NiTech® Technology Industrial Application Examples

*These slides summarise cases where NiTech® technology has been applied in industry.*
Content

Industrial Applications

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**Seeded Crystallisation Example 1**

AstraZeneca published a paper on the benefits of a COBC:


### Problems in batch
- Poor size distribution
- Variations in morphology

### Desired benefits from going continuous
- More efficient use of reagents and energy
- Reduced space requirement
- Less waste

### Initial batch optimisation
- Cooling rate
- Oscillation intensity
- Feed concentration
- Hold time
- Seeding

### Continuous operation design
- Batch results specified a 25 mm diameter, 25 m long vessel
- Two 12 L COBCs can replace three 6.4 m³ stirred tanks
Seeded Crystallisation Example 1

Key Findings

- Overall isolation time reduced from 9 hrs 40 mins to 12 mins
- An estimated 20% capital cost saving
- £0.3m projected annual operating cost reduction
- Credited to increased specific surface area and plug flow nature
- Linear and reliable scale up
Seeded Crystallisation Example 2

A major pharma company was interested in the benefits of NiTech’s technology.

Key success criteria for a representative API crystallisation:

- Demonstrate robustness (>8 h trouble-free operation)
- Ultrasound not needed to induce nucleation
- No encrustation or sedimentation (prone in the batch)
- Achieving good yields
- Much lower process times
- Satisfactory product purity

Batch feasibility:
- Process time reduced from ~7 hr to ~1 hr

Continuous (Lab-scale):
- 15 mm diameter, 33 m long
- Optimised variables (oscillation, temperature profile, flow rates)

Continuous (Pilot-scale):
- Achieved success criteria

A major pharma company was interested in the benefits of NiTech’s technology.
Seeded Crystallisation Example 2

Continuous (Pilot-scale)

- Ultrasound was not required to initiate nucleation – leading to capital, maintenance and energy savings.
- Process time was drastically reduced while maintaining purity and yield levels.
- Operability and robustness were demonstrated by using an appropriate seeding strategy.
- Continuous trouble-free operation for at least 8 hr, without sedimentation or blockage.
**Cooling-only Crystallisation Example**

- NiTech’s technology was of interest to a large agrochemical producer for dewaxing/crystallisation of vegetable oils. They were interested in the potential for:
  - more uniform mixing;
  - better temperature control; and
  - plug flow under laminar conditions.

- The key objectives were to demonstrate at pilot-scale an improved:

<table>
<thead>
<tr>
<th>Product</th>
<th>Process</th>
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<tbody>
<tr>
<td>• separation of precipitated solid from oil</td>
<td>• reduced crystallisation time</td>
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<tr>
<td>• homogeneous crystallisation (larger sizes and desired shape)</td>
<td>• shorter filtration time</td>
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<tr>
<td></td>
<td>• effective heat control for a linear temperature profile</td>
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<td>• reduced temperature difference between the process and utility mediums</td>
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Cooling-only Crystallisation Example

Batch trials were conducted to save on resources while the optimum parameters and initial feasibility of the technology were determined.

Rapid cooling was used to bring the feed solution to saturation, before a slow, controlled cooling was used to crystallise the material.

A pilot COBC (25 mm wide, 24 m long, 10.4 L) was constructed for up to 8 L/min.

Key Outcomes

- Showed the viability of a COBC
- Successful scale-up from a batch, with no obvious differences
- Halving of crystallisation time
- Fast, consistent and repeatable filtration times were achievable
- A homogenous crystallisation was achieved
- A smaller temperature difference between process and utility fluids
- Linear, controllable cooling was demonstrated