Oral Drug Product Administration via Enteral Feeding Tubes: In Vitro Testing

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FDA Guidance: Enteral Tube Administration of Oral Drug Products

In Vitro Testing Prior to Labeling Claims

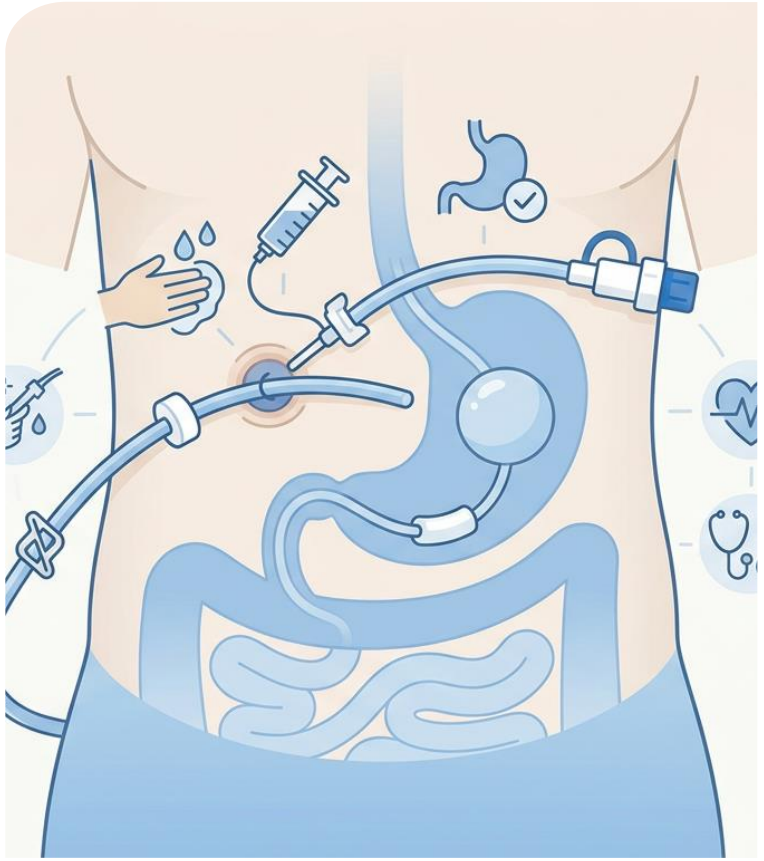
FDA recommends in vitro testing before claiming enteral tube administration in labeling, focusing on dose recovery, clogging risk, stability, and performance for modified-release or enteric-coated products.

Risk-Based Testing & Documentation Standards

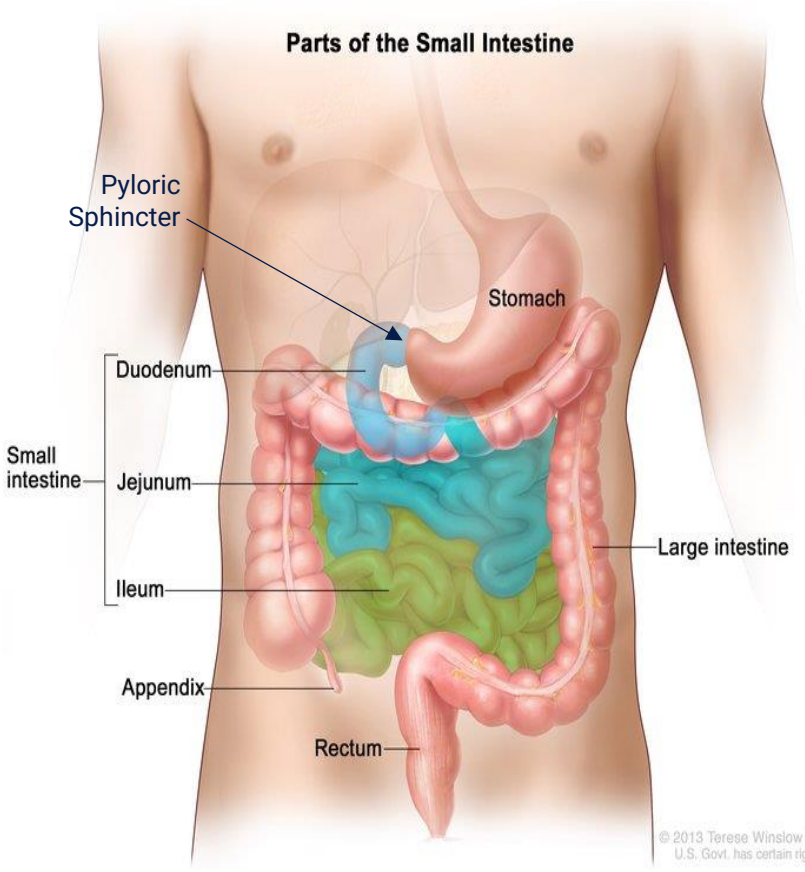
Testing should be risk-based and use representative tube types/sizes, dispersion media, and administration conditions; applicants must document protocols, analytical methods, visual observations, and justification for selected conditions.

Labeling Requirements Based on Data

If supported by data, labeling should specify suitable dosage forms, tube characteristics, preparation/administration steps, flushing, storage, and timing. If not supported, labeling must state the product should not be administered via enteral tube.



Enteral Feeding Tubes (EFT)



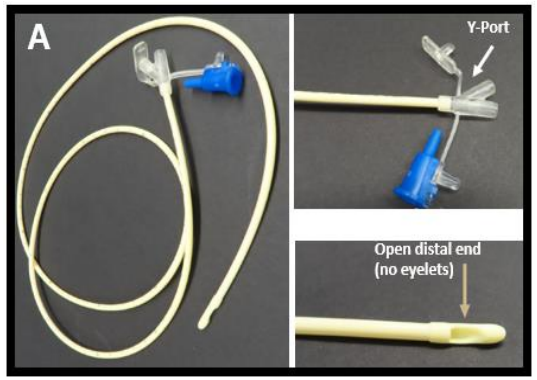
	Feeding Tube Name	Entry Point	Termination Point	
IN SCOPE	Nasogastric (NG)	Nose	Stomach	Pre-Pyloric
IN SCOPE	Gastrostomy (G, PEG)			
OUT OF SCOPE	Gastrojejunostomy (G/J)†	Through abdominal wall	Gastric decompression and medication administration	
OUT OF SCOPE	Gastrojejunostomy (G/J)†	Through abdominal wall	Nutritional feedings only	
OUT OF SCOPE	Jejunostomy (J, PEJ)		Jejunum	Post-Pyloric
OUT OF SCOPE	Nasojejunal (NJ)	Nose	Jejunum	Post-Pyloric
OUT OF SCOPE	Nasoduodenal (ND)*	Nose	Duodenum	Post-Pyloric

†G/J tubes out of scope because of the dual lumen design and variance between manufacturers
*Duodenal placements not common due to tendency for tube displacement/migration and reflux

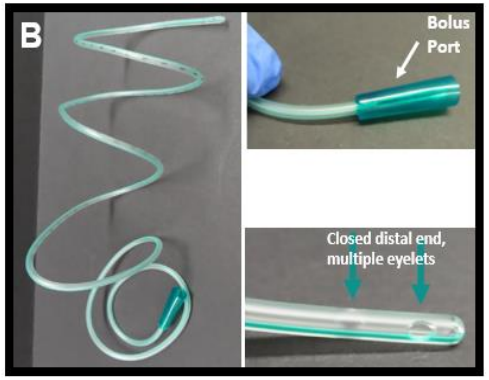
World J Gastroenterol 2009; 15(11): 1281-1288 [PMID: 19294757 DOI: 10.3748/wjg.15.1281]

Enteral Feeding Tubes – Configurations

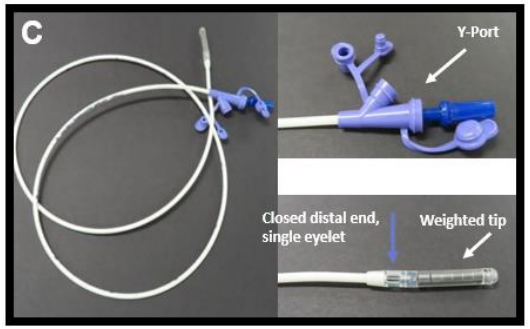
Nasogastric Tubes



A. Legacy NG-tube with Y-Port and open distal end



B. Legacy NG-tube with bolus port, closed distal end, and multiple eyelets



C. Legacy NG-tube with Y-port, closed distal end, weighted tip, and single eyelet

D. ENFit syringe and ENFit Y-port on NG-tube

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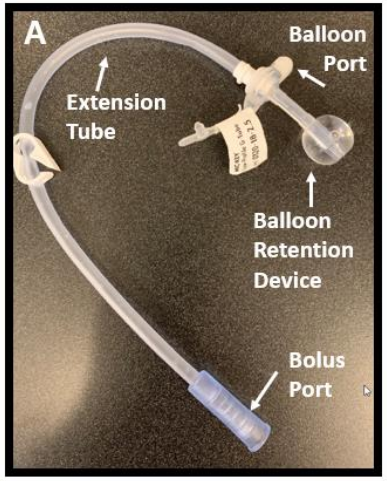
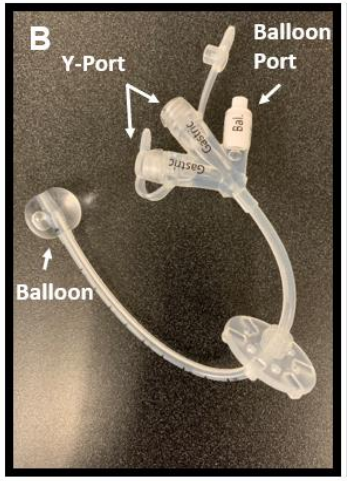
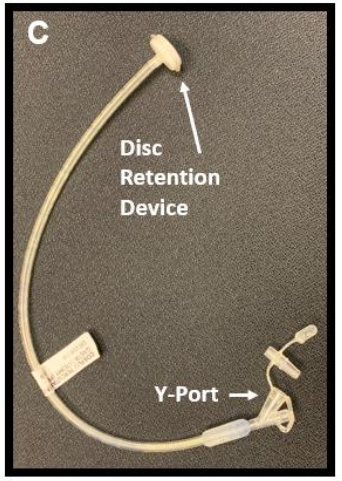
Gastrostomy Tubes



A. Legacy low-profile ('button') G-tube with bolus extension tubing attached

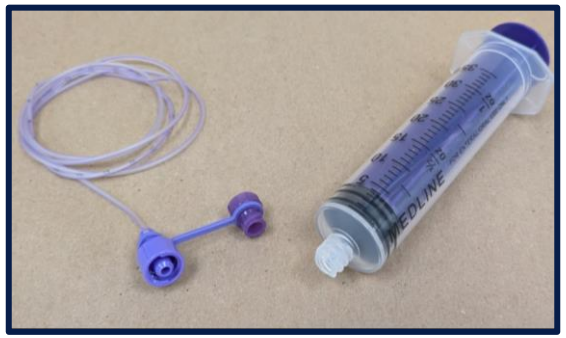


B. Legacy 'standard' G-tube with Y port and balloon retention device

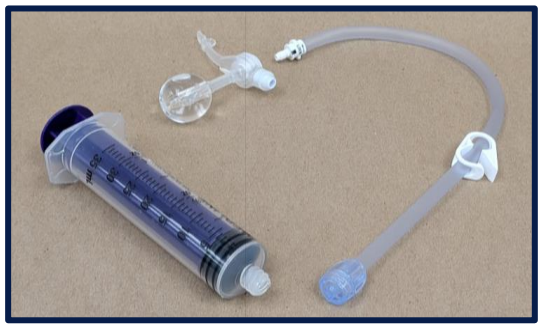


C. Legacy 'standard' G-tube with Y-port and disc retention device

Following ISO 80369-3, healthcare organizations worldwide have transitioned to ENFit enteral tubes and syringes to help reduce the risk of misconnections and medication errors.



Covidien Argyle™ NG Tube (PVC) w/ EN Fit syringe



Avanos Mic-Key™ Balloon with extension tube and EN Fit syringe.

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General Principles

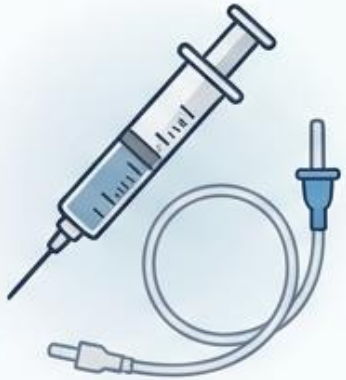
Minimize manipulation of the dosage form

Preserve drug integrity and coating (where applicable)

Achieve uniform suspension before administration

Tablets / Capsules

- Crush tablets or open capsules only if appropriate
- Disperse in minimum volume of vehicle
- Rinse mortar/syringe to capture residual drug



Liquid Formulations

- Dilute if required; verify compatibility with EFT

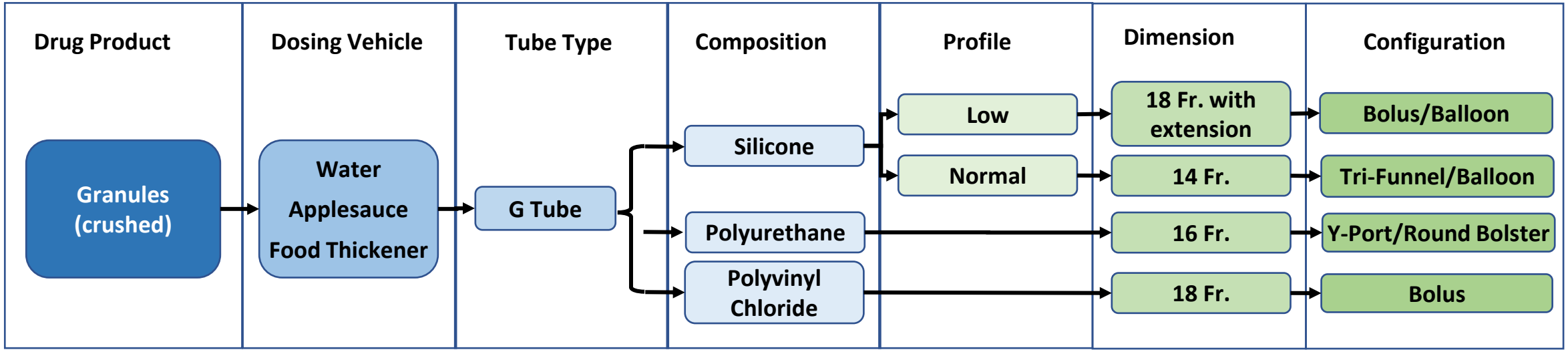
Key Parameters to Define

- Crushing / dispersion method and equipment
- **Contact time** before administration
- **Vehicle** volume and type
- **Flushing protocol** (pre/post dose)

Testing Recommendations Overview

Test	Purpose	Method	Acceptance Criteria
Dose Recovery	Confirm drug passes through tube without significant loss	Flush syringe + tube; assay eluate	≥ 90% label claim
Sedimentation / Redispersibility	Assess suspension settling and ease of resuspension	Allow to stand; timed shake/swirl; resample	Uniform suspension restored within 10 s
In-Use Stability	Confirm potency over preparation-to-admin window	Assay at initial at end of in-use period	≥ 90% label claim at target time
Particle Size	Ensure particles pass tube bore; no blockage	Laser diffraction or sieve analysis	D90 < 250 µm (or per tube bore spec)
Acid Resistance (delayed-release dosage form)	Evaluate coating integrity in gastric pH	Incubate in pH 1.2 HCl; sample and assay	Drug release < 10% at 2 h
Dissolution (extended-release dosage form)	Confirm drug release profile after tube passage	USP apparatus II; pH-matched media	Meets label dissolution specification

Case Study: Granules (2 mm film-coated)



Granules are too large to pass through G tube without crushing

Help with dispersing crushed granules and administration

General consideration: smallest Fr. Size, different construction materials, at least one with balloon, configurations with highest risk of occlusion identified by mechanical evaluation.

Case Study: Granules-Feasibility Studies

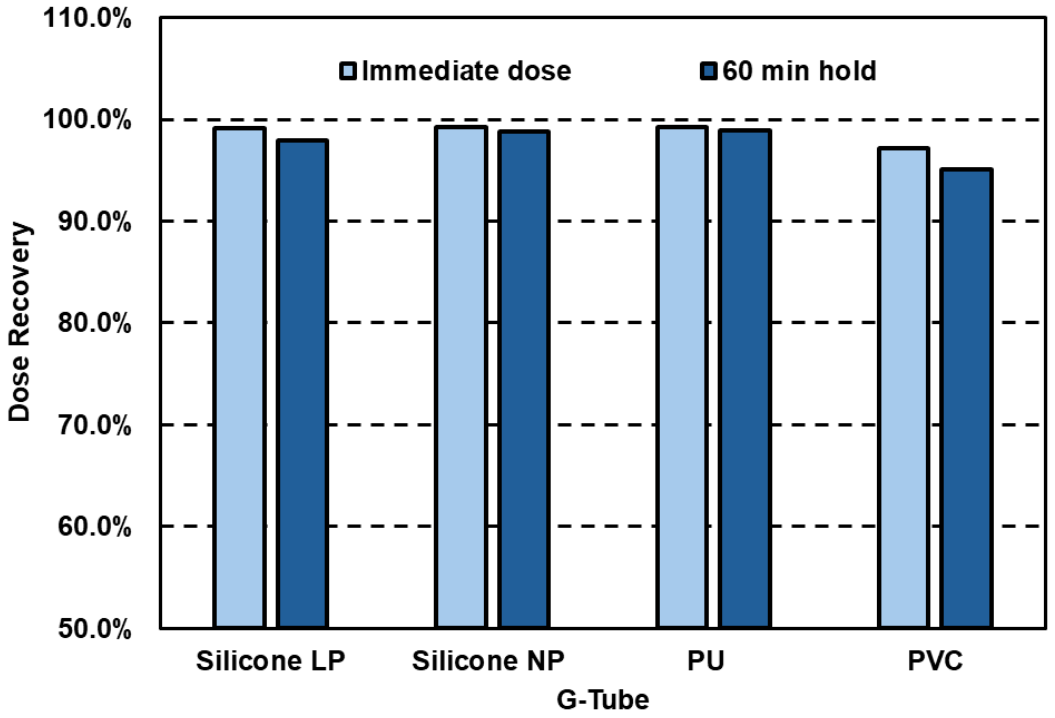
Phase I: Visual Observation

Water Applesauce Food Thickener

When coarsely grounded:

- Water and food thickener didn't disperse crushed granules adequately and caused agglomeration, which led to tube occlusion.
- Applesauce worked better to push granule chunks through the tubes

Phase II: Dose Recovery with Applesauce



LP: low profile; NP: normal profile; PU: Polyurethane; PVC: Polyvinyl Chloride.

Case Study: Granules-Feasibility Studies Cont.

Limitations with Applesauce Dosing

- Harder to rinse from mixing cup for complete delivery
- Risk of squirting mixture when placing syringe plunger
- Higher degradation due to acidic pH
- Availability of applesauce at dosing sites

Benefits with Water Dosing

- ✓ Easier to mix and rinse
- ✓ Drawing up with syringe mitigates squirting risk
- ✓ No meaningful increase in degradation
- ✓ Widely available anywhere

Required a better pill crusher that gives flour like consistency!

Crushing and transferring powder

DP water mixture

Syringe with DP mixture

Deliver dose via G-tube

Pill crusher after rinsing

Syringe and G tube after rinsing

Case Study : Granules-Analytical Testing

Triplicate at T0 and singlet at T1h holding

Visual Observation

- No clogging or sticking was observed up to one hour holding.
- Grinding to fine powder was the key to deliver dose with water mixture.

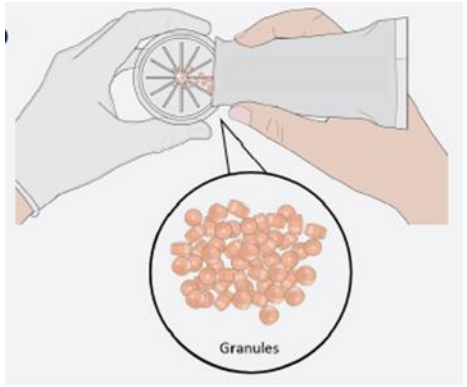
Dose Recovery

- Some loss in recovery is expected during dose preparation and rinse steps.
- Acceptable recovery for all individual preparations.

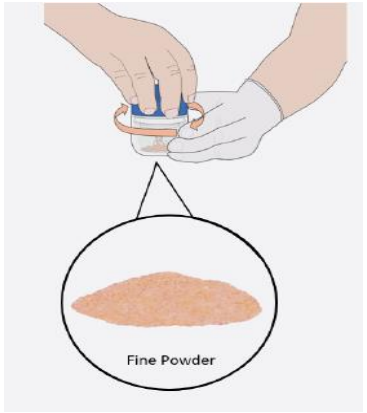
Degradation

No meaningful increase in impurities up to one hour holding. All met acceptance criteria.

Instruction for Use Developed Based on Analytical Testing -Granules G-Tube Dose Preparation and Administration Process

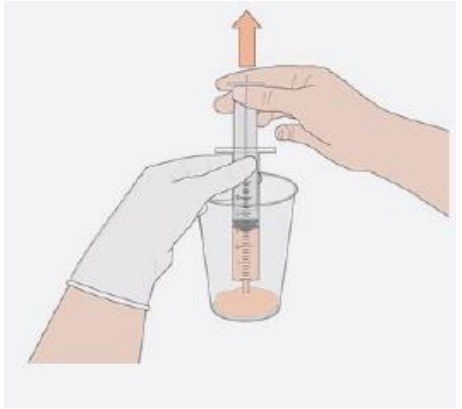


Pour granules into pill crusher

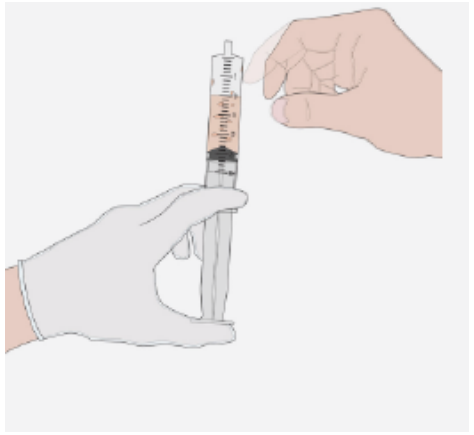


Grind to fine powder

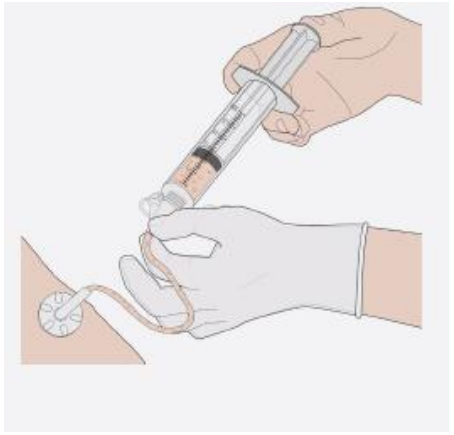
Add water and mix



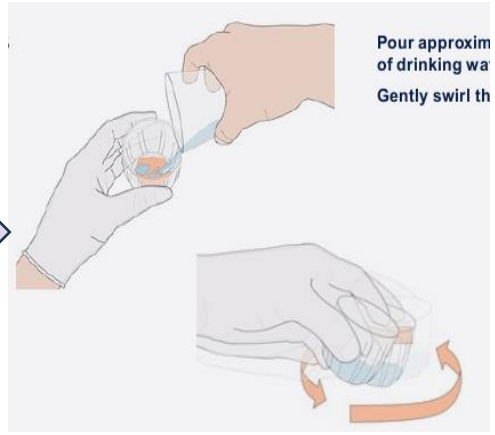
Draw mixture up with syringe



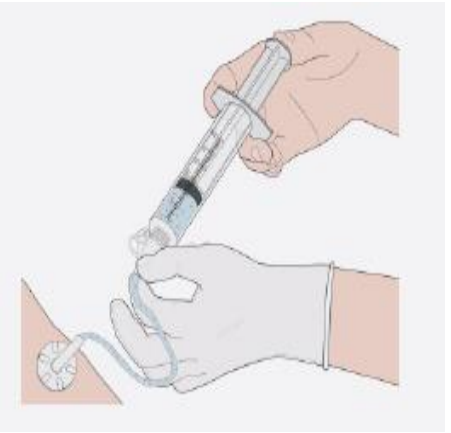
Remove any air bubbles



Connect to G tube and dose

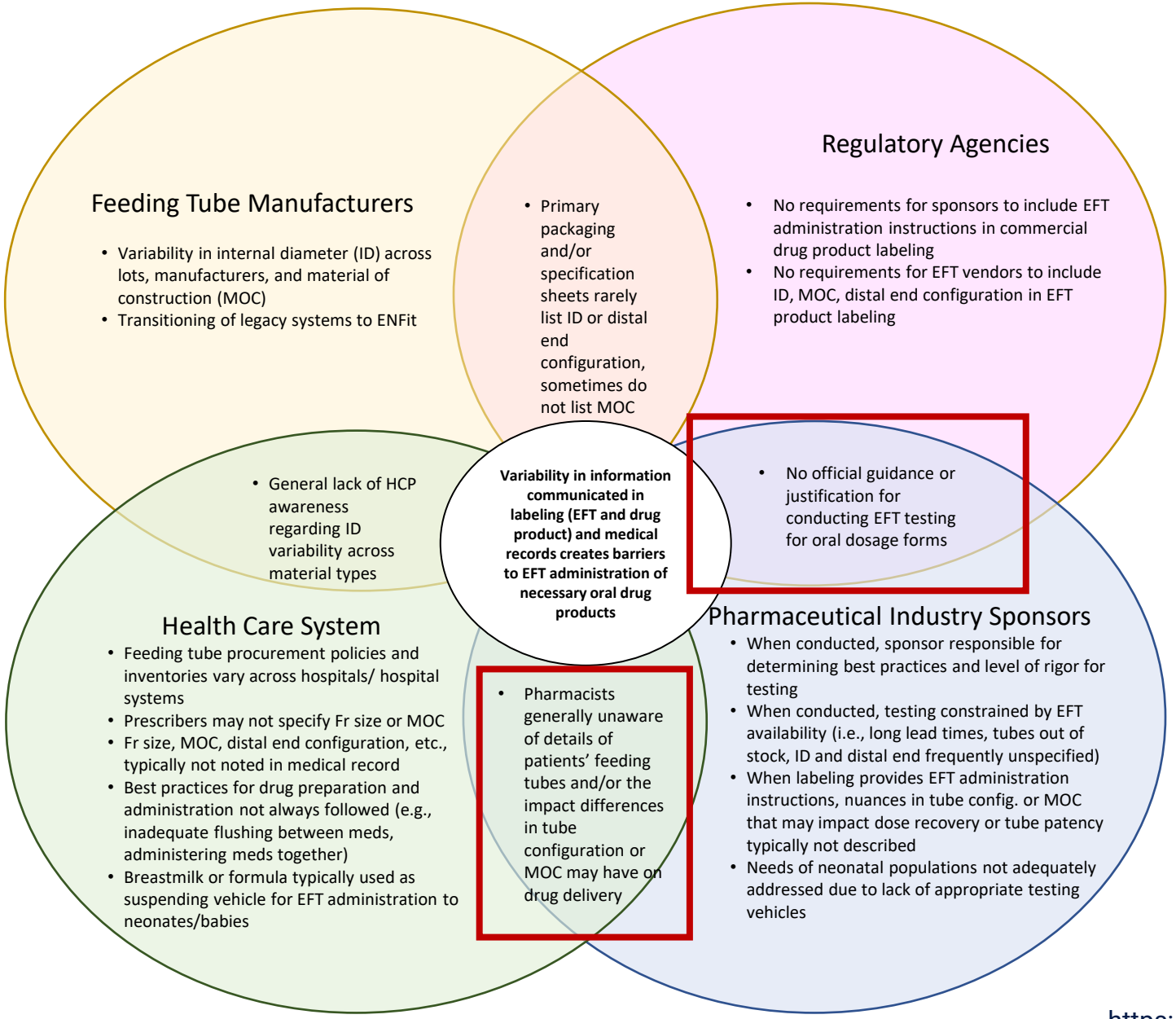


Rinse pill crusher, mixing cup by swirling



Connect to G tube and dose

CURRENT State



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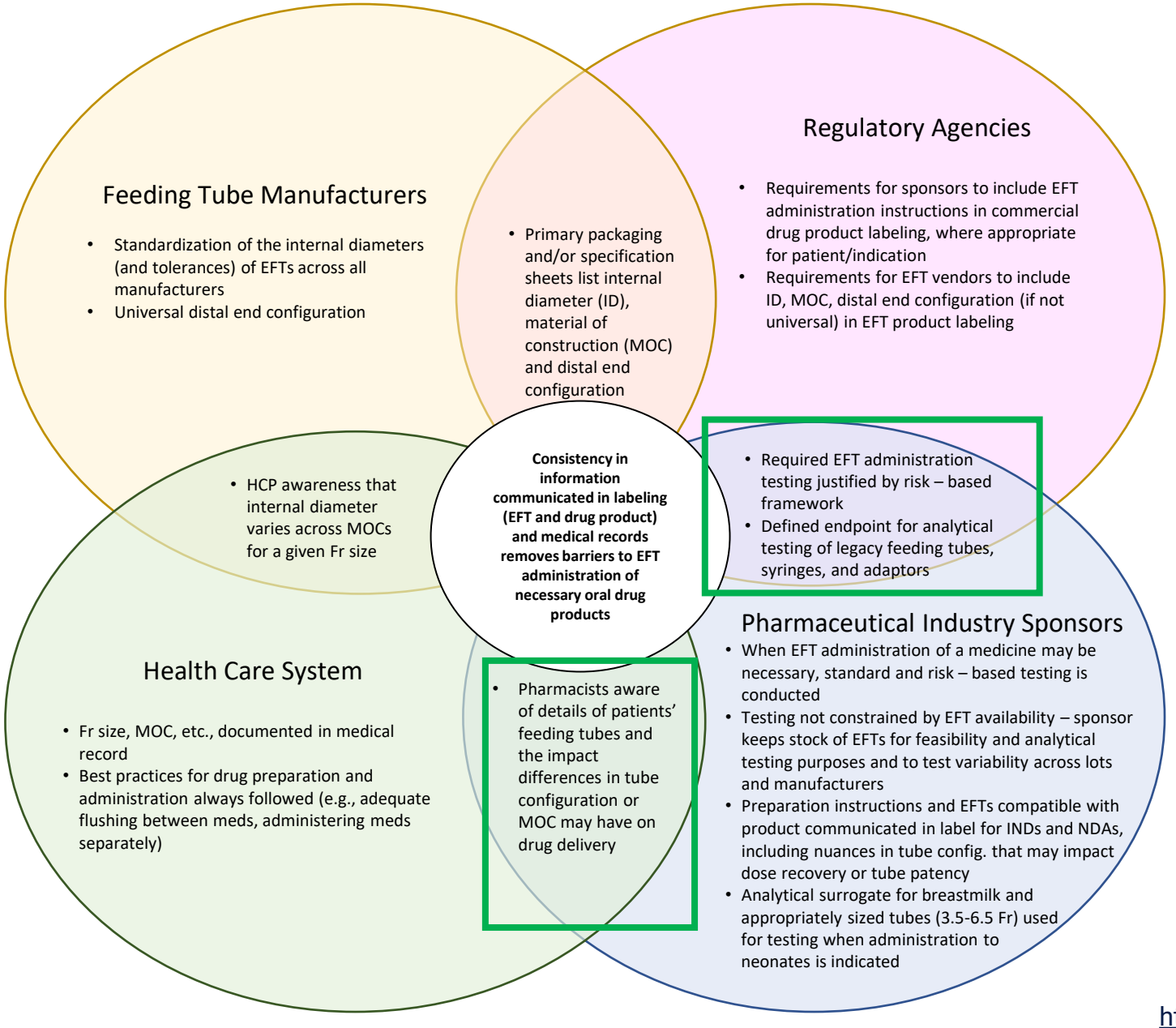
DESIRED State



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Acknowledgement

Selina Wilson (Eli Lilly)

Julianne Farabaugh (Merck & Co., Inc., Rahway, NJ, USA),

Rachel Meyers (Rutgers University, Cooperman Barnabas Medical Center),

Karen Thompson (Merck & Co., Inc., Rahway, NJ, USA)

Zahid Iqbal (AbbVie Inc.)

Thomas Huemann (AbbVie Inc.)

Sujani Nannapaneni (AbbVie Inc.)

And More!


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