Mid-production | Unlikely | High material demand |
| Laser | Live | No | Design challenges |
| Adhesion punch | Live | No | Ambiguity in measurements |

Currently, none of the empirical methods used in literature have been developed to predict sticking. Therefore, there is an urgent need for an empirical method/tool to quantifiably detect and assess the propensity of sticking for a given powder during the early stages of drug development with minimal material and one that is practical in complexity and accessibility.**References:**1. Chattoraj, Sayantan, et al. “Sticking and Picking in Pharmaceutical Tablet Compression: An IQ Consortium Review.” *Journal of Pharmaceutical Sciences*, vol. 107, no. 9, Sept. 2018, pp. 2267–82. [*www.jpharmsci.org*](file:///C%3A%5CUsers%5Cvergisjm%5CAppData%5CLocal%5CMicrosoft%5CWindows%5CINetCache%5CContent.Outlook%5CQP8JCUU3%5Cwww.jpharmsci.org), <https://doi.org/10.1016/j.xphs.2018.04.029>.
2. Thomas, James V. *Evaluation and Study on the Adhesion of Powder onto Punch Faces during Tablet Compaction*. Drexel University, 2015.
3. Tsosie, Henrietta, et al. “Scanning Electron Microscope Observations of Powder Sticking on Punches during a Limited Number (N<5) of Compactions of Acetylsalicylic Acid.” *Pharmaceutical Research*, vol. 34, no. 10, Oct. 2017, pp. 2012–24. *link.springer.com*, [<https://doi.org/10.1007/s11095-017-2186-3>](https://doi.org/10.1007/s11095-017-2186-3).
4. Mullarney, M. P., et al. “Assessing tablet-sticking propensity by weighing accumulated powder on a removable punch tip.” *Pharmaceutical Technology*, vol. 36, no. 1, 2012, pp. 57–62.
5. Thomas, James, and Antonios Zavaliangos. “An In-Line, High Sensitivity, Non-Contact Sensor for the Detection of Initiation of Sticking.” *Journal of Pharmaceutical Innovation*, Dec. 2018. *Springer Link*, <https://doi.org/10.1007/s12247-018-9367-4>.
6. Mollereau, Germinal, et al. “Image Analysis Quantification of Sticking and Picking Events of Pharmaceutical Powders Compressed on a Rotary Tablet Press Simulator.” *Pharmaceutical Research*, vol. 30, no. 9, Sept. 2013, pp. 2303–14. *CrossRef*, <https://doi.org/10.1007/s11095-013-1074-8>.
7. McDermott, Todd S., et al. “A material sparing method for quantitatively measuring tablet sticking.” *Powder Technology*, vol. 212, no. 1, Sept. 2011, pp. 240–52. *ScienceDirect*, <https://doi.org/10.1016/j.powtec.2011.05.023>.
 |

## Sticking Assessment Tool Requirements

### General Requirements

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| The developed Sticking assessment tool should have the ability to: * Demonstrate tool/technique can detect/measure sticking when material doesn't visibly show sticking at early stages of tablet development.
	+ Measure sticking with as minimal material as possible (ideally <10g of active compound).
* Must measure sticking for any given powder (including pure active compound, active powder blend, processed powders - granules).
* Quantitatively measure the intensity of sticking between material (ex- composition, particle size, hardness) and instrument conditions (ex- speed, pressure, humidity).
	+ Test materials that are both known to stick and those that are not.
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### Optional Hardware and Software Requirements

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| As optional requirements, the developed electronic device or software package should result in the ability to: * Device capable of securely capturing data in an open and/or standardized data format and readily accessible for processing software (Excel, Spotfire, etc.)
* Seamlessly integrate with commonly used programming frameworks (e.g., C, C++, MATLAB, VBA, Python, etc.)
* Software code must be open source.
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### Availability Requirements

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| * The expected output is a commercial device that is adequately sensitive, can quantitatively measure sticking and predict its propensity for a given formulation during large scale manufacturing.
* A prototype of the device should be made available free of charge on loan to each ETC company for on-site evaluation.
* Any accompanying or required software should be made available free of charge to each ETC company for on-site evaluation.
* Timing for development and prototype availability can be negotiated, but proposals that can deliver a prototype for evaluation within one (1) year of project start will be considered favorably.
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### Licensing Requirements for Commercialized Product

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| 1. A prototype of the device and if applicable, any accompanying software will be licensed to ETC participants at no cost during (i) development and (ii) a mutually agreed beta testing period.
2. Thereafter, device/software will be available for licensing on a perpetual basis or for purchase. The vendor shall make available industry-standard support for the device and any accompanying software.
3. Any accompanying software shall be available for self-hosting by (or on behalf of) the ETC participants even if the vendor elects to make software as a service (SaaS) alternative available.
4. Ownership of data generated using the device/software during development phase and in future with commercial device/software will reside 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 Sticking Assessment 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 are related 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)*

*We encourage all respondents to review the* [***Enabling Technologies Consortium FAQ***](https://www.etconsortium.org/_files/ugd/d6fa33_6713713d571d490ba451f348126fcc35.pdf)*to aid in the development of your response to the RFI.*

## 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:

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| --- | --- |
| A | Current capability |
| 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 |
| Device | Simple and readily accessible tool to measure sticking. |  |  |
| Device | Detect/measure sticking with high sensitivity. |  |  |
| Device | Ability to measure the relative magnitude of sticking between powder blends. |  |  |
| Device | Ability to measure the relative magnitude of sticking with varying compaction parameters. |  |  |
| Device | Ability to assess the propensity of sticking for a given powder with <10 grams of active compound. |  |  |
| Method | Establish a method to assess consistency of baseline performance of device. |  |  |
| Method | Establish a method specifying punch tip preparation and testing process for reproducible measurements of sticking. |  |  |
| Method | Ability to predict propensity of sticking during large scale tablet manufacturing. |  |  |
| Software | Any accompanying software must be readily accessible and deployable. |  |  |

## 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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