**Check One: ☒Project ☐Review ☐Collaboration**

 **☐Workshop ☐Other**

| **Descriptive Title** | Mechanical activation of organic crystalline materials during breakage in dry systems |
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| **Working Title[[1]](#footnote-0)** | Mechanical activation of crystalline materials |
| **Technical Area[[2]](#footnote-1)** | Size Reduction |
| **Date** | 17th June 2025 |
| **Short Description** | **Problem statement**Particle breakage of organic crystalline materials is often associated with mechanical activation and negative implications on process performance and product attributes. Typical issues associated with this behavior are (a) limited throughput, limitations in product fineness and caking in process operations, and (b) particle size growth, solid form transformation, loss in crystallinity, and chemical degradation in manufactured products. This is industrial relevant for processes including body breakage of organic crystalline materials, mainly dry milling and compression. The fundamental problem is little understood (Descamps and Willart 2016, Iyer et at. 2023). Industry can handle these issues in most cases only by trial-and-error approach.**Scientific scope**Mechanical activation and the corresponding material behavior of organic crystalline materials following from the initiation of breakage, including preferable crack planes, evolution of temperature, mechanochemical reaction, formation of disorder, relaxation/recrystallization, and atmospheric interactions is in the scientific scope of this project proposal. This is an interdisciplinary topic across particle breakage, crystallography, mechanochemistry, organic chemistry and solid-state science. The work by Boldyrev and co-workers on mechanical activation (Boldyrev 2018) and Beyer and Clausen-Shaumann on activation of covalent bonds (Beyer and Clausen-Shaumann 2005) should be considered as starting points.**Motivation**Creation of the fundamental understanding on the dynamic material behavior following from the initiation of breakage and addressing the relationship between input material attributes, mechanical stress characteristics/atmospheric conditions and physical and chemical product material attributes would lead to opportunities for early-on risk assessment and guiding directions for process and product improvement in industry.**References*** [Beyer and Clausen-Shaumann, *Chem. Rev.* 105 (2005) 2921-2944](https://doi.org/10.1021/cr030697h)
* [Boldyrev, *Her. Russ. Acad. Sci.* 88 (2018) 142-150](https://doi.org/10.1134/S1019331618020016)
* [Descamps and Willart, *Adv. Drug Deliv. Rev.* 100 (2016) 51-66](https://doi.org/10.1016/j.addr.2016.01.011)
* [Iyer et al., *J. Pharm. Sci.* 112 (2023) 1539-1565](https://doi.org/10.1016/j.xphs.2023.02.019)
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| **Objectives** | The project should have both experimental and computer-based components. The objectives of this project are* **Deconvolute the fundamental principles, main impacting parameters and their interrelation** considering (a) physical and chemical input material attributes, (b) stress conditions, and (c) following from the initiation of breakage, preferable crack planes, mechanochemical reaction, formation of disorder, relaxation/recrystallization, and atmospheric interactions on (d) the physical and chemical product material attributes.
* **Establish a validated workflow for the risk assessment** of process induced transformations on the physical and chemical product material attributes considering different mechanical stress and atmospheric conditions. The workflow should be based on analytical data from the input material attributes, scenarios for mechanical stress and atmospheric conditions, and a computer-based risk assessment, ideally derived from first-principles models, of process induced transformations of the physical and chemical product material attributes. The workflow should minimize, ideally prevent from processing effort beyond the analytical and computational effort.
* **Establish a validated workflow to direct optimization** for the reduction/prevention of process induced transformations of the physical and chemical product material attributes. The workflow should build upon the previous objective and derive a process safe space for mechanical stress and atmospheric conditions to minimize/prevent process induced transformations of the physical and chemical product material attributes by a computer-based framework.
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| **Scope** | * **Organic crystalline materials** (aligned with industrial project liaisons) of single, non-agglomerated particles; particle shape as applicable; brittle fracture characteristics of initial solids material
* **Solids material**: Particle size average range of 100 to 500 µm and temperature of about -20 to 40°C, when appropriate
* **Stress conditions**: Compression stress between rigid walls (single particle and powder bed) and impact stress against rigid wall, both at different levels of stress, strain rate and multiple stress events, when appropriate
* **Atmospheric conditions**: Temperature of about -20 to 40°C, rel. humidity of about 0 to 80% rh and nitrogen and air gas, when appropriate
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| **Recommended Contractors (2 or 3)** |
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1. Title used in meeting agendas and file archives [↑](#footnote-ref-0)
2. One or more from the following list: W = wet systems; D = dry systems; F = particle formation; SR = size reduction; M = modeling; SE = systems engineering [↑](#footnote-ref-1)