U.S. FOOD & DRUG ADMINISTRATION

A Closer Look into the Nasogastric and Gastric Feeding Tube Study Requirements and Recommendations

SBIA 2020: Advancing Innovative Science in Generic Drug Development Workshop
Session 4: In Vitro Feeding Tube Testing and GI Locally-Acting Products

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Learning Objectives

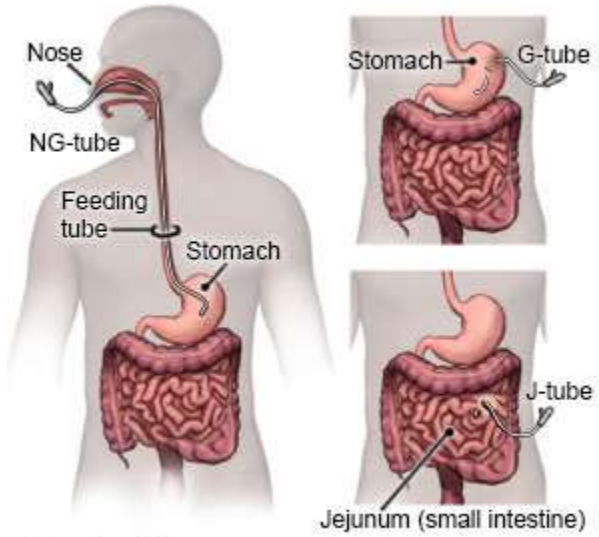
- Describe the history of enteric feeding tubes testing
- List in vitro testing recommendations
- Apply lessons learned to a Case study: Lansoprazole Orally Disintegrating Tablets

What are Enteral Feeding Tubes?

- Enteral tubes are medical devices to allow for the delivery of food and medicine for patients who are unable to swallow oral dosage forms due to a variety of medical conditions

Type	Outer Tube Diameter (Fr*,**)
Nasogastric	4-18
Nasoduodenal	3.5-12
Nasojejunal	3.5-12
Gastrostomy	12-30
Gastrojejunal	12-22
Jejunostomy	12-18

* Fr = French
** 3 Fr = 1 millimeter



Feeding Tube
https://www.drugs.com/cg/images/en3432827.jpg

- Varies by
  - Diameter (inner and outer)
  - Tube composition (e.g., type of polymer)
  - Inner tube geometry (e.g., balloon)
  - Port number and configuration
  - Connector type
  - Etc.

Tube Size Primer

- Range of tube sizes, types, and configurations
  - Size of patient, type of food, material, etc.

- FR is the unit of size that measures <u>outer</u> diameter
  - one FR = 0.33 mm
  - Inner is variable due to material, type, etc.
  - Balloons halve the internal volume

NG tube with 2 eyes, closed distal tip

	I.D./O.D. RATIO
Polyurethane	
Polyvinylchloride (PVC)	
Silicone	


G tube with balloon

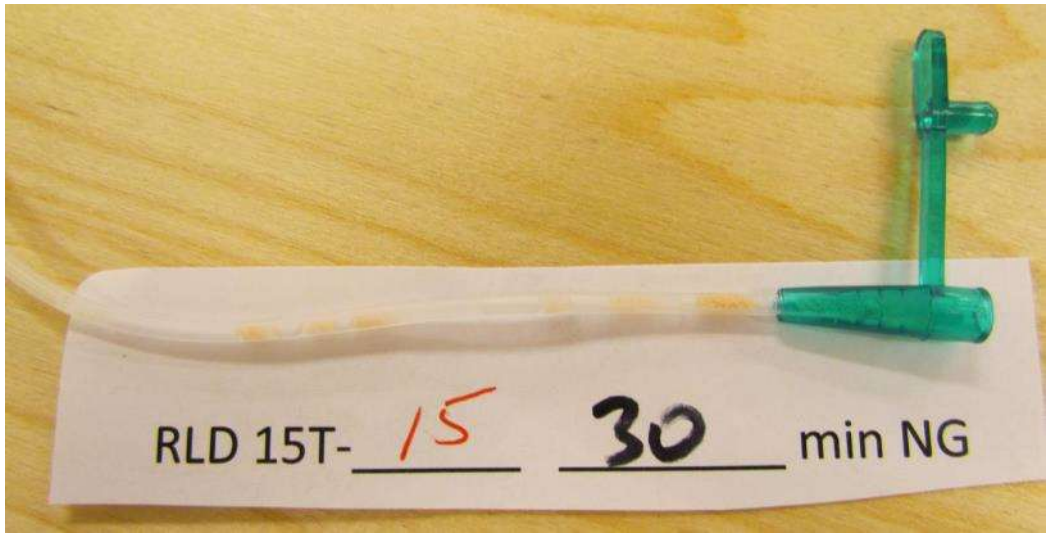
Risk Considerations for Delivery Through Enteric Tubes

- Clinical data suggest enteral tube occlusions and clogs occur with a frequency of 23 to 35 percent during routine use

- The risks of enteral tube occlusion increase under a number of conditions, including, but not limited to, the following
  - Presence of insoluble ingredients
  - Aggregation in dispersion media
  - Selection of an inappropriate vehicle to serve as the dispersion media
  - Inadequate flushing of the enteral tube before and after drug administration
  - Inadequate drug product dispersion before administration
  - Large particle size
  - Drug product-enteral tube interactions

Risk Considerations for Delivery Through Enteric Tubes

- Clogging/material build up for products administered via feeding tubes
  - Incomplete delivery of medicine
  - Removal and replacement of tube



- Multiple examples within the literature and clinic

FDA Laboratory Studies

- FDA performed laboratory studies to assess the risk of various conditions on delivery of drugs via enteric feeding tubes
  - Percent recovery
  - Acid stability (as applicable)
  - Holding time
  - Dispersant (e.g., source and pH)
  - Tube and syringe configurations
  - Sedimentation
  - Particle size distribution
  - Holding angle

- The design of the enteral feeding tube, specifically the size and location of the eyes/tube openings and open/closed distal tip as well as the size and location of a gastric balloon, affect the risk of tube obstruction.
  - The length of the tubing did not have an effect on the risk of clogging.

- Rinsing/flushing of the tube is a critical step to fully administer the dose.

https://pubmed.ncbi.nlm.nih.gov/28416417/

In Vitro Testing Recommendations

- Considerations when developing in vitro tests*
  - Selection of tubes for testing
  - Dispersion media and dispersion preparation
  - Based upon proposed administration

- Quality
  - Recovery testing under a variety of conditions
  - In-use conditions (holding time, repeat administration)
  - Sedimentation volume and redispersibility testing

- Bioequivalence (test versus reference)
  - Recovery testing (12 units)
  - Particle size distribution study
  - Acid resistance testing (as applicable)

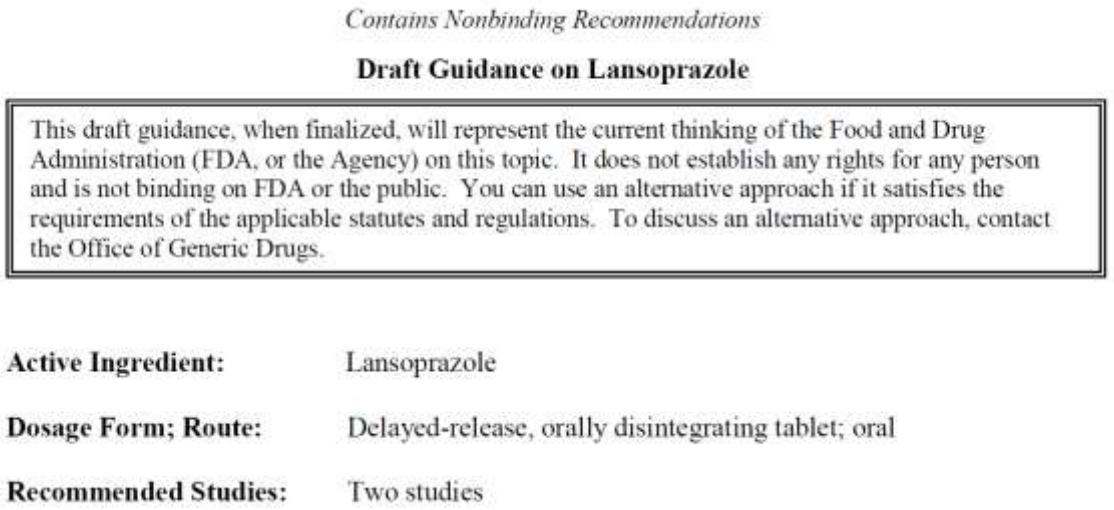
*Excludes oral solutions, which present a low risk for forming occlusions versus other oral dosage forms containing solid or insoluble components

Lansoprazole Delayed-Release Orally Disintegrating Tablets: Case Study

Prevacid SoluTab (RLD)-Nasogastric Tube (≥ 8 French) administration

For administration via a nasogatric tube, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in a syringe and draw up 4 mL of water, or place a 30 mg tablet in a syringe and draw up 10mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, inject through the nasogastric tube into the stomach within 15 minutes.
- Refill the syringe with approximately 5 mL of water, shake gently, and flush the nasogastric tube.



Contains Nonbinding Recommendations

Draft Guidance on Lansoprazole

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient:	Lansoprazole
Dosage Form; Route:	Delayed-release, orally disintegrating tablet; oral
Recommended Studies:	Two studies

https://www.accessdata.fda.gov/drugsatfda_docs/psg/Lansoprazole_draft_Oral%20tab%20delayed-release%20OD_RLD%2021428_RC02-18.pdf

Lansoprazole ODT: Risk Assessment

- Formulation
  - Orally disintegrating tablet (insoluble excipients)
  - Delayed release (enterically coated) microgranules
  - Granules (large particle size)
- Conditions of use
  - Disperse tablet in water
  - Administer through an nasogastric tube (FR 8 or larger) within 15 minutes.
  - Flush the nasogastric tube with water
  - Up to 3X daily
- Risk
  - Agglomeration of insoluble excipients (clogging risk)
  - Enteric coating degradation
  - Large granule size (clogging risk)
- Tests
  - % Recovery with multiple tube configurations (FR 8)
  - Sedimentation studies
  - Repeat administration
  - Hold times up to labeled amount in dispersions of varying pH
  - Particle size distribution study
  - Acid resistance study

Summary

- In vitro testing is used to demonstrate low risk of clogging for drug formulations delivered via enteric feeding tubes

- There are a variety of in vitro tests that can be performed based upon formulation and conditions of use

- Product specific guidances are available

Challenge Questions

- Yes/No Oral solutions are considered to be high risk for clogging enteral feeding tubes?

- Name two different design characteristics of enteral feeding tubes that impact risk for obstruction.

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