GFD®

Scaling up filtration and drying processes with the smart lab assistant GFD® Lab Filter Dryer

psl

www.powdersystems.com

PSL is a global provider of innovative technologies and process services that accelerate and improve the development and manufacture of therapeutics and fine chemicals. We have a rich heritage of delivering unique process expertise and quality solutions to our industry partners since 1989.

PSL's innovative Filtration and Drying technology has been globally used and proven at all levels of API production, from early R&D activities up to clinical trials and commercial manufacturing.

Sylvain Querol

Head of Business Development

With 15 years of experience in the pharmaceutical industry, supporting clients in selecting the right equipment tools for their process challenges. Since joining PSL in 2014, Sylvain has partnered with end-users worldwide to implement the right processing solutions with a strong focus around their solid/liquid separation needs and vacuum tray dryings. With a strong focus on pharmaceutical based projects, his mechanical engineering scholar background has also been a valuable asset in cross-industry applications such as aerospace or precious metal applications".

Agenda

1. Introduction to Nutsche Filter Dryer technology

- Solid Liquid Separation
- Nutsche Filter Dryer Features
- Nutsche Filter Dryer Process Steps

2. Filtration Considerations

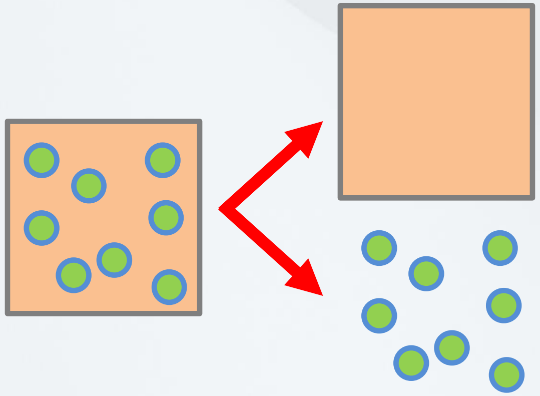
- Filtration Approach
- Filtration Size
- Product Washing
- Cake compressibility

3. Drying Considerations

- Equipment set-up
- Loss on Drying
- Agitator Effect (Case Study)

Introduction to Nutsche Filter Dryer technology

Types of Solid Liquid Separation

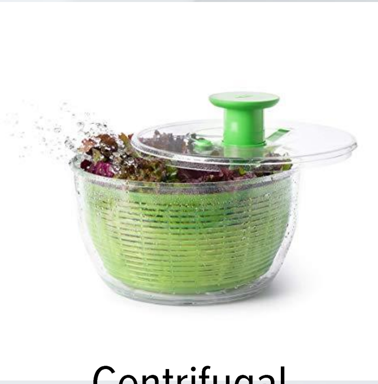


Solid / Liquid Separation

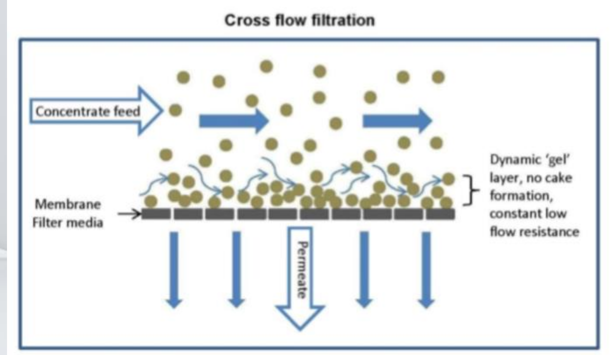
Gravity

Vacuum

Pressure



Centrifugal

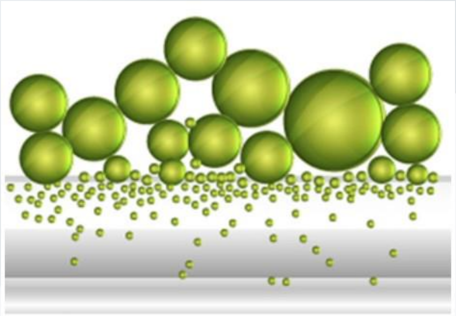


Cross Flow Filtration

Granular Bed

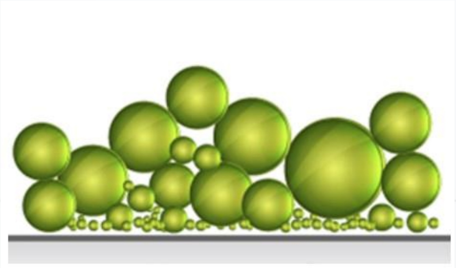
Filtration Types

- In Depth Filtration the filter medium is porous and uses its depth to trap and hold smaller particles with the filter medium.
- Typically used when the solids are not the product (water treatment etc) and rate isn't critical. Technique can be replicated on an ANFD using filter aid. Higher Contamination Risk



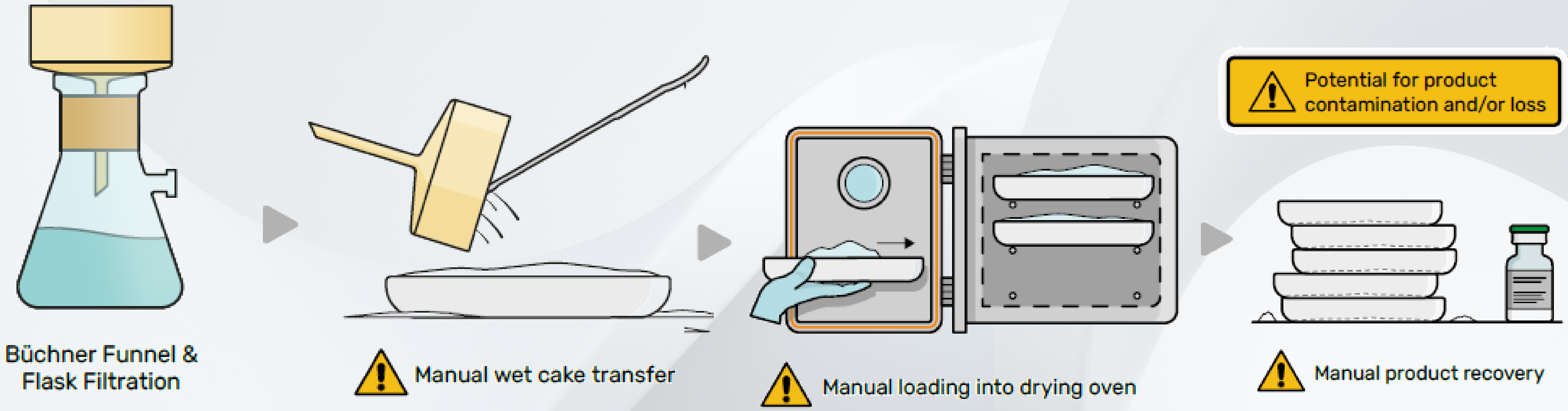
Depth Filtration

- In Surface Filtration the filter medium uses a mesh to retain the solids with any undersized material passing through the mesh
- Typically used when the solids are the product and are to be recovered



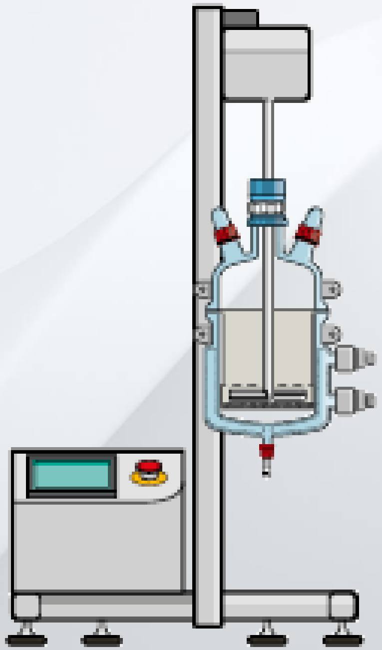
Surface Filtration

Traditionnal Methods



- Product Loss / Lower Yields
- Labour Intensive
- Multiple Equipment / Larger Footprint
- Higher Contamination Risk
- Poor Batch Repodocibility

- Slurry Filtration
- Product Washing
- Re-slurry



All-in-one Solution

- Vacuum Drying
- Product Sampling
- Product Discharge

Nutsche Filter Dryer

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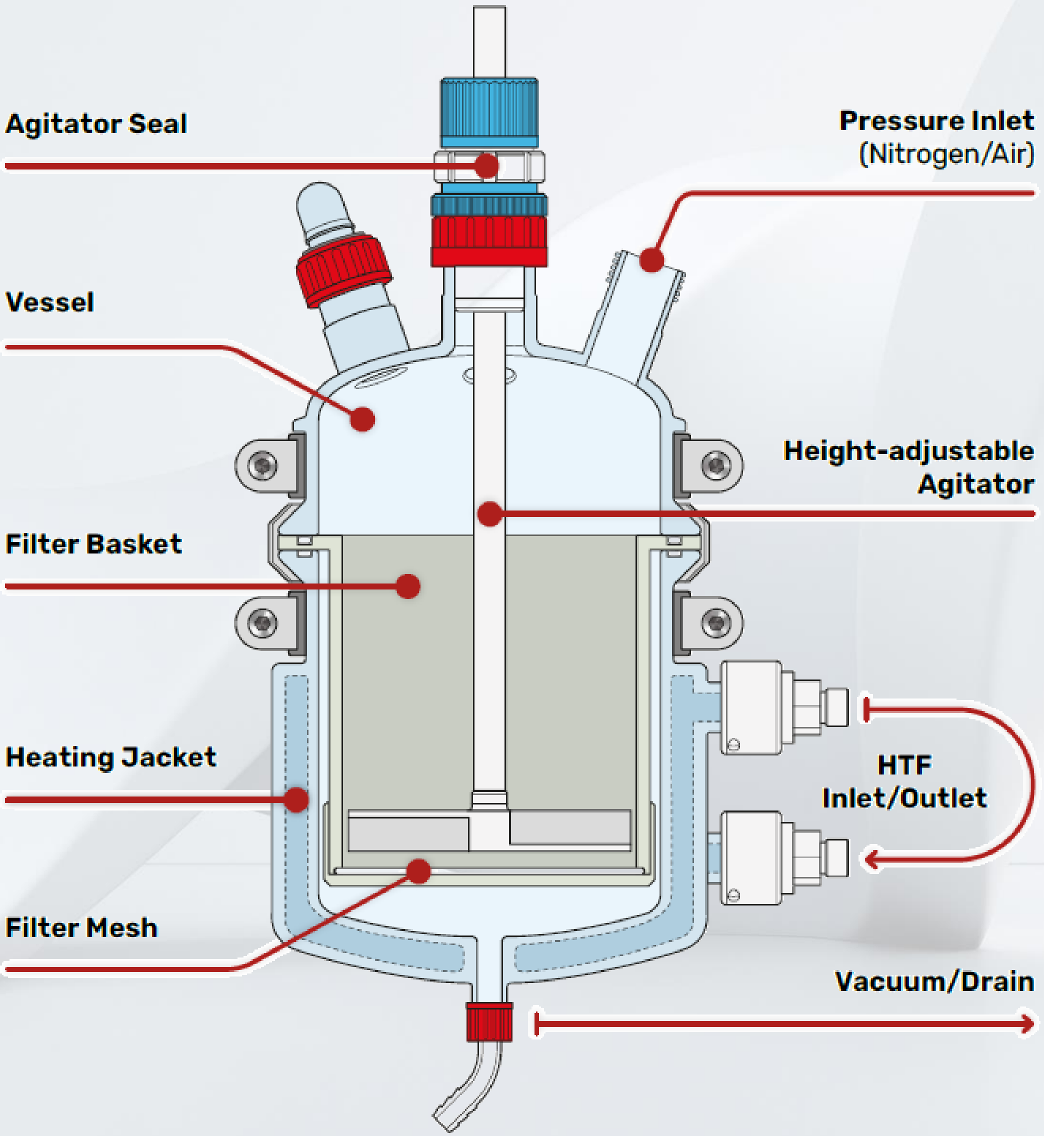
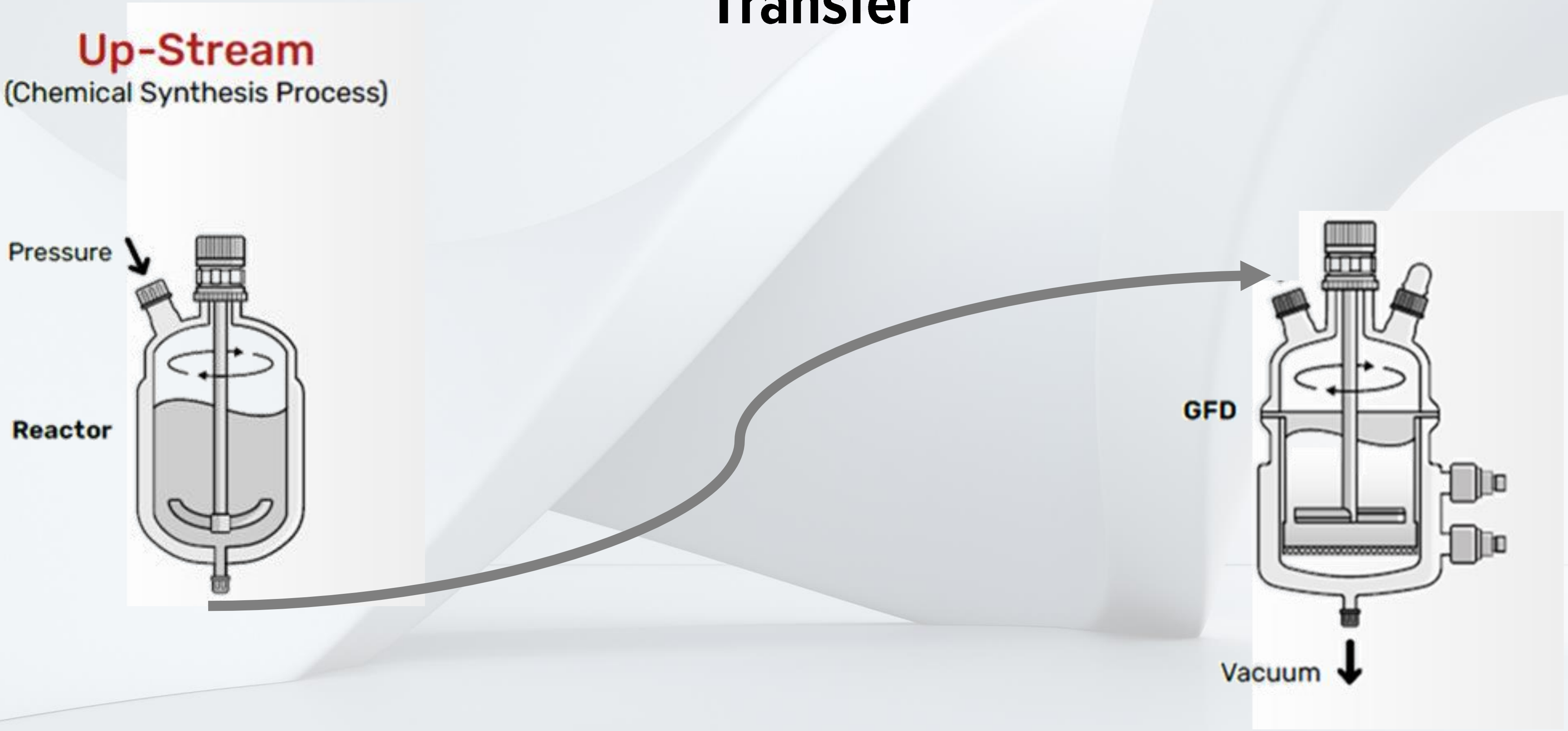
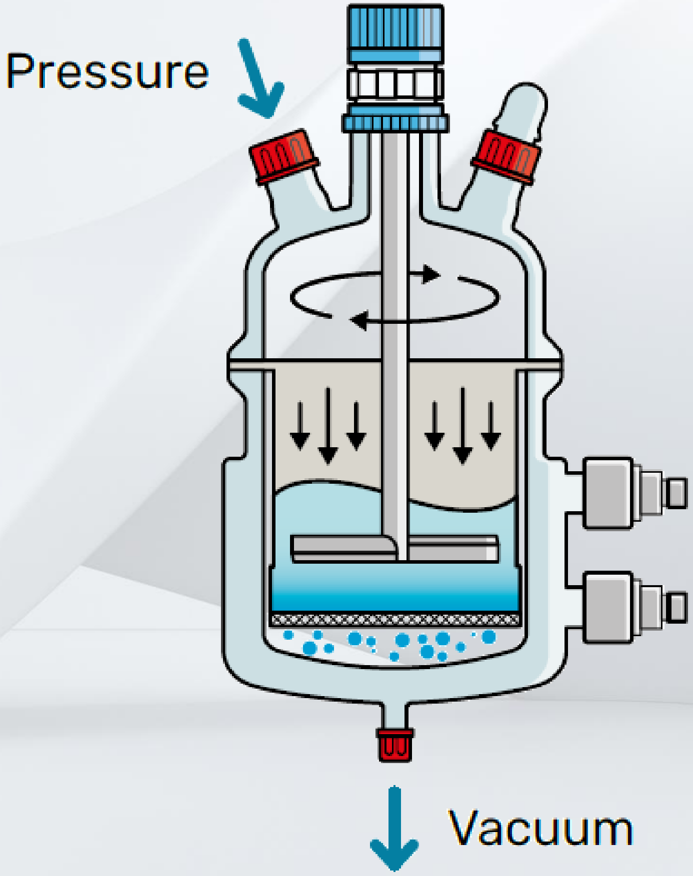
Nutsche Filter Dryer Features



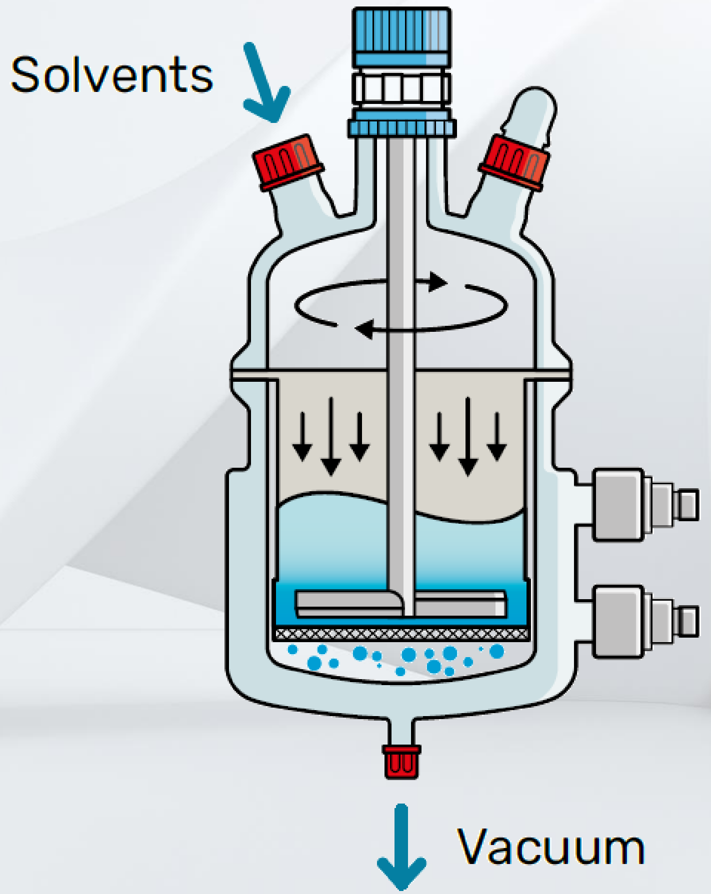
Slurry / Suspension Transfer



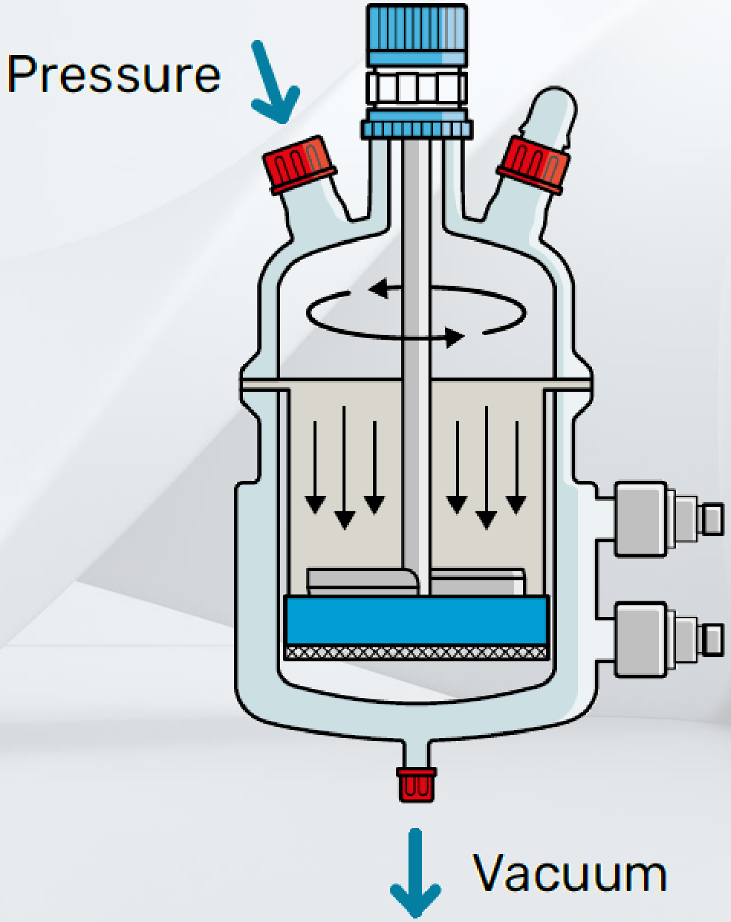
Dewatering / Filtration



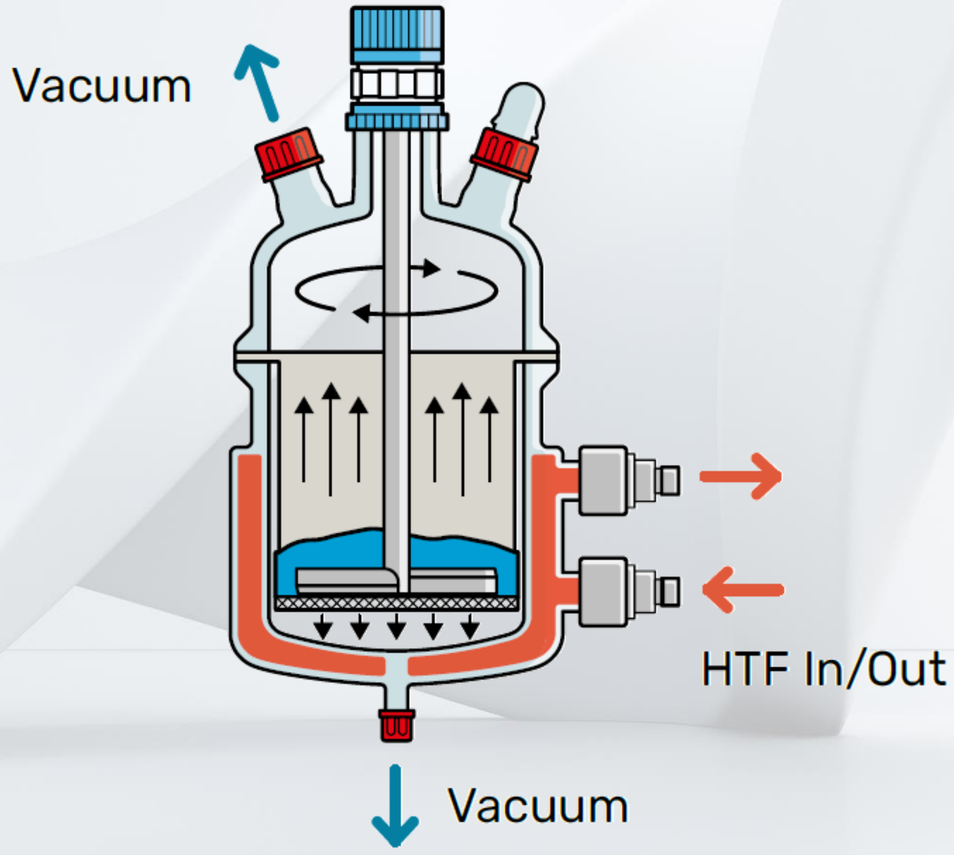
Washing / Reslurry



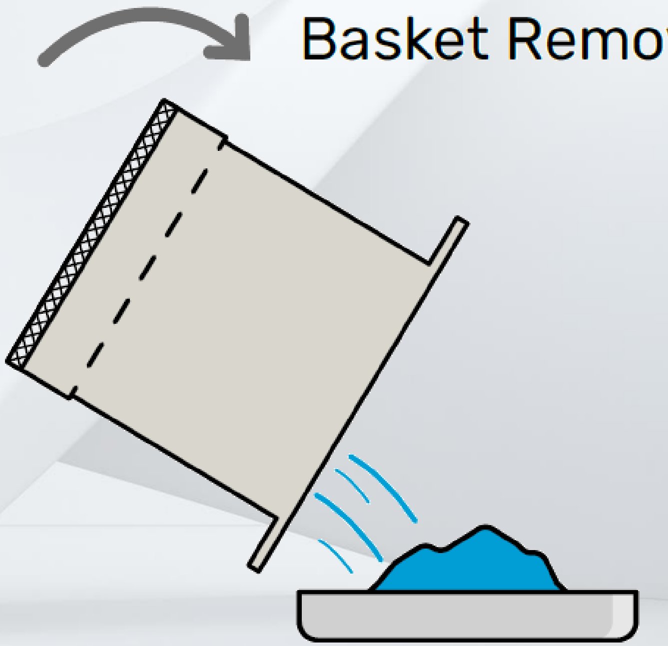
Pressure Filtration



Drying



Product Recovery



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Filtration Rate

Although the interaction of many factors can impact upon Filtration Rate they typically fall under one of the following areas

- Resistance of the Filter:

  Porosity and Design of the Mesh being used to separate solids from liquids

- Viscosity of the Filtrates:

  A Physical property of the liquid being filtered

- Resistance of the Filter Cake

  How the solids retained on the filter mesh impact upon filtration

Filtration Rate

Filtration time will be a key parameter when considering scaling up your process, e.g.

- 10min to go through 50mm of cake
- 30min to go through 100mm of cake

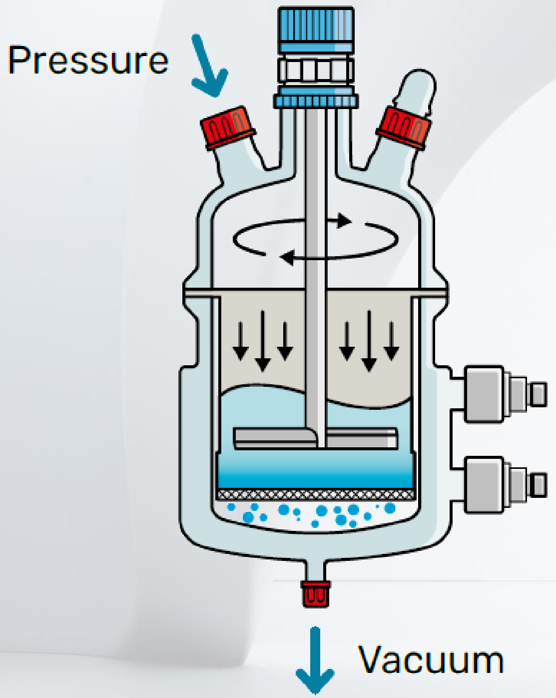
Filtration rate is the target to maintain constant when moving up in scale.

- Monitoring this easily at lab scale: filtrate container on weigh scale + operator monitoring (or video recording).
- When moving up in scale, with pilot/industrial systems and advanced automation, use of flow meters (cumulative) or filtrate vessels on load cells.

Selecting Right Approach

Constant Differential pressure.

- Maintaining the same differential pressure across the filtration element throughout process.
- Usually means a drop in the filtration throughput as product cake builds up. Cake resistance.
- Easier to implement at lab scale.



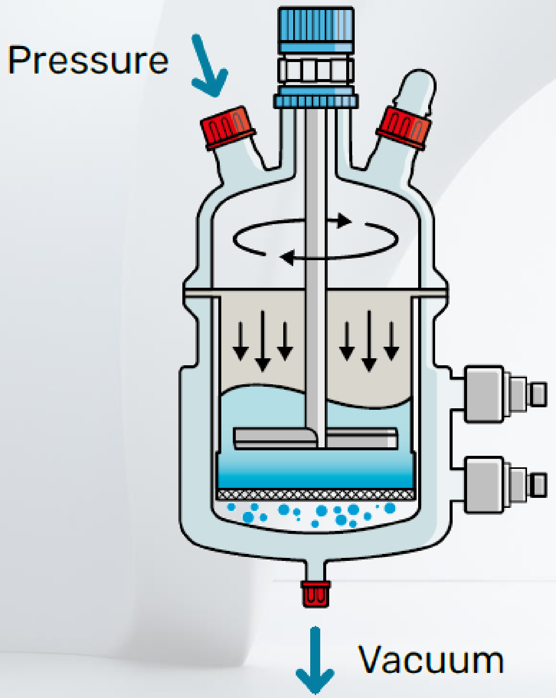
$\Delta P_{t1} = \Delta P_{t2}$

$F_{t1} > F_{t2}$

Selecting Right Approach

Constant Filtration rate.

- A need for increasing the differential pressure for compensating cake resistance.
- Could be detrimental to product quality if differential pressure becomes too high (see cake compressibility).
- More complex to implement at lab scale as limited monitoring/automation.



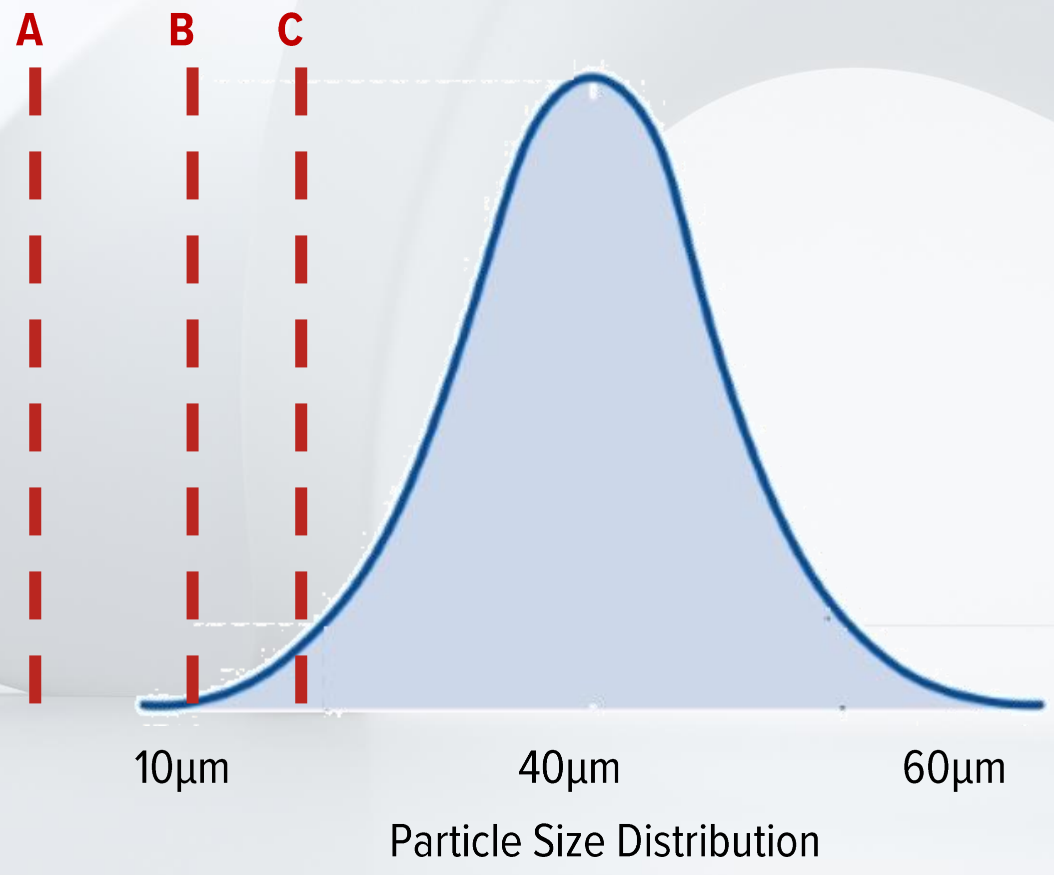
$\Delta P_{t1} < \Delta P_{t2}$

$F_{t1} = F_{t2}$

Filtration Porosity

Filtration size selection relies on various considerations:

- Retention efficiency vs. filtration rate.
  - Smaller porosity would give better retention but would increase resistance, impacting filtration rate (cut-off "A")
- Is my product malleable, prone to deformation ?
  - If cut-off ("B") is too close to the PSD lower end risk of particulate ingress in the porosity/blind mesh.
- Are undersize/debris an issue for my product ?
  - Sometimes removing fines can be needed for product quality ("C")



Filtration Porosity

Important to select a development equipment which can allow an easy porosity change, using mesh which translate to industrial equipment.

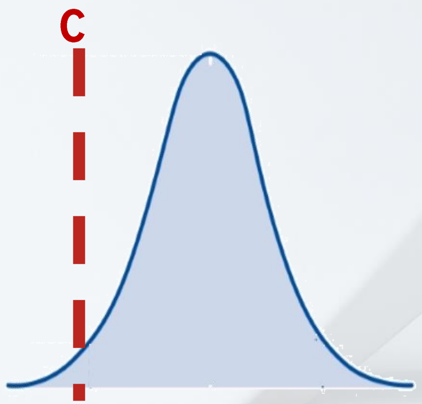
Filter Basket MoC	Filtration Media MoC	Pore Sizes
Polypropylene	Polypropylene, PEEK, Polyester, Nylon - **Interchangable**	7µm, 8µm, 12µm, 15µm, 20µm, 30µm, 40µm & more
PTFE		
316L Stainless Steel	316L Stainless Steel - **Welded**	5µm, 10µm, 20µm & more
Alloy 22	Alloy 22 - **Welded**	

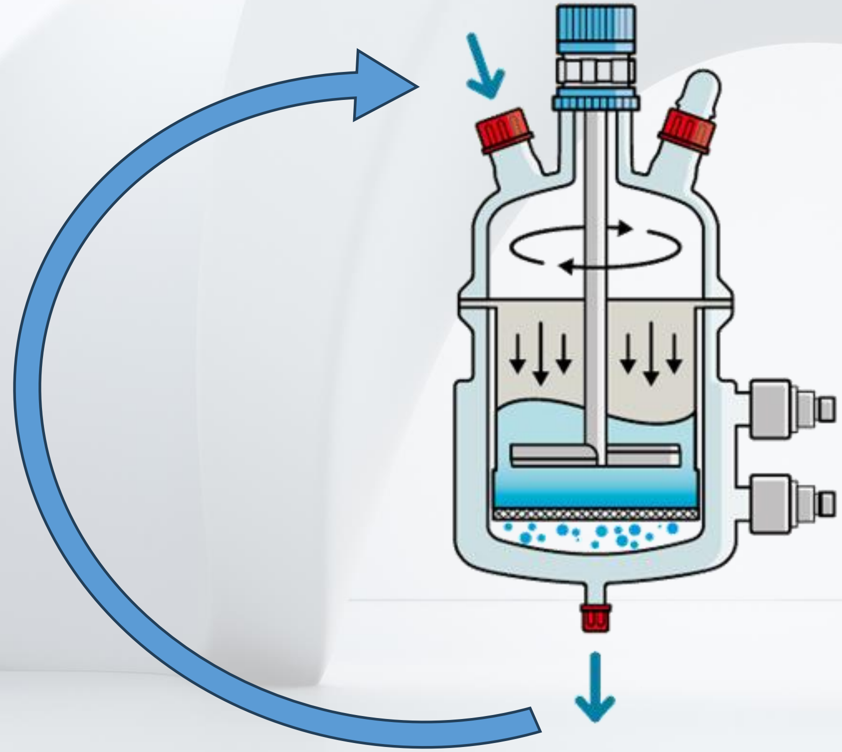
050 Series Polypropylene basket with removable mesh

Filtration Porosity

Further considerations when selecting a higher cut-off ("C"):

- Using recirculation of initial filtrates.
- Use product cake as filtering media.





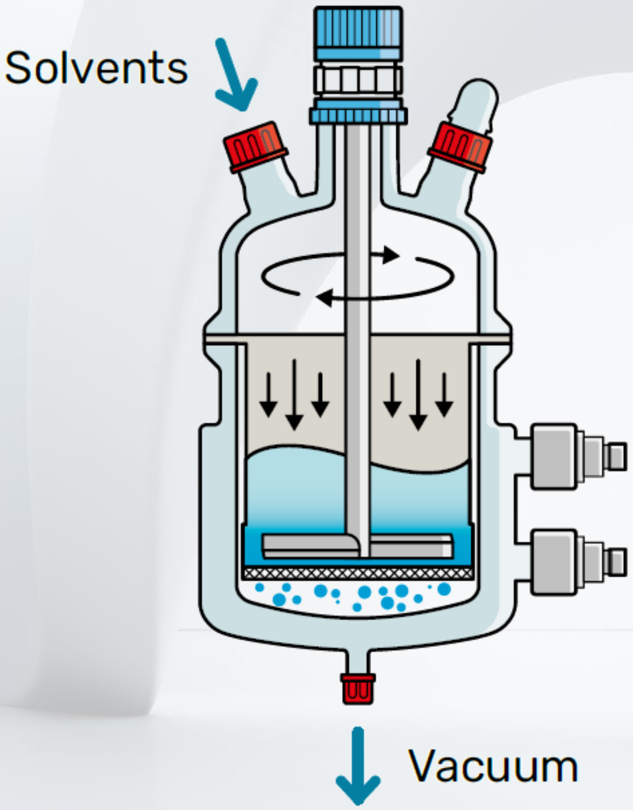
Displacement wash vs. Slurry wash

Displacement wash

- Agitator not used.
- Volume filled with solvent before it is "pushed out"/filtering out under pressure.
- Used if product is prone to soluble. Less prone cracking/channeling.

Slurry wash

- Volume filled with washing solvent and agitator used to re-slurry solids.
- More effective in removing the traces, or if you're wanting to remove fines/debris, freeing mesh pore to remove.

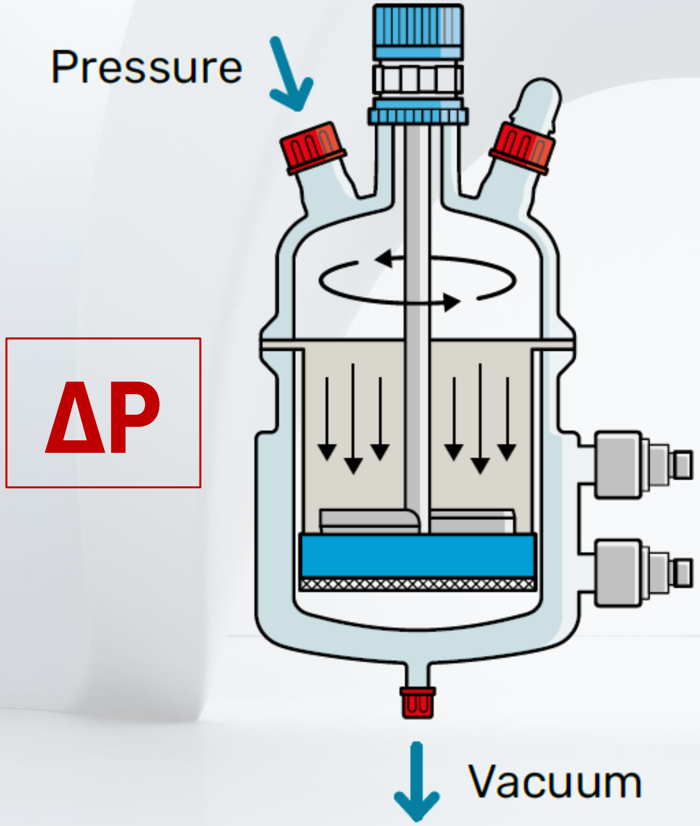


In both cases, conductivity of the filtrates can be used to monitor the washing efficiency

Compressibility of cake (pressure filtration)

Pressure filtration is beneficial to remove filtrate traces and moisture content further prior to dyring, but attention must be paid :

- Product deformation which can be an issue/agglomeration.
- Avoid mesh ingress/blockage.
- Sometimes higher pressure is detrimental to filtration efficiency.
- Compressed solid / plaster (inefficacy to process further).
- Is the extra time gain worth it for product quality ?



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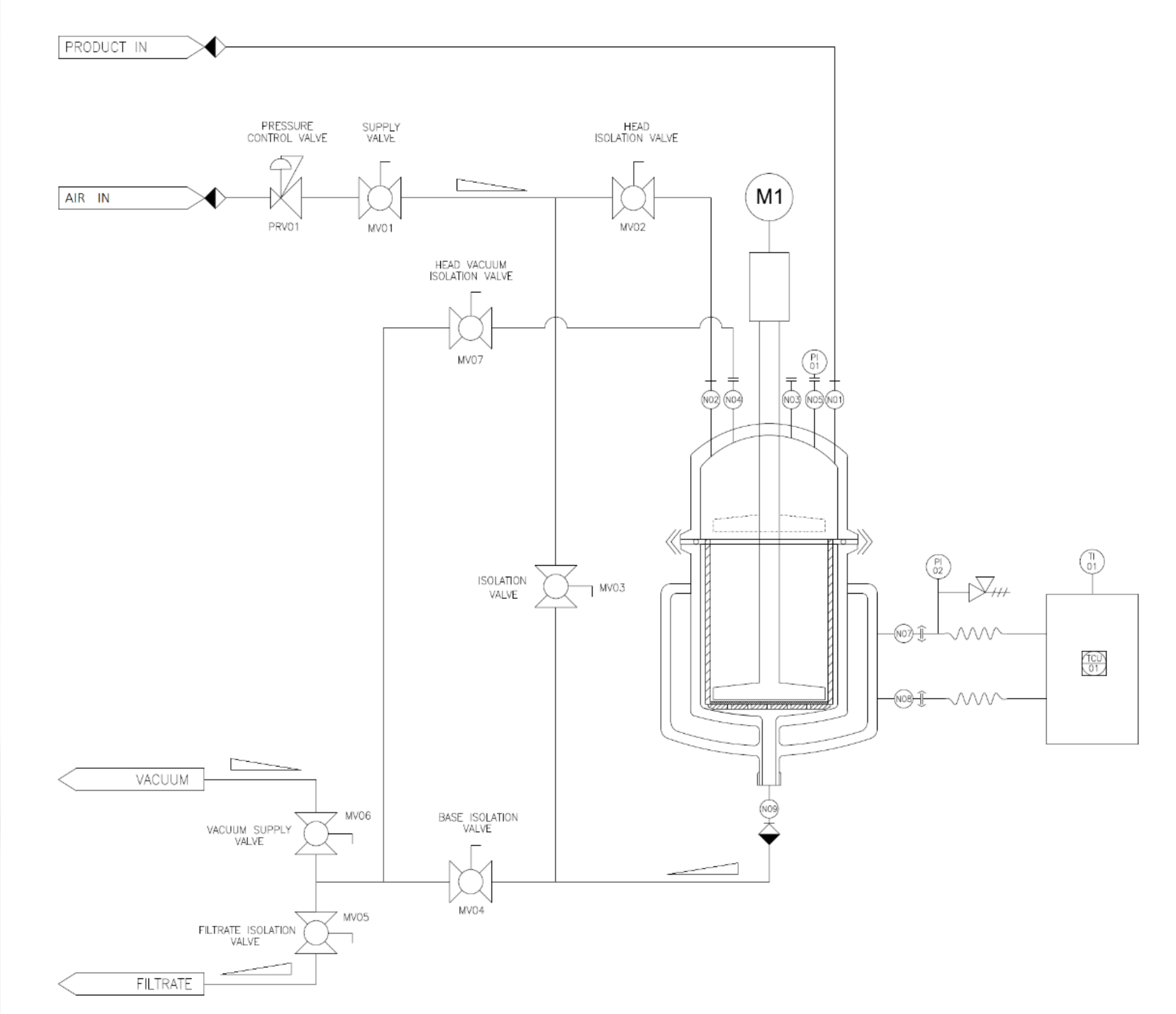
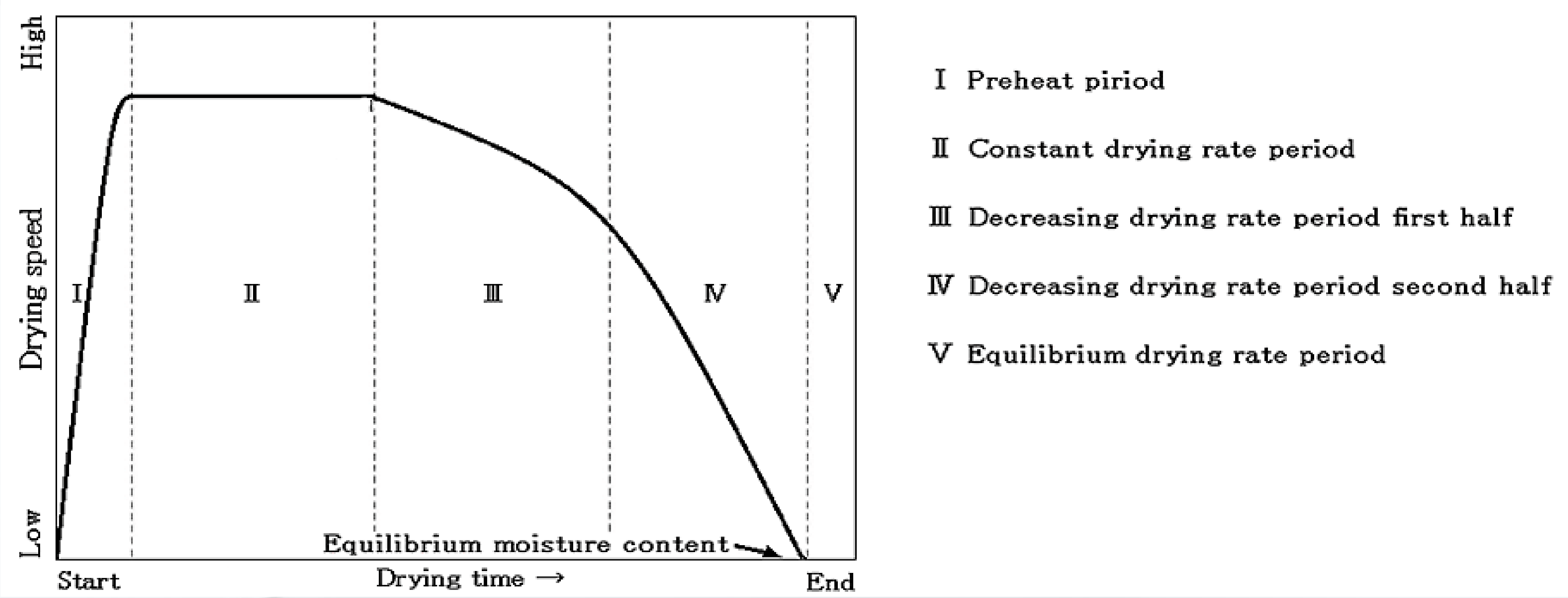
Equipment Set-up

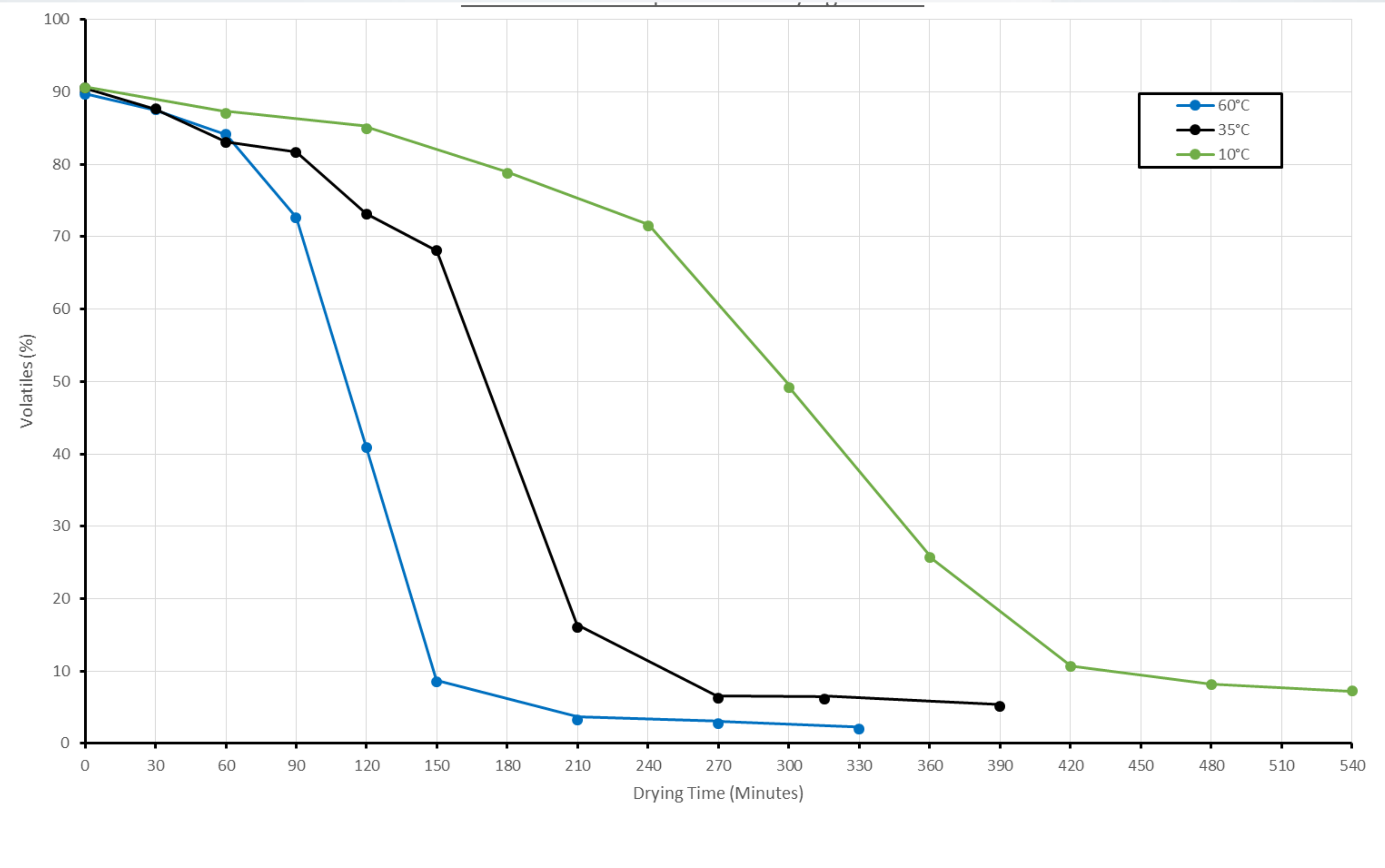
- Temperature Control Unit
- Vacuum line(s)
- Purging Gas



Drying Curves



Drying Curve – Loss on Drying (volatiles)



- Material was modified starch

Drying Curve – Loss on Drying

Some challenges for consideration at small scale:

- Having enough material for taking samples and plotting LoD curves
- Evaporative cooling: a way to see when we reach end of drying. Temperature remains stable throughout evaporation and as we get dryer the temperature would ramp up. Less need for sampling.
- Would be able to notice heat treatment issues/date: threshhold temperatures creating agglomeration, product deformation, flash-off surfaces and fusing particulate, colour deformation, etc…

Agitator speeds or tip speeds

- Agitator speeds can have an effect on drying effects. Modifying RPM.

- RPM should not be increases without consideration: shear or heat inducing issues can be noticed with heat sensitive materials. Small scale equipment should allow higher RPM to replicate tip speed found at industrial.
  - For example on a 0.01m^2 (050 Series GFD), tip speed at 100rpm would be same as on a 1m^2 at 10 RPPM.

Drying Effects – Case Study

- Single Direction used only
- No height adjustment

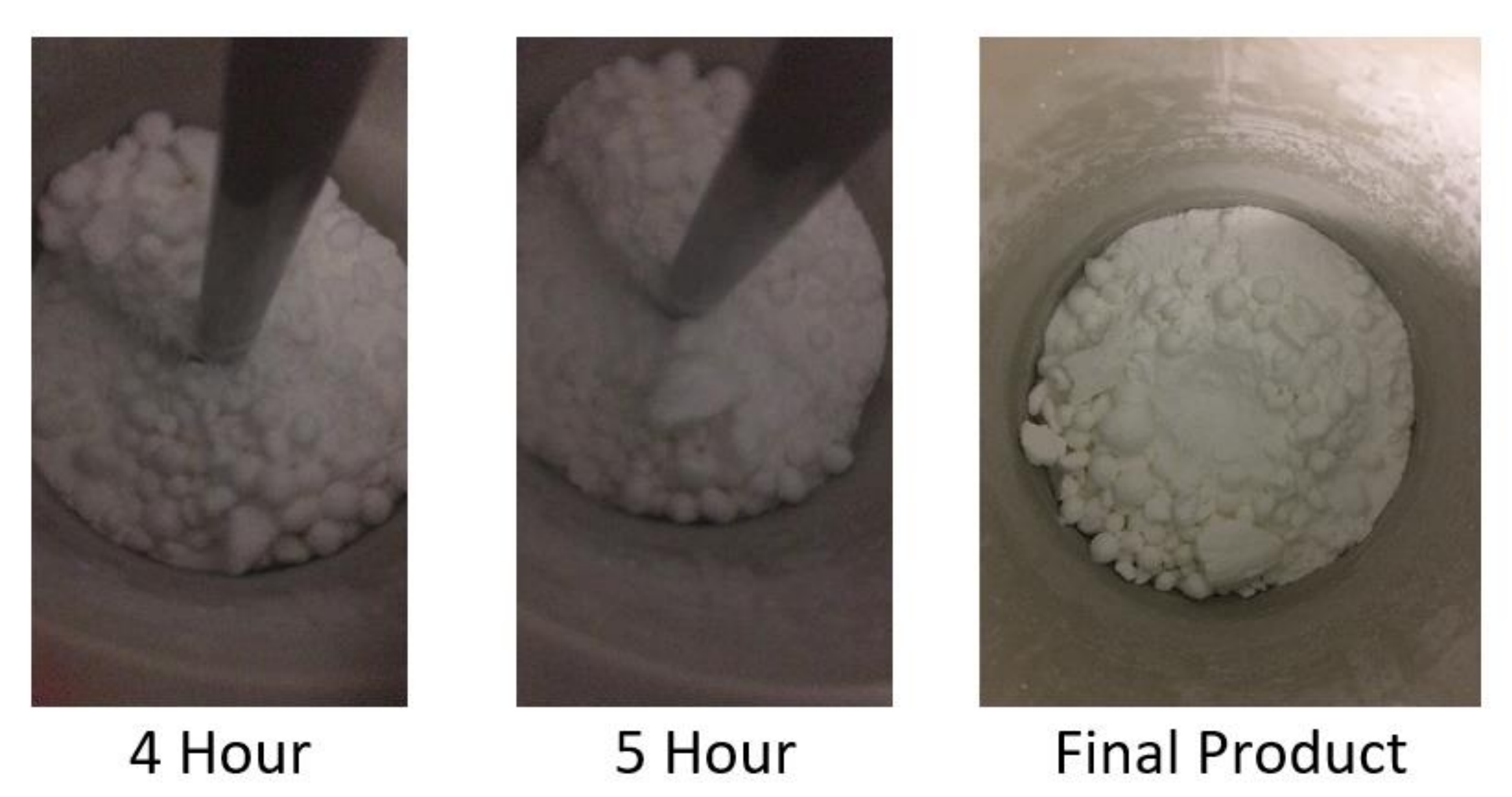
1 Hour

2 Hour

3 Hour

Drying Effects – Case Study

- Single Direction used only
- No height adjustment

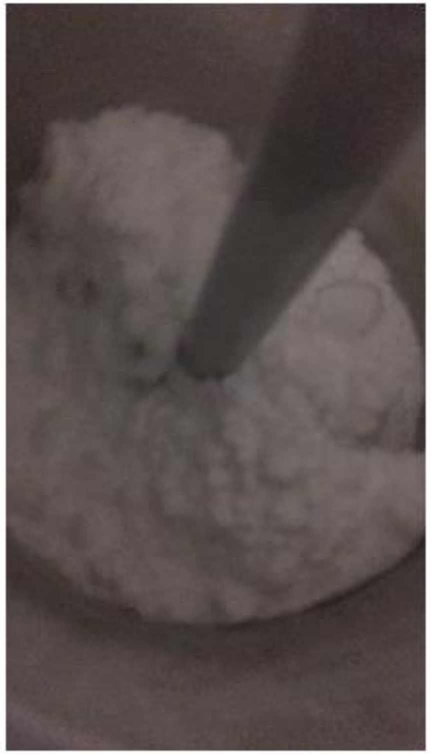


Drying Effects – Case Study

- Direction Change during trial
- Raise/Lower cycles of Agigtator through cake thickness

1 Hour

2 Hour



3 Hour

Drying Effect – Case Study

- Direction Change during trial
- Raise/Lower cycles of Agigtator through cake thickness

4 Hour

5 Hour

Final Product

Drying Curve – Conclusions

Transcribing scale-up on the drying phase is more complicated (than filtration):

- More difficult to guage in parameters to transcribe in scaling up as down to heat efficiency and heat transfers

- The rate of drying is harder to scale-up and small scale evaluation will be more about gaining information, setting boundary limits and rely on cheaper trials and error with less material.

Questions

Learn more about PSL at powdersystems.com

Thank You

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Taking Your Process Further, **Together**