



A new versatile blister-based DPI platform

Intertek Inhaled & Nasal Biologics | DNA Forum 2026

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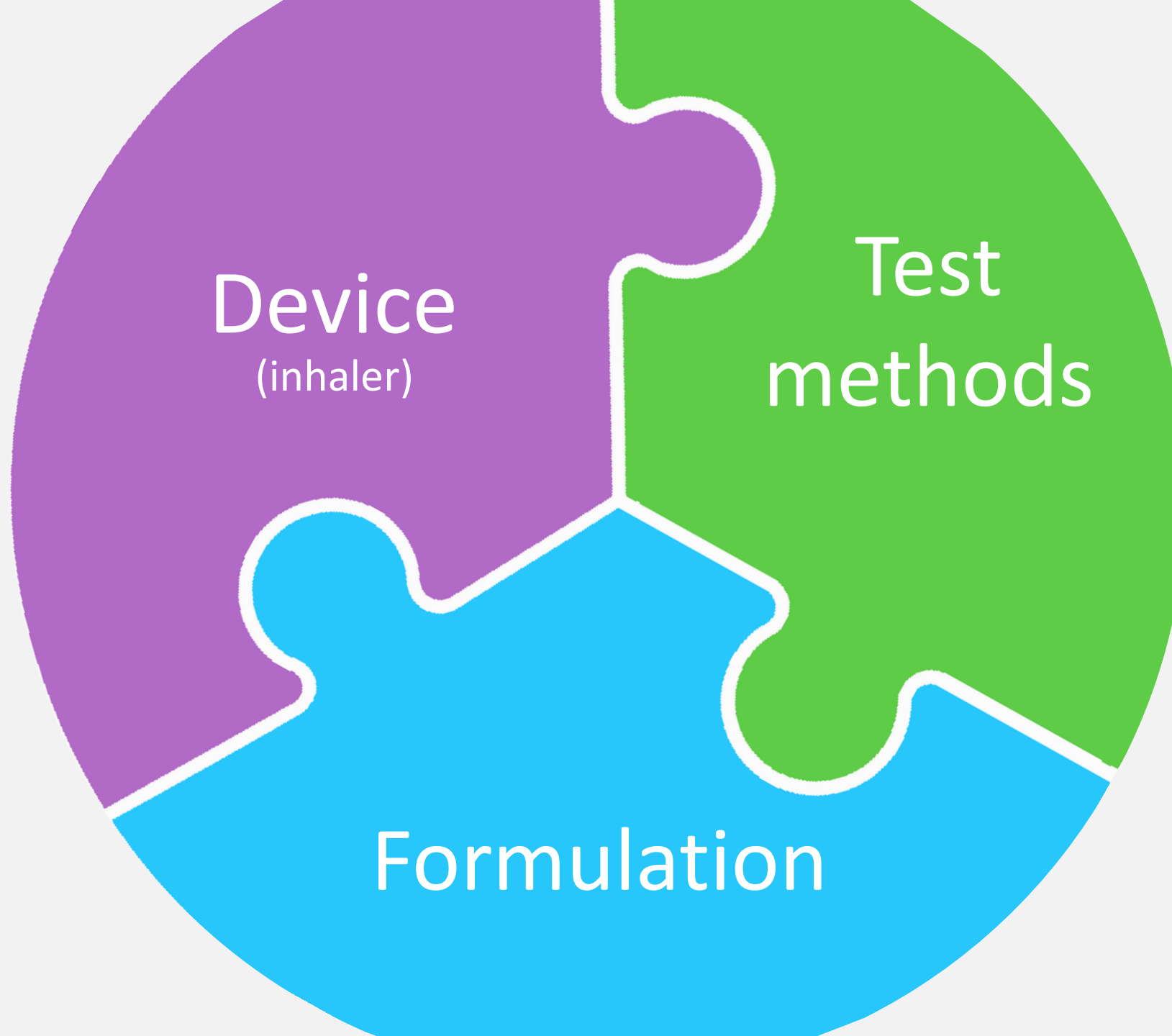
Quattrii carrier-free (QCF) Dry Powder Inhaler (DPI)

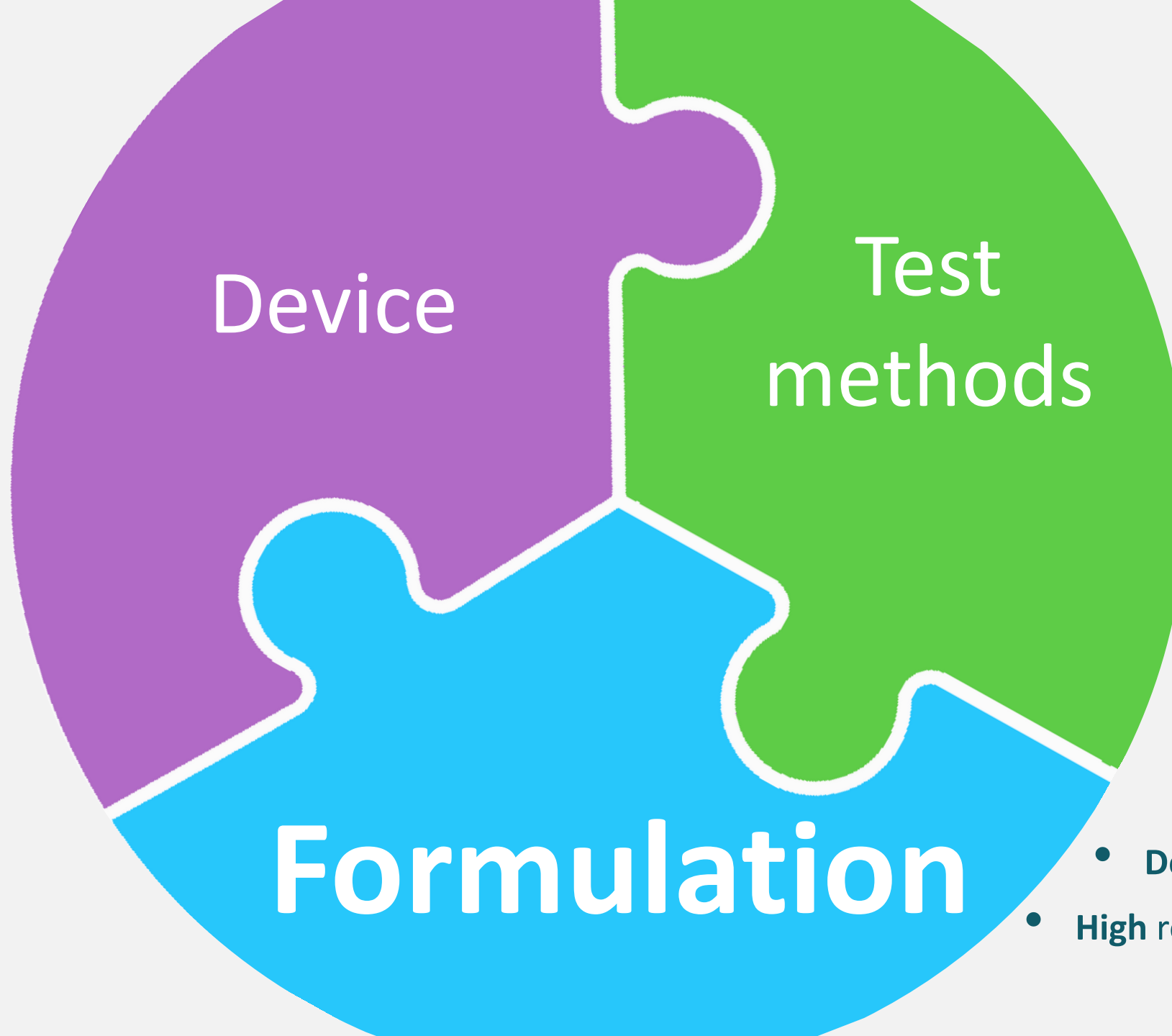
- ✓ Delivery of carrier-free spray-dried formulations
- ✓ Reloadable, foil blister-based
 - superior moisture protection
- ✓ Versatile platform:
 - One product for a wide range of fill masses



Disclaimer: AI has been used to create the sandcastle, giant spanner, and Rubik's cube

- but not the data!





- **Delicate** molecules
- **High** respirable doses



**Biologic
analogy**

A young girl with long brown hair, wearing a colorful patterned swimsuit, is kneeling on a sandy beach. She is smiling and looking towards a large, ornate sandcastle she has built. The sandcastle features multiple towers, turrets, and a central archway. In the background, a massive, powerful wave is crashing, creating a large plume of white foam and spray against a clear blue sky. The water is a vibrant turquoise color. The scene is bright and sunny, capturing a moment of childhood joy at the beach.

Atmospheric moisture

Robust moisture protection is crucial

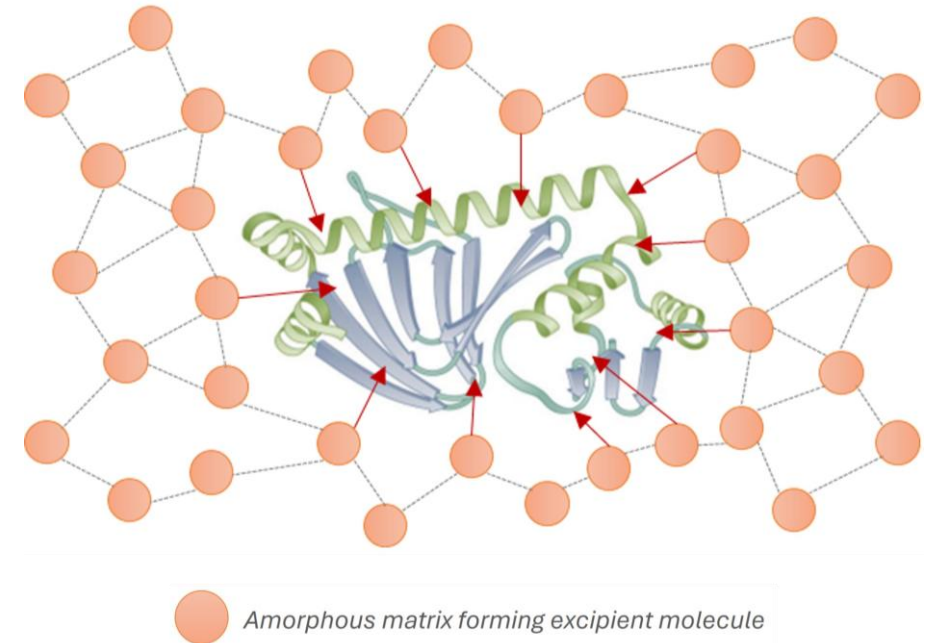
**Denatured
biologic**



Robust moisture protection is crucial

- Formulating biologics as a dry-powder has **many advantages**, including **stability** and **convenience** of DPIs over nebulisers
- **Dry powder biologics** are often **spray-dried**
- Complex biologic molecule structure **protected** in a sugar matrix
- The amorphous matrix is very **hygroscopic**
- Absorbing moisture compromises the matrix which **damages** the biologic

Biologic structure
protected in sugar matrix



Dry powder biologics need foil.

Quattrii blisters protect the biologic right up to use



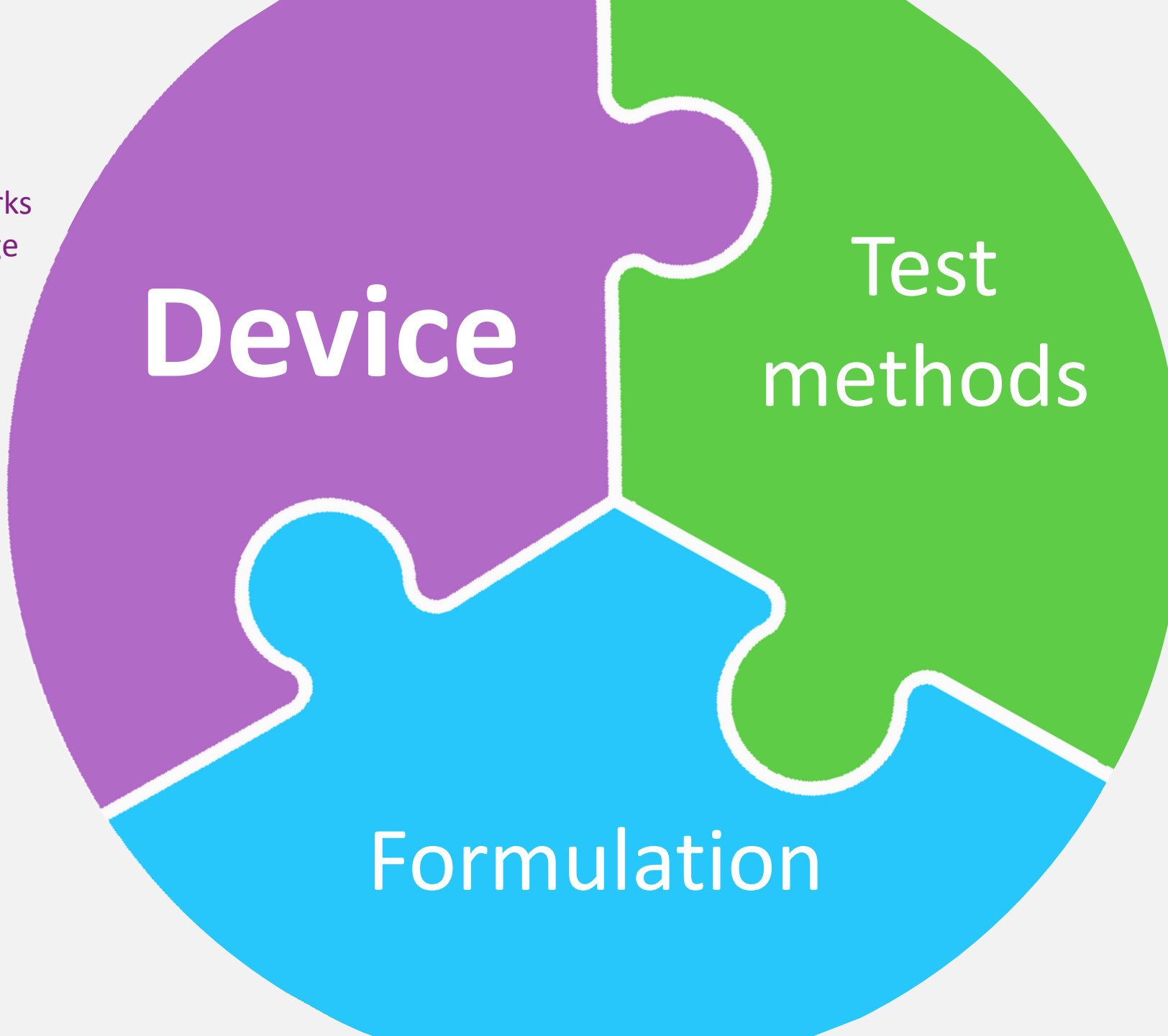
Pierced
QCF blister

90 mg of spray-dried
formulation in QCF
800 μ L blister



- Quattrii carrier-free (QCF) uses 800 μ L **foil** blisters (vs. size 0 capsules $\sim$ 680 μ L)
- Blisters are **pierced** not peeled
 - stronger heat seal
 - better moisture protection
- **Versatility** across fill masses (payloads)

- **Versatile:** works for a wide range of fill masses
- Inherent **moisture protection**
- Good drug delivery **performance**



Study aim: To evaluate the powder delivery performance of Quattrii carrier-free (QCF) across a range of fill masses

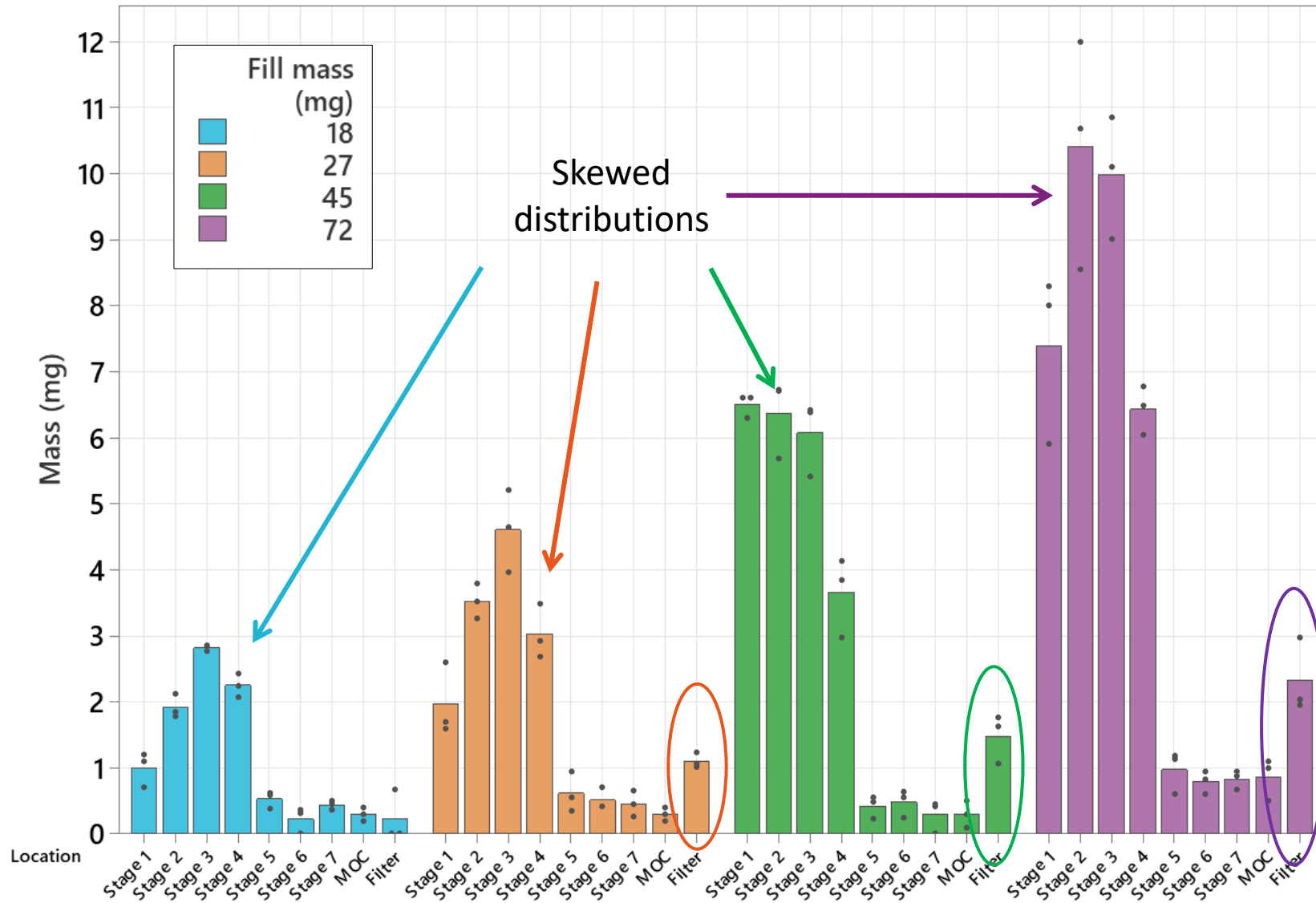
Fill masses of 18, 27, 45 and 72 mg



NGIs based on USP<601> → should work, right?

- Spray-dried Trehalose-leucine based biologic placebo formulation
- D_{50} of $\sim 2.5 \mu\text{m}$, D_{10} of $\sim 1.0 \mu\text{m}$
- Gravimetric analysis method used with Next Generation Impactor (NGI)
- Flowrate (Q) 34 & 48 LPM @ 2 & 4 kPa
 - Quattrii is a high resistance DPI

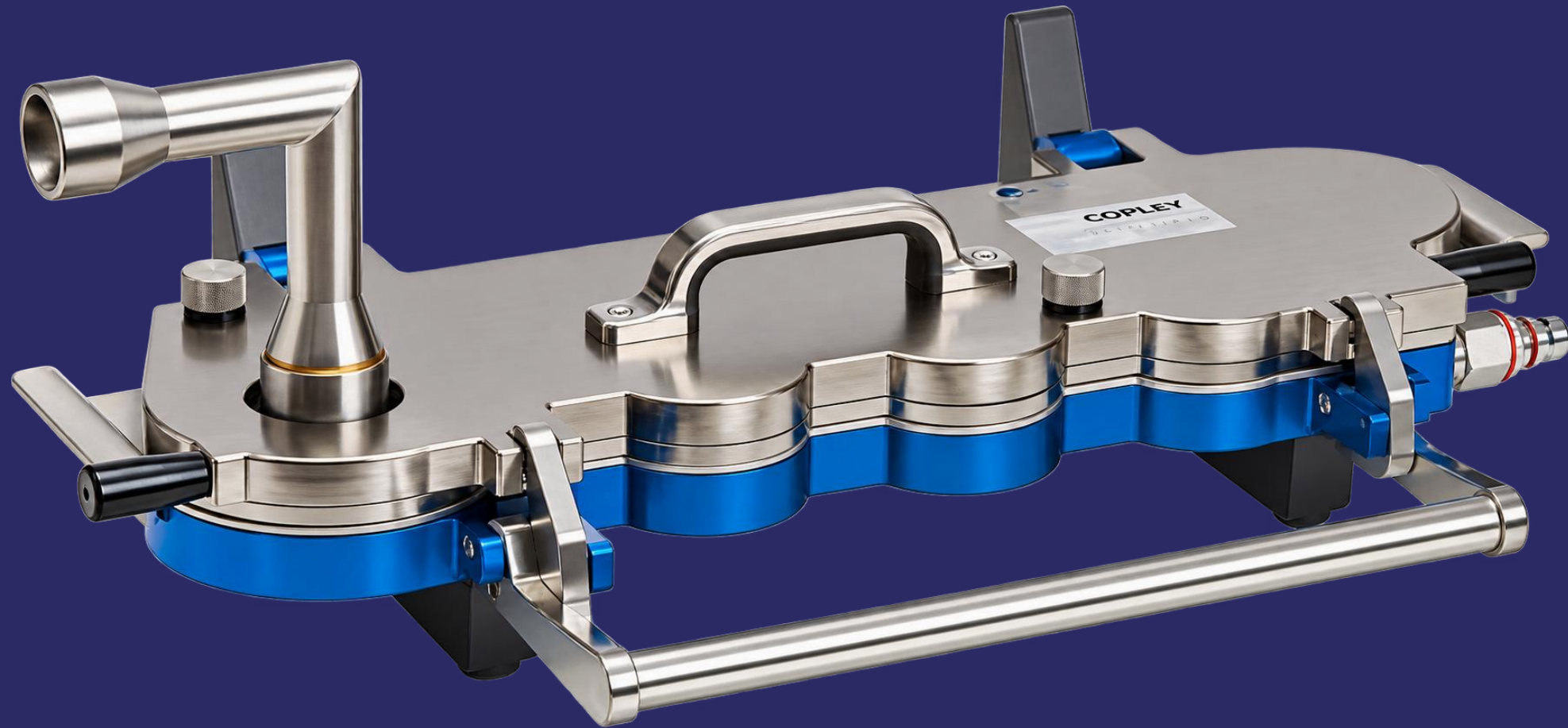
NGIs based on USP<601> → should work, right?



- We noticed high deposition on the filter
- **Skewed** stage deposition profiles
- Worse at higher fill masses

What's going on?

Next Generation Impactor (NGI)





What's wrong with this picture?



72 mg

Powder
hitting jets

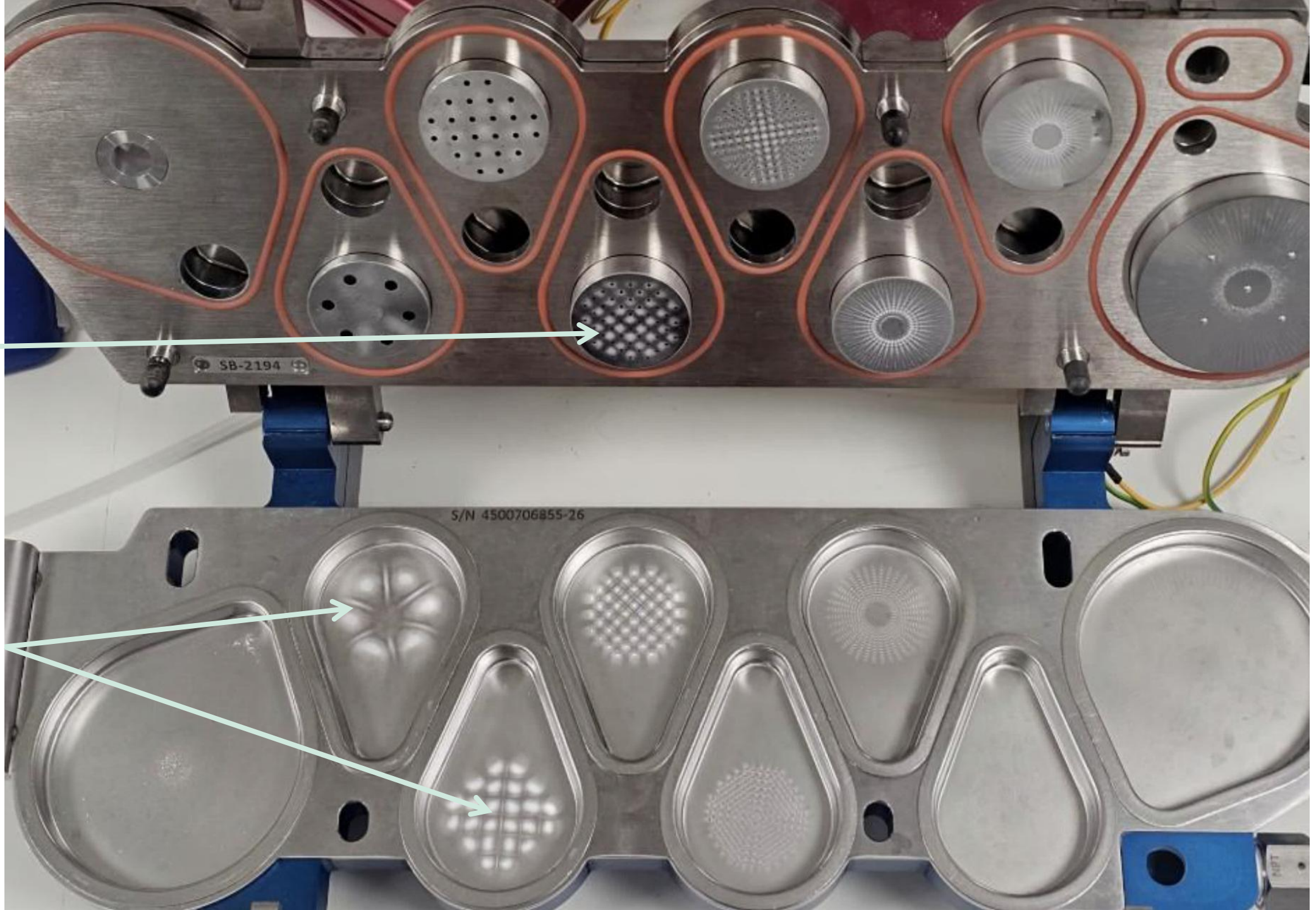
Bounce
patterns



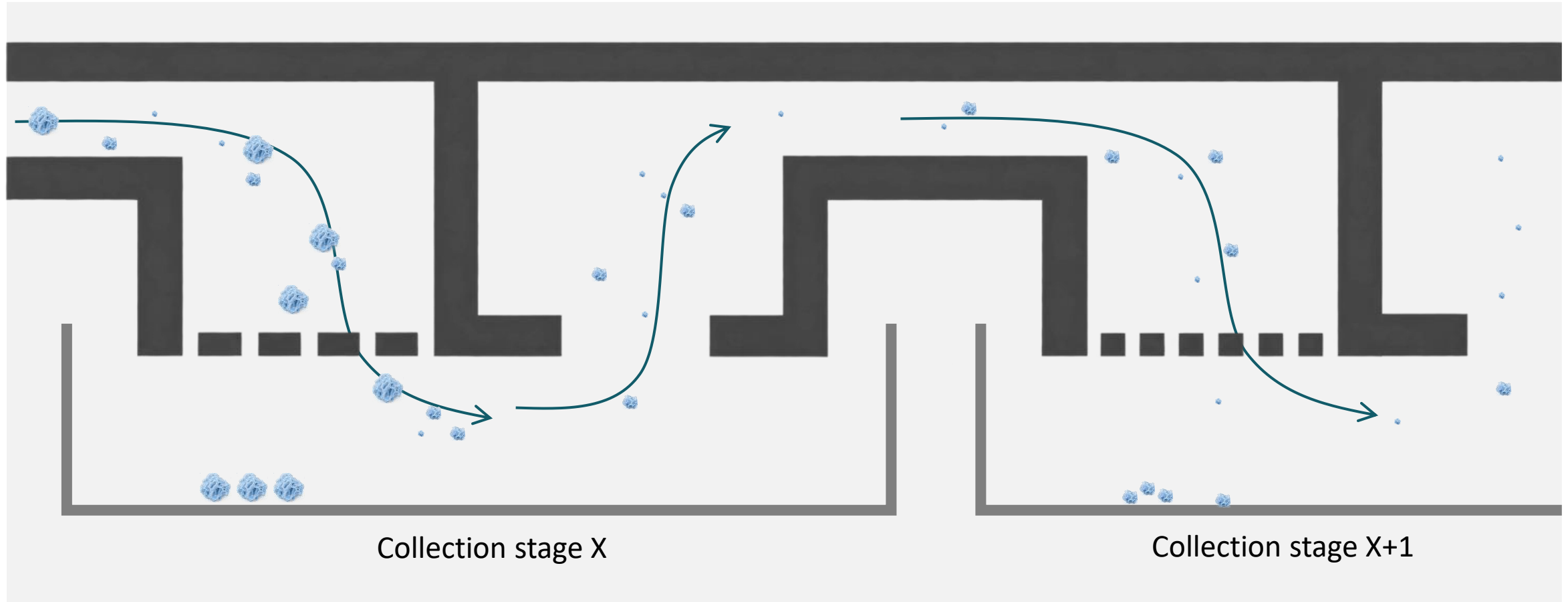
18 mg

Powder
hitting jets

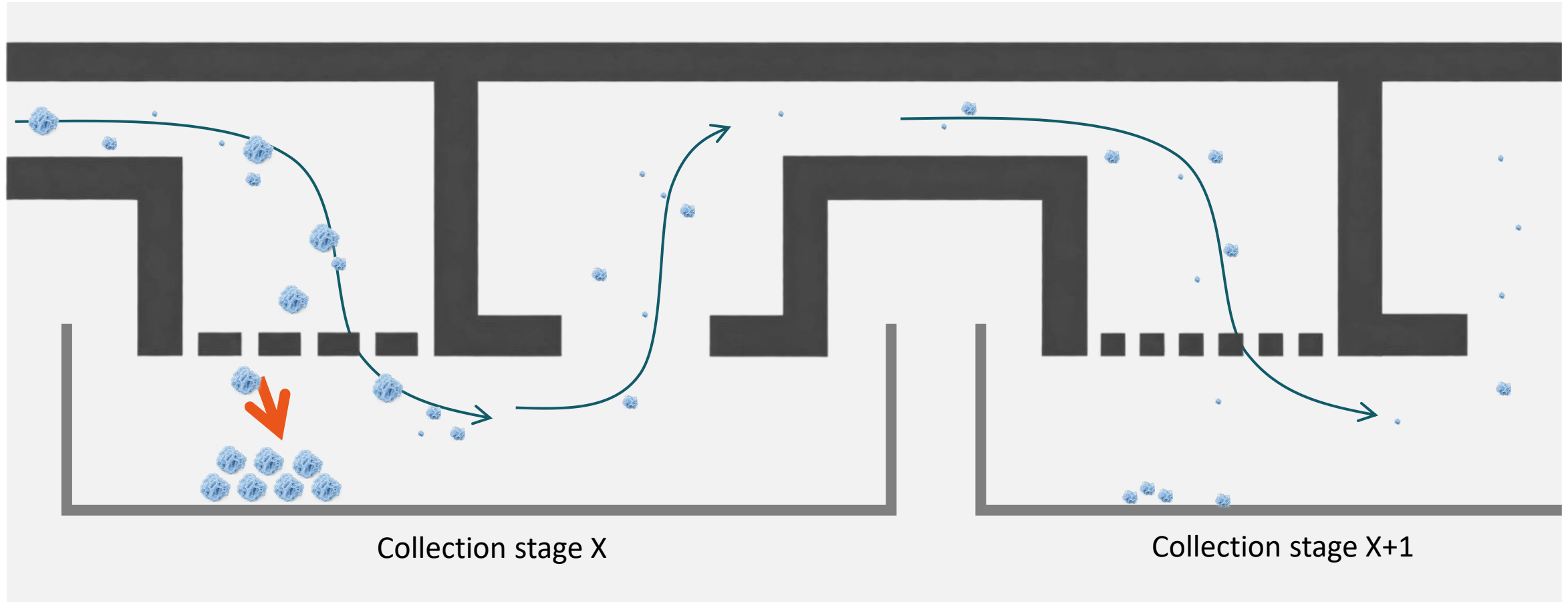
Bounce
patterns



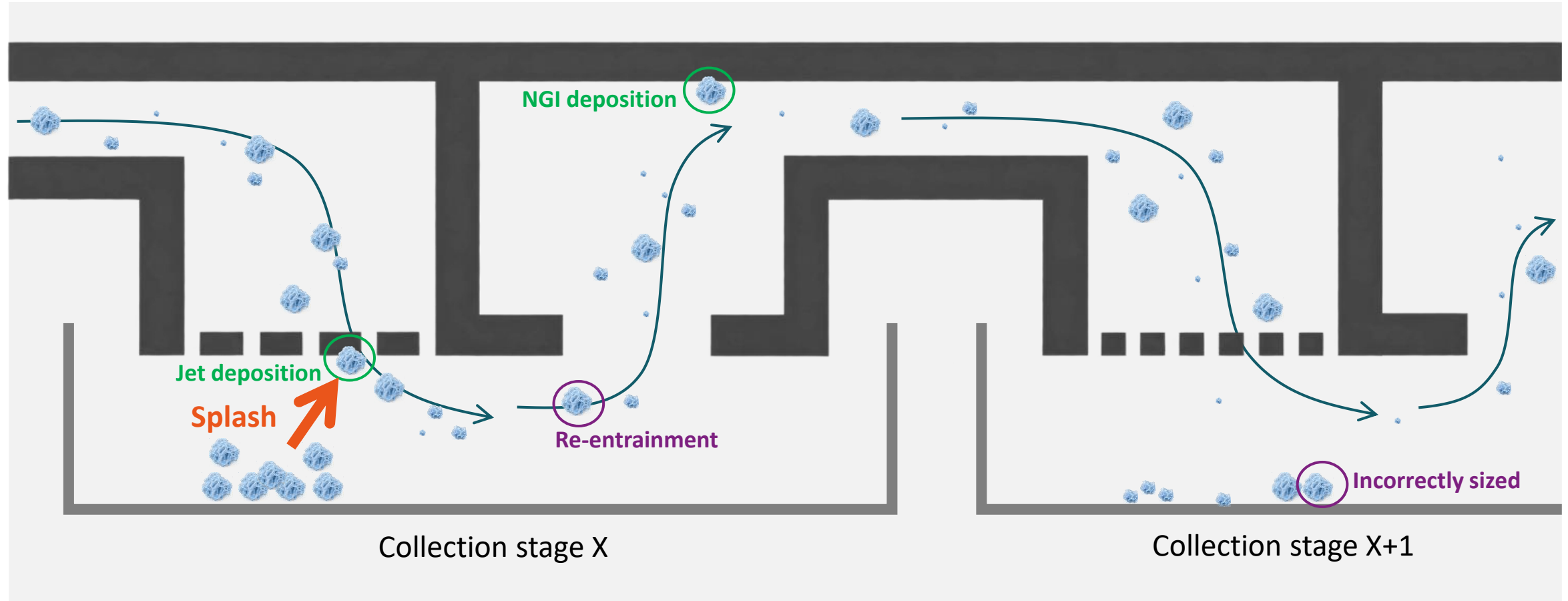
Stage overloading & particle re-entrainment

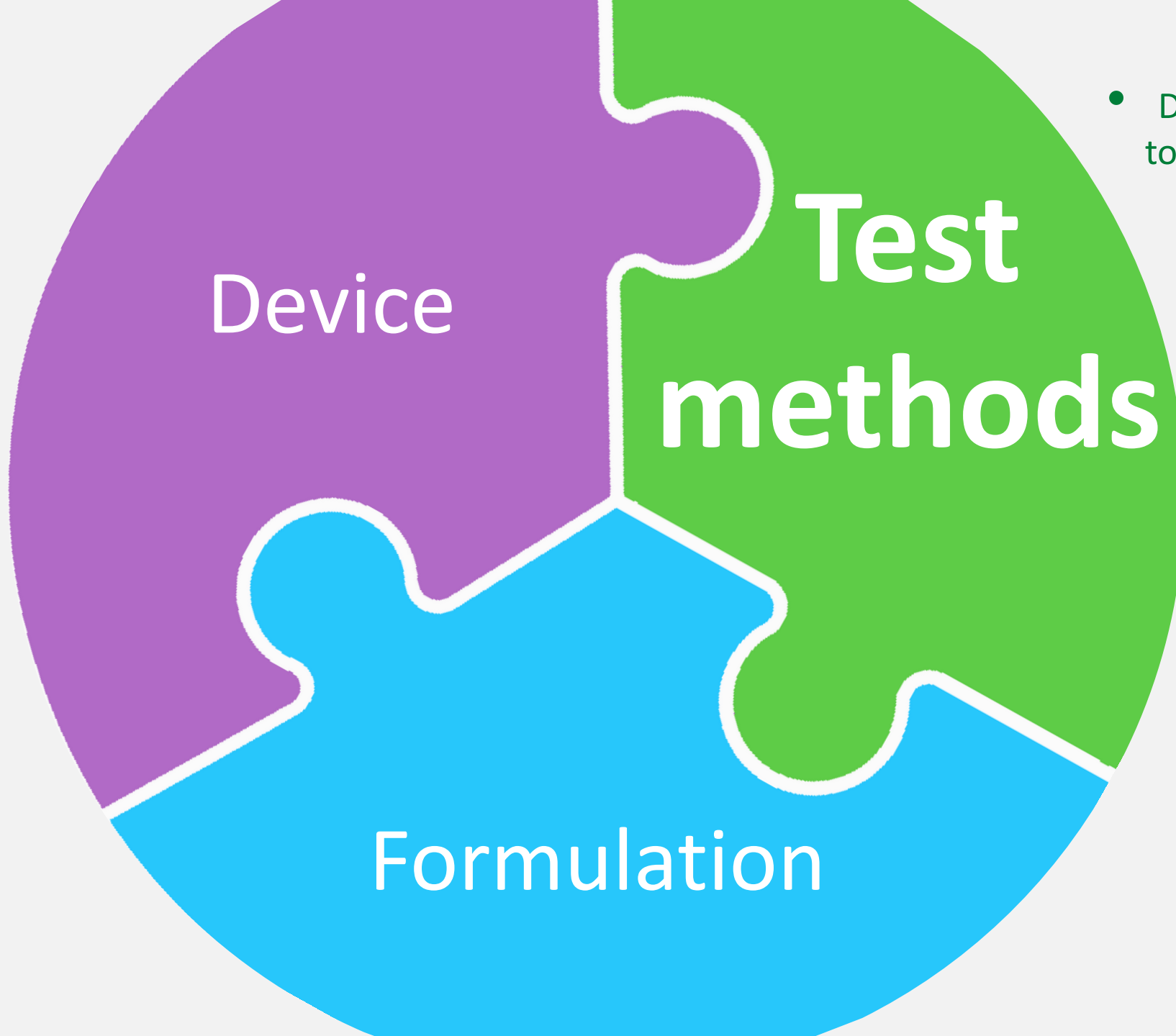


Stage overloading & particle re-entrainment



Stage overloading & particle re-entrainment





- Do we need to adapt test methods for **higher respirable doses?**

Previous studies: how to stop bounce for high respirable doses?

Method	Studies	Successful?	Potential problems
Conventional cup coating incl. more of it	Peterson et al., 2023	No	Powder impacts powder → re-entrainment not addressed
Aqueous solution in NGI cups	Rissler, Asking & Dreyer, 2009; Peterson et al., 2023	Yes	- Affects stage cut offs by closing gap between NGI cup and jet. - Potential separation of liquid by fast moving air jets
Aqueous solution-soaked fibrous filters in NGI cups	Dunbar, Kataya & Tiangbe, 2005; Rissler, Asking & Dreyer, 2009; Grasmeijer et al., 2012; Peterson et al., 2023	Yes	Affects stage cut offs by closing gap between NGI cup and jet.
Dry loose filter in NGI cups	Grasmeijer et al., 2012	No	- Affects stage cut offs by closing gap between NGI cup and jet. - Filter papers have volume so may act as powder filter and trap small particles which would otherwise pass to the next stage
Copley gravimetric cups	Wu et al., 2013; Duan et al., 2013; Acosta et al., 2021; Kadrichu et al., 2021	Maybe	One study with 45 mg carrier-free fill mass showed better results with wetted filters.
Multi-Stage Liquid Impinger (MSLI)	Wong et al., 2010; Grasmeijer et al., 2012	Yes	- Old tech from 1990s, labour intensive, hard to mechanise. - Less granular than NGI by stage breakdown.



We're a team of engineers and physicists,
so, we come at things from a different perspective...

What about a different approach?

- Reduce powder overloading in cups
- Reduce NGI flowrate (to reduce particle momentum)

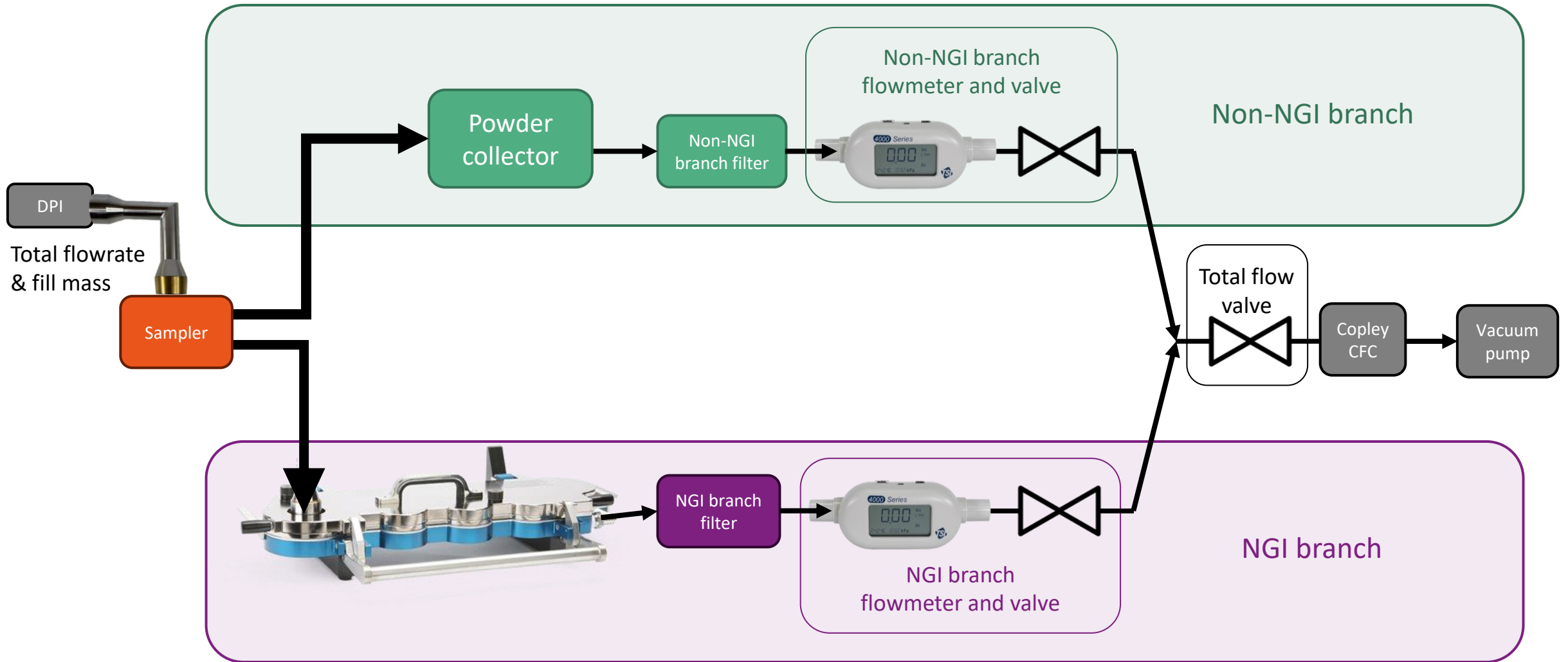
BUT

- Do not reduce DPI fill mass
- Do not reduce DPI flowrate

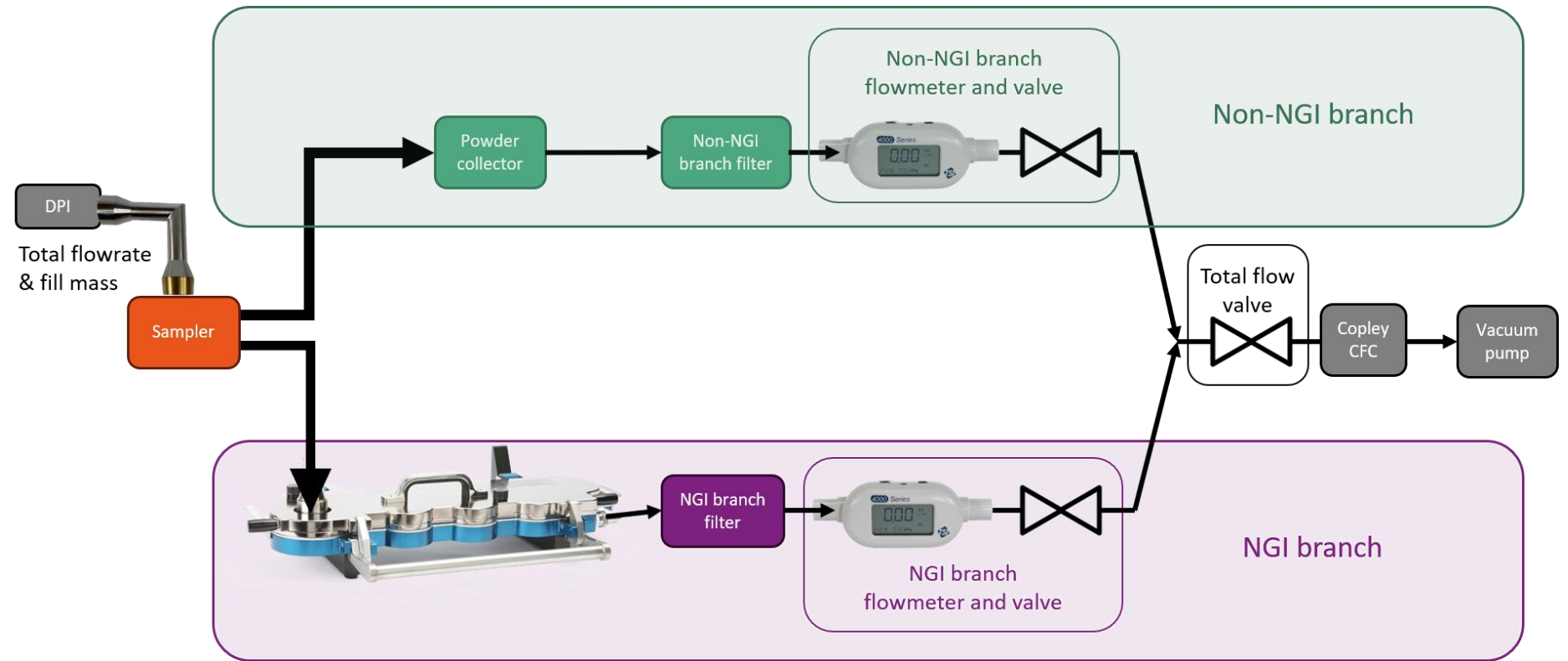


Can we measure a **sample** of the respirable powder?

Introducing the “sample” method



“Sample” method



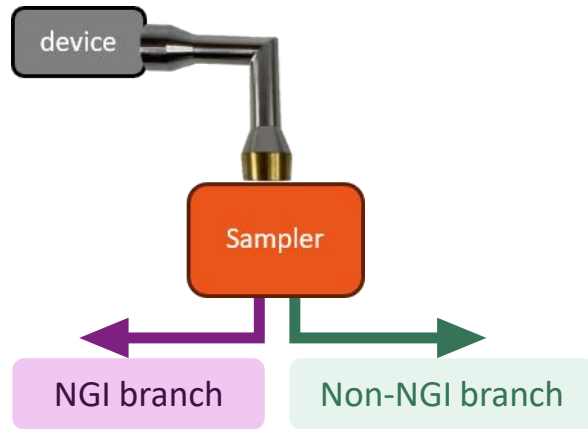
Benefits:

- Less powder going into NGI = reduce overloading of NGI cups
- Lower flowrate through NGI → Lower velocity → powder enters with less momentum, reducing bounce

Challenges:

- How to ensure sample is representative?

How to ensure a representative sample?



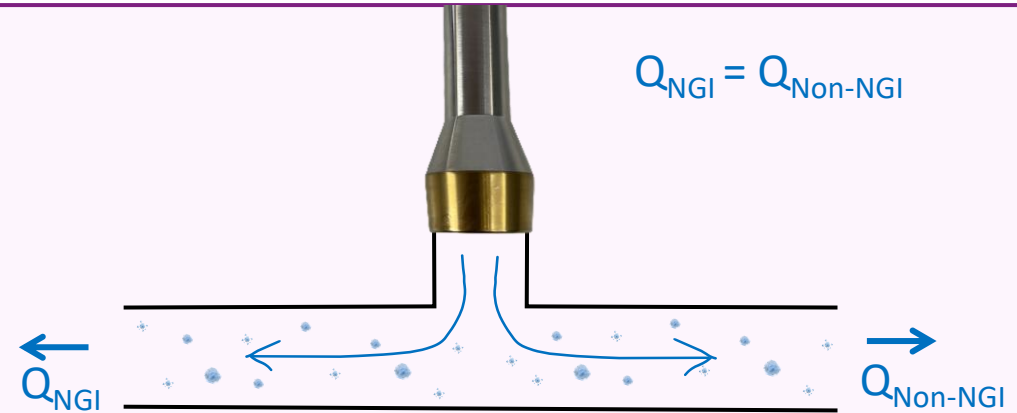
Sampler requirements

Two branches must have equivalent particle size distributions

Known flowrate through the NGI

Recover all the powder

Known proportion of powder mass per branch



Sampler method 1: Equal Split

- Equal flowrate (Q) and velocity (V) down NGI branch and non-NGI branch
- T-junction (not Y-junction) for equal split of larger particles
→ but increases chance of deposition in the sampler

Equal split method: 72 mg

Respirable dose ~ 40 mg $\rightarrow$ still ~ 20 mg through the NGI

But the flowrate has also halved (from 48 to 24 LPM)

$\rightarrow$ powder momentum greatly reduced

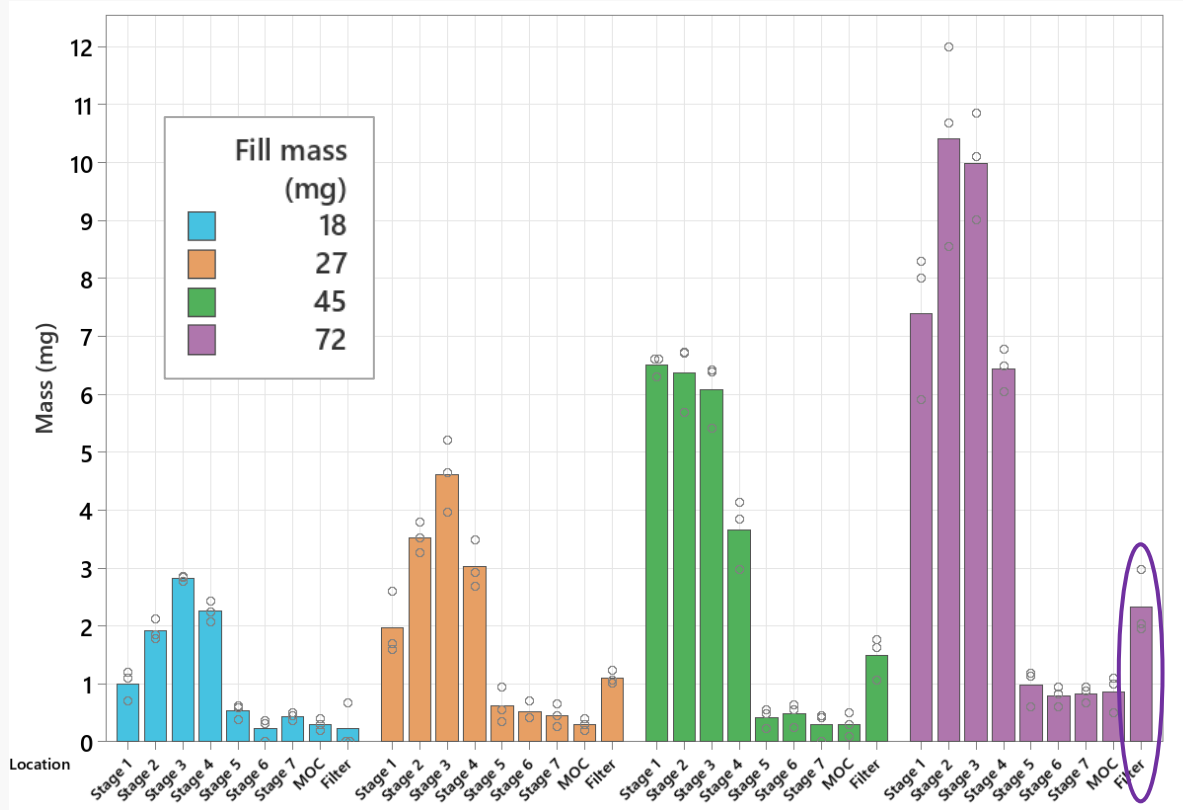
No deposition
on jets

Minimal bounce pattern



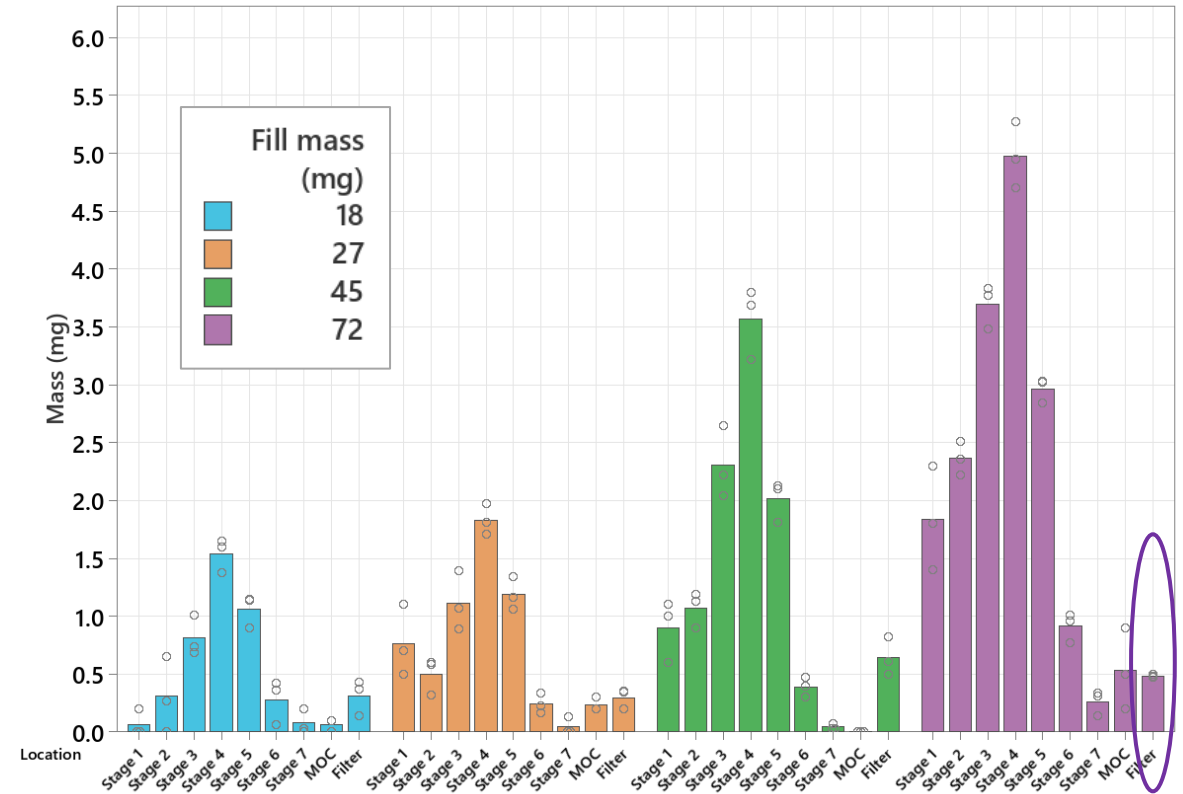
Std NGIs based on USP<601>

Flowrate (Q) = 48 LPM



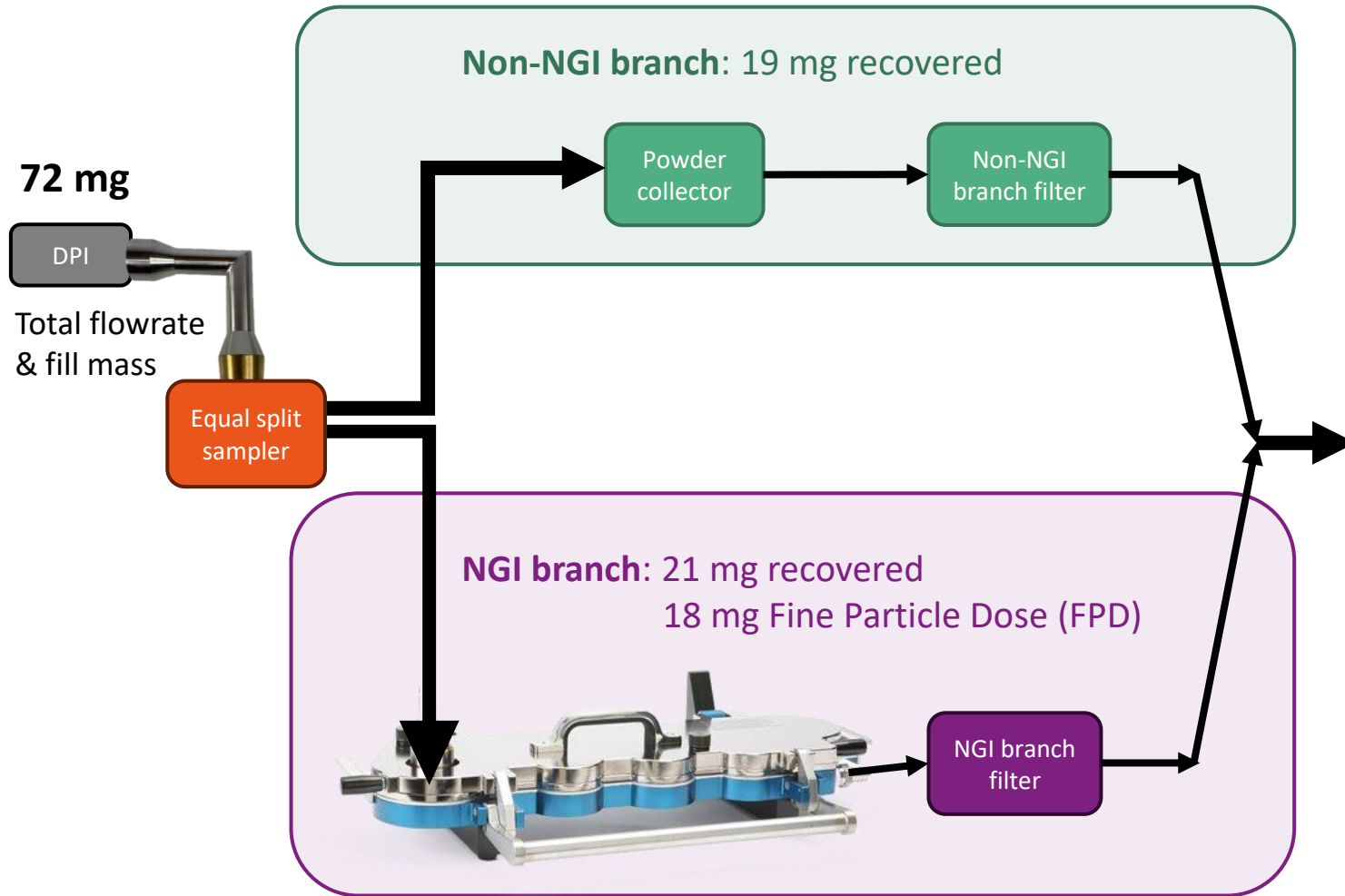
Equal split - sample method

Flowrate (Q) = 24 LPM



Y axis half scale for equal split method
→ half of powder recovered in NGI

- Distributions less skewed
- Proportionally less mass on filter



APSD calculations

(Aerodynamic Particle Size Distribution)

Recovery ratio of 19:21

$$\text{Total FPD} = \text{FPD}_{\text{NGI}} \times \frac{\text{Total recovered mass}}{\text{NGI recovered mass}}$$

$$= 18 \times \frac{19+21}{21}$$

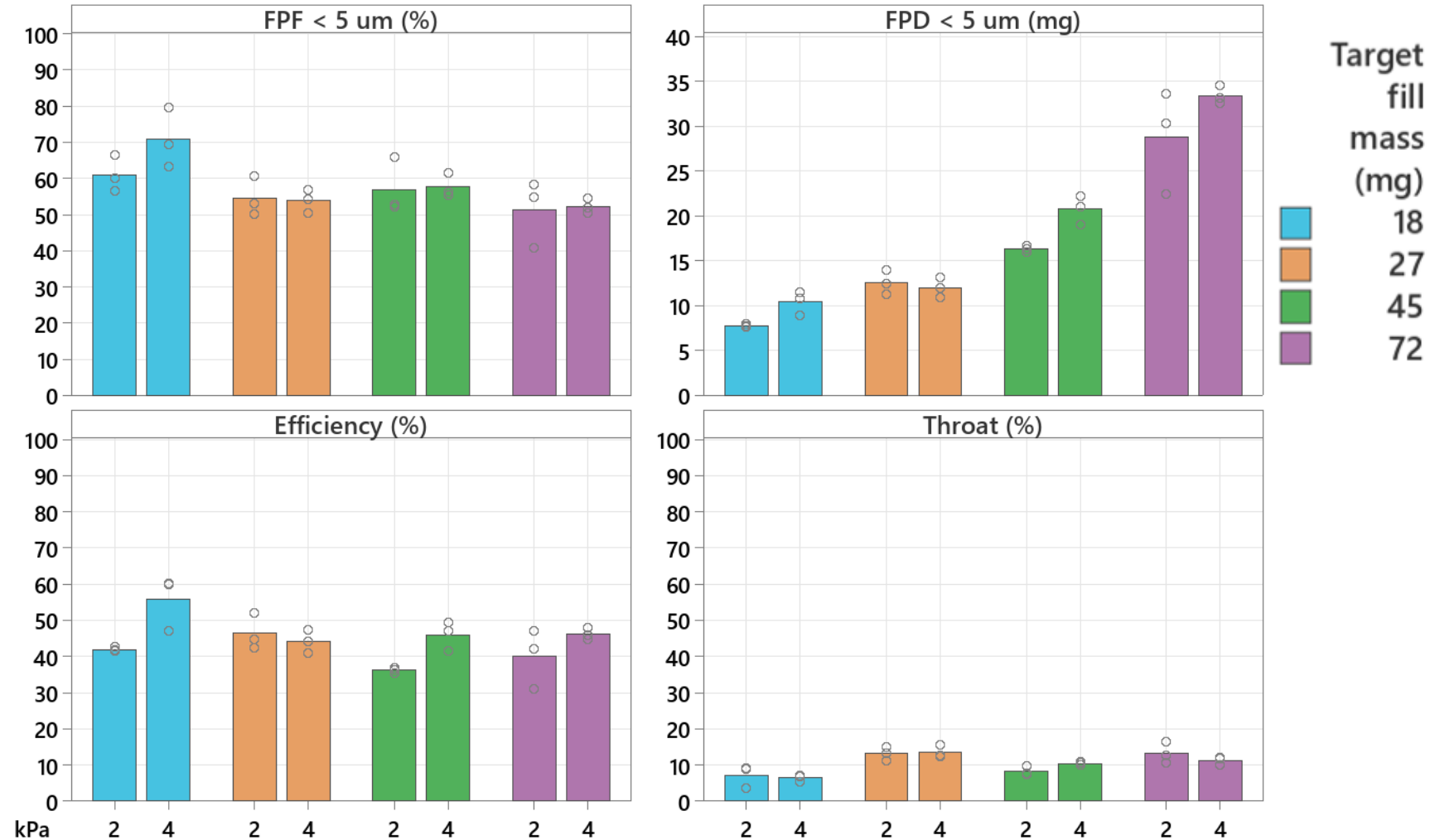
$$= 18 \times 1.9$$

$$= 34 \text{ mg}$$

Quattrii CF performance from 18 to 72 mg

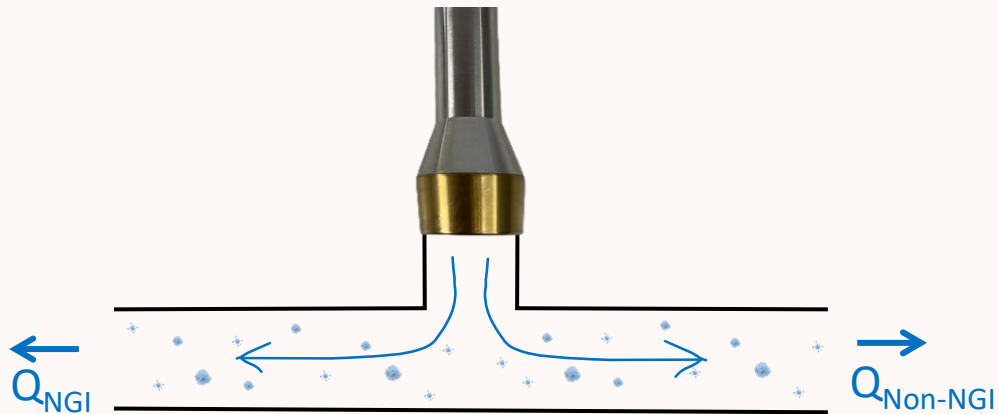
- Spray-dried biologic placebo
- Equal-split “sample” method
- Consistently good performance, even at 4x fill mass
- FPDs from 5 mg to 35 mg
- FPF > 50% consistently @ 2 & 4 kPa
- Good efficiency even at high fill masses
- Low throat deposition

Quattrii CF offers a **versatile** platform for biologics



Next steps: Improve sampling method

Sampler method 1: Equal split T-junction



$$Q_{\text{NGI}} = Q_{\text{Non-NGI}}$$

Issues:

- Deposition in T-junction reduces recovery
- Equal flowrates not always optimal:
 - What if DPI flowrate is 90 LPM?
 - What if DPI flowrate is < 30 LPM?

Learnings:

- Reducing the NGI flowrate had a big effect – can we minimise it?



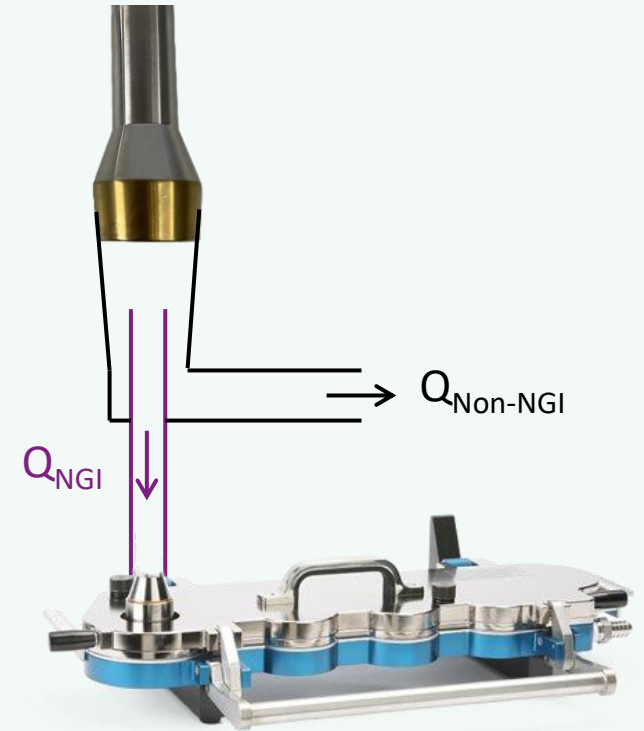
We got our thinking caps on...

and came up with a new concept

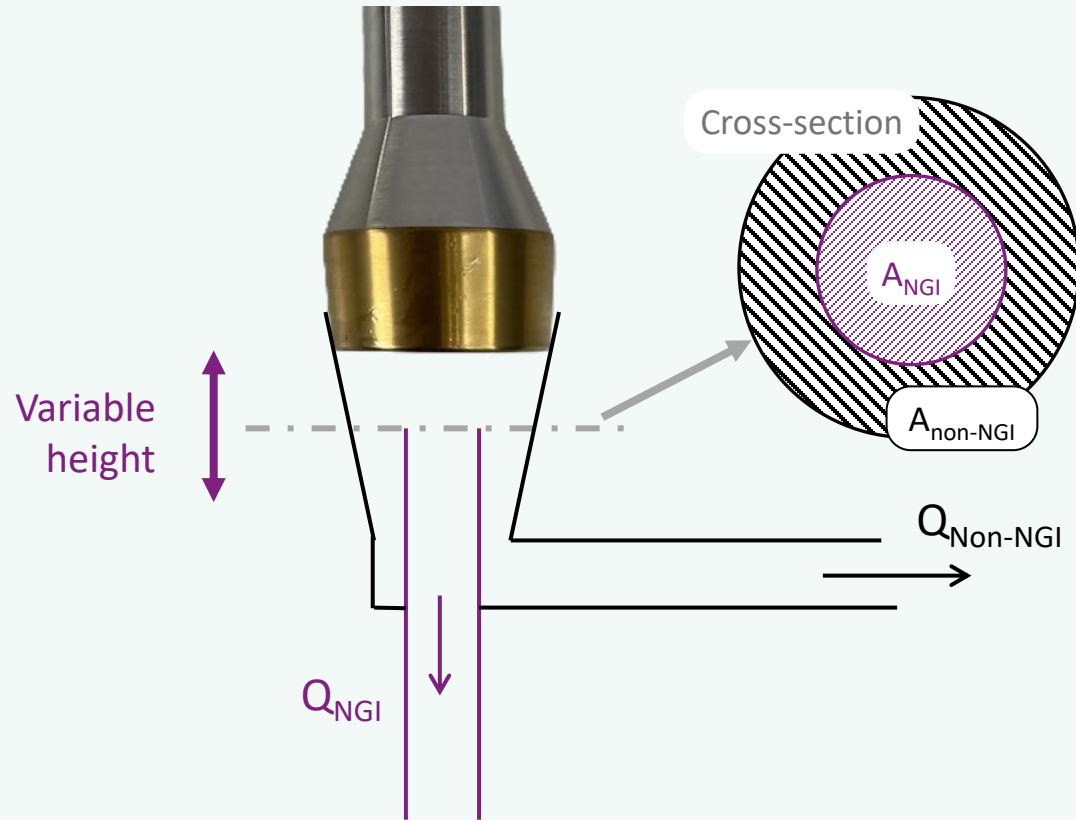
Method 2: Fixed NGI flowrate – Design concept

Key idea: NGI flowrate (Q_{NGI}) is fixed at 15 LPM (minimum NGI flowrate as specified)

- Minimise powder loading and flowrate through NGI
→ Minimise bounce & re-entrainment
- New in-line design concept to replace T-junction



Method 2: Fixed NGI flowrate (Q)



$$Q_{NGI} \neq Q_{Non-NGI}$$

$$Velocity_{NGI} = Velocity_{Non-NGI}$$

To avoid biasing the powder distributions, the velocities must be equal

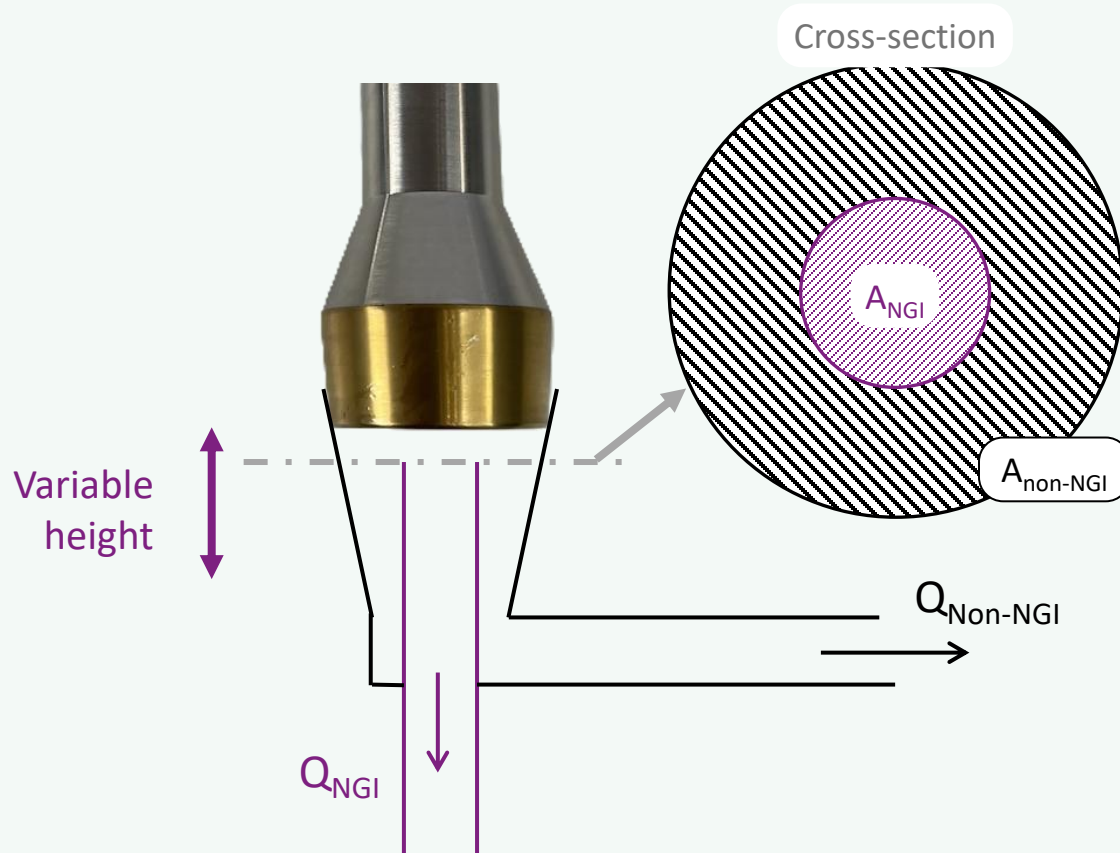
$$Velocity (V) = \frac{Flowrate (Q)}{Area (A)}$$

Method 2: Fixed NGI flowrate (Q)

Flowrates (Q) not equal

Velocities need to match

→ Control the cross-sectional area



Example 1: high DPI flowrate

$$Q_{DPI} = Q_{NGI} + Q_{Non-NGI}$$

$$90 \text{ LPM} = 15 \text{ LPM} + 75 \text{ LPM}$$

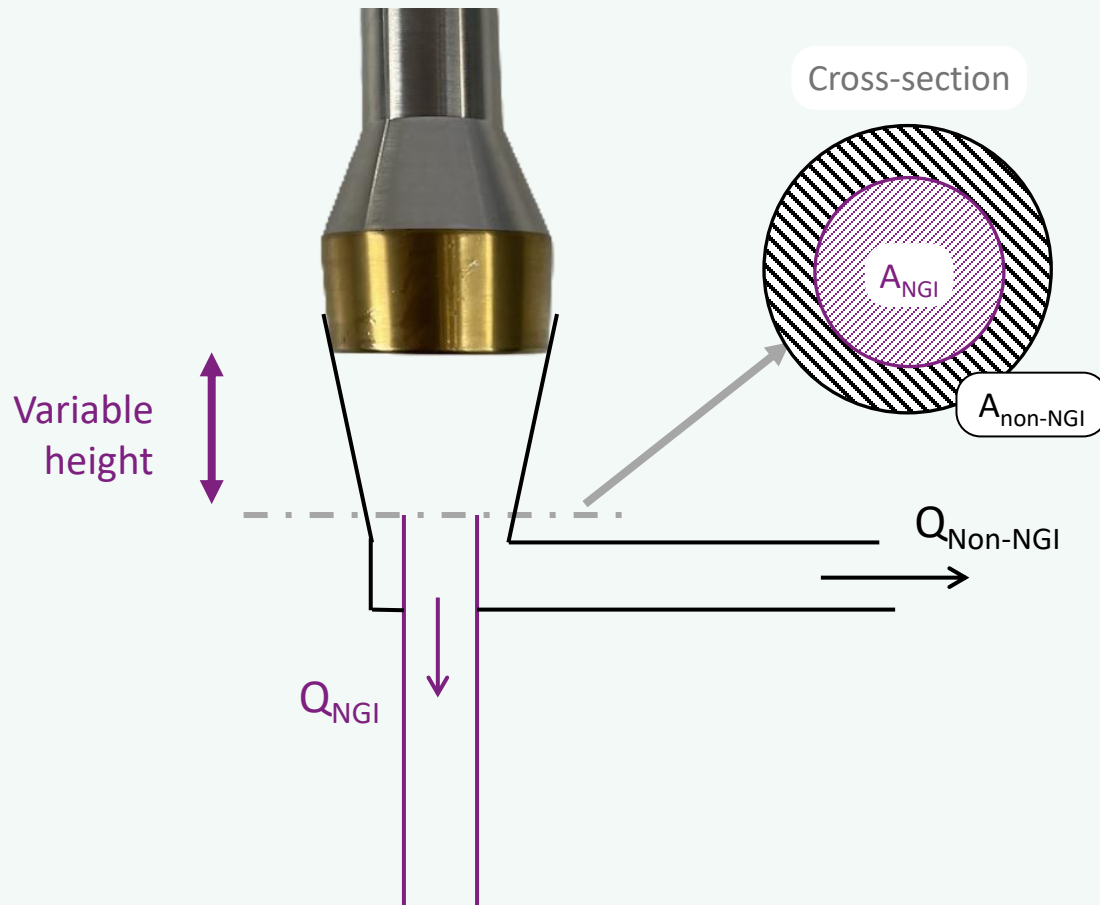
$$\frac{A_{Non-NGI}}{A_{NGI}} = \frac{75}{15} = 5:1$$

Method 2: Fixed NGI flowrate (Q)

Flowrates (Q) not equal

Velocities need to match

→ Control the cross-sectional area



Example 2: low DPI flowrate

$$Q_{DPI} = Q_{NGI} + Q_{Non-NGI}$$

$$25 \text{ LPM} = 15 \text{ LPM} + 10 \text{ LPM}$$

$$\frac{A_{Non-NGI}}{A_{Non-NGI}} = \frac{10}{15} = 0.7:1$$

Method 2: Fixed NGI flowrate (Q)

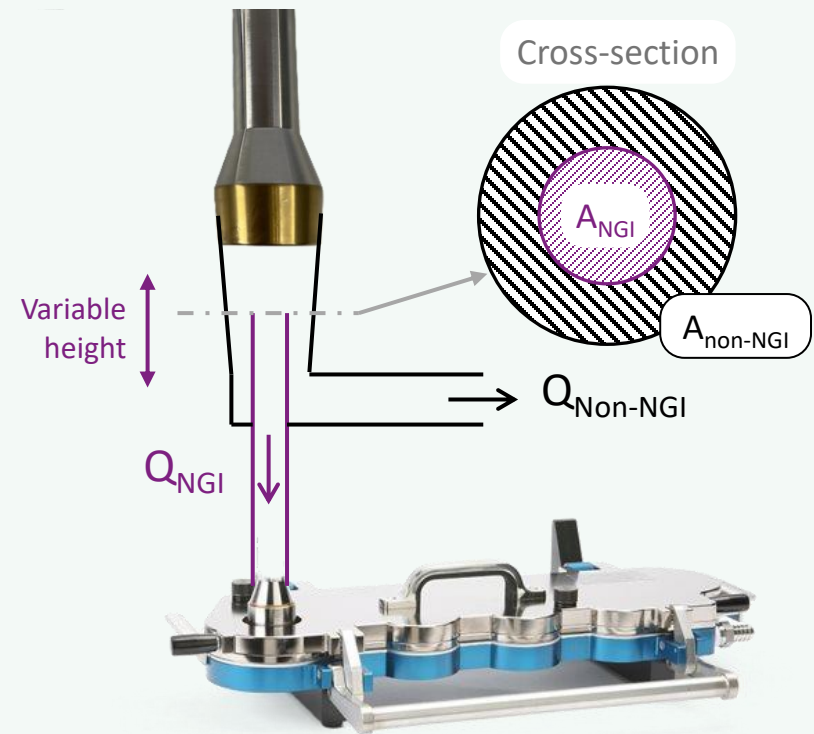
Flowrates (Q) not equal

Velocities need to match

→ Control the cross-sectional area

Benefits:

- No T-junction = **improve powder recovery** by reducing deposition in sampler
- Minimise powder loading and flowrate through NGI
→ **Minimises bounce & re-entrainment**
- Fixed NGI flowrate → **same cut-off diameters** for all testing
 - **Convenient comparison** of stage deposition even for different DPI flowrates



- **Versatile:** works for a wide range of fill masses
- Inherent **moisture protection**
- Good drug delivery **performance**

Device
(inhaler)

Test
methods

- Test methods appropriate for **changing landscape** of therapies

Formulation

- **Delicate** molecules
- **High** respirable doses



Thank you

Jamie, David and I are happy to discuss further

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