Precision Packaging for Pediatric Drug Products

When packaging becomes part of the dose delivery system

Granule Sachet Scale-Up: Implications for CMO Selection, Dose Control, and Regulatory Readiness

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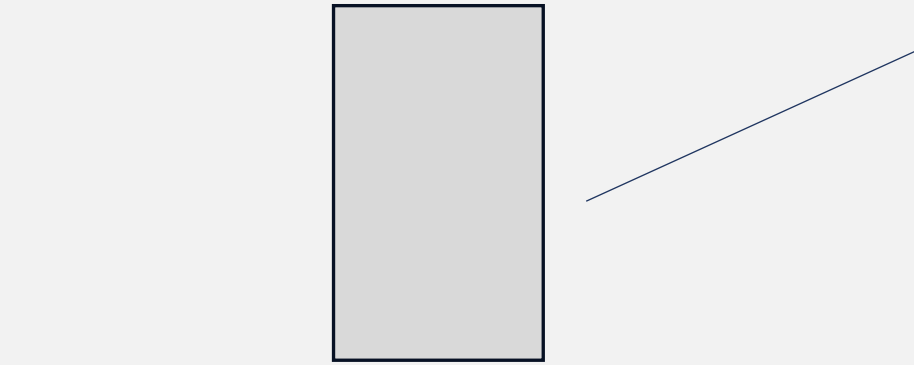
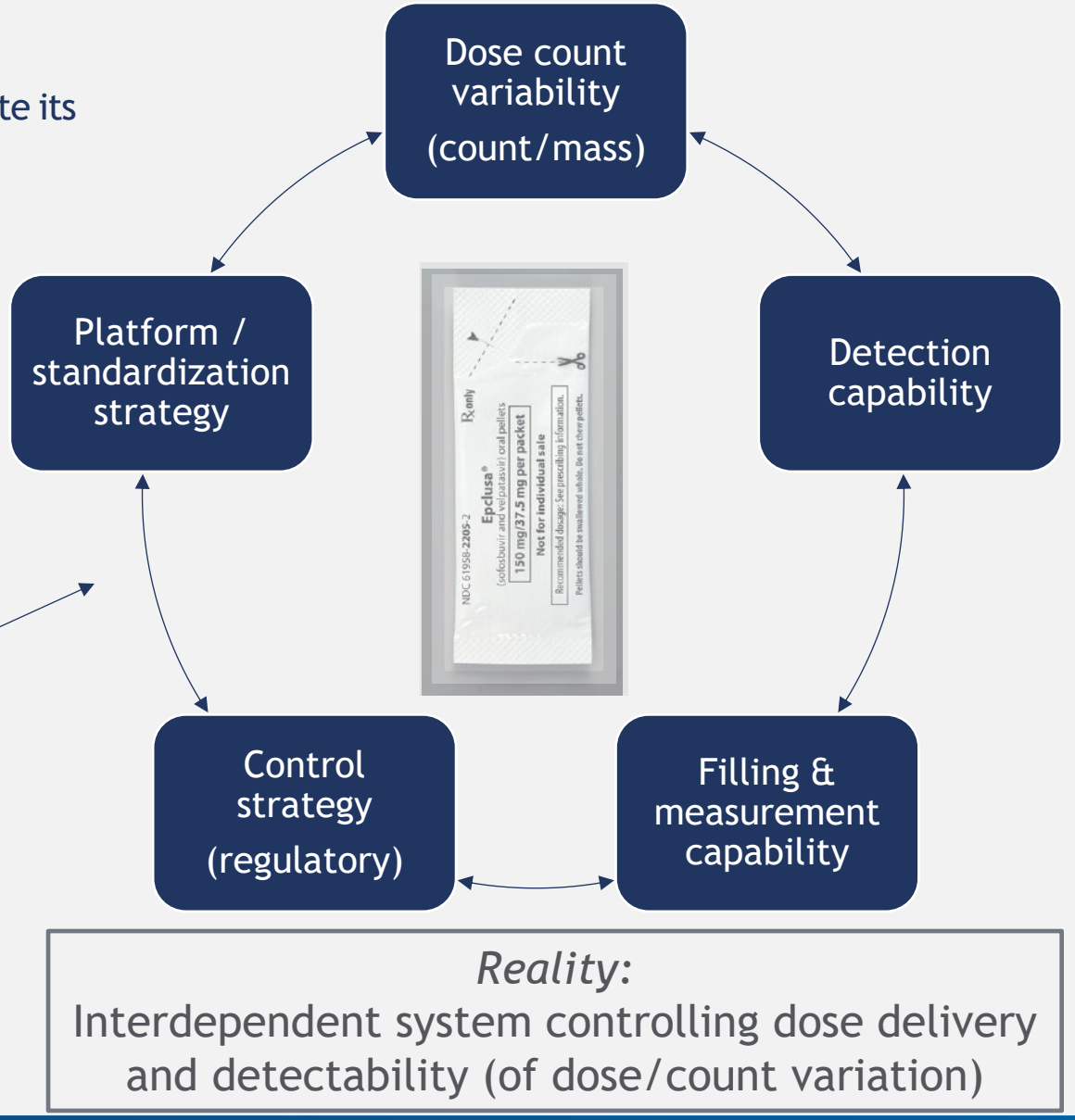
GILEAD
Creating Possible

It’s NOT “just” packaging.

- Packaging is often assumed to be the simplest part of the system—despite its critical roles in protection (moisture, light, oxygen), containment, communication, and enabling safe and effective use.
- For stick packs, these functions directly impact dose delivery, making packaging the highest-risk element:
  - Dose variability
  - Detectability
  - Regulatory readiness



Perception:
Simple container

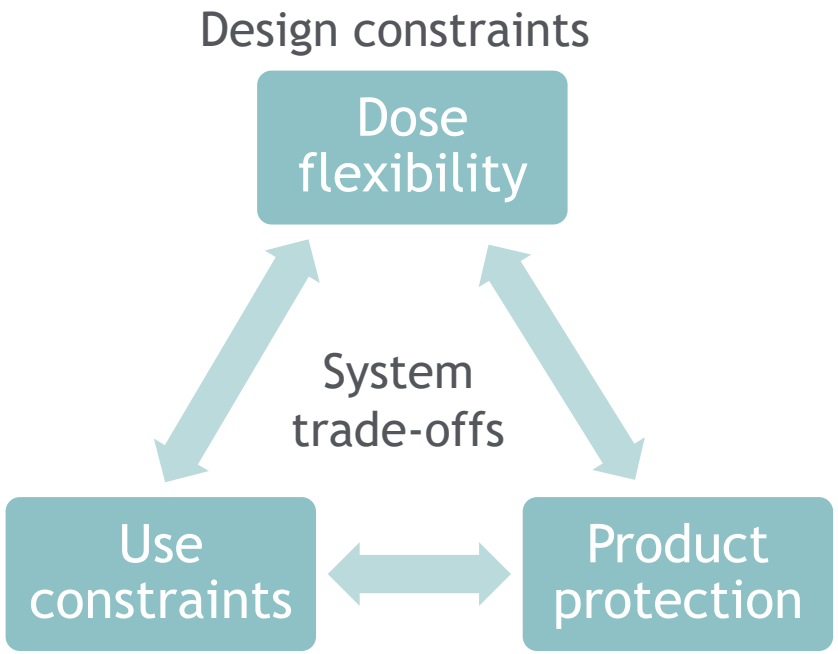


Reality:
Interdependent system controlling dose delivery and detectability (of dose/count variation)

Why granules in stick packs matter

- Pediatric dosing demands flexibility, but packaging introduces variability that must be measured and controlled.
- Stick packs require a robust control strategy across:
  - Dose accuracy (low-count variability & detectability limits)
  - Product protection (moisture sensitivity & physical integrity)
  - Patient/caregiver usability (unit-dose handling & administration)

Packaging defines how the dose is delivered, measured, and controlled.



CMO capability for stick packs is more limited than expected

Limited number of CMOs **with true experience** in pediatric stick pack / sachet filling.

The key challenge is not the pack – it is whether the CMO can execute the required control strategy. At low counts, measurement and control capability becomes the limiting factor.

"Can run packets" is not the same as "can commercialize robustly".

Hidden Gaps

- Low-count fill capability (precision at low unit counts)
- Detection capability (limits of detection vs process variability)
- GMP / commercial readiness (validated control strategy)

What to verify

- Demonstrated experience with low count sachets
- Equipment fit for mini-tablets (not powders)
- Inspection + IPC capability
- FDA / inspection readiness

CMO capability requirements

CMO capability—not packaging material—drives commercialization risk.

From development to commercialization: critical lessons learned

Mistakes to avoid:

1. Engaging packaging too late
   - Early assumptions lock in downstream constraints
2. Designing for dose without integrating detectability
   - Variability becomes difficult to measure and control
3. Equating engineering success with commercial readiness
   - Successful runs do not demonstrate sustained process capability
4. Delaying regulatory strategy rather than building it in parallel
   - Late alignment creates rework and filing risk

Key insight: Commercialization risk is created by early assumptions - especially around detectability and control - not late-stage execution.

Other system drivers of variability and complexity

Granule agglomeration / twinning

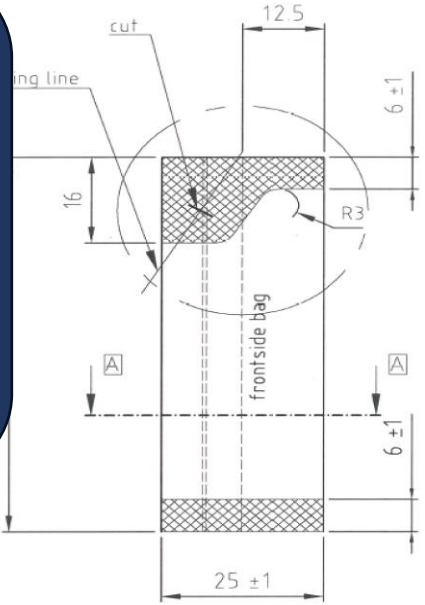
- ✓ Non-uniform counts
- ➢ Sifting

Granule static charge

- ✓ Erratic feeding → fill variability
- ➢ Deionization

Desiccation / moisture protection

- ✓ Limited in-sachet desiccant options
- ➢ Over-engineering → cost and supply risk



Example stick pack geometry

In-line printing / MOQ (minimum order quantity)

- ✓ Low volume → MOQ constraint
- ➢ Reduce variants
  - ➢ SKU variability→ increased complexity
  - ➢ Label variants→more lots + release complexity (no britestock-like flexibility)

Standardizing / platforming

- ✓ SKU variability increases complexity
- ➢ Standardize formats

Key insight: Material, handling, and supply constraints - agglomeration, static, moisture, MOQ, and platforming - drive variability and commercialization complexity in low-count systems

Case Study 1: Dual product granules – co-packaging complexity in stick packs

As dosing complexity increased (dual products + lower counts), existing equipment could not deliver the required precision and control.

Challenge:

- Co-packaging two granule types into a single stick pack
- Low fill counts required (potentially **down to 3 granules**)

What Changed:

- Legacy equipment insufficient
- Required:
  - Multi-dosing stations
  - Integrated weigh systems
- Enabled accurate filling at low counts

Outcome:

- Dual dosing at low counts became feasible
- Packaging architecture defined manufacturability and dose control

Key takeaway:

Ultimately, it is packaging—and its ability to measure and control dose—that defines feasibility in dual-product and low-count systems.

Case Study 2: MOQ and artwork strategy in low-volume stick pack programs

During development, large volumes of pre-printed stick pack material expired before use, highlighting the mismatch between MOQ-driven supply and low product demand.

Challenge:

- Country-specific artwork across multiple SKUs
- High MOQ for pre-printed film
- Low demand → expired material

Decision Point

- Continue with pre-printed, country-specific materials (risk: scale waste across SKUs)
- Or shift to in-line printing with a common base film (benefit: print only what is needed, lot-by-lot)

What Changed:

- Evaluated and upgraded in-line printer capability
- Enabled singe-color variable printing
- Printed country-specific content lot by lot

Outcome:

- Eliminated material obsolescence
- Reduced SKU complexity and inventory risk
- Aligned supply with actual demand
- Trade-off: Increased number of small lots and release activities (no britestock-like flexibility)

Key takeaway:
In low-volume products, **MOQ and artwork strategy, not primary packaging, drive supply risk** unless flexibility is designed into the system.

What ultimately drives success with pediatric stick packs

Case Study 1 – Technical Constraint

- Low-count dosing introduced control limits
- Legacy equipment could not ensure accuracy
- Capability—not formulation—became limiting

Case Study 2 – Supply Constraint

- Low demand + high MOQ → material obsolescence risk
- Country-specific artwork increased complexity
- Supply strategy—not primary packaging—became limiting

In low-count pediatric systems, success is not defined by formulation alone—it is defined by the ability to control, measure, and flex the entire system.

Questions?

Backup Slides

Schematic of new line with controls for dual dosing and low fill count