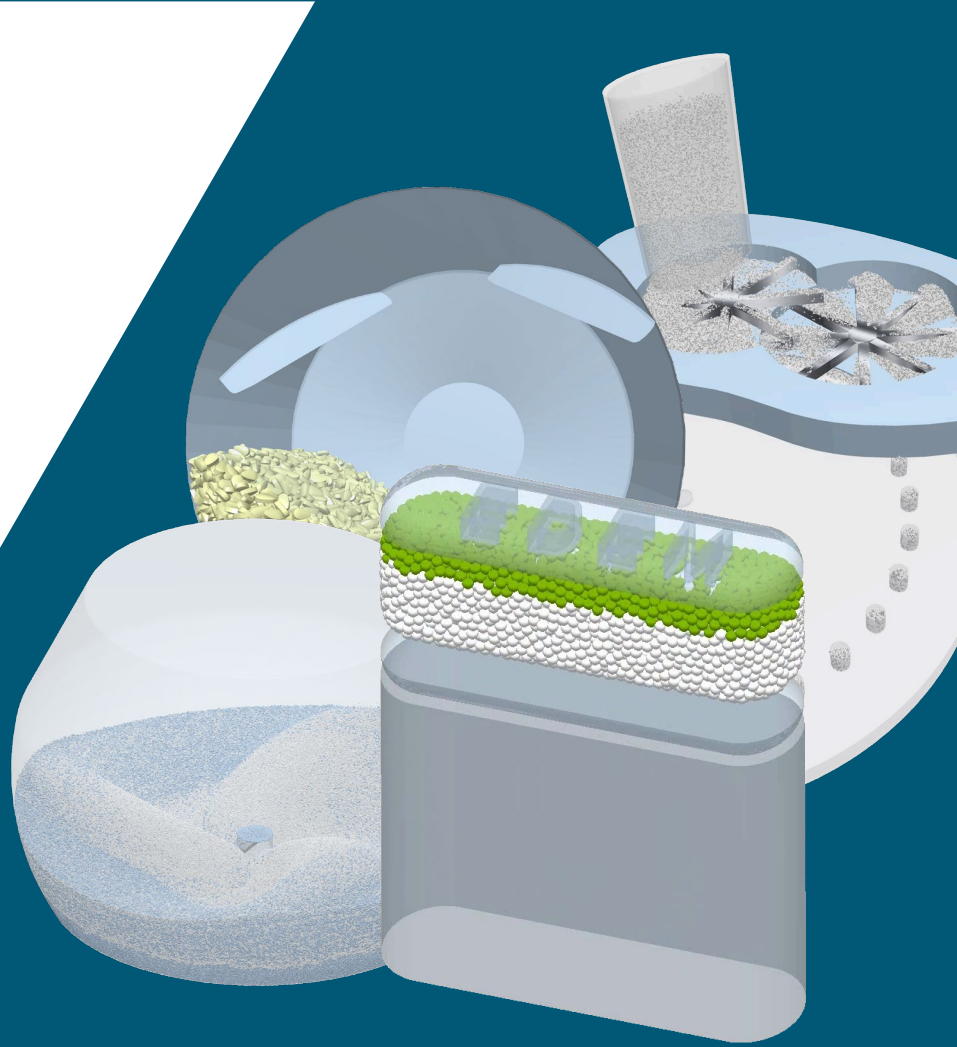
EBOOK

Applications of EDEM for Pharmaceutical Manufacturing Processes



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Context and Challenges

Over 75% of all pharmaceutical products are in the solid dosage form and particulates are involved in almost every stage of the manufacturing process. Efficient handling and processing of particulates is critical to profitable manufacture of pharmaceutical products.

A typical drug manufacturing work-stream involves several unit operations such as blending, granulation, milling and coating, all of which involve particulates in the form of powders, capsules, or tablets. Common problems areas include poor mixing, uneven coating, non-uniform die filling and pill breakage. These can have a strong impact on the productivity of operations and the final product quality.

An inefficient mixing process for instance can negatively impact downstream processes such as granulation, milling and tableting. It can adversely impact product quality and result in potential batch failure and added costs due to production delays.

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Context and Challenges

When handling powders and particulates, process engineers and operators are also faced with many questions such as what device/design to use for a given powder, what mixing speed will help achieve a uniform blending, what is the maximum fill level possible, etc.

Understanding the behavior of powders and bulk solids is critical for minimizing these problems, ensuring manufacturing efficiency and avoiding product quality issues.

Traditionally, process engineers have had to rely on empirical methods such as physical testing to understand their systems and operations. These methods are time and labor intensive as well as expensive and they do not provide all the answers.

To overcome these challenges new and fundamental insight into the micro and macro mechanics of pharmaceutical processes is required - beyond what is obtainable through experimentation or classical numerical methods alone.

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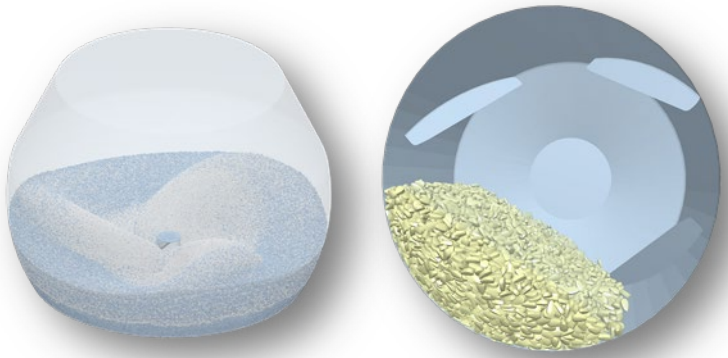
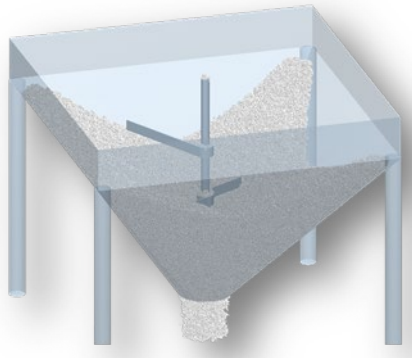
Introducing EDEM simulation technology

Powered by the Discrete Element Method (DEM), EDEM software enables companies to simulate the complex behavior of particulate solids at the individual particle level - providing information on their micro and macro-mechanical behavior which is difficult or impossible to obtain experimentally.

This enables the detailed analysis of processing operations for a wide range of materials, from powders to tablets and beyond.





EDEM is a powerful predictive tool for simulating pharmaceutical manufacturing processes including powder mixing, tablet coating, die filling, granulation, milling and more.

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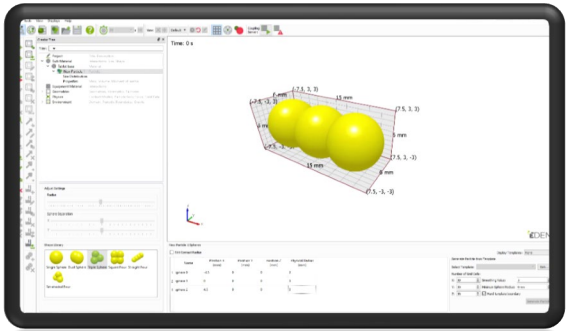
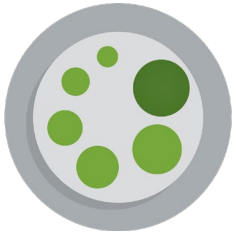
Overview of EDEM components

EDEM CREATOR

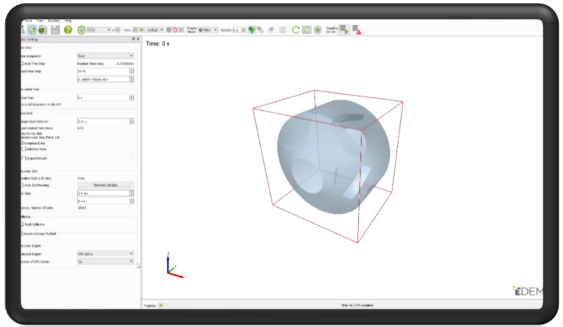
Create materials, particles, geometry and physics models





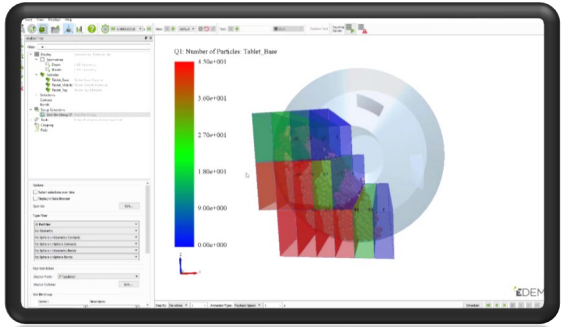
EDEM SIMULATOR

Define run-time and simulation settings and process the simulation on CPU or GPU



EDEM ANALYST

Visualize your results, create videos, graphs and export data



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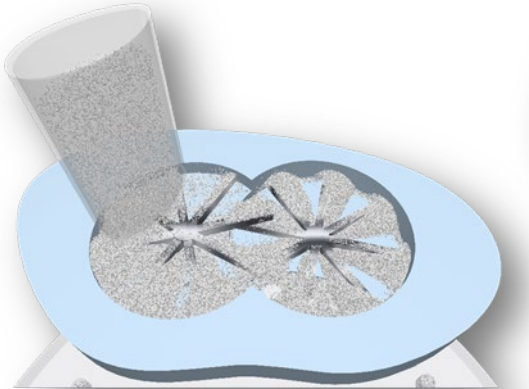
Benefits of EDEM simulation

By including EDEM in their design workflow, researchers, scientists and engineers are able to:

- **Obtain** a greater understanding of powder behavior
- **Increase** process efficiency and capability
- **Reduce** costs and dependence on physical prototyping and testing
- **Drive** product and process innovation
- **Improve** scale-up procedures
- **Improve** product quality
- **Get** products to market quicker



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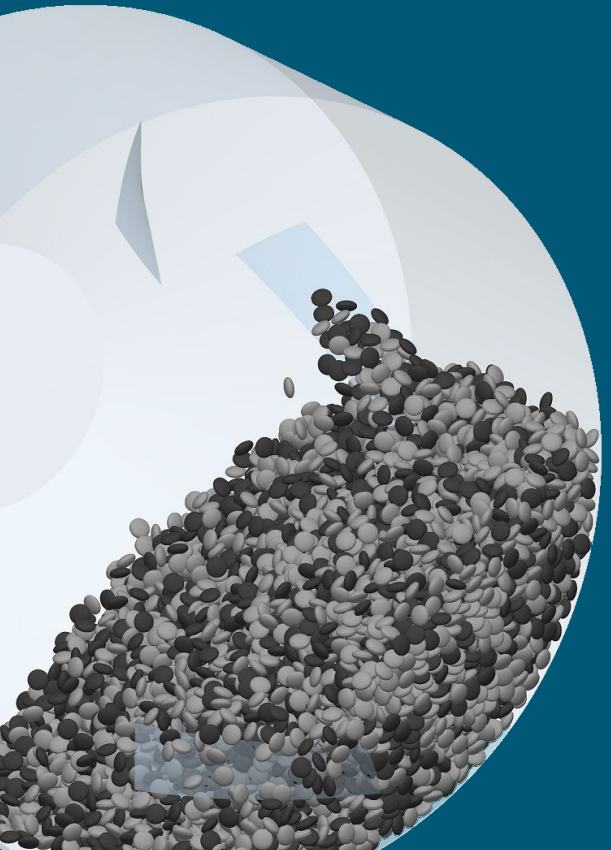

APPLICATION EXAMPLES

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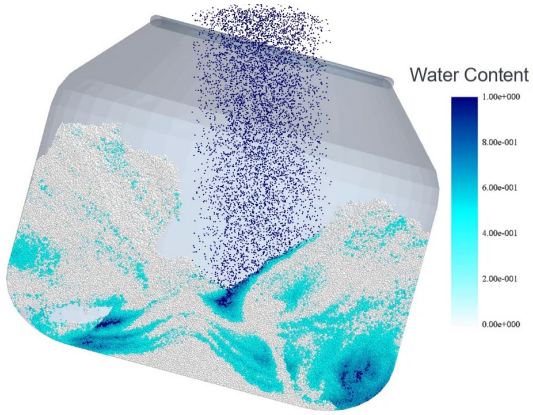
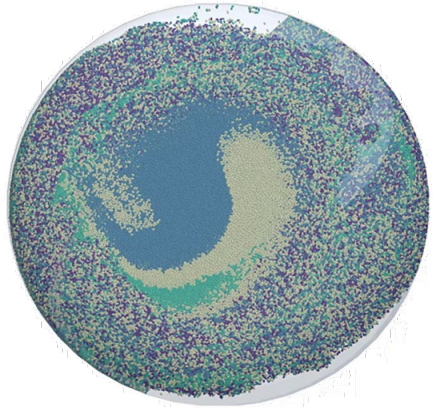
Mixing

- **Understand** mixing and segregation mechanics by analyzing:
  - Convective and diffusive patterns
  - Particle trajectories and velocities
  - The evolution mixture component concentrations
- **Identify** dead zones
- **Predict** mixing rates
- **Inform** scale-up



Wet mixing

Bin blender
(courtesy of Pfizer)



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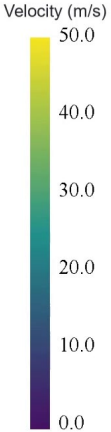
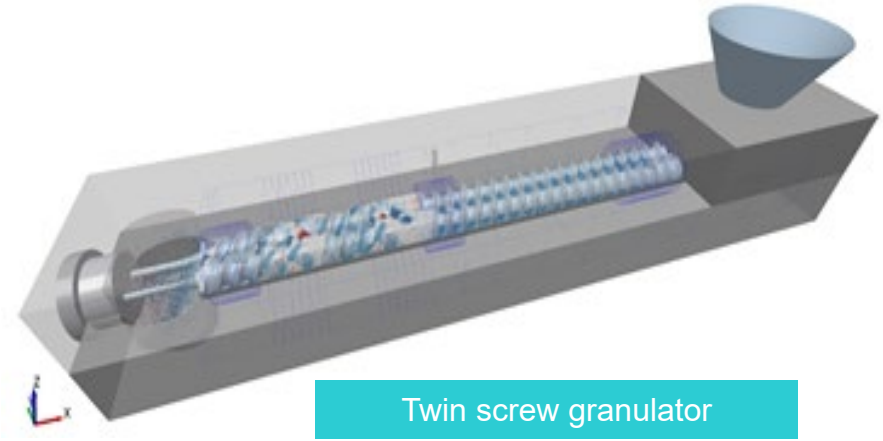
Changing particle size - Agglomeration and Comminution

- **Understand** agglomeration and comminution by analyzing:
  - Micro-mechanical forces, stresses and velocities
  - The spatial and temporal evolution of agglomerate sizes
- **Determine** the effect of material properties and operational parameters on process performance
- **Predict** and **optimize** performance



Pin mill



Twin screw granulator

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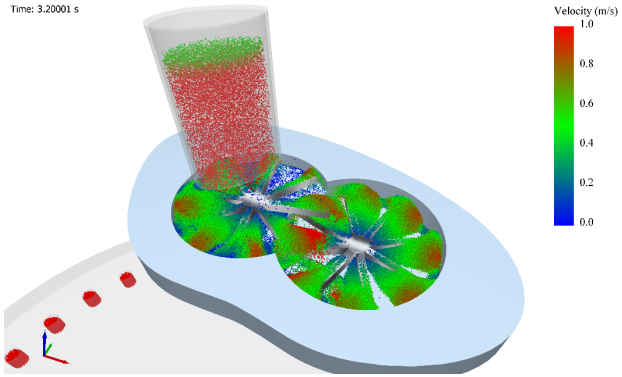
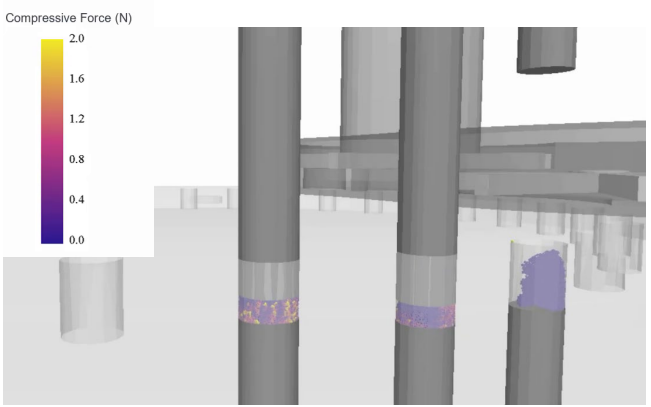
Die Filling and Tablet Compaction

- **Understand die filling** by analyzing:
  - Particle velocities and trajectories
  - Segregation and agglomeration
  - Pre-compaction porosity distribution
- **Understand compaction** mechanics by analyzing:
  - Particle forces and bulk stresses
  - The spatial and temporal evolution of porosity and tortuosity
- **Predict** structural defects
- **Study** the effect of powder properties and operational parameters on the final product quality attributes



Die filling



Tablet compaction

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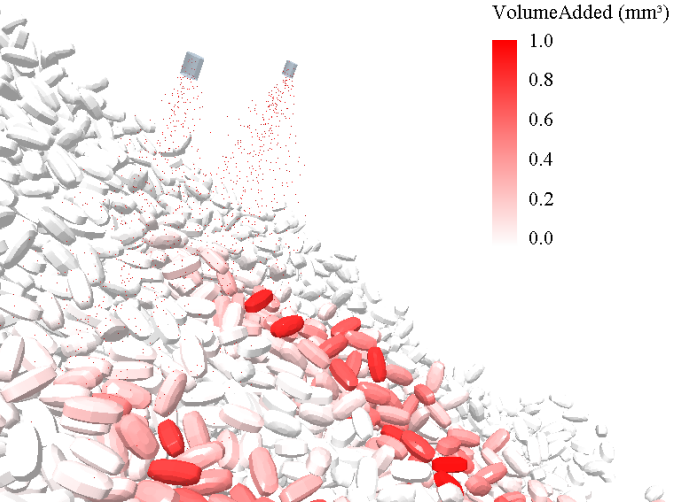
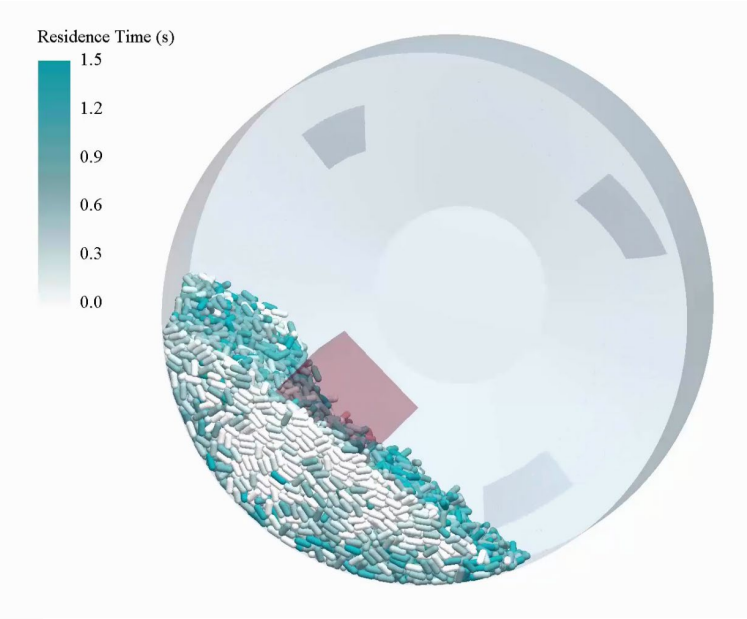
Tablet Coating

- **Predict** the spatial and temporal evolution of tablet coating
- **Examine** effect of spray pattern, spray rate, fill level and rotational speed
- **Compare** different tablet shapes
- **Optimize** design with respect to coating uniformity





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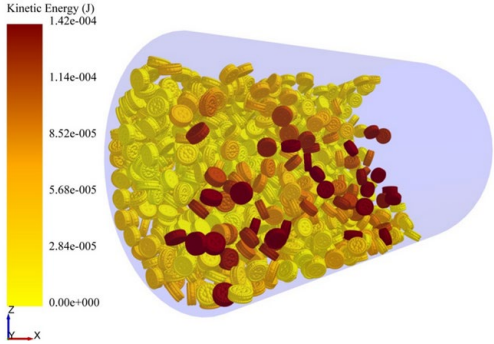
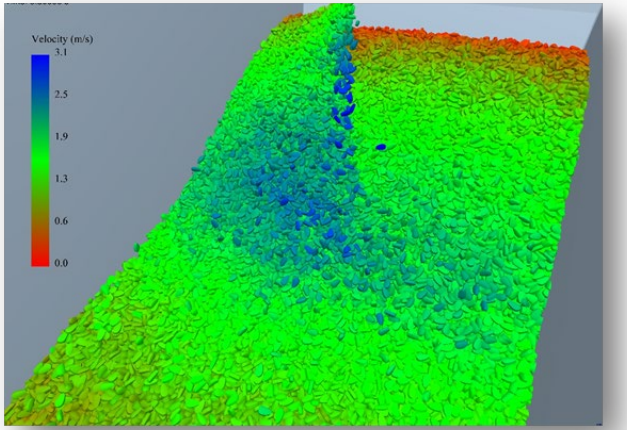
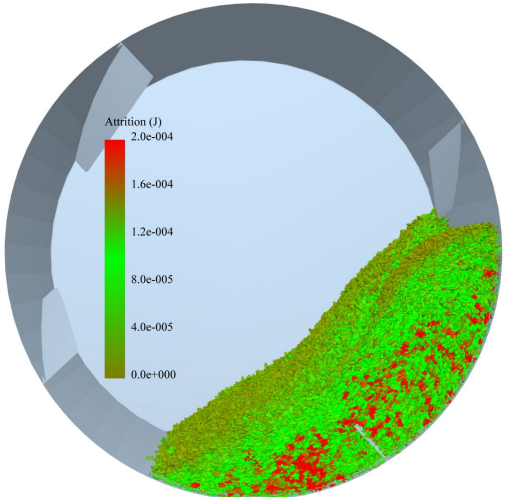
Tablet Coating - attrition

- **Investigate** attrition and breakage of tablets during transportation
- **Ensure** no defective tablets are commercialized to meet quality standards
- **Predict** and assess risk of tablet attrition based on:
  - pan speed
  - tablet volume
  - fill level



Damaging of tablets within a tumbling drum





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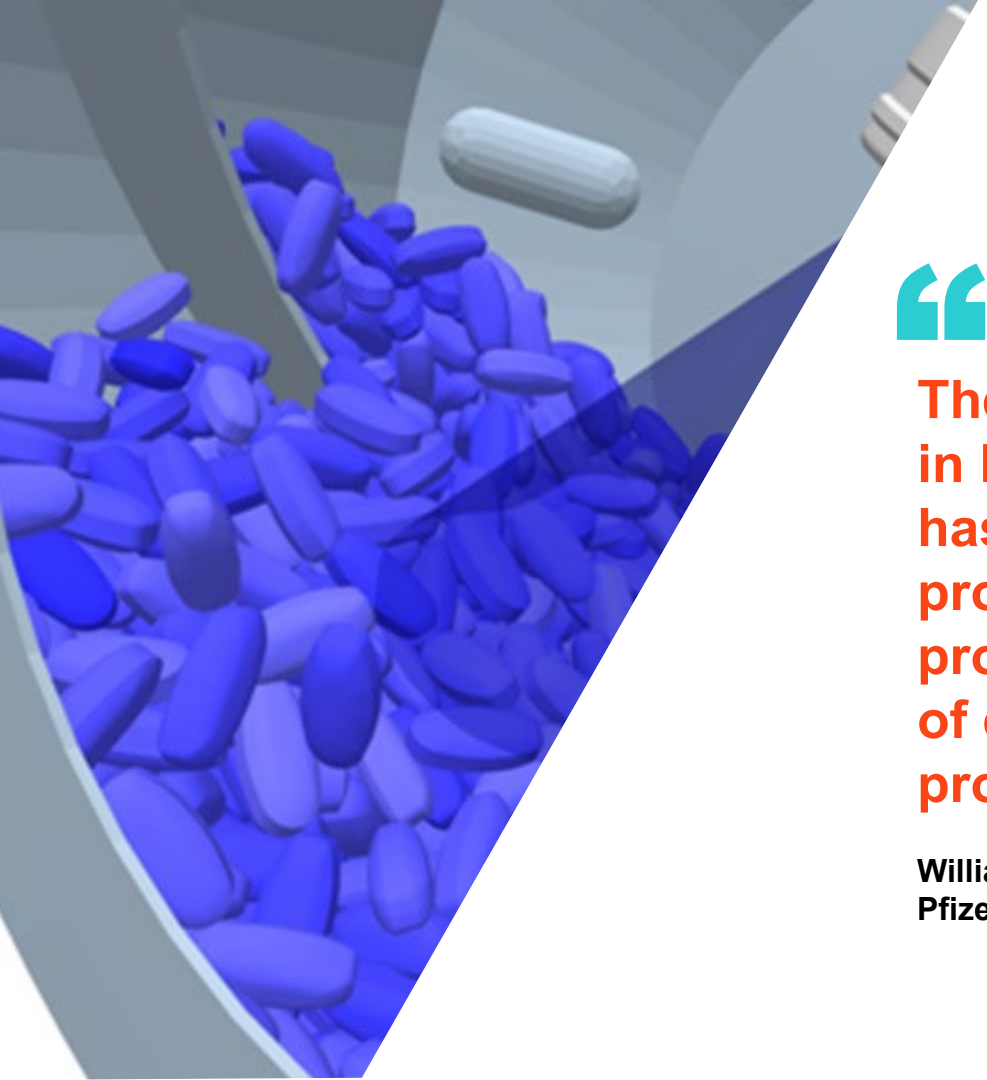

The deployment of EDEM modelling in Pfizer drug product development has accelerated the decision-making process by predicting, before process scale-up, the performance of commercial tablet shapes at process scale.

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Pfizer Worldwide Research & Development

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www.altair.com/edem

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