Going with the flow: how syringe orientation impacts dosing accuracy

Research findings concerning dosing accuracy with ENFit™ syringes

Keliana O'Mara, PharmD
NICU Clinical Pharmacy Specialist
UF Health Shands Hospital
omarak@shands.ufl.edu

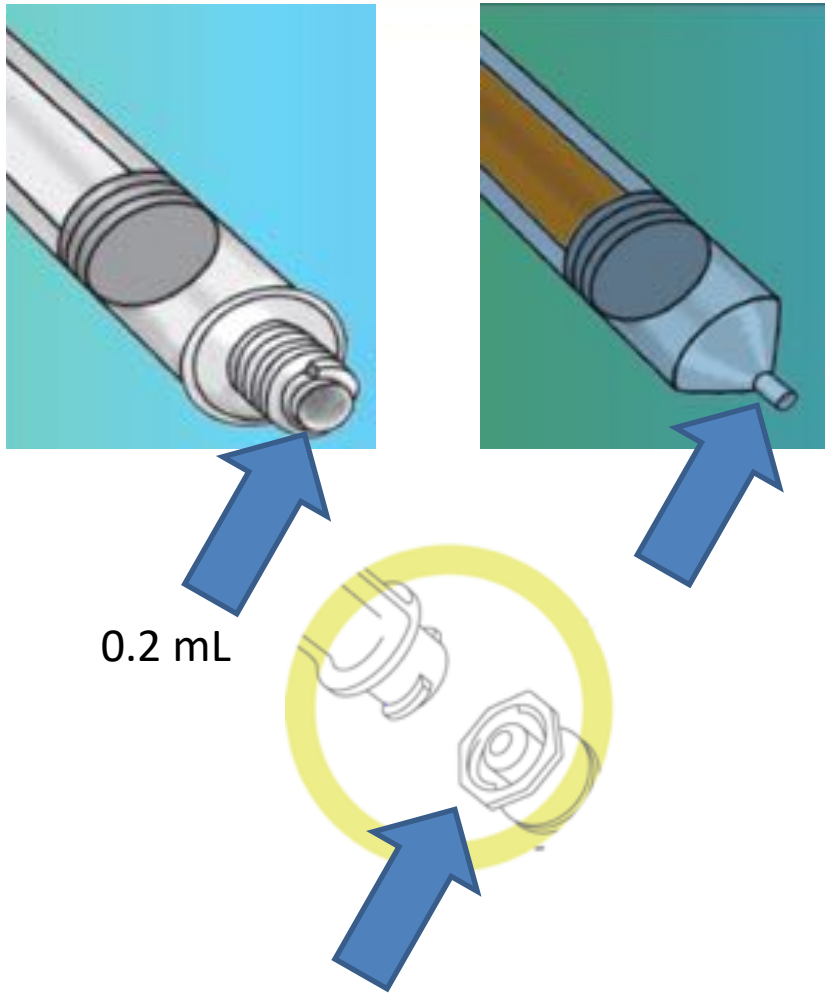
UFHealth
UNIVERSITY OF FLORIDA HEALTH

Objectives

- Discuss pertinent background of International Organization for Standardization (ISO) standards for enteral systems
- Review ENFit™ syringe and accessory designs to highlight potential for dosing inaccuracy
- Examine recent peer-reviewed literature regarding dosing accuracy of ENFit™ syringes

Background

- ENFit™ female syringe system
  - Endorsed by GEDSA as a solution for ISO 80369-3
  - Reverse orientation from male oral syringes
  - Enteral formula vs. medication administration
  - Enteral and oral application
- Design concerns
  - Syringe tip: dosing risk
  - Tubing tip: dosing and contamination risk



Images from: http://stayconnected.org

Standard Female ENFit™ Dosing Risk

- ISMP issued dosing accuracy warning in 2015
- Low volume medications vulnerable to clinically significant under and over-dosage
- Several work-around proposals given without addressing actual design flaw

Correct:

Incorrect:

ISMP ENFit Devises Are On Their Way…Important Safety Considerations For Hospitals. April 9, 2015
ISMP Update on Implementation of the New ENFit Enteral Connectors. July 30, 2015.

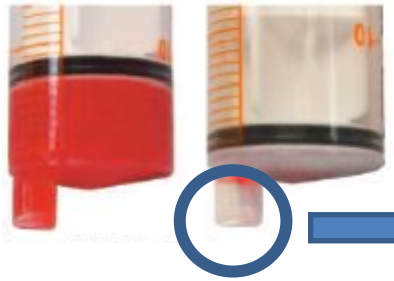
Images from: https://www.ismp.org/resources/enfit-enteral-devices-are-their-wayimportant-safety-considerations-hospitals

Clinical Concerns

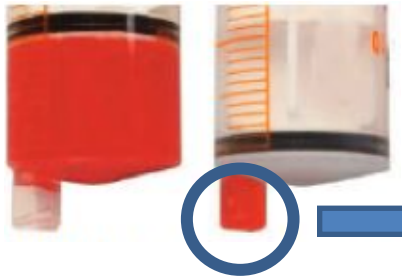
- Multidisciplinary meeting (Jul 2015) at CHOP
  - Representation from ISMP, ASHP, GEDSA, A.S.P.E.N., NANN, PPAG, and FDA
- Clinician input
  - More than 80 medications have liquid doses in volumes less than 2 mL
  - 1,250 doses each day

Example:
Digoxin 50 mcg/mL
Patient weight: 1 kg

Intended:
Dose: **5 mcg**
Volume: **0.1 mL**



Actual:
Dose: **15 mcg**
Volume: **0.3 mL**



Actual:
Dose: **0 mcg**
Volume: **0 mL**

Standard female syringe tip is not safe for low volume medication doses

CHOP: The Children's Hospital of Philadelphia
ISMP: Institute for Safe Medication Practices
ASHP: American Society of Health-System Pharmacists

GEDSA: Global Enteral Device Supplier Association
A.S.P.E.N.: American Society for Parenteral and Enteral Nutrition

NANN: National Association of Neonatal Nurses
PPAG: Pediatric Pharmacy Advocacy Group
FDA: Federal Drug Administration

Images from: https://www.ismp.org/resources/enfit-enteral-devices-are-their-wayimportant-safety-considerations-hospitals

ENFit™ with Low Dose Tip Feature

- ISMP 2016 Update:
  - Developed to address industry-wide problem concerning ENFit™ syringe dead space and associated concerns with dosing accuracy with small volumes of medications
- New areas of concern:
  - Creation of moat
  - Oral adapters

Moat: area between male lumen and outer ring

ENFit™ with Low Dose Tip Feature

Moat volume:
0.15 mL*

Actual:
Dose: **12.5 mcg**
Volume: **0.25 mL**

Example:
Digoxin 50 mcg/mL
Patient weight: 1 kg

Intended:
Dose: **5 mcg**
Volume: **0.1 mL**

Oral Adapters

DoseMate

Actual:
Dose: **10 mcg**
Volume: **0.2 mL**

DoseMateDL

Priming volume:
0.1 mL

*Unpublished data

Images from: https://www.neomedinc.com/dosemate/

ENFit™ with Low Dose Tip Feature

Did the Low Dose Tip (LDT) feature fix the known issue of dosing inaccuracy with ENFit™ Syringe?

Actual:
Dose: **15 mcg**
Volume: **0.3 mL**

Dose: **~~22.5 mcg~~**
Volume: **0.25 mL**

Actual:
Dose: **10 mcg**
Volume: **0.2 mL**

Intended:
Dose: **5 mcg**
Volume: **0.1 mL**

Complexity of Use

Syringe Type	FDA-approved Instructions for Use	DoseMate	DoseMate-DL: Bedside Fill	Dose Mate-DL: Pre-filled Syringe
Legacy	1. Ensure that the plunger is fully depressed before filling dispenser. 2. Draw medication into dispenser. For accurate measurement, use the edge of the black silicone ring closest to the medication. 3. Slowly depress plunger, directing fluid towards inside cheek to allow for natural swallowing. Forceful squirting to the back of the throat may cause choking.	N/A	N/A	N/A
ENFit	1. Ensure that the plunger is fully depressed before filling dispenser. 2. Draw medication into dispenser. For accurate measurement, use the edge of the black silicone ring closest to the medication. 3. For syringe sizes 6 mL and below, ensure the moat is free of fluids and re-verify doses (repeat as necessary). 4. Before feeding, to minimize potential for clogging, mix any supplements or additives thoroughly to achieve uniform consistency. 5. Slowly depress plunger, directing fluid towards inside cheek to allow for natural swallowing. Forceful squirting to the back of the throat may cause choking.	Screw adapter completely onto syringe. **NOTE**: No clarification on bedside fill & pre-filled scenarios.	Screw adapter completely onto syringe <u>prior</u> to drawing up medication from cup.	Screw adapter completely onto pre-filled syringe. **NOTE**: Approximate priming volume is 0.1 mL. Air flushing may be used to fully expel syringe contents.
		Manufacturer recommendations: Dosing accuracy is maximized when ENFit compatible connectors are used throughout the process of filling, plunger operation and dispensing.		

Complexity in Medication Safety

- Major cause of medication errors
  - Leads to variation in practice
  - Opportunities for error
  - Increased risk of patient harm
- Reducing complexity key to improving safety and productivity
  - Simply
  - Standardize
  - Automate
  - Integrate
- ***Every step in a process is an opportunity for error***

Institute of Medicine Report. Preventing Medication Errors. 2006
Vanderveen T. Patient Safety and Quality Healthcare. Sept 2007

Oral/Enteral Syringe Target Dosing Accuracy

- No specific oral device performance standards
  - Intravenous syringe: ± 5% intended dose/volume
- ENFit™ industry-sponsored testing utilized ± 10%
- No standard within clinical community for acceptable dosing variance

Category	Unintended Adverse Effects Dependent on Dose	Impact of Effect Dependent on Dose	Narrow Therapeutic Index	Rounding Tolerance, %
Avoiding unintentional adverse effects	Yes	No	No	10–15
Controlling intended effects	No	Yes	No	5–10
Avoiding toxicity	No	No	Yes	1–5
Insufficient data	NA	NA	Usually	0–1

NA indicates not available.

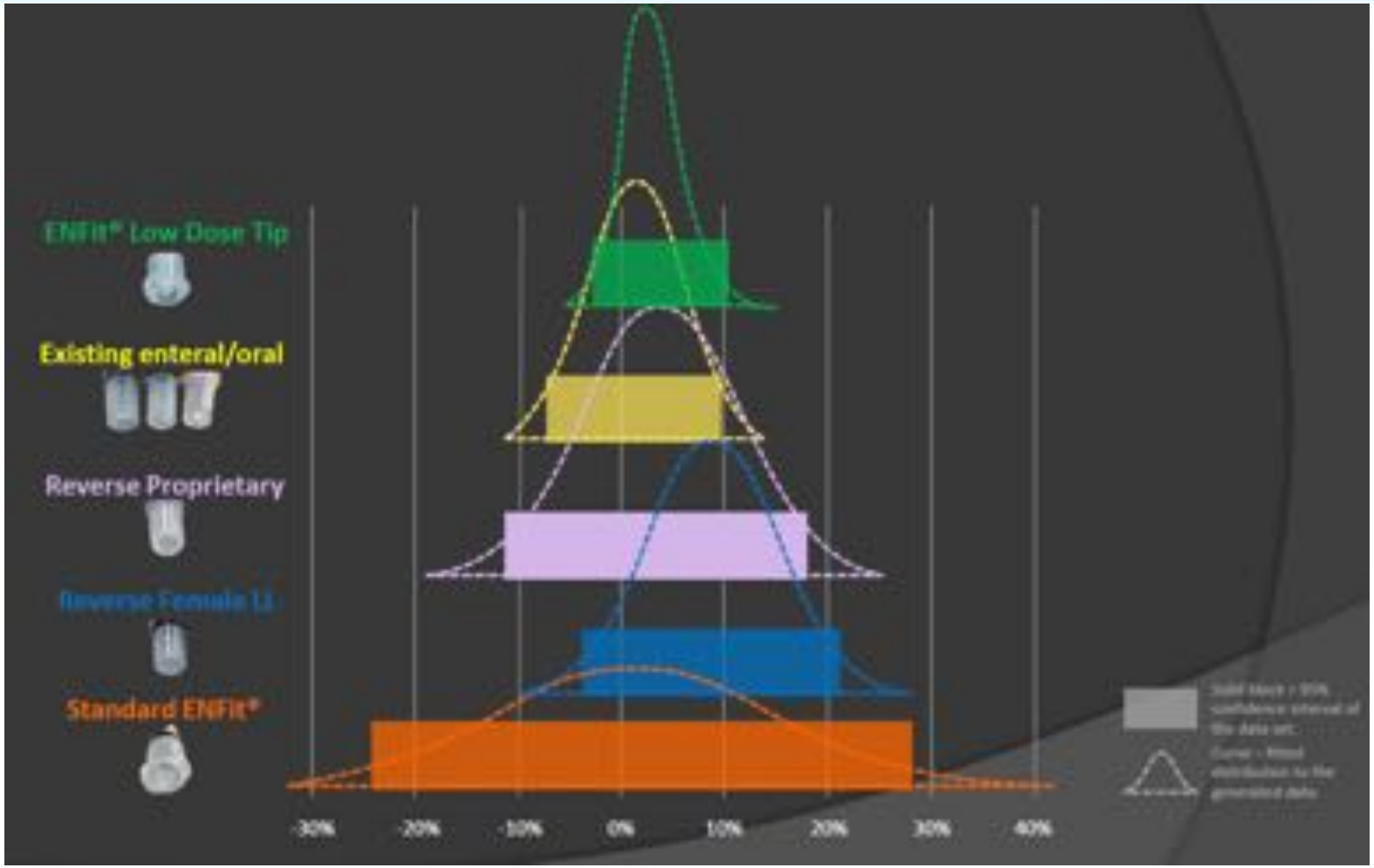
ISO 7886-1:2017. Sterile hypodermic syringes for single-use—Part 1: Syringes for manual use. Published May 2017.
Johnson KB. *Pediatrics* 2011; 128:e422-428.

Enteral Route-Does Accuracy Matter?

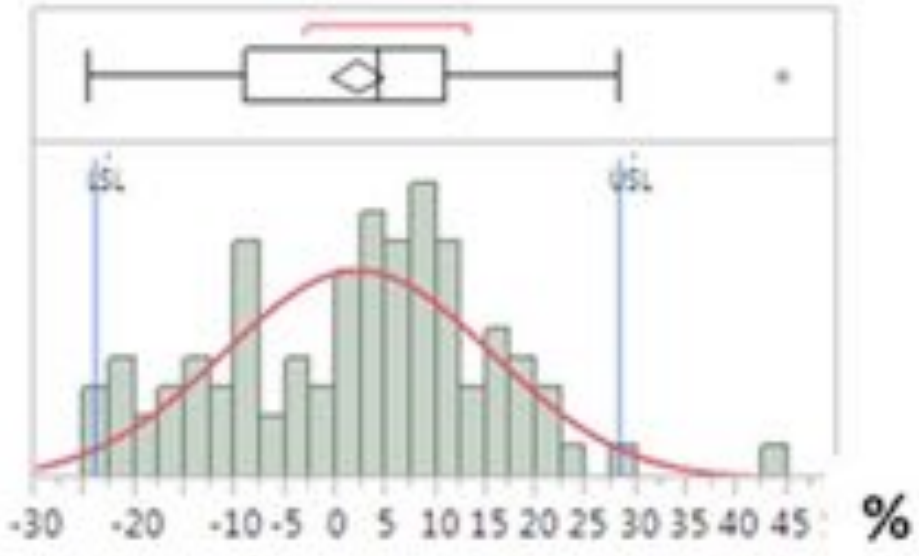
Medication	Concentration	Neonatal dose (volume)	20% DV (volume)	Pediatric dose (volume)	20% DV (volume)
Tacrolimus	0.5 mg/mL	--	--	1 mg (2 mL)	0.2 mg (0.4 mL)
Cyclosporine	100 mg/mL	--	--	20 mg (0.2 mL)	4 mg (0.04 mL)
Phenytoin	125 mg/5 mL	6 mg (0.24 mL)	1.2 mg (0.05 mL)	20 mg (0.8 mL)	4 mg (0.16 mL)
Phenobarbital	20 mg/5 mL	3 mg (0.75 mL)	0.6 mg (0.15 mL)	20 mg (5 mL)	4 mg (1 mL)
Clonidine	10 mcg/mL	1 mcg (0.1 mL)	0.2 mL (0.02 mL)	33 mcg (3.3 mL)	6.6 mcg (0.66 mL)
Clonazepam	0.1 mg/mL	0.1 mg (1 mL)	0.02 mg (0.2 mL)	1 mg (10 mL)	0.2 mg (2 mL)
Morphine	2 mg/mL	0.1 mg (0.5 mL)	0.02 mg (0.01 mL)	1 mg (0.5 mL)	0.2 mg (0.1 mL)
Methadone	2 mg/mL	0.1 mg (0.05 mL)	0.02 mg (0.01 mL)	1 mg (0.5 mL)	0.2 mg (0.1 mL)
Gabapentin	50 mg/mL	5 mg (0.1 mL)	1 mg (0.02 mL)	50 mg (1 mL)	10 mg (0.2 mL)
Digoxin	50 mcg/mL	5 mcg (0.1 mL)	1 mcg (0.02 mL)	50 mcg (1 mL)	10 mcg (0.2 mL)
Enalapril	1 mg/mL	100 mcg (0.1 mL)	20 mcg (0.02 mL)	1 mg (1 mL)	0.2 mg (0.2 mL)
Zidovudine	10 mg/mL	3 mg (0.3 mL)	0.6 mg (0.06 mL)	60 mg (6 mL)	12 mg (1.2 mL)
Lamivudine	10 mg/mL	2 mg (0.2 mL)	0.4 mg (0.04 mL)	50 mg (5 mL)	10 mg (1 mL)

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

GEDSA: ENFit™ Dosing Accuracy



ENFit Standard Syringes



http://stayconnected.org/wp-content/uploads/2016/04/GEDSA-Low-Dose-Syringe-End-User-LDT-Preso-FINAL.pdf

Deken A. Dose Accuracy—Performance Testing of Enteral, Oral, ENFit, and ENFit LDT syringes. Available at: www.stayconnected.org

GEDSA: ENFit™ Dosing Accuracy

- Research poster available per GEDSA

Syringe Type (1 mL)	Lower Bound % (Under-dosing)	Upper Bound % (Over-dosing)
Standard ENFit	-24.1	28.2
Male tip	-7.4	9.7
ENFit LDT	-2.9	10.5

- Critique:
  - Only tested 1 mL syringes
  - Did not evaluate adapters
  - Did not provide information regarding volume of drug tested or method for determining dosing accuracy (i.e. volumetric vs. gravimetric)

Deken A. Dose Accuracy—Performance Testing of Enteral, Oral, ENFit, and ENFit LDT syringes. Available at: www.stayconnected.org

ENFit™ Dosing Accuracy Concerns

- Lack of peer reviewed literature documenting performance of ENFit™ syringes or the available oral adapters
- Lack of published male legacy device performance
- UF Health Shands Study
  - Establish baseline for performance of male oral and ENFit™ syringes
  - Determine if oral adapters and deviation from strict adherence to filling criteria would impact dosing accuracy
  - Clarify if dosing accuracy of LDT syringes was impacted by route of administration

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Dosing Accuracy of ENFit™ LDT

- In vitro study comparing three types of enteral medication syringes

Syringe	Sizes (mL)	Volumes tested (syringe capacity)
Baxter® male legacy	0.5, 1, 5, 10	Low volume: 20% High volume: 80%
Neomed® male legacy	0.5, 1, 6	Low volume: 20% High volume: 80%
Neomed® ENFit™ female	LDT: 0.5, 1, 6 Standard: 12	Low volume: 20% High volume: 80%

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Dosing Accuracy of ENFit™ LDT

- FDA-approved instructions for use were followed for each syringe and any associated adapters
- Medications tested:
  - Children's Dimetapp Cold and Cough
  - Aspirin 81 mg chewable tablets
- Dosing accuracy assessed by dosing variance (DV)
  - Actual dose vs. intended dose
  - Primary assessment: >10% variance = unacceptable
- Gravimetric analysis to determine actual volume dispensed
  - Mettler Toledo® electronic scale utilized

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Testing Conditions

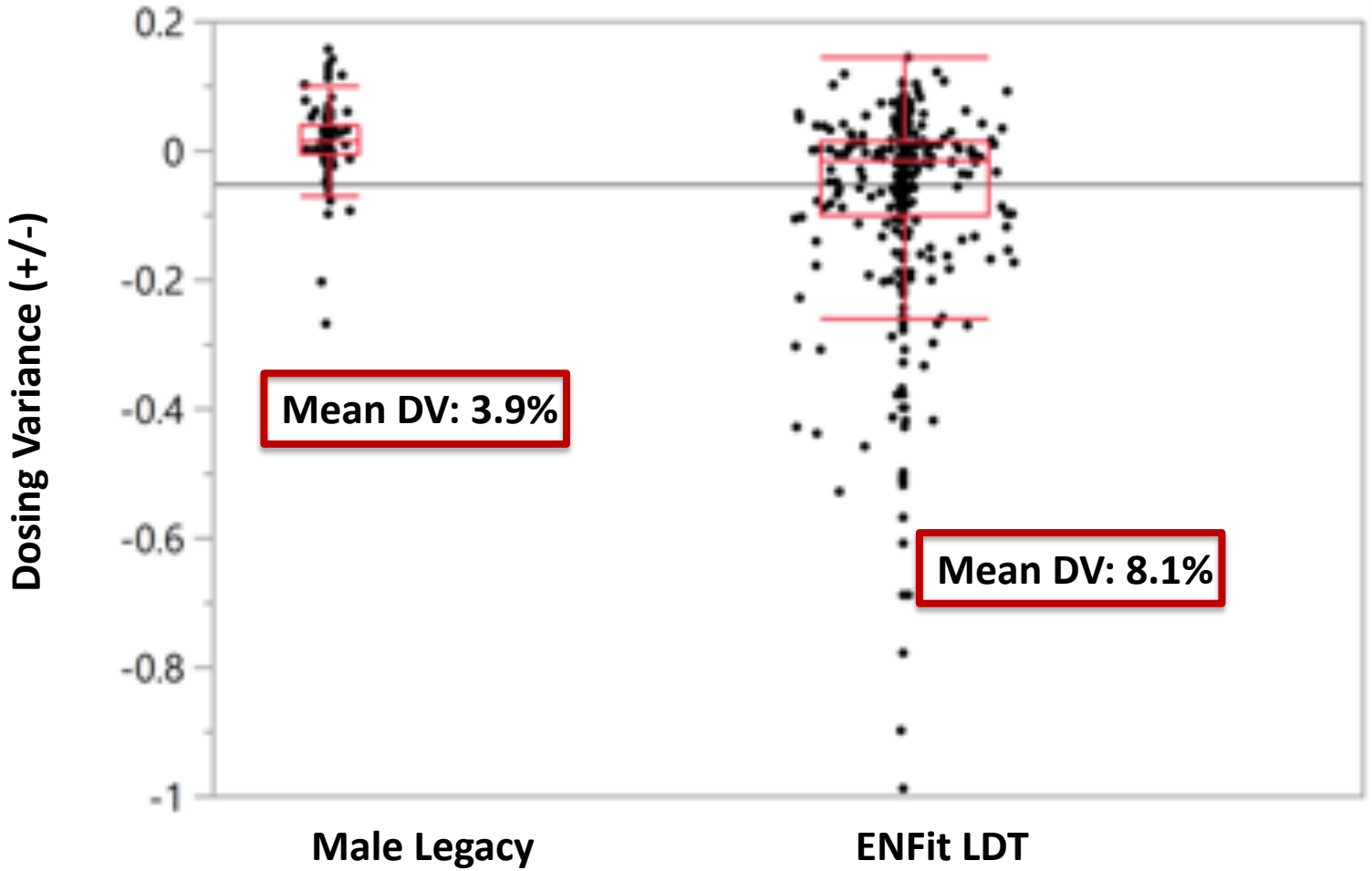
Dispensing sources	Dispensing adapters	Administration adapters
Bulk bottle*	No adapter	No adapter
Medication cup	Pharmacy (straw)	DoseMate
Crushed tablet	Nursing (DoseMate, DoseMateDL)	DoseMateDL

*Bulk bottle adapter caps were used for legacy and ENFit™ syringes

- Adapter use with ENFit™ compared against no dispensing/administration adapters with male legacy syringes
- Variety of combinations assessed with adapters
- See study for full list of conditions evaluated

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Dosing Accuracy of ENFit™ LDT



Overall dosing variance (±) of male and LDT syringes

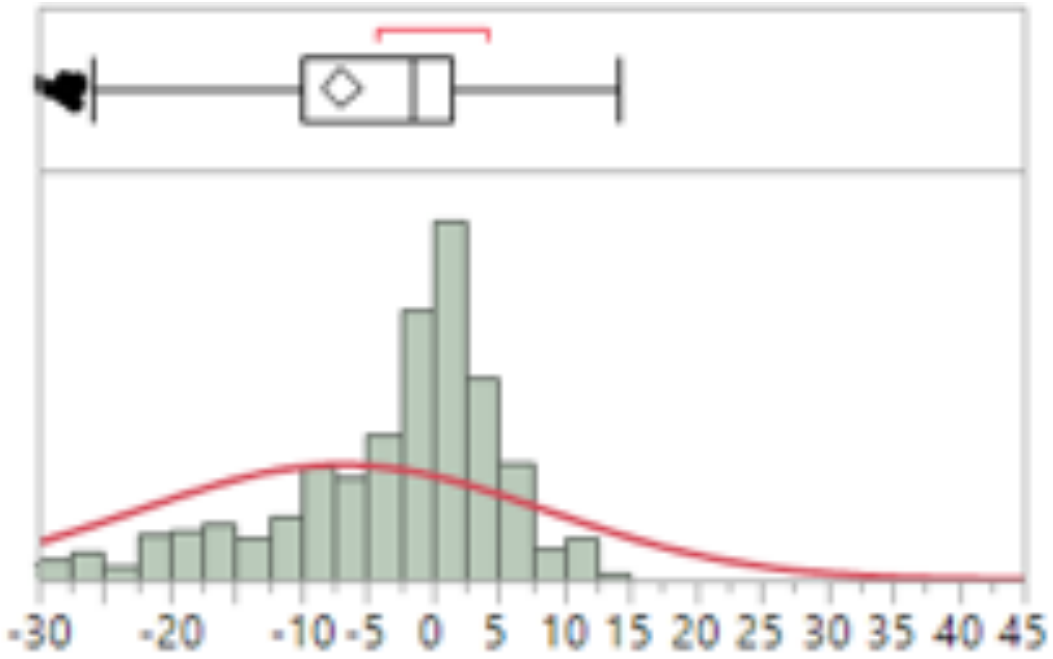
*Note wide distribution of DV range with LDT despite mean DV being within 10%

LDT: low dose tip
DV: dosing variance

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

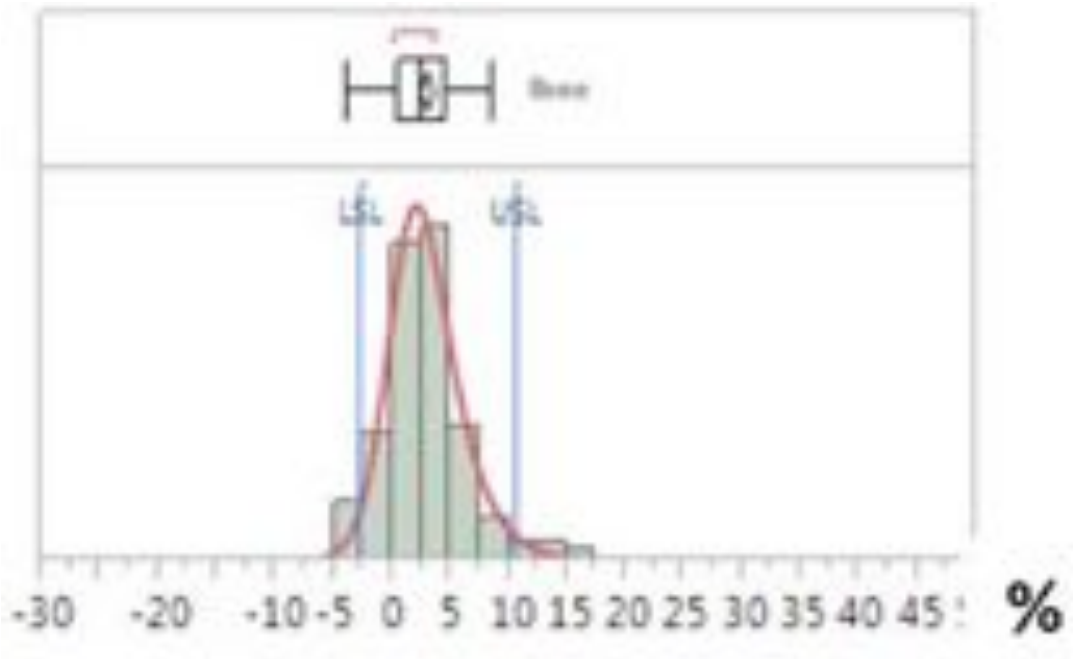
Dosing Accuracy of ENFit™ LDT

O'Mara et al.



% Dosing Variance (+/-)

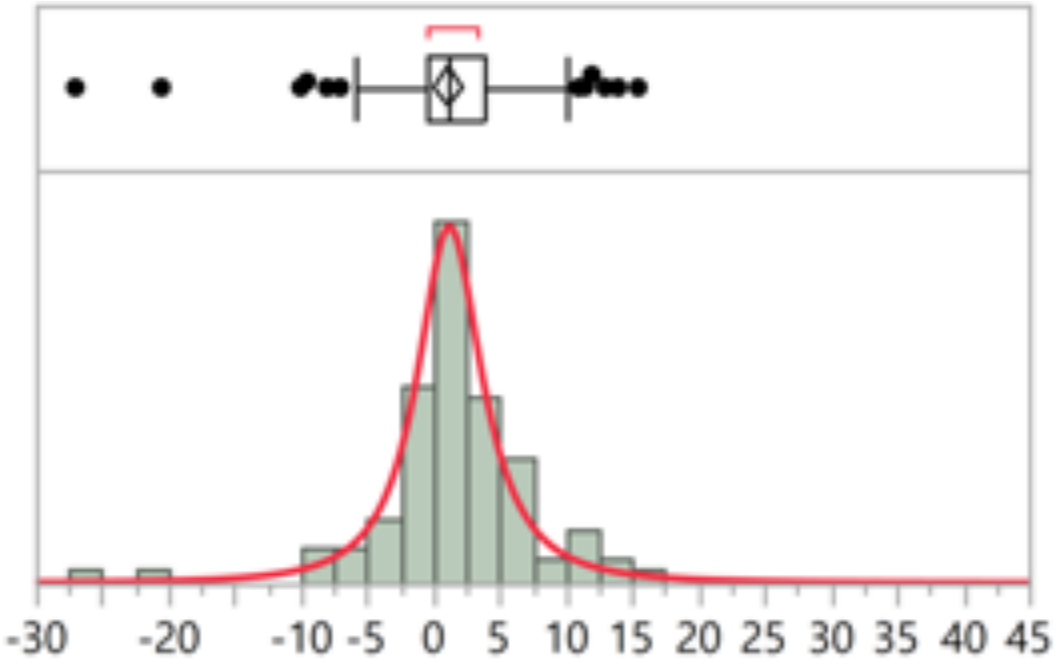
Deken et al.



% Dosing Variance (+/-)

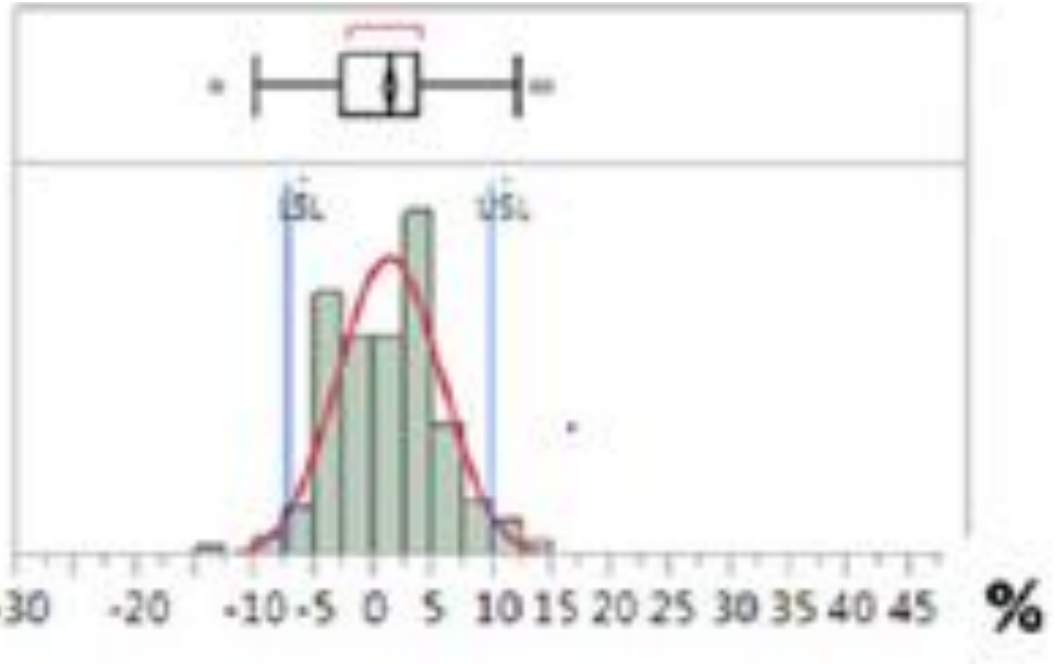
Dosing Accuracy of Male Syringes

O’Mara et al.



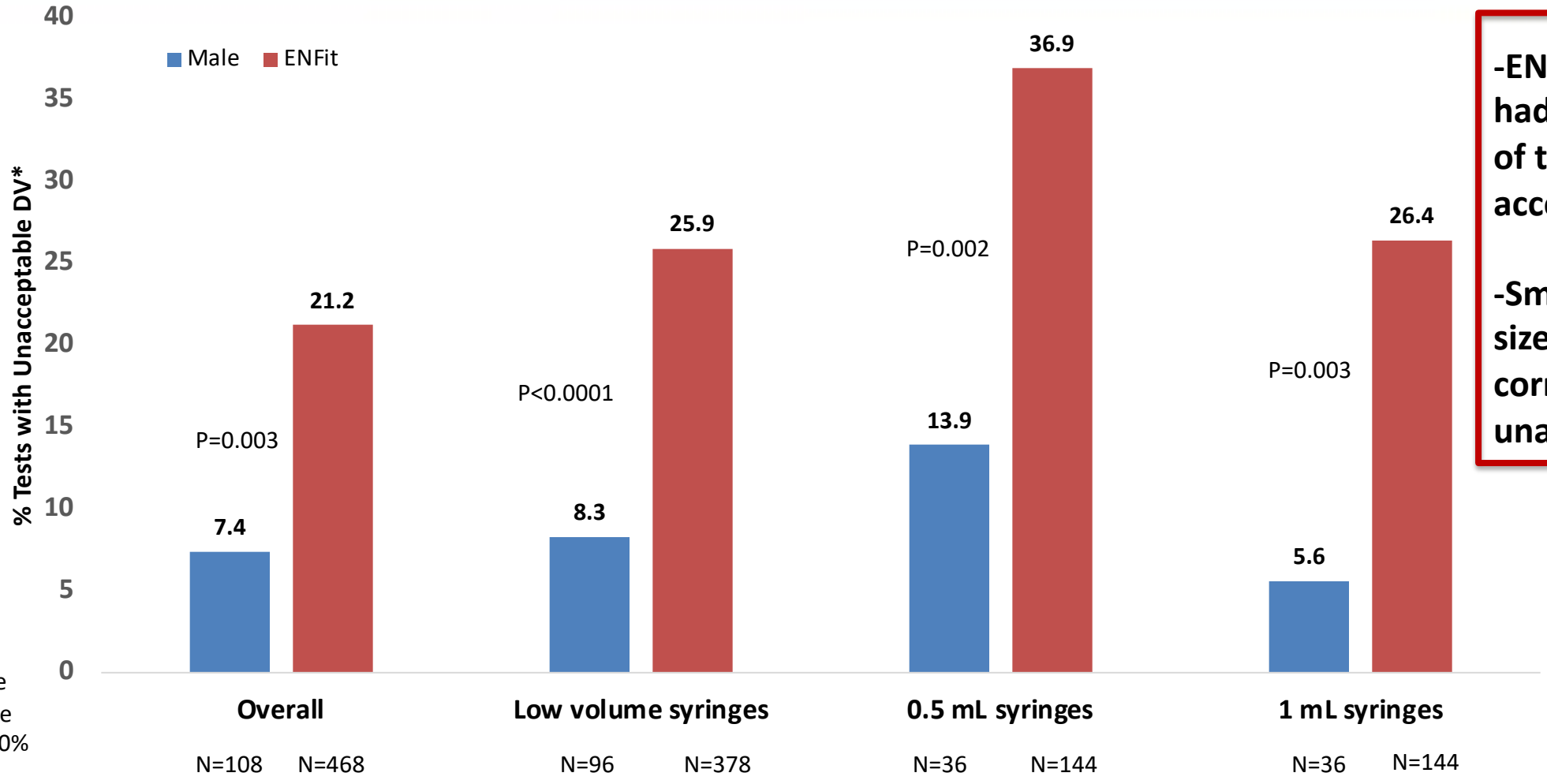
% Dosing Variance (+/-)

Deken et al.



% Dosing Variance (+/-)

Dosing Accuracy by Syringe Size



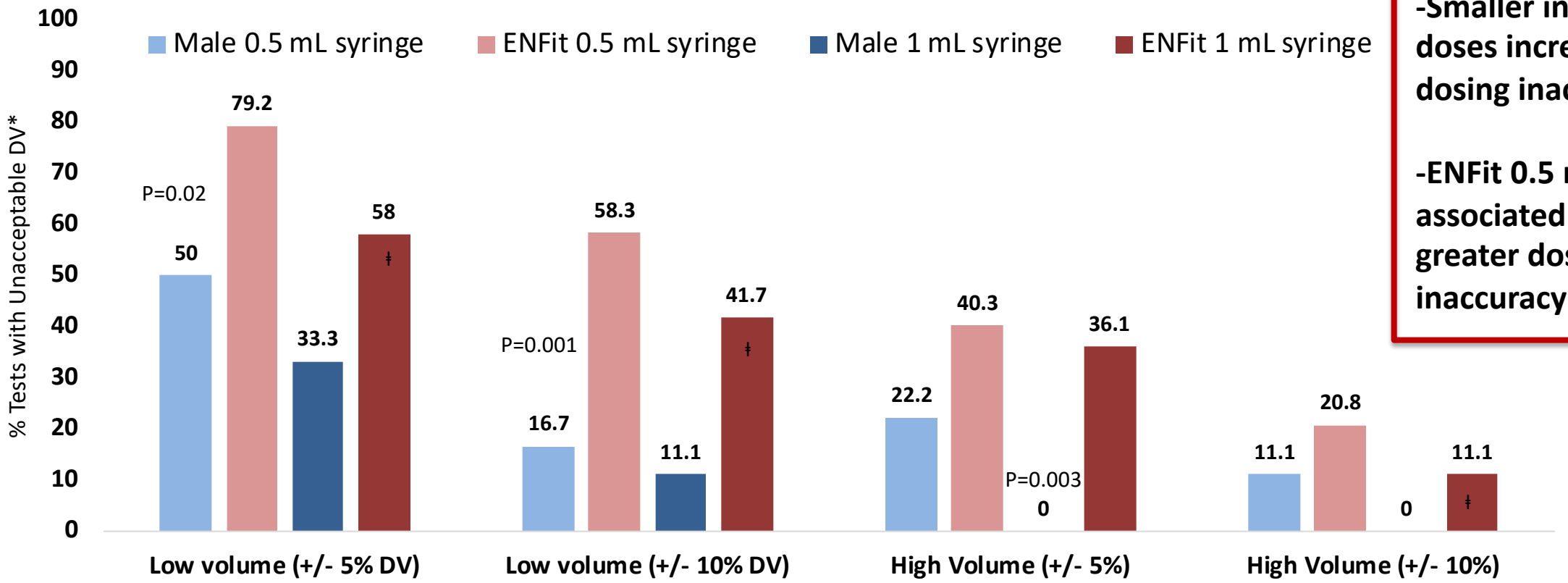
-ENFit syringes had increased % of tests outside of acceptable DV

-Smaller syringe size inversely correlated with unacceptable DV

*Unacceptable DV: actual dose more than ± 10% intended dose

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Dosing Accuracy By Intended Volume



-Smaller intended doses increased dosing inaccuracy

-ENFit 0.5 mL LDT associated with greater dosing inaccuracy

*Unacceptable DV: actual dose outside of intended dose limits

ǂp=0.05

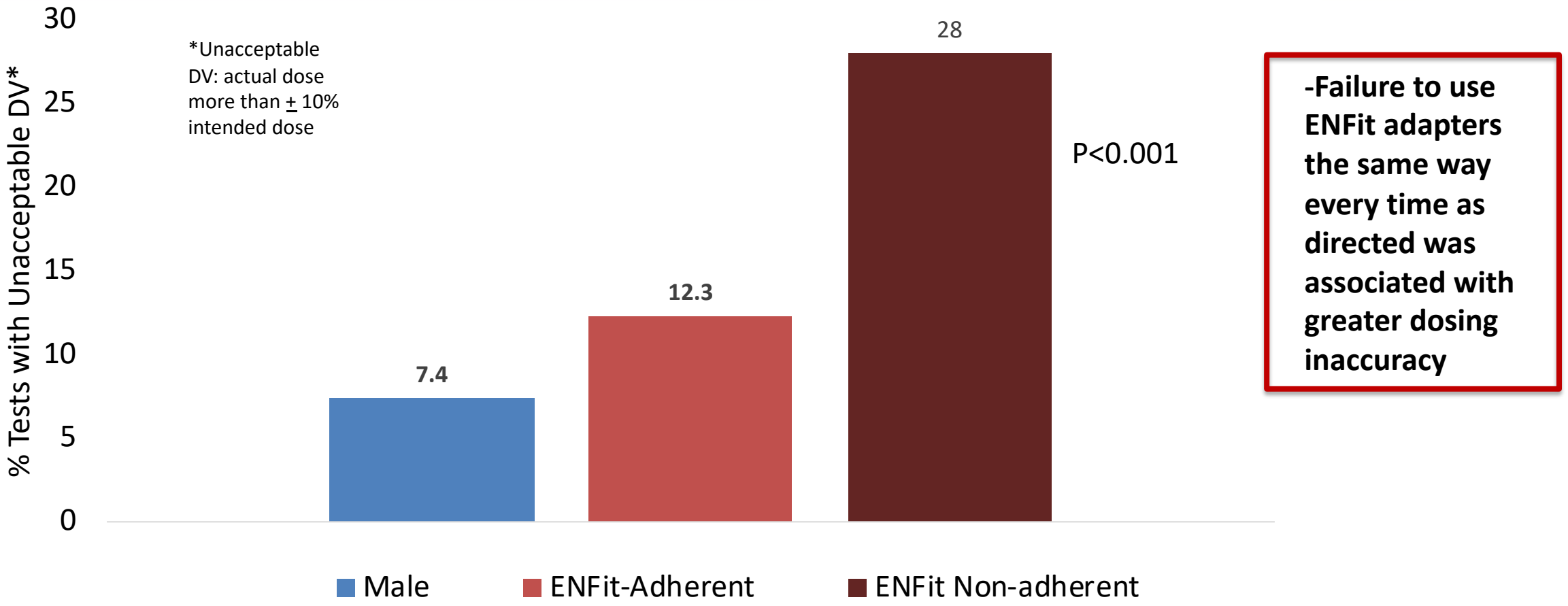
O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Dosing Accuracy by Dispensing and Administration Technique

Condition Tested	Male	ENFit™	P value
Bulk Bottle, (%)	0	9.5	0.06
Medication Cups, (%)	2.4	18.4	0.002
Crushed Tablets, (%)	8.3	38.9	0.002
Pharmacy Dispense, (%) (Patient-specific dose)	N/A	18.8	0.06
Bedside Dispense, (%) (RN dose)	N/A	5.6	

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

Dosing Accuracy by Adapter Use



-Failure to use ENFit adapters the same way every time as directed was associated with greater dosing inaccuracy

O'Mara K et al. *J Clin Pharm Ther.* 2019;44(3):463-470.

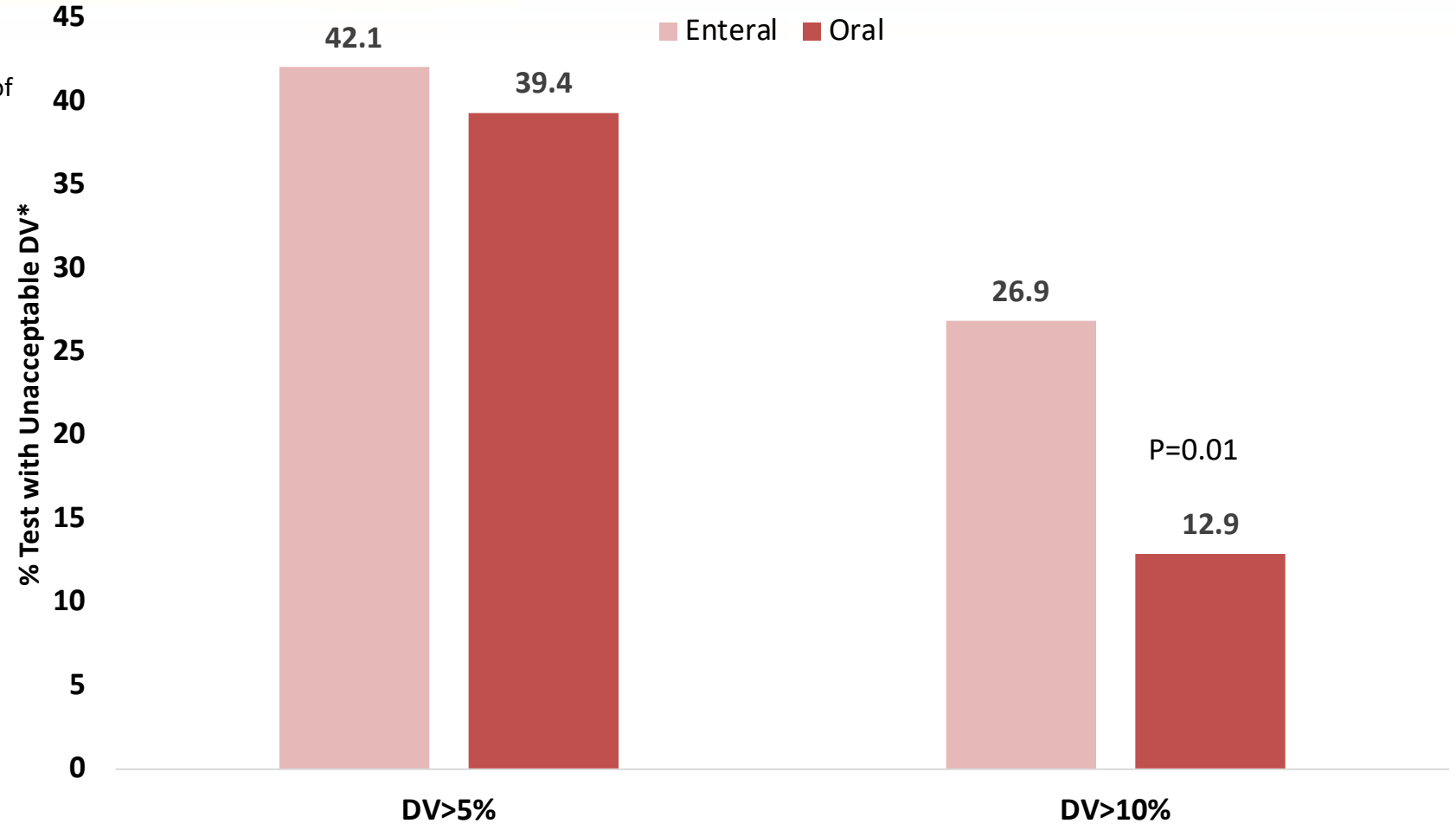
Dosing Accuracy by Route of Administration

	Enteral (n=96)		Oral (n=168)	
	Dispense	**Administer**	**Dispense**	**Administer**
Medication Cup	No Adapter Pharmacy Straw N/A	No Adapter No Adapter N/A	DM DM-DL Pharmacy Straw	DM DM-DL No Adapter
Bulk Bottle	Bottle Adapter N/A	No Adapter N/A	Bottle Adapter Bottle Adapter	DM DM-DL
Crushed Tablet	No Adapter Pharmacy Straw	No Adapter No Adapter	DM DM-DL	DM DM-DL

O'Mara K et al. *J Clin Pharm Ther.* 2019. doi: 10.1111/jcpt. 13079

Dosing Accuracy of LDT by Route

*Unacceptable DV: actual dose outside of intended dose limits



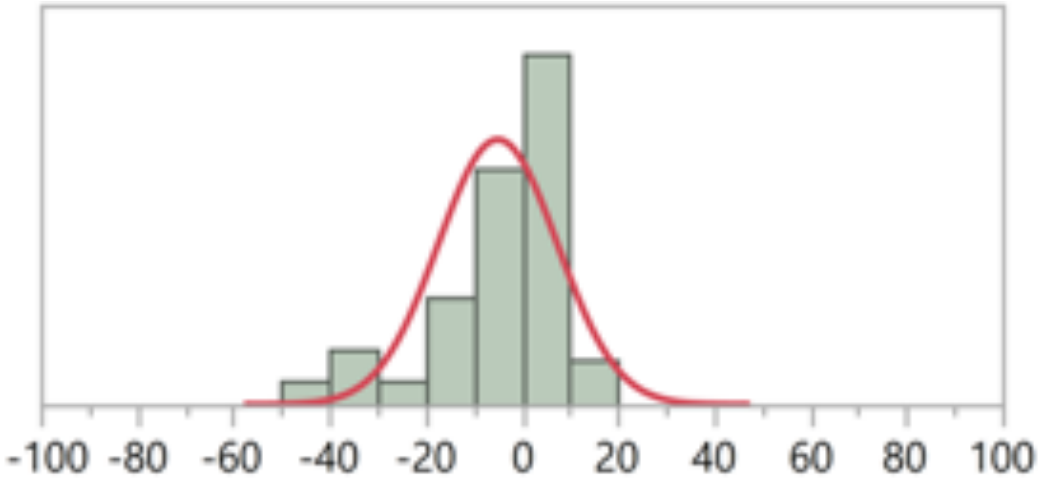
-At higher thresholds for dosing inaccuracy, enteral route is associated with greater risk of unacceptable DV

-When lower threshold for dosing inaccuracy used, both routes yield high rates of unacceptable DV

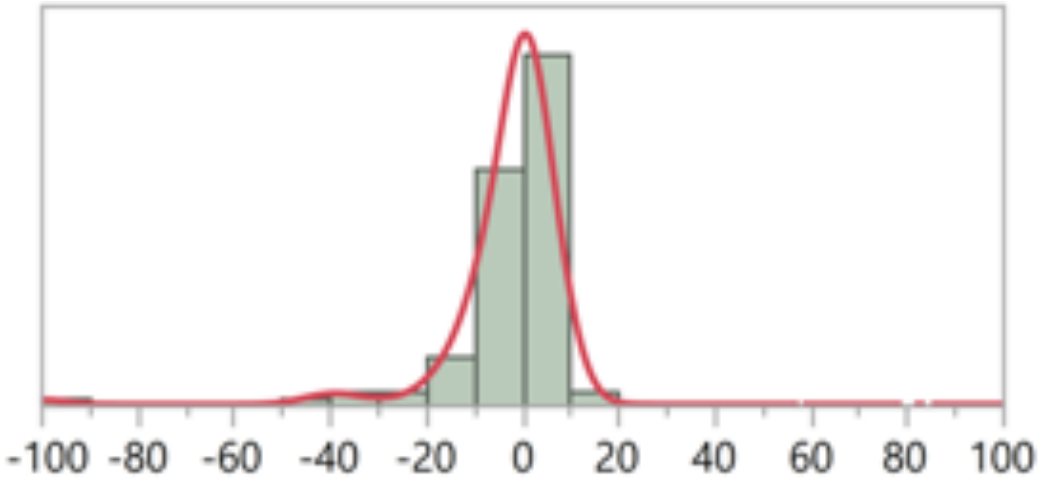
O'Mara K et al. *J Clin Pharm Ther.* 2019. doi: 10.1111/jcpt. 13079

Dosing Accuracy by Route of Administration

Enteral



Oral



-ENFit was originally intended for enteral use only, but enteral may carry even higher rates of dosing inaccuracy

-Oral use has less overall variability but still has significant proportion of tests exceeding acceptable dosing variance limits

O'Mara K et al. *J Clin Pharm Ther.* 2019. doi: 10.1111/jcpt. 13079

Literature Summary

- ENFit™ LDT syringes have increased dosing inaccuracy compared to male slip tip (legacy) syringes
  - 21% of doses outside of acceptable range
- Smaller syringes and lower volumes are associated with higher rates of dosing inaccuracy across both syringe designs
  - 40-80% of LDT doses outside of acceptable range based on size and volume
- ENFit™ adapters appear to have a negative impact on dosing accuracy, particularly if not used the same way each time
- Enteral administration of ENFit™ LDT may be even more vulnerable to dosing inaccuracy than oral administration practices

Where does the ENFit™ LDT Fit in ISO Standards?

- The ENFit™ LDT is not ISO 80369-3 compliant
  - Does not meet the device design specifications
  - Considered a ***compatible*** design
- ISO 20695: Enteral feeding systems standard
  - First draft: 2017 (disapproved)
    - LDT originally incorporated into the standard
    - Concerns for potential over-dosage with the moat
  - Second draft: 2019 (approved)
    - LDT is recognized as not reliably increasing dose accuracy
    - LDT has been removed from the mandatory requirements and is included as informational only
    - LDT is now an “enteral alternative syringe tip” because of its inability to ensure dosing accuracy

Unresolved Questions

- Is there a way to modify current ENFit designs to maintain misconnection safety and improve dosing accuracy?
- How should health systems address the concerns for dosing accuracy with the LDT and its new designation as an alternative enteral tip in ISO 20695?
- How should health systems address use of the ENFit™ LDT and its lack of compliance with ISO 80369-3?
- How can health systems using ENFit™ that cannot switch to an alternative device provide protection for their patients most vulnerable to dosing inaccuracies?

Future Directions

- Open and transparent communication of potential risks between industry and clinical communities
- Active surveillance of high risk patient populations and high risk medications
- Device/flow modification (i.e. one design for all volumes of doses)?

Key Takeaway Points

- ENFit™ standard tip syringes have a known issue with dosing accuracy
  - Identified by clinical community
  - Acknowledged by industry and safety organizations
- ENFit™ syringes with the low dose tip feature do not resolve the issue of dosing accuracy with the female syringe
  - Reversal of flow from female-to-male has an inherent design flaw for precise and accurate delivery of medication doses
- ISO has recognized the impact of the LDT on dosing accuracy
  - Enteral standards acknowledge the failure of the LDT to reliably deliver accurate doses
  - The LDT is only compatible with ISO-compliant devices

Going with the flow: how syringe orientation impacts dosing accuracy

Research findings concerning dosing accuracy with ENFit™ syringes

Keliana O'Mara, PharmD
NICU Clinical Pharmacy Specialist
UF Health Shands Hospital
omarak@shands.ufl.edu

UFHealth
UNIVERSITY OF FLORIDA HEALTH

Managing Safe Use of Enteral Syringes

KATHY GHOMESHI, PHARMD, MBA, BCPS, CPPS

Goal: Patient Safety

Prevent Harmful Tubing Misconnections

System Design vs User Error

Unanticipated, Unreconciled Sources of Latent/Active Error

System Design vs User Error

Legislature

LEGISLATIVE COUNSEL BUREAU
STATE OF CALIFORNIA
AUTHENTICATED
ELECTRONIC LEGAL MATERIAL

Assembly Bill No. 444

CHAPTER 198

An act to amend Section 1279.7 of the Health and Safety Code, relating to health facilities.

[Approved by Governor August 13, 2015. Filed with Secretary of State August 13, 2015.]

LEGISLATIVE COUNSEL'S DIGEST

AB 444, Gipson. Health facilities: epidural and enteral feeding connectors.

Existing law, as of January 1, 2016, prohibits a health facility, as defined, from using an epidural connector or an enteral feeding connector, that would fit into a connector other than the type it was intended for, unless an emergency or urgent situation exists and the prohibition would impair the ability to provide health care. Existing law also requires a health facility to develop a patient safety plan and, until January 1, 2016, requires that plan to include measures to prevent adverse events associated with misconnecting enteral feeding and epidural lines. Violation of these provisions is a misdemeanor.

This bill would make the provisions relating to an epidural connector operative as of January 1, 2017, and would make the provisions relating to an enteral feeding connector operative as of July 1, 2016. The bill would make conforming changes.

The people of the State of California do enact as follows:

SECTION 1. Section 1279.7 of the Health and Safety Code is amended to read:

1279.7. (a) A health facility, as defined in subdivision (a), (b), (c), or (f) of Section 1250, shall implement a facility-wide hand hygiene program.

(b) Commencing January 1, 2017, a health facility, as defined in subdivision (a), (b), (c), or (f) of Section 1250, is prohibited from using an epidural connector that would fit into a connector other than the type it was intended for, unless an emergency or urgent situation exists and the prohibition would impair the ability to provide health care.

(c) Commencing January 1, 2016, a health facility, as defined in subdivision (a), (b), (c), or (f) of Section 1250, is prohibited from using an intravenous connector that would fit into a connector other than the type it was intended for, unless an emergency or urgent situation exists and the prohibition would impair the ability to provide health care.

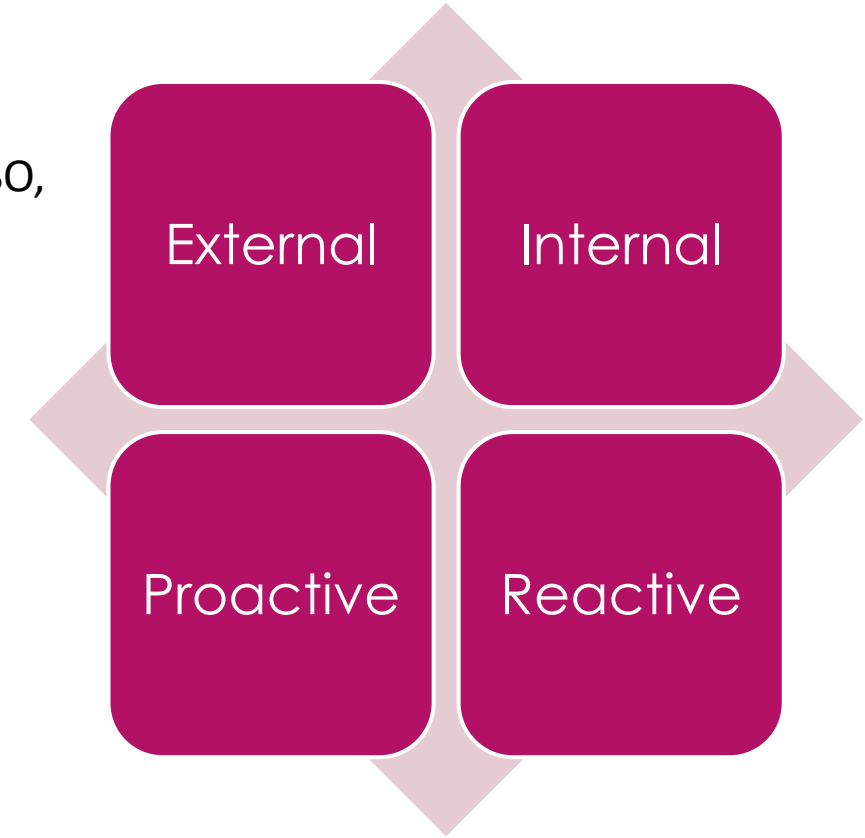
(d) Commencing July 1, 2016, a health facility, as defined in subdivision (a), (b), (c), or (f) of Section 1250, is prohibited from using an enteral feeding

Safety Review Strategies

FDA, GEDSA, TJC, ISMP, PSO, ASPEN

Vendors
Early Adopters

External Error Reporting



Subject matter experts, FMEA

Implementation

Incident reports and follow-up

FDA: Food & Drug Administration, GEDSA: Global Enteral Device Supplier Association, TJC: The Joint Commission, ISMP: Institute for Safe Medication Practices, PSO: Patient Safety Organization, ASPEN: American Society for Parenteral and Enteral Nutrition, FMEA: Failure Mode and Effects Analysis

Medication Management
Medication-Use Processes

Safety Planning Considerations

Planning	Procuring	Storing
Background information	Which vendor	Pharmacy
FMEA	Which items	Patient Care Area
Multidisciplinary	Wholesale distributor	
Patient Populations	Medications vs Nutrition	
Patient Care Settings	Preparing vs Administering	
Pre/Mid/Post Implementation	Shortages	

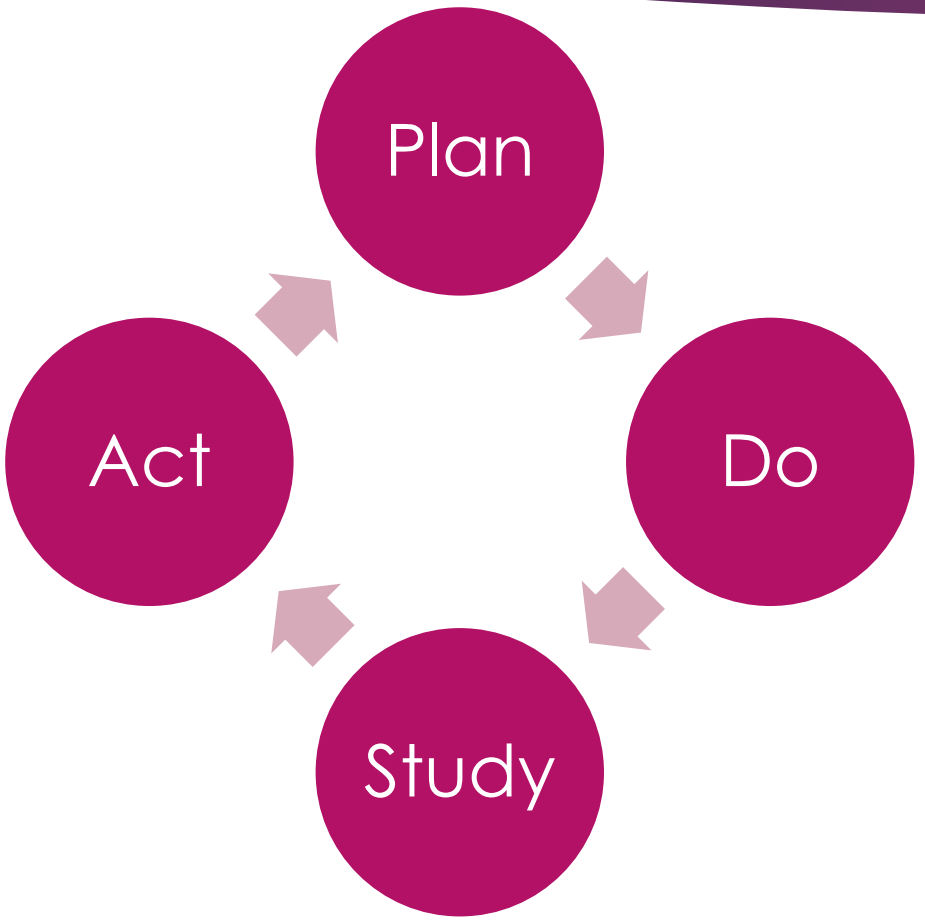
Safety Planning Considerations

Prescribing	Preparing/ Compounding	Dispensing
Enteral vs Oral	Pharmacy	Enteral vs Oral
	Nursing	Tamper evident
	Nutrition/Dietary Support	Protect from light

Safety Planning Considerations

Administering	Monitoring	Educating	Evaluating
With adapters	Patient concerns	Front line staff	Unresolved issues
Additional Valves	Front line user concerns	Patients	Error Reports
Other routes (eg, rectal)			Lessons learned (NRFit)

Goal: Patient Safety



Sharp End

Patients

Healthcare Teams

Healthcare Facilities

Global

Industry

Regulators

Blunt End

Conclusion

- Multi-phase global initiative to prevent harmful wrong route of administration errors through unique connector design
- Use of enteral connectors prevent inadvertent IV administration, but may contribute to other unintended safety concerns
- Post-market surveillance information and reporting important to continue to identify and improve safe use globally as well as point of care
- Incorporate lessons learned from enteral connector for other/future routes to be standardized