

ACCEPTABLE DOSE ACCURACY VARIABILITY OF SINGLE USE PLASTIC SYRINGES  
USED IN INTRAVENOUS AND ORAL/ENTERAL MEDICAL APPLICATIONS – USERS’  
PERSPECTIVE

by

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(Under the Direction of David W. Mullis, Jr.)

ABSTRACT

The study assessed USA based healthcare professional’s expectations of acceptable dose accuracy variability of single use (disposable) plastic syringes when used for intravenous injection and oral/enteral delivery of medication and nutrition. The study’s primary purpose was to determine if healthcare professionals expect these syringes to be standardized by using a common test method and dose accuracy variability specification, and if so, to what level of variability. The study included several subparts to ascertain the target population’s current thinking related to the dose accuracy of these type syringes when used to administer medication or nutrition to neonatal, pediatric and adult patients. This was an online survey that resulted in a total of 357 completed responses. Participants were primarily nurses (50.4%) and pharmacists (41.2%) with only (8.4%) physicians. The results suggest that regardless of the healthcare professional’s occupation, they agree the standardization of these type syringes to specific dose accuracy variability specifications is warranted.

INDEX WORDS: Syringe, Plastic, Single Use, Disposable, Dose Accuracy, Variability,  
Intravenous, Oral, Enteral

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## CHAPTER 1

### INTRODUCTION

#### *The History of Single Use Plastic Syringes*

Syringes are the most widely used medical devices in the world. Wide spread use of single use (disposable) plastic syringes in the United States of America (USA) did not occur until the 1960s. The introduction of single use plastic syringes was not well received, as physicians deemed sterilization of reusable syringes to be comparably safe and more economical than single use syringes. Even though reusable syringes were sterilized between each patient use; they still contributed to disease spread<sup>1</sup>. It was not until December of 1961 that the safety of these practices was questioned. Dr. Albert L. Weiner, O.D. sealed the fate of reusable syringes when he was convicted of 12 counts of manslaughter after 41 of his patients contracted serum hepatitis, of which, 12 resulted in death<sup>2</sup>. The root cause of these incidents was attributed to the use, sterilization and reuse of glass syringes. Single use syringe demand dramatically increased after this incident, and within a year, single use syringes secured one-third of the USA syringe market<sup>3</sup>.

There are several competing claims to the design of the first single use plastic syringe, however, the most plausible is that of the Monoject syringe developed in the USA by Roehr products in 1955<sup>4</sup>. New Zealand pharmacist Colin Albert Murdoch developed and patented one further refinement in 1956 to give us the single use plastic syringe general design that is still in use today<sup>2</sup>. The development of the Monoject syringe spurred Becton Dickinson (BD) into the development of similar plastic syringes (they had previously been developing glass

disposable syringes) and BD introduced its own single use plastic syringe “Plastipack” in 1961<sup>3</sup>. Ultimately, BD, with its introduction of the Plastipak, brought the single use plastic syringe into wide spread use and turned it into the preferred syringe used globally today.

Although materials have improved and designs have been refined, the single use syringes in use today still carry the same fundamental and technological characteristics of those of more than 50 years ago. To this day, there is not a common test method or defined specification for dose accuracy or the variability of dose accuracy for single use plastic syringes recognized by regulatory bodies for the standardization of these type syringes.

#### *Purpose of Research*

The objective of this study was to utilize the experience of healthcare professionals in the USA related to their affiliation with single-use plastic syringes for intravenous injection and oral/enteral delivery of syringe contents in acute care settings to research end user’s expectations of the variability of syringe dose accuracy and the need to standardize a common test method and define a dose accuracy variability specification of single-use plastic syringes. The goal of this survey was to statistically extrapolate the results of the study to the target population to formulate conclusions related to the dose accuracy variability expectations of single use plastic syringes to the target population.

#### *Statement of Problem*

Currently, a standardized dose accuracy variability requirement does not exist for single-use plastic syringes in any recognized international standard for syringe manufacturers to utilize when designing and manufacturing single-use plastic syringes. A review of current literature is

unclear if the target population expects single use plastic syringes to be standardized and if so, to what level of dose accuracy.

## CHAPTER 2

### LITERATURE REVIEW

There is very little published literature associated with the accuracy of single use plastic syringes. Current literature regarding the dose accuracy of syringes is focused on specific uses of syringes such as pre-filled syringes and glass syringes used with pre-defined pharmaceutical medications. The researcher was unable to identify specific literature related to the dose accuracy or the variability of dose accuracy of single use plastic syringes for non-specific pharmaceutical uses. There are International Organization of Standardization (ISO) standards associated with the general characteristics of single use plastic hypodermic syringes (i.e. Luer and Luer Lock syringes), however, there is currently no ISO standard that denotes the general requirements for single use plastic oral/enteral syringes, reverse luer syringes or catheter tip syringes. There is also no global standardized requirement or test method (ISO, AAMI, ASTM, EN, etc.) to determine or prescribe the evaluation of dose accuracy for single use plastic syringes.

Standardized general requirements for single-use plastic syringes were not formalized until 1993 and have not changed since. In 1993 the international organization of standardization (ISO) published ISO 7886-1:1993 *Sterile hypodermic syringes for single use – Part 1: Syringes for manual use*<sup>5</sup>. ISO 7886-1 includes requirements and test methods for various syringe parameters including tolerance on graduated capacity (ISO 7886-1:1993, Section 9), however it does not provide a specification or test method for the variability of dose accuracy of single use plastic syringes. The variability of dose accuracy can be defined as the ratio of the actual volume delivered to the patient in relation to the intended volume (prescribed dose) and is defined as a

percentage. For example, an intended dose is 1.0 mL, the syringe is filled to the 1.0 mL graduation mark and then the syringe contents are administered to the patient. If the administered volume is 0.9 mL, the variability of syringe dose accuracy would be -10%. If this same scenario is repeated and the administered volume is 1.1 mL, the variability of syringe dose accuracy would be +10%. If this was repeated multiple times with accuracy ranges from -10% to +10%, it could be inferred that the variability of syringe dose accuracy of that syringe is +/- 10%.

ISO 7886-1:1993 defines tolerance on graduated capacity as the variability of the volume of water at  $(20 \pm 5) ^\circ\text{C}$  [or, for tropical countries  $(27 \pm 5) ^\circ\text{C}$ ] expelled from the syringe when the fiducial line on the piston traverses a given scale interval or intervals and is calculated using the nominal capacity of the syringe and the intended dose to be delivered<sup>6</sup>. This means, the specification is only considering the graduation markings on the syringe. To be clear, ISO 7886-1:1993 does not define dose accuracy or the variability of dose accuracy. The standard defines only the tolerance for graduated capacity (Section 9, Tolerance on Graduated Capacity). ISO 7886-1:1993 does not define the tolerance for graduated capacity in linear or simple percentage terms. The tolerance for graduated capacity defined within ISO 7886-1:1993 is dependent on both the nominal capacity (maximum graduation marking volume) of the syringe used and the desired volume of fluid to be expelled and is disproportionately greater when low doses are considered. This is because the standard defines tolerance on graduated capacity requirements for two different and distinct use scenarios:

1. Tolerance Requirement 1: For a syringe fully dispensing a dose volume that is less than half ( $< 50\%$ ) the nominal capacity of the syringe

2. Tolerance Requirement 2: For a syringe fully dispensing a dose volume that is equal to or greater than half ( $\geq 50\%$ ) nominal capacity of the syringe.

The standard also does not define when each use scenario should be utilized to meet tolerance on graduated capacity requirements. The standard allows for either use scenario to be utilized to claim compliance to ISO 7886-1:1993, Section 9 Tolerance on graduated capacity.

Table 1 denotes the requirements documented in ISO 7886-1:1993 for tolerance on graduated capacity. From the table, syringes sizes of less than 5 mL nominal capacity, if tested to the specification of *equal to or greater than half nominal capacity*, should maintain  $\pm 5\%$  tolerance on graduated capacity. For syringe sizes of more than 5 mL nominal capacity, syringes should maintain  $\pm 4\%$  tolerance on graduated capacity.

Table 1: Tolerance of graduated capacity requirements of ISO 7886-1:1993

Nominal capacity of syringe, $V$ (mL)	Tolerance on any graduated capacity	
	Less than half nominal capacity	Equal to or greater than half nominal capacity
$V < 2$	$\pm (1.5 \% \text{ of } V + 2 \% \text{ of expelled volume})$	$\pm 5 \% \text{ of expelled volume}$
$2 \leq V < 5$	$\pm (1.5 \% \text{ of } V + 2 \% \text{ of expelled volume})$	$\pm 5 \% \text{ of expelled volume}$
$5 \leq V < 10$	$\pm (1.5 \% \text{ of } V + 1 \% \text{ of expelled volume})$	$\pm 4 \% \text{ of expelled volume}$
$10 \leq V < 20$	$\pm (1.5 \% \text{ of } V + 1 \% \text{ of expelled volume})$	$\pm 4 \% \text{ of expelled volume}$
$20 \leq V < 30$	$\pm (1.5 \% \text{ of } V + 1 \% \text{ of expelled volume})$	$\pm 4 \% \text{ of expelled volume}$
$30 \leq V < 50$	$\pm (1.5 \% \text{ of } V + 1 \% \text{ of expelled volume})$	$\pm 4 \% \text{ of expelled volume}$
$50 \leq V$	$\pm (1.5 \% \text{ of } V + 1 \% \text{ of expelled volume})$	$\pm 4 \% \text{ of expelled volume}$

When utilizing the tolerance on graduated capacity specification of *less than half nominal capacity*, the requirements drastically changes and now requires a calculation to determine compliance. To understand the drastic difference in these requirements, three examples are provided below.

1. Any 1 mL syringe dispensing 0.2 mL may have a graduated capacity error of  $\pm 9.5\%$  and still comply with ISO 7886-1:1993, Section 9.

2. Any 2mL syringe dispensing 0.2mL may have a graduation capacity error of  $\pm 17\%$  and still comply with ISO 7886-1:1993, Section 9.
3. Any 3mL syringe dispensing 0.5mL may have a graduation capacity error of  $\pm 11\%$  when dispensing 0.5mL and still comply with ISO 7886-1:1993.

Based on the above information, the standard can clearly be manipulated to the benefit of the single use plastic syringe manufacturer. A 2mL plastic single use syringe can be tested to *equal to or greater than nominal capacity* and must maintain less than  $\pm 5\%$  graduated capacity error. However, the exact same syringe can be tested to *less than half nominal capacity* and have a graduated capacity error of  $\pm 17\%$ . Both scenarios allow a single use plastic syringe manufacturer to claim compliance to ISO 7886-1:2003, however one method requires a variance less than  $\pm 5\%$ , while the other method allows for a variance of up to 17%. If a syringe manufacturer chose the test method that allowed for a variance of less than  $\pm 5\%$ , they would be placing a 2mL syringe on the market that has a variance of up to 17% for volumes measured in the syringe that were below half the syringe's nominal capacity and still claim compliance the standard. This difference in results from the two provided methods of measurement in ISO 7886-1 normalizes with larger volume syringe sizes, however dose accuracy of a syringe is significantly more critical for small volume syringe sizes, as seen with most measuring devices, the smaller the measured volume, the more critical the accuracy. Clearly, there are flaws in this standard.

The variability of dose accuracy, not just tolerance on graduated capacity should be considered when designing a single use plastic syringe. Critically, the tolerance of graduated capacity defined within ISO7886-1: 1993 for *graduated capacity* can be considered only part of the acceptable performance for delivered dose accuracy of a single use plastic syringe. In

practice, dose accuracy is also limited by the ability to manipulate the syringe piston/plunger and read the fiducial line circumscribing the end of the piston/plunger in relation to the graduation scale, as well as the ability or opportunity to eliminate headspace and/or ullage.

Tolerance on graduated capacity and dose accuracy were terms that may have been considered synonymous in the past. It was not until the introduction to the market of ISO 80369-3 (*Small-bore connectors for liquids and gases in healthcare applications -- Part 3: Connectors for enteral applications*) compliant enteral syringes that single use plastic syringe manufacturers and users realized there is more to syringe dose accuracy than just tolerance on graduated capacity<sup>7</sup>. Tolerance on graduated capacity assumes the piston/plunger movement is the only variable of the syringe. It does not consider human factors or general usability of single use plastic syringes, nor does it consider the connection state of the syringe when filling and delivery its contents. Human factors become relevant for the accuracy of syringes for many reasons. Proper lighting, vision of the user, understanding the precision of the fiducial line's alignment to the graduation markings on the syringe all become factors to consider when determining dose accuracy variability of a syringe.

Historically, the most commonly used syringes in medical applications have been male tipped. The fluid lumen of the syringe (syringe tip) inserts into the patient access device (needle, I.V. line connection, feeding tube, etc.). This allows for the dead space of the syringe (volume that never transfers to the patient access device) to remain static. However, with female tipped syringes, the patient access device inserts into the syringe tip, potentially displacing the dead space volume and thus causing an under delivery of its contents. Over deliveries may also occur if the syringe is filled using a device that inserts into the syringe tip and then its contents are delivered to the patient in a non-connected state (i.e. directly into the mouth).

Since single use plastic syringe manufacturers are no longer following the design of 50 years ago as well as the fact that ISO 7886-1:1993, Section 9 *Tolerance on graduated capacity* is clearly flawed and can be subject to manipulation. ISO 7886-1:1993 should no longer be the gold standard for single use plastic syringes. Research is therefore required to understand the expectations of healthcare professionals regarding variability for dose accuracy of single use plastic syringes, regardless if the syringe is male or female tipped, or if it is filled and/or delivered in a connected or non-connected state to adequately define a variability of dose accuracy specification that cannot be manipulated to accurately standardize the dose accuracy of plastic single use syringes.

## CHAPTER 3

### METHODOLOGY

#### *Study Design*

This observational study was based on the two most common uses (intravenous and oral/enteral delivery) of single-use plastic syringes in acute care hospital settings. The study analyzed single-use plastics syringes among healthcare professionals (nurses, pharmacists, pharmacy technicians, physicians, nurse practitioners, physician's assistants) related to route of administration (intravenous injection versus oral/enteral delivery), patient type (neonatal, pediatric and adult patients), and the margin of safety of the syringe contents to be administered to the patient. The research utilized an Google Forms internet-based questionnaire (survey) and distributed via mass email deployments and webpage posts. Relevant factors for determining the most appropriate dose accuracy variability of a single-use plastic syringe include the patient type in which the syringe contents are being delivered, the route of administration and the patient safety of the contents of the syringe.

The study was designed to include two background questions related to the participant's occupation and years of experience. These questions enabled the researcher to ensure respondents were within the target population and allowed the researcher to extrapolate potential differences in sub-populations where the research provided adequate sample size per sub-population. Due to distribution limitations, the survey contained a question requiring participants to answer if they live and work within or outside the United States. Data analysis excluded those

who are not considered part of the target population and those who are considered part of the target population but do not live and work within the USA.

Qualifying questions were also added to the survey to guide the participant to questions that are relevant to their experience. If the participant did not have experience with filling or administering syringes, they were not required to answer the two questions related to the types of syringes they most commonly use. If the participant did not have experience with neonatal patients, they were not required to answer dose accuracy variability questions related to the neonatal patient population. If the participant did not have experience with pediatric patients, they were not required to answer dose accuracy variability questions related to the pediatric patient population. If the participant did not have experience with adult patients, they were not required to answer dose accuracy variability questions related to the adult patient population. These qualifier questions were included as part of the study design to ensure responses are based on participant's experience, rather than their current thinking. All qualifier questions were required and the survey software directed each participant to the next question based on their response to these qualifier questions. All survey questions (if qualified) required participant responses for survey submission. This ensured incomplete surveys were not submitted.

The survey was divided into six (6) subparts. Subpart 1 was defined as the Introduction and Informed Consent. Participants were required to read introduction information and IRB approved consent and respond to the question with "yes" before the survey software would proceed to the next survey questions. If a participant responded "no" to this question, the survey software did not permit view of any of the survey questions and immediately forwarded to the submission page where the participant submitted the survey.

Subpart 2 of the survey collected participant information. The survey asked three background questions that defined inclusion and exclusion criteria as well as subpopulations.

The questions were as follows:

Which of the following choices best describes your occupation? (Only choose one)?

- Nurse (i.e. RN, LPN, BSN, MSN)
- Physician, Nurse Practitioner, Physician Assistant (i.e. MD, DO, NP, PA)
- Pharmacist (i.e. Pharm. D., RPh.)
- Pharmacy Technician (i.e. CPhT)
- Other, Specify \_\_\_\_\_

How many years have you been in the occupation you selected in the above question?

- less than 5 years
- 5 to 10 years
- 10 to 15 years
- 15 to 20 years
- more than 20 years

Where do you live and work?

- United States
- Outside the United States.

Participants that responded to the question of what best describes your occupation with “other”, were required to document their occupation. These responses were then filtered by the

researcher during data analysis based on their response and the relevance of their occupation to the target population.

Subpart 3 of the survey was related to the types of single use plastic syringes most commonly used in the participant’s day-to-day functions. This subpart consisted of a qualifying question that asked the participant if they have experience filling and/or administering the contents of a syringe to a patient. If they responded “no”, the survey software skipped the remaining questions of Subpart 3 and continued to Subpart 4. If the participant responded “yes”, the participant was provided pictures of different types of single use plastic syringes (Figure 1) and was asked to rank them based on the frequency they used each type (most common, 2<sup>nd</sup> most common, 3<sup>rd</sup> most common, etc.) for eventual intravenous injection.






Luer Lock	
Luer Slip	
Reverse Luer	
Oral/Enteral	
Catheter	

Figure 1: Syringe choices provided in Subpart 3 of the survey

If the participant had never used one type of syringe for eventual intravenous injection, they were provided an option “I have never filled or administered this type syringe for eventual intravenous injection”. The identical questions were then asked related to the use of the same syringes for eventual oral/enteral delivery of the syringe contents.

Subpart 4 of the survey consisted of four general questions regarding the participants current thinking or opinion related to when dose accuracy is most important. The questions were designed to segregate route of administration from syringe contents (nutrition or medication), patient population and dose size. This subpart did not contain a qualifier question. The questions were as follows:

Question 1: Of the choices below, which do you think requires a higher level of dose accuracy regardless of the route of administration?

- Medication (drug)
- Nutrition (parenteral or enteral)
- I think medication and nutrition require the same level of accuracy

Question 2: Of the administration routes listed below, which do you think requires a higher level of dose accuracy regardless of what (drug or nutrition) is being administered?

- Intravenous Injection
- Oral/enteral delivery
- I think intravenous injection and oral/enteral delivery require the same level of accuracy

Question 3: Of the choices below, which patient type do you think requires the highest level of dose accuracy regardless of what (drug or nutrition) is being administered or route of administration?

- a neonatal patient
- a pediatric patient
- an adult patient
- I think a neonate, a pediatric patient and an adult all require the same level of dose accuracy

Question 4: Of the choices below, which do you think requires a higher level of dose accuracy?

- Small volume dose (less than 2 mL)
- Dose over 2 mL
- I think all doses regardless of dose size should have the same level of accuracy.

Subpart 5 of the survey consisted of asking the participant the identical question for each of the following patient populations: neonatal patient population, pediatric patient population and adult patient population. For each patient population subsection, the following qualifier question was asked: Do you have experience with any of the following: filling syringes that will be administered to [neonatal] [pediatric] [adult] patients, administration of syringe contents to [neonatal] [pediatric] [adult] patients and/or treatment of [neonatal] [pediatric] [adult] patients? If the participant responded no to the qualifier question, the survey software skipped the specific question related to that patient population. If the participant responded yes to the qualifier question, they were provided with two definitions that may have been beneficial to them when responding to the specific questions. These definitions can be found in Table 2.

Table 2: Definitions provided for specific questions of Subpart 5

**VARIABILITY OF SYRINGE DOSE ACCURACY**

The ratio of the actual volume delivered to the patient in relation to the intended volume (prescribed dose) and is defined as a percentage. For example, an intended dose is 1.0 mL, the syringe is filled to the 1.0 mL graduation mark and the syringe contents are administered to the patient. If the administered volume is 0.9 mL, the variability of syringe dose accuracy would be -10%. If this same scenario is repeated and the administered volume is 1.1 mL, then the variability of syringe dose accuracy would be +10%. If this was repeated multiple times with accuracy ranges from -10% to +10%, it could be inferred that the variability of syringe dose accuracy of that syringe is +/- 10%.

**MARGIN OF SAFETY**

The range between the minimum therapeutic dose and the minimum toxic dose. This is also known as the therapeutic window or therapeutic index. The below table lists a few narrow margin of safety (therapeutic index) drugs.

Examples of Narrow Therapeutic Index Drugs (NTIDs) include:

5-fluorouracil, amphotericin B, carbamazepine, cyclosporine, phenytoin, digoxin, flecainide, gentamicin, lithium, phenobarbital, theophylline, warfarin

The following specific question was asked for each patient population:

Specific Question: Understanding that syringe dose accuracy variability does exist, what is the MAXIMUM variability of syringe dose accuracy you deem acceptable for a(n) [NEONATAL] [PEDIATRIC] [ADULT] patient for each of the scenarios below?

Scenarios	Variability of Syringe Dose Accuracy (%)						
	0	+/- 3	+/- 5	+/- 10	+/- 15	+/- 20	More than +/- 20
Intravenous injection of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of nutrition (TPN)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of nutrition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(survey software requires only one response per row)

Subpart 6 of the survey was designed to assess the participants current thinking regarding the need to standardize single use plastic syringe dose accuracy variability by using a common test method and dose accuracy variability specification. The question was asked for both intravenous injection and oral/enteral delivery of the syringe contents. If the participant responded yes, the survey software forwarded to the next question, if the participant responded no, the survey software required the participant to free-text document why the responded no.

Each question of Subpart 6 was written as follows:

Do you think the dose accuracy of all single-use plastic syringes used for [intravenous injection] [oral/enteral delivery] should be standardized by using a common test method and dose accuracy variability specification?

### *Target Population*

The target population of the study was healthcare professionals in the United States that are affiliated with intravenous and/or oral/enteral delivery of syringe contents to patients. Affiliation includes users of single-use plastic syringes in hospital settings where users include those that fill and/or administer the contents of a syringe intravenously or oral/enterally to a patient. Affiliation also includes those that provide treatment to neonatal, pediatric or adult patients, but do not necessarily fill and/or administer the contents of a syringe intravenously or oral/enterally to a patient. Such healthcare professionals include nurses (LPN, RN, BSN, MSN), pharmacists, and pharmacy technicians. Affiliation also includes healthcare professionals that prescribe medication and/or nutrition to be delivered intravenously and/or oral/enterally to a patient via syringes. This includes physicians, nurse practitioners, and physician assistants.

Based on the target population descriptions, the below sub-populations were pre-populated in the survey:

- Nurse (i.e. RN, LPN, BSN, MSN)
- Physician, Nurse Practitioner, Physician Assistant (i.e. MD, DO, NP, PA)
- Pharmacist (i.e. Pharm. D., RPh.)
- Pharmacy Technician (i.e. CPhT)

### *Research Hypotheses*

Primarily, the researcher proposed to examine the following hypothesis on a quantitative scale:

1. The researcher hypothesized that at least 95% of healthcare professionals have not used an oral/enteral syringe for intravenous injection, however more than 50% have used a Luer Lock or Luer Slip syringe for oral/enteral delivery.
2. The researcher hypothesized that generally, the majority of healthcare professionals will agree:
  - Medications require a higher level of dose accuracy than nutrition regardless of route of administration,
  - intravenous injection requires a higher level of dose accuracy than oral/enteral delivery regardless of what (drug or nutrition) is being administered,
  - neonatal patients require the highest level of dose accuracy regardless of what (drug or nutrition) is being administered or route of administration

- small volume doses (less than 2 mL) require a higher level of dose accuracy than doses over 2 mL.
3. The researcher hypothesized that for each patient population, the expectation of the acceptable dose accuracy variability of single-use plastic syringes, regardless of the participant's occupation will be:
- Generally, smaller for medications versus nutrition,
  - smaller for medications with narrow therapeutic margins versus medications with wide therapeutic margins, and
  - smaller for intravenous injection versus oral/enteral delivery.
4. The researcher hypothesized majority of participants will agree that regardless of route of administration, single-use plastic syringes should be required to meet a dose accuracy variability specification utilizing a common test method.

### *Survey Design Validation*

The survey design validation was performed in multiple stages. Stage one pilot test of the survey utilized industry colleagues (n=5), syringe experts (n=15) of which were mostly engineers, and thesis committee members (n=4) to first qualify the questions as they related to the intent of the study and review of each question's response options to ensure the response options made sense, were exhaustive and mutually exclusive. This process consisted of several iterations of the survey being distributed with changes/clarifications being made at each distribution. Once no further questions/clarifications were required, the validation process moved to stage two. Stage two pilot test of the survey incorporated target population individuals (n=10) executing the survey and providing feedback related to the structure of the questions, the

ease of understanding the questions, the validity of each questions' response options, and any feedback related to the reasoning behind each question. Stage two resulted in the inclusion of qualifier questions for Subpart 3 and Subpart 5 of the survey. Once no further questions/clarification was required, the validation process moved to stage three. Stage three pilot test of the survey reviewed the post stage two survey version with stage one reviewers again. Small changes were made to the survey at the end of stage three for clarification reasons. Stage four pilot test of the survey reviewed the post stage three survey version with stage two reviewers again. This review resulted in no changes to the survey. Stage five of the survey validation involved three laymen (individuals outside the target population and not considered subject matter experts) executing the survey and providing feedback to the researcher. All three laymen communicated to the researcher that the survey was easy to follow, the questions were easy to understand, the response options were easy to interpret and choose, and overall the survey made sense. This completed the validation and the survey content was frozen.

#### *Institutional Review Board Process*

Prior to subject recruitment, the survey design and recruitment materials were submitted to the University of Georgia's Institutional Review Board (IRB) for review and approval which is a required element to ensure the protection of Human Subjects per University policy and federal law as set forth in 45 Code of Federal Regulations (CFR) Part 46<sup>14</sup> and 21 CFR 56<sup>16</sup>. The draft survey submitted to the IRB included the participant consent as the first question of the survey. This question required the participant to select "Yes" to the question "By clicking YES (I agree to participate in this survey) below, you are agreeing to participate in the above described survey." By selecting YES, the online survey continued to the next page. If a participant

selected NO to this question, the survey skipped all questions and took the participant to the submission page for participant to submit the survey with no responses. The consent page included the title and purpose of the study, why and how the participant was selected, the approximate time required to complete the survey, the fact that survey participation was voluntary and anonymous, the risks associated with survey participation, and how the results would be used. The IRB application, survey design, recruitment materials and participation informed consent were approved on September 29, 2016.

### *Subject Recruitment*

The target population was recruited utilizing recruitment emails from the researcher to known email addresses of the target population, from GEDSA (Global Enteral Device Suppliers Association) to their known distribution list, and from GSHP (Georgia Society of Health-System Pharmacist) to their known distribution list. Recruitment also included posting the recruitment email content on the RN (Registered Nurse) Network group on LinkedIn. Distribution software such as ConstantContact, MailChimp and ExactData was utilized for deployment to aid in reducing the number of bounced/blocked emails. Target population email addresses were obtained from reputable sources including physicians, nurses and pharmacist friends/colleagues of the researcher that provided contact information of their colleagues; non-profit organizations that were willing to aid in distribution (such as GEDSA and GSHP), medical device manufacturer's contact lists (such as NeoMed, Inc.) and purchased email addresses of the target population from ExactData.

Recruitment email contents contained the subject matter, why the participant was selected, how their email address was obtained, organization and reason for the study, link to the

survey, any incentives associated with the study, directions for the ability to opt out of future recruitment emails and the due date to complete the survey. The recruitment emails also contained a statement that informs the participant that their participation is voluntary and their responses are anonymous. Follow-up recruitment emails were also sent, but no more than three (3) follow-up recruitment emails were sent to obtained email addresses. Follow-up emails were only sent to those email addresses that did not chose to opt out of future correspondences regarding the study when they received the first correspondence.

Deployment of the recruitment email occurred in multiple phases. Original recruitment email deployment occurred on October 1, 2016 to 4,923 potential target population email addresses. On October 7, 2016, GEDSA (Global Enteral Device Suppliers Association) deployed to their known distribution list of 636 potential target population email addresses. On October 20, 2016, a recruitment email deployed to 10,000 additional target population email addresses through ExactData. This third deployment was required due to the low response rates of the first two deployment groups. This deployment was managed by ExactData. ExactData is a third-party marketing company that aids industry in deployments of marketing newsletters, surveys, etc. Their database of target population individuals was utilized to ensure all 10,000 email addresses were that of the target population. Due to pour response rates of this deployment, other means of deployment were utilized including, GSHP (Georgia Society of Health-System Pharmacist) deploying to their known distribution list on November 1, 2016. Recruitment also included posting the recruitment email content on the RN (Registered Nurse) Network group on LinkedIn on November 2, 2016. Follow-up emails were sent to the original distribution list, the GEDSA distribution list and the ExactData distribution lists, but no more than three follow-up emails were sent to ensure alignment with the IRB approval.

### *Data Collection*

Data collection was in the form of an internet based questionnaire (survey) utilizing Google Forms. Only the researcher had access to the responses. The survey was anonymous and as such, did not require any personal information from the participants as that information is not relevant to the analysis. The survey software (Google Forms) did not collect personal data, including IP addresses of participants. The data was continuously monitored by the researcher during the fielding of the survey. Upon completion of the survey, the data was exported from Google Forms to a Microsoft<sup>®</sup> Excel workbook (Microsoft<sup>®</sup> Office 2010). The researcher manually reviewed the exported data compared to the data collected in Google Forms to ensure the data export process did not compromise the data. All data exported from Google Forms collection software was deemed valid.

### *Statistical Rationale*

Prior to survey deployment, a sample size of 384 participants was projected to be adequate to analyze the data with 95% confidence and a 5% margin of error. To determine this number, the researcher used the following formula:

$$\text{Sample size (n)} = \frac{(\text{Z-score})^2 * \text{StdDev} * (1-\text{StdDev})}{\text{Margin of Error}^2 (\text{ME})}$$

where:

$$\text{Z-score} = 1.96$$

$$\text{StdDev (p)} = 0.5 \text{ (unknown, therefore utilized most forgiving number to ensure the sample size will be large enough)}$$

$$ME = 5\% (0.05)$$

However, after survey deployment, the researcher realized that each subpart of the survey may have a different number of responses based on some subparts containing qualifying questions. Based on this information, a statistical rationale to determine adequate sample size was no longer required as the format of the subparts of the survey did not lend to power analysis.

### *Data Analysis*

The primary statistical analysis techniques that were used to analyze the data consisted of the use of descriptive statistical methods for general demographic interpretations and percentages for sample proportions. Contingency tables were also used to provide a means of summarizing counts and percentages. Inferential statistics were used to extrapolate the survey results to the target population so inferences could be made regarding USA based healthcare professionals' views towards the dose accuracy of single use plastic syringes. These included chi-square test for a single proportion, chi-square test of proportions, chi-square test for equality of proportions and chi-square test for independence. Wald and binomial confidence intervals for proportions were also utilized. Where required, continuity and Bonferroni corrections were used to control type 1 errors. Data was presented in the form of tables and graphs to further aid in visualization of the results.

### *Disclosure*

The researcher wished to disclose her experience with the subject matter. The researcher has worked in the medical device industry, specifically quality and regulatory affairs, for over 15 years. The researcher is currently the Vice President of Quality and Regulatory Affairs for

NeoMed, Inc. NeoMed, Inc. is a medical device manufacturer of enteral devices specific to the neonatal and pediatric patient populations. NeoMed, Inc. manufactures medical devices such as feeding tubes, extension sets and oral/enteral syringes. The researcher has been heavily involved in the ISO standards process for the introduction and publication of ISO 80369-3. The implementation of medical devices with ISO 80369-3 compliant connectors has been ongoing for over seven (7) years. The researcher is also a committee member of standards working group TC205 WG16. This working group committee is responsible for the drafting, revision review and publication of ISO 20695. ISO 20695 is a draft standard for enteral devices which includes specific requirements for the test methods related to dose accuracy of enteral syringes.

## CHAPTER 4

### RESULTS

#### *Data Collection and Exclusion Criteria Results*

The survey closed on November 9, 2016 at 5:00 PM EST. Upon closure of the online survey, 407 completed surveys were obtained. Of these, nine (9) participants, did not agree to participate as they chose no to the question “I agree to participate in this survey”. The remaining 398 completed surveys were then reviewed for exclusion criteria. Per predetermined exclusion criteria, all participants that did not live and work in the United States were excluded from the data analysis, therefore 27 (6.8%) completed survey responses were removed from the data analysis leaving 371 completed surveys. The data was then reviewed for completed surveys that were performed by participants that were not considered to be within the target population. The target population consisted of prepopulated fields for 1) Nurse (i.e. LPN, RN, BSN, MSN), 2) Physician, Nurse Practitioner, Physician Assistant (i.e. MD, DO, NP, PA), 3) Pharmacist (i.e. Pharm. D., RPh.), 4) Pharmacy Technician (i.e. CPhT), and 5) other. If a participant chose “Other”, they were required to document their occupation. There were 22 completed surveys that chose “Other” as an occupation and provided free-text descriptions of their occupation. The researcher reviewed these free-text descriptions and collapsed eight completed surveys into one of the four pre-populated occupation fields based on the respondent’s occupation description. A few examples include, “CRNA (nurse anesthetist)” was grouped with nurses, “RN BSN MBA Clinical Resource Manager” was also grouped with nurses, and “Respiratory Therapist RRT” was grouped with physicians. The other 14 respondents that chose “Other” as their occupation

were excluded based on their provided occupation description clearly not being within the target population. Examples of these included syringe manufacturers, sales representatives, and supply chain/materials management personnel. Table 3 below denotes how each of these 22 completed surveys were grouped or excluded.

Table 3: Analysis of “Other” free-test responses regarding participant’s occupation

Participant Response	Target Population (Yes/No)	Sub-population grouping
Device Sales	No	
Point of Care Technology Provider	No	
RN BSN MBA Clinical Resource Manager	Yes	Nurse (i.e. LPN, RN, BSN, MSN)
Respiratory Therapist RRT	Yes	Physician, Nurse Practitioner, Physician Assistant (i.e. MD, DO, NP, PA)
Director, Supply Chain	No	
Registered Dietitian	Yes	Nurse (i.e. LPN, RN, BSN, MSN)
Sales Representative	No	
Consumer Support Organization Executive Director	No	
Salesman	No	
Materials Manager	No	
Supplier	No	
Syringe Manufacturing and Sales	No	
Nutritionist	No	
Speech Language Pathologist	No	
Director of Materials Mgt.	No	
Phlebotomist	Yes	Nurse (i.e. LPN, RN, BSN, MSN)
Lab Manager	Yes	Pharmacy Technician
Paramedic	Yes	Nurse (i.e. LPN, RN, BSN, MSN)
CRNA (nurse anesthetist)	Yes	Nurse (i.e. LPN, RN, BSN, MSN)
Pharmacy Buyer	Yes	Pharmacy Technician
Buyer	No	
Materials Manager	No	

### *Subject Demographics*

After exclusion criteria analysis, the final number of completed surveys analyzed was 357. There were only six (6) participants that chose (or were reassigned above to) pharmacy technician, therefore the researcher combined these completed surveys with Pharmacist to have a total of three (3) sub-populations for final data analysis. The total number of participants per sub-population for data analysis is denoted in Table 4. It should be noted that only 30 (8.4%) of the participants were Physicians, Nurse Practitioners or Physician Assistants. Based on this extremely low response rate for this sub-population, the researcher was not able to compare the sub-populations for every subpart of the survey with a valid level of significance to determine if the three sub-populations responded differently to the questions. Therefore, the analysis of the results of certain subparts of the survey were only analyzed for the general population of healthcare professionals by analyzing all sub-populations as one population.

Table 4: Total Number of Participants per Sub-population

Nurse (i.e. LPN, RN, BSN, MSN)	180 (50.4%)
Physician, Nurse Practitioner, Physician Assistant (i.e. MD, DO, NP, PA)	30 (8.4%)
Pharmacist (i.e. Pharm. D., RPh.)	147 (41.2%)
Total	357

The survey background section (Subpart 2) also inquired as to the number of years each participant has been in their selected occupation. Of the three sub-populations analyzed, the data showed that 217 (60.8%) participants, regardless of their occupation, have over 20 years of experience. Overall, only 17 (4.8%) respondents had less than five (5) years of experience and 123 (34.4%) respondents had at least five years but no more than 20 years of experience. See Figure 2 for a comparison of each sub-population by number of years of experience. The fact

that over 60% of responses were generated from healthcare professionals with over 20 years of experience is a good indicator that the responses were based on experience and not the opinion of the participants.

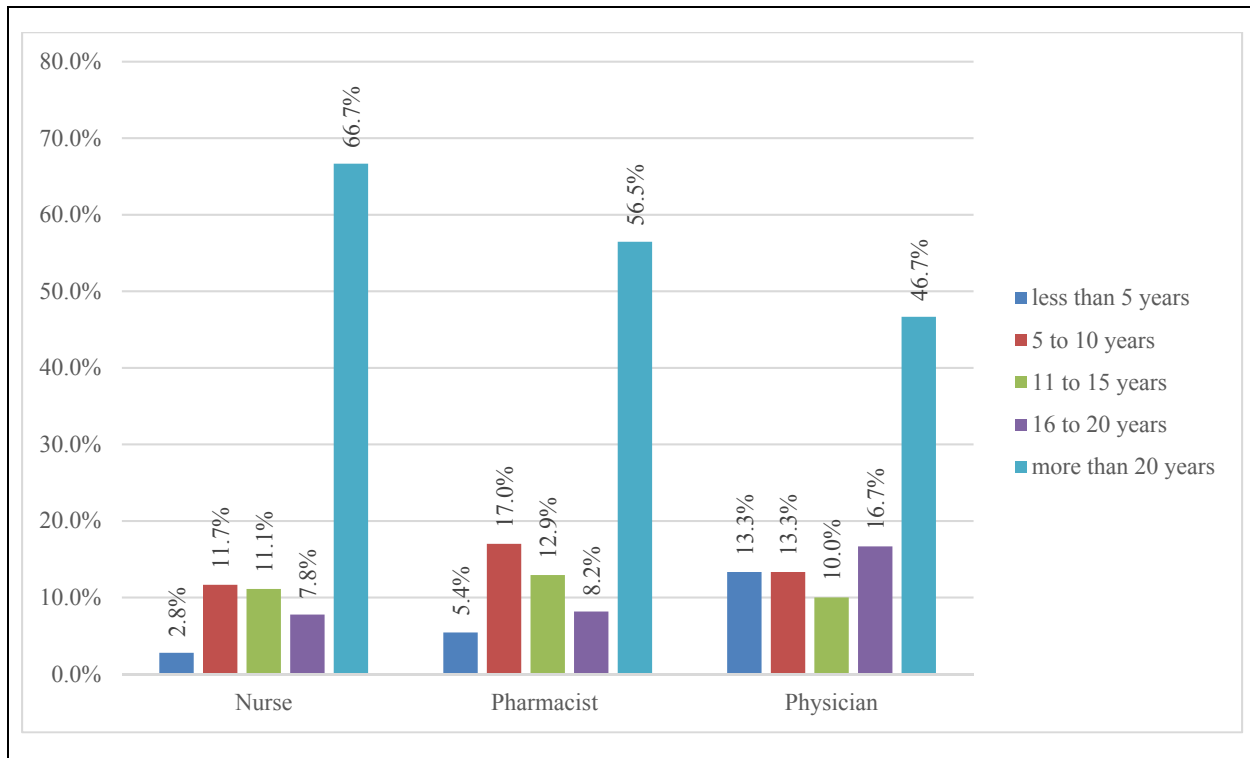


Figure 2: Sub-populations by years of experience

### *Analysis of Subpart 3*

Subpart 3 of the research involved understanding the most common uses of single-use plastic syringes based on the experience of the participants. The survey questions were designed to answer the researcher’s first hypothesis question; however, a qualifying question was added to Subpart 3 to ensure those that responded to these research questions were responding based on their experience and not just their opinion. Therefore, before participants could respond to questions related to what types of syringes they use for certain medical applications and how often they use them, they first had to respond to a yes/no question regarding their experience

with filling syringes and/or administering syringe contents to patients. Of the 357 total respondents utilized for data analysis, 345 (96.6%) participants responded yes to the qualifying question. Only 12 participants did not have experience filling syringes and/or administering syringe contents to patients. Therefore, there was a total of 345 responses analyzed for Subpart 3 data analysis.

Subpart 3 contained two questions. The questions were identical except for changing the eventual route of administration of the syringe contents. The first question of Subpart 3 required the participant to rank their usage of the different syringe types for eventual intravenous injection and the second question required them to rank the different syringes types for eventual oral/enteral delivery. The questions required the respondent to detail the frequency for which they fill and or administer different types of syringes for eventual intravenous administration and then again for oral/enteral delivery. The different types of syringes to choose from were described in Chapter 3, however, were a Luer Lock, a Luer Slip, a Female Luer (Reverse Luer), an Oral/Enteral and a Catheter tipped syringe. The participants were required to rank the syringe types by most common, second most common, third most common, fourth most common and fifth most common. The participant was also provided one last choice for each syringe type “I have never filled or administered this type syringe for eventual [intravenous injection] [oral/enteral delivery]”. This additional response was added during the survey design validation to ensure that all available options were mutually exclusive and exhaustive.

To analysis the results of Subpart 3, the researcher reviewed each of the syringe types by route of administration separately. Luer Lock syringes were by far the most common syringe type used for intravenous injection regardless of the participant’s sub-population (nurse, pharmacist, physician) as 318 (92.2%) respondents chose a Luer Lock syringe as their most

common syringe type for intravenous injection. This result was not unexpected, as a Luer Lock syringe is the global gold standard for single use plastic syringes used for intravenous injection. This is confirmed with the publication of ISO 7886-1, which is specially intended for hypodermic syringes and denotes the details of the syringe in the standard with the assumptions that they are Luer Lock and Luer Slip syringe designs.

The results for the Luer Slip style syringe were aligned with the results for the Luer Lock style syringe being the second most common syringe type used for eventual intravenous injection with 155 (50%) participants denoting it as the second most common. These results are consistent with the researchers thinking as Luer Slip syringes are in the same family and covered by the same requirements of ISO 7886-1 as a Luer Lock syringe. Luer Slip syringes are most commonly found in small volume (<2 mL) syringes as it is extremely difficult to design a Luer Lock syringe tip for a small volume syringe based on the engineering and manufacturability of the device.

The results for the Female Luer (reverse Luer) syringe were also as expected by the researcher as reverse Luer syringes are quite common in the United Kingdom, however are not common in the USA and the target population only included respondents from the USA. Two hundred sixty-four (76.5%) respondents documented that they have never used a reverse Luer syringe for an eventual intravenous injection. The results for catheter tipped syringes also showed that the majority of respondents have never used a catheter syringe for eventual intravenous injection with 243 (70.4%) respondents choosing this answer.

The responses for oral/enteral syringes used for eventual intravenous injection was not as the researcher hypothesized. The researcher hypothesized that at least 95% of participants have not used an oral/enteral syringe for intravenous injection; however, survey results showed only

243 (70.4%) participants had never used this type of syringe in this capacity. To test this hypothesis, a one-sample test of proportions was employed at a 5% significance level. Testing the hypotheses:  $H_0: p = 0.95$  against  $H_a: p > 0.95$ , SAS<sup>®</sup> Version 9.4, PROC FREQ was used to perform a normal approximation to the binomial distribution without a continuity correction. Wald confidence limits were also calculated. These 95% confidence limits were (0.656, 0.753), which indicates that the true proportion of healthcare professionals who have never used an oral/enteral syringe for eventual intravenous injection is between 66% and 75%. The researcher based the hypothesis on her experience in the oral/enteral syringe manufacturing industry as the Institute of Safe Medication Practices (ISMP) has published several medication safety alerts recommending that oral/enteral syringes should not be used for intravenous injection as well as stating that Luer Lock and Luer Slip syringes should not be used for oral/enteral delivery due to the potential to misconnect and wrong route administer medications or nutrition. The ISO 80369-3 initiative began over seven years ago, to encourage syringe manufacturers to design out the ability for a delivery device (i.e. single use plastic syringe) to connect to a patient access device of a wrong route. The state of California also set into law a similar requirement in 2016 with Assembly Bill 1867. AB 1867 states in part (b) commencing July 1, 2016, a healthcare facility, ..., is prohibited from using 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 impart the ability to provide health care.<sup>20</sup>

To test the hypothesis that more than 50% of the participants have used a Luer Lock or Luer Slip syringe for eventual oral/enteral delivery, the same methods were used. The 95% Wald confidence limits were (0.6440, 0.7398), which indicates that the true proportion of healthcare professionals who have used a Luer Lock or Luer Slip syringe for eventual

oral/enteral delivery is between 66% and 75%. These results support the researcher's hypothesis that more than 50% of healthcare professionals have used a Luer Lock or Luer Slip syringe for eventual oral/enteral delivery.

The results of Subpart 3 showed that only 70.4% of healthcare professionals have never used an oral/enteral syringe for eventual intravenous injection with a 95% confidence interval of 66% to 75%. These results are far less than what the researcher hypothesized. The researcher hypothesized that more than 95% of the participants have never used an oral/enteral syringe for eventual intravenous injection yet hypothesized that at least 50% of the participants have used a Luer Lock or Luer Slip syringe for eventual oral/enteral delivery. The researcher estimated such hypotheses because Luer Lock and Luer Slip syringes are known to be the most common syringe types used in acute care hospital settings. Single use plastic syringe tips must mate with the patient access device to ensure adequate administration without leakage. There are numerous patient access devices that are designed to mate with Luer Lock or Luer Slip syringe tips regardless of the route of administration. For example, patient access devices that are designed to mate with a Luer Lock or a Luer Slip syringe include intravascular access devices, intramuscular needles, epidural needles, urinary catheters, Foley catheters, tracheostomy tubes, limb cuffs, and even enteral feeding tubes. However, there are not many patient access devices that are specifically designed to mate with an oral/enteral syringe.

Many hospitals in the USA contain segregated pharmacies that unit-dose medications in single use plastic syringes based on physician orders. This unit-dosing practice follows United States Pharmacopeia (USP) compendium for proper pharmaceutical closure container (i.e. syringe) materials, but USP does not specifically denote that syringes designed for a certain route of administration should only be used for that route of administration. Requiring a pharmacy to

unit-dose in specified syringe types requires pharmacies to stock multiple types of syringes. It would also require physician's orders to specify the syringe type on the order. These additional processes are considered to impede patient care even though they increase the risk of misconnections that may result in wrong route administration.

Unfortunately, cost must also be considered when stocking multiple types of syringes in the pharmacy or on the patient floor. When acute care facilities determine the medical devices that will be routinely stocked for patient use, clinical efficacy and potential risks are determining factors, but cost is also heavily weighed. Single use plastic syringes are normally not reimbursable by insurance; therefore, they are considered routine, low risk medical devices of which the hospital purchasing departments tend to become the final decision makers.

The fact that the medical device industry is a for profit industry also must be considered. Medical device manufacturers have core missions and policies that lend to safe and effective medical devices, but they will also not invest the resources or finances to design a medical device that will not return a profit. The costs of the pre-market development work of placing a medical device on the market must be considered when designing a medical device. This seems obvious for life-sustaining medical device, but it also holds true for the simplest types of devices.

Subpart 3 was not designed to address the purpose or the problem statement of this research. Subpart 3 was designed to ascertain a level of understanding of what types of single use plastic syringes are most frequently utilized for the two most common routes of administration that hold the highest associated risks with wrong route administration.

### *Analysis of Subpart 4*

Subpart 4 of the survey was designed to ask general questions based on the participant's experience filling and/or administering the contents of a syringe as it relates to:

- the dose accuracy expectations based on the route of administration (intravenous injection versus oral/enteral delivery) regardless of the syringe contents (medication or nutrition),
- the dose accuracy expectations based on the contents of the syringe (medication versus nutrition) regardless of the route of administration (intravenous injection or oral/enteral delivery)
- the dose accuracy expectations based on eventual administration to a certain patient population (neonatal patients versus pediatric patients versus adult patients regardless of the route of administration (intravenous injection or oral/enteral delivery) or the syringe contents (medication or nutrition)
- the dose accuracy expectations based on the dose volume (small volume dose of less than 2mL versus dose volumes greater than 2mL).

Each question of Subpart 4 asks the respondent to only consider one variable when answering each of the four questions. The questions were designed this way to ascertain a general understanding of healthcare professionals current thinking for dose accuracy as it relates to what is being administered (contents of the syringe), the route of administration, the patient type and the dose volume independent of each other.

Subpart 4 did not contain any qualifying questions; therefore 357 responses were analyzed for each of the bullet points described above. For these research questions concerning

dose accuracy, chi-square tests for a single proportion, where the null proportion was 0.50 were implemented.

### Medication versus Nutrition

For the first question of Subpart 4, the researcher hypothesized that the majority of healthcare professionals would agree that medication requires a higher level of dose accuracy than nutrition, regardless of the route of administration to the patient. To test whether participants perceived medication to require a higher level of dose accuracy than nutrition regardless of route of administration, the researcher tested  $H_0: p = 0.50$ , where  $p$  is the proportion of healthcare professionals who believe medication requires a higher level of dose accuracy than nutrition, against  $H_a: p > 0.50$ . The results of this question showed that 235 participants (65.8%) felt that medication required a higher level of dose accuracy than nutrition, while 157 (33.9%) felt medication and nutrition required the same level of dose accuracy, while just one participant (0.3%) felt that nutrition required a higher dose accuracy. SAS<sup>®</sup> Version 9.4, PROC FREQ was used to compute the binomial proportion and p-value for the hypothesis test. The p-value is  $< 0.0001$ , which indicates that the null hypothesis was rejected in favor of the alternative hypothesis of greater than 50% of healthcare professionals consider medication to require a higher dose accuracy than nutrition, therefore the researcher's hypothesis was aligned with the results of the survey.

To test if there were any significant differences between the sub-populations, a chi-square test of proportions was implemented to test the hypothesis  $H_0: p_1 = p_2 = p_3$ , where  $p_1$  = the percentage of physicians who believe medication requires a higher level of dose accuracy than nutrition,  $p_2$  = the percentage of pharmacists who believe medication requires a higher level of

dose accuracy than nutrition, and  $p_3$  = the percentage of nurses who believe medication requires a higher level of dose accuracy than nutrition. The alternative hypothesis,  $H_a$ , is that the perception is different among these three sub-populations. Since only one participant responded that he/she felt that nutrition requires a higher level of dose accuracy than medication, this response was combined with the responses of participants that believe there should be no difference between the dose accuracy of medication and nutrition. The results are described in Table 5.

Table 5: Sub-population comparison of dose accuracy related to medication versus nutrition

	Nurses	Pharmacists	Physicians	Total
Dose accuracy is more important for medication	101 (56.1%)	110 (74.8%)	24 (80.0%)	235
Dose accuracy is not more important for medication	79 (43.9%)	37 (25.2%)	6 (4.9%)	122
Total	180	147	30	357

A chi-square test for equality of proportions was performed using SAS<sup>®</sup> Version 9.4, PROC FREQ. The chi-square statistic was 15.53 with a p-value of 0.0004, indicating that there are differences among the sub-populations' perceptions regarding acceptable dose accuracy. To test this hypothesis further, a Bonferroni correction was used to control the type I error. To be considered statistically significant, the pairwise comparison must have a p-value of less than 0.0167. Physicians and pharmacists did not have a statistically significant difference when compared ( $p=0.5473$ ), though there was a statistically significant difference in the current thinking of pharmacist and physicians when compared to nurses, as more pharmacists perceived the dose accuracy of medication to be more important than nutrition than did nurses ( $p=0.0004$ ), as did physicians compared to nurses ( $p=0.0136$ ). The differences between the sub-populations

could be due to many factors, such as years of education, frequency of use of syringes, and whether the participant was more familiar with filling syringes versus administering the contents of syringes. Of note, the differences between physicians and nurses could also be contributed to the low number of responses obtained from physicians.

#### Intravenous Injection versus Oral/enteral Delivery

For the second question of Subpart 4, the researcher hypothesized that the majority of participants would agree that intravenous injection requires a higher level of dose accuracy than oral/enteral delivery, regardless of the syringe contents (medication or nutrition). To test whether participants perceived intravenous injection to require a higher level of dose accuracy than oral/enteral delivery regardless of the syringe contents, the researcher tested  $H_0: p = 0.50$ , where  $p$  is the proportion of healthcare professionals who believe intravenous injection requires a higher level of dose accuracy than oral/enteral delivery. The alternative hypothesis was  $H_a: p > 0.50$ . One hundred eighty-five (51.8%) survey participants responded that they felt intravenous injection requires a higher level of dose accuracy than oral/enteral delivery, while 171 (47.9%) felt there should be no difference, and one (0.3%) responded that oral/enteral delivery required a higher level of dose accuracy. SAS<sup>®</sup> Version 9.4, PROC FREQ again was used to calculate binomial proportions, and the one-sided p-value was 0.2457, which causing the researcher to fail to reject the null hypothesis and conclude that no more than half of healthcare professionals feel that intravenous injection requires a higher level of dose accuracy than oral/enteral delivery, which does not support the researcher's hypothesis.

To test if there were any significant differences between the sub-populations, a chi-square test of proportions was implemented to test the hypothesis  $H_0: p_1 = p_2 = p_3$ , where  $p_1 =$  the

percentage of physicians who believe intravenous injection requires a higher level of dose accuracy than oral/enteral delivery,  $p_2$  = the percentage of pharmacists who believe intravenous injection requires a higher level of dose accuracy than oral/enteral delivery, and  $p_3$  = the percentage of nurses who believe intravenous injection requires a higher level of dose accuracy than oral/enteral delivery. The alternative hypothesis,  $H_a$ , is that the perception is different among these three sub-populations. Since only one participant responded that he/she felt that oral/enteral delivery requires a higher level of dose accuracy than intravenous injection, this response was combined with the responses of participants that believed there should be no difference between the dose accuracy for intravenous injection and oral/enteral delivery. The results are described in Table 6.

Table 6: Sub-population comparison of dose accuracy related to route of administration

	Nurses	Pharmacists	Physicians	Total
Dose accuracy is more important for intravenous injection	77 (42.8%)	90 (61.2%)	18 (60.0%)	185
Dose accuracy is not more important for intravenous injection	103 (57.2%)	57 (38.8)	12 (40.0%)	172
Total	180	147	30	357

A chi-square test for equality of proportions was performed using SAS<sup>®</sup> Version 9.4, PROC FREQ. The chi-square statistic was 11.91 with a p-value of 0.0026, indicating that there are differences among the sub-populations' perceptions regarding acceptable dose accuracy for the two routes of administration. To test this hypothesis further, a Bonferroni correction was used to control the type I error. To be considered statistically significant, the pairwise comparison must have a p-value of less than 0.0167. Physicians and pharmacist's responses did not have a statistically significant difference when compared ( $p=0.9000$ ), though there was a

statistically significant difference in the current thinking of pharmacist when compared to nurses, as more pharmacists perceived the dose accuracy of intravenous injection to be more important than oral/enteral delivery than did nurses ( $p=0.0009$ ). It could be deducted that this could be attributed to the primary functions of these professions, as pharmacist more often fill syringes whereas nurses more often administer the contents of syringes to patients. When comparing the responses of physicians to those of nurses ( $p=0.0793$ ), there were no significant differences.

#### Neonatal versus Pediatric versus Adult Patient Populations

For the third question of Subpart 4, the researcher hypothesized that the majority of participants would agree that the neonatal patient population requires the highest level of dose accuracy compared to pediatric and adult patient populations, regardless of the route of administration to the patient or of the syringe contents (medication or nutrition). To test whether participants perceived the neonatal population to require a higher level of dose accuracy than the pediatric or adult patient populations regardless of route of administration or syringe contents, the researcher tested  $H_0: p = 0.50$  where  $p$  is the proportion of healthcare professionals who believe the neonatal patient population requires a higher level of dose accuracy than the pediatric and adult patient populations, against  $H_a: p > 0.50$ . In response to this question, 192 (53.8%) felt that a neonatal patient requires a higher level of dose accuracy than a pediatric or adult patient, while no participants thought a pediatric or adult patient required a higher level of dose accuracy, and 165 (46.2%) felt that neonates, pediatrics, and adults all require the same level of dose accuracy. The p-value of the hypothesis test was 0.0765, indicating that there is not sufficient statistical evidence to conclude that more than 50% of healthcare professions feel that there is a

greater need for higher dose accuracy in the neonatal patient population. Therefore the researcher’s hypothesis was not aligned with the results of the survey.

To test if there were any significant differences between the sub-populations, a chi-square test of proportions was implemented to test the hypothesis  $H_0: p_1 = p_2 = p_3$ , where  $p_1$  = the percentage of physicians who believe the neonatal population requires a higher level of dose accuracy than the pediatric or adult patient populations,  $p_2$  = the percentage of pharmacists who believe the neonatal population requires a higher level of dose accuracy than the pediatric or adult patient populations, and  $p_3$  = the percentage of nurses who believe the neonatal population requires a higher level of dose accuracy than the pediatric or adult patient populations. The alternative hypothesis,  $H_a$ , is that the perception is different among these three sub-populations. The results are described in Table 7.

Table 7: Sub-population comparison of dose accuracy related to patient type

	Nurses	Pharmacists	Physicians	Total
Dose accuracy is more important for neonatal patients	81 (45.0%)	93 (63.3%)	18 (60.0%)	192
Dose accuracy is not more important for neonatal patients	99 (55.0%)	54 (36.7%)	12 (40.0%)	165
Total	180	147	30	357

A chi-square test for equality of proportions was performed using SAS<sup>®</sup> Version 9.4, PROC FREQ. The chi-square statistic was 11.37 with a p-value of 0.0034, indicating that there are differences among the sub-populations’ perceptions regarding acceptable dose accuracy for the two routes of administration. To test this hypothesis further, a Bonferroni correction was used to control the type I error. To be considered statistically significant, the pairwise comparison must have a p-value of less than 0.0167. Physicians and pharmacists did not have a statistically significant difference when compared (p=0.7361), though more pharmacists

perceived the dose accuracy for the neonatal patient population to be more important than dose accuracy for pediatric or adult patient populations when compared to nurses ( $p=0.0010$ ), however, physicians compared to nurses ( $p=0.1276$ ) did not show a statistically significant difference. This too, could be attributed to the low number physician responses.

#### Small Volume (< 2 mL) versus Larger Volume (> 2mL) Doses

For the final question of Subpart 4, the researcher hypothesized that the majority of participants would agree that small volume doses (2mL or less) require a higher level of dose accuracy than doses over 2mL, regardless of the route of administration (intravenous injection or oral/enteral delivery, the syringe contents (medication or nutrition) or the patient population (neonate, pediatric, or adult). To test whether participants perceived doses less than 2mL to require a higher level of dose accuracy than doses greater than 2mL regardless of route of administration, syringe contents, or patient population, the researcher tested  $H_0: p = 0.50$  where  $p$  is the proportion of healthcare professionals who believe doses 2 mL or less require a higher level of dose accuracy than doses larger than 2 mL, against  $H_a: p > 0.50$ . The survey responses indicate a different result than expected. Only 137 (38.4%) felt that a dose 2 mL or less required a higher level of accuracy than a dose larger than 2 mL, while the remainder of participants 220 (61.6%) felt that doses 2 mL or less did not require a higher level of dose accuracy. The null hypothesis was rejected ( $p < .0001$ ), concluding that less than 50% of participants think the dose accuracy should be higher for doses smaller than 2mL. From these results, the researcher must conclude that the majority of healthcare professionals do not think dose volume should be considered when determining the accuracy variability of the dose when administered from a single use plastic syringe.

To test if there were any significant differences between the sub-populations, a chi-square test of proportions was implemented to test the hypothesis  $H_0: p_1 = p_2 = p_3$ , where  $p_1$  = the percentage of physicians who believe a small volume dose (< 2mL) requires a higher level of dose accuracy than a larger volume dose (> 2 mL),  $p_2$  = the percentage of pharmacist who believe a small volume dose (< 2mL) requires a higher level of dose accuracy than a larger volume dose (> 2 mL), and  $p_3$  = the percentage of nurses who believe a small volume dose (< 2mL) requires a higher level of dose accuracy than a larger volume dose (> 2 mL). The alternative hypothesis,  $H_a$ , is that the perception is different among these three sub-populations. The results are described in Table 8.

Table 8: Sub-population comparison of dose accuracy related to dose volume

	Nurses	Pharmacists	Physicians	Total
Dose accuracy is more important for small volume doses (< 2mL)	41 (22.8%)	82 (55.8%)	14 (46.7%)	137
Dose accuracy is not more important for small volume doses (< 2mL)	139 (77.2%)	65 (44.2%)	16 (53.3%)	220
Total	180	147	30	357

A chi-square test for equality of proportions was performed using SAS<sup>®</sup> Version 9.4, PROC FREQ. The chi-square statistic was 38.22 with a p-value of < 0.0001, indicating that there are differences among the sub-populations' perceptions regarding acceptable dose accuracy for small volumes compared to larger volumes. To test this hypothesis further, a Bonferroni correction was used to control the type I error. To be considered statistically significant, the pairwise comparison must have a p-value of less than 0.0167. There was not a statistically significant difference in the current thinking of physicians and pharmacists (p=0.3611), as both professions see validity in a higher level of dose accuracy for smaller volume doses. However, when comparing the current thinking of pharmacist to nurses (p < 0.0001) and that of physicians

to nurses ( $p = 0.0059$ ), there was a statistically significant difference in the results. The results showed that nurses think the level of dose accuracy should be independent of the dose volume, meaning the accuracy of the dose should be the same regardless of the dose volume.

Based on the overall number of nurses that participated in the research compared to that of pharmacists and physicians (50.4% of all responses were provide by nurses), it could be deducted that the researcher's hypothesis, the majority of healthcare professionals would agree the smaller the volume, the more accurate the dose, could possibly been accurate if the total number of participants had been evenly distributed amongst the three sub-populations.

#### *Analysis of Subpart 5*

Subpart 5 of the survey analyzed the participant's expectation of dose accuracy variability as it related to patient population and the contents of the syringe. The researcher asked the participants the exact same six questions for each of the three patient populations (neonatal patients, pediatric patients, and adult patients). The intend of this subpart was to analyze the current thinking of healthcare professionals based on their experience with each type patient population regarding dose accuracy variability of single use plastic syringes. The six questions asked for each patient population were:

What is the maximum variability of single use plastic syringe dose accuracy you deem acceptable for:

1. intravenous injection of a drug with a wide margin of safety?
2. intravenous injection of a drug with a narrow margin of safety?
3. intravenous injection of parenteral nutrition?
4. oral/enteral delivery of a drug with a wide margin of safety?

5. oral/enteral delivery of a drug with a wide margin of safety?
6. oral/enteral delivery of nutrition?

The participants were provided the following choices for: 0%,  $\pm$  3%,  $\pm$  5%,  $\pm$  10%,  $\pm$  15%,  $\pm$  20%, more than  $\pm$  20%. For each of the three patient populations, a qualifying yes/no question was asked regarding the participant's experience with working with each type patient population. The question was worded as follows: Do you have experience with any of the following: filling syringes that will be administered to [patient population] patients, administration of syringe contents to [patient population] patients, and/or treatment of [patient population] patients. If the participant responded no, the survey skipped the six questions related to that patient population. This qualifying question was added to the survey for each patient population based on feedback obtained during the survey design validation. To eliminate responses based on the participant's current thinking rather than their actual experience, the qualifying questions removed those participants that did not have actual experience with each patient population. If the participant did not have experience with each patient population, the participant was not permitted to respond to dose accuracy variability questions related to that patient population. The addition of these qualifying questions, however, hindered the ability of the researcher to statistically compare the results of each patient population. This is discussed further in each patient population section below.

Of the 357 completed surveys, there was a total of 267 (74.8%) responses for the neonatal patient population, 229 (64.1%) for the pediatric patient population and 232 (65.0%) for the adult patient population. Each of the six questions were analyzed for each patient population independent of each other as well as independent of the responses to the same questions for the other two patient populations. The data was also tabulated by each scenario comparing the three

patient populations and route of administration. This analysis is presented in the General Results section below.

### Neonatal Patient Population Results

The results of all six questions regarding acceptable dose accuracy variability in the neonatal patient population for the 267 respondents that answered these questions is presented in Figure 3. Graphical visualization of the results allowed the researcher to easily see the differences in the results for intravenous injection compared to oral/enteral delivery, as well as visually compare narrow margin of safety drugs to wide margin of safety drugs to nutrition. The graphs show that the respondents understood the differences of the three types of syringe contents, as the results indicate the participants clearly expect the smallest level of dose accuracy variability to be when administering a narrow margin of safety drug intravenously. The same conclusions can be made regarding the participant's expectations of dose accuracy variability for oral/enteral delivery of nutrition. Since the questions were not formatted in the survey to be mutually exclusive, inferential statistics were not able to be performed. This was a flaw in the survey design identified after the survey launched. However, SAS® Version 9.4, PROC FREQ was used to determine either the Wald or binomial confidence intervals for each of the six scenarios for neonatal patients with 95% confidence. Binomial confidence intervals were used when  $(np < 5)$  and  $(n(1-p) < 5)$ . The results of this analysis are presented in Table 8.

The 95% confidence intervals calculated show that for intravenous injection of a drug with a narrow margin of safety, 94.5% to 98.8% of healthcare professionals would expect the dose accuracy variability of a single use plastic syringe to be less than  $\pm 5\%$ , whereas only 1.2% to 5.5% of healthcare professionals would expect the same syringe to have no more than  $\pm 10\%$

variability. Confidence intervals were not calculated for dose accuracy variability results of greater than 10% due to the low number of respondents that chose this dose accuracy variability for each of the scenarios. As one can see from the results presented in Table 9, the other five scenarios resulted in similar findings. It should be noted that the confidence intervals for all six scenarios clearly showed the majority of healthcare professionals would agree that their expectation for single use plastic syringe's dose accuracy variability lies below  $\pm 5\%$ , regardless of the contents of the syringe. The data also shows that the participants allowed their dose accuracy variability expectations to increase based on the risk of the route of administration (intravenous injection poses a higher risk than oral/enteral delivery), as well as the contents of the syringe (narrow margin of safety drugs pose a higher risk than wide margin of safety drugs which pose a higher risk than nutrition). These results support the researcher's hypothesis that for each patient population, the expectation of the acceptable dose accuracy variability of single-use plastic syringes, regardless of the participant's sub-population, will be generally smaller for medications versus nutrition, smaller for medications with narrow therapeutic margins versus medications with wide therapeutic margins, and smaller for intravenous injection versus oral/enteral delivery.

Table 9: Neonatal patient population - Dose accuracy variability percentages per scenario			
Dose Accuracy Variability	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$
Scenario	$\hat{p}$ (95% CI)	$\hat{p}$ (95% CI)	$\hat{p}$
Intravenous injection of a drug with a narrow margin of safety	96.6% (0.9446, 0.9879)	3.4% (0.0121, 0.0554)	0.0%
Intravenous injection of a drug with a wide margin of safety	85.0% (0.8074, 0.8930)	12.7% (0.0841, 0.1631)	2.3%
Intravenous injection of parenteral nutrition	85.4% (0.8116, 0.8963)	12.0% (0.0809, 0.1588)	2.6%
Oral/enteral delivery of a drug with a narrow margin of safety	92.1% (0.8891, 0.9536)	7.1% (0.0403, 0.0102)	0.8%
Oral/enteral delivery of a drug with a wide margin of safety	78.3% (0.7333, 0.8322)	17.2% (0.1270, 0.2176)	4.5%
Oral/enteral delivery of nutrition	71.9% (0.6652, 0.7730)	22.5% (0.1747, 0.2748)	5.6%

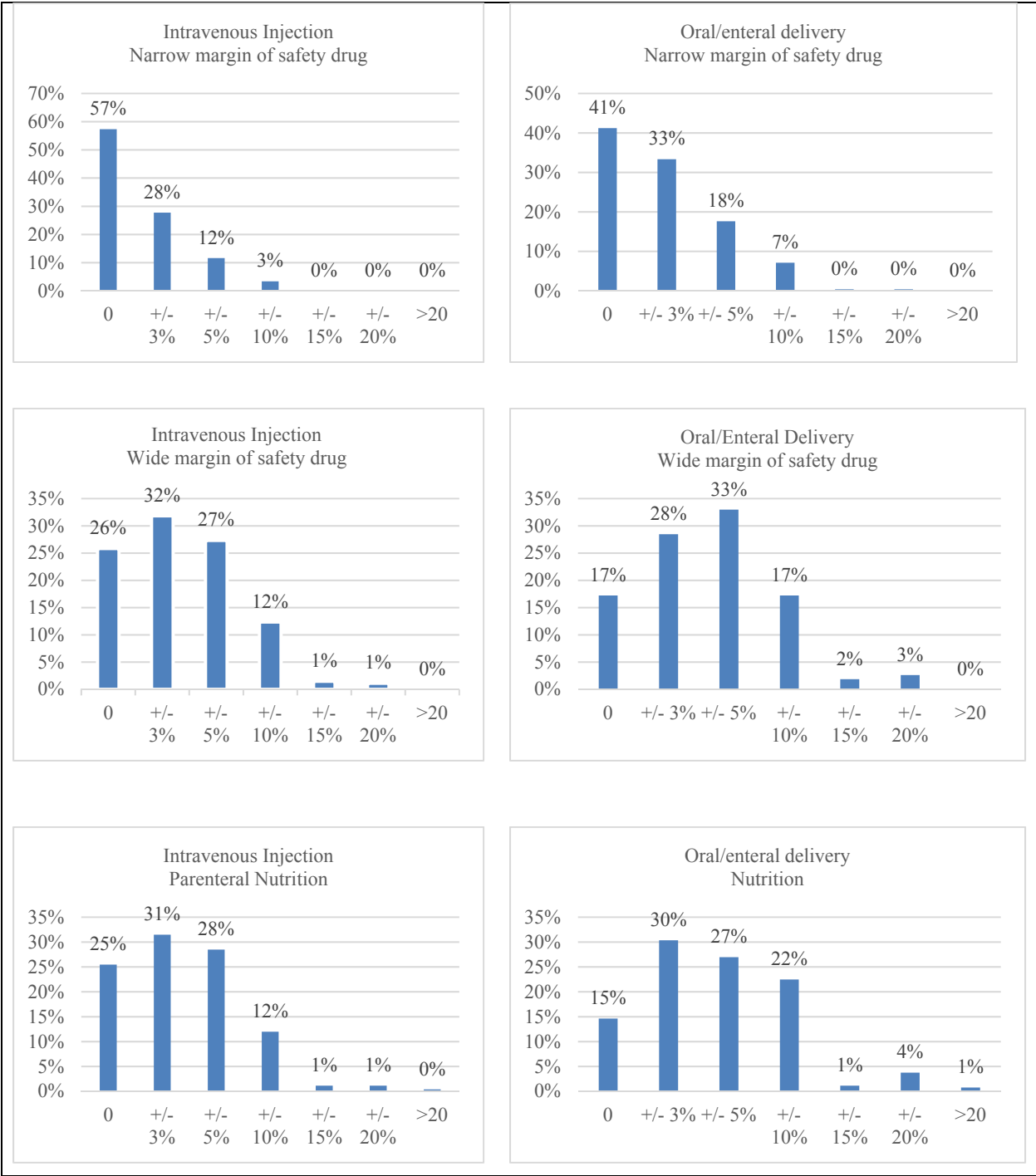


Figure 3: Neonatal patient population - Dose accuracy variability per scenario

### Pediatric Patient Population Results

The results of all six questions regarding acceptable dose accuracy variability in the pediatric patient population for the 229 respondents that answered these questions is presented in Figure 4. Graphical visualization of the results again allowed the researcher to easily see the differences in the results for intravenous injection compared to oral/enteral delivery, as well as visually compare narrow margin of safety drugs compared to wide margin of safety drugs compared to nutrition. The graphs for the pediatric patient population were very similar to those for the neonatal patient population. The results again showed that the participants clearly expect the smallest level of dose accuracy variability to be when administering a narrow margin of safety drug intravenously. The same conclusions can be made regarding the participant's expectations of dose accuracy variability for oral/enteral delivery of nutrition. Since the questions were not formatted in the survey to be mutually exclusive, inferential statistics were not able to be performed. This was a flaw in the survey design identified after the survey launched. However, SAS® Version 9.4, PROC FREQ was used to determine either the Wald or binomial confidence intervals for each of the six scenarios for neonatal patients with 95% confidence. Binomial confidence intervals were used when  $(np < 5)$  and  $(n(1-p) < 5)$ . The results of this analysis are presented in Table 9.

The 95% confidence intervals calculated show that for intravenous injection of a drug with a narrow margin of safety, 94.1% to 98.9% of healthcare professionals would expect the dose accuracy variability of a single use plastic syringe to be less than  $\pm 5\%$ , whereas only 1.1% to 5.8% of healthcare professionals would expect the same syringe to have no more than  $\pm 10\%$  variability. Confidence intervals were not calculated for dose accuracy variability results of

greater than 10% due to the low number of respondents that chose this dose accuracy variability for each of the scenarios. As one can see from the results presented in Table 10, just as those presented in Table 9, the other scenarios resulted in similar findings. It should be noted that the confidence intervals for all six scenarios clearly showed the majority of healthcare professionals would agree that their expectation for single use plastic syringe's dose accuracy variability lies below  $\pm 5\%$ , regardless of the contents of the syringe. The data also shows that the participants allowed their dose accuracy variability expectations to increase based on the risk of the route of administration (intravenous injection poses a higher risk than oral/enteral delivery), as well as the contents of the syringe (narrow margin of safety drugs pose a higher risk than wide margin of safety drugs which pose a higher risk than nutrition). These results also support the researcher's hypothesis that for each patient population, the expectation of the acceptable dose accuracy variability of single-use plastic syringes, regardless of the participant's sub-population, will be generally smaller for medications versus nutrition, smaller for medications with narrow therapeutic margins versus medications with wide therapeutic margins, and smaller for intravenous injection versus oral/enteral delivery.

Dose Accuracy Variability	0%, $\pm 3\%$ , or $\pm 5\%$	$\pm 10\%$	$> 10\%$
Scenario	$\hat{p}$ (95% CI)	$\hat{p}$ (95% CI)	$\hat{p}$
Intravenous injection of a drug with a narrow margin of safety	96.5% (0.9413, 0.9888)	3.5% (0.0112, 0.0587)	0.0%
Intravenous injection of a drug with a wide margin of safety	80.8% (0.7568, 0.8589)	17.9% (0.1294, 0.2287)	1.3%
Intravenous injection of parenteral nutrition	82.1% (0.7713, 0.8706)	14.4% (0.0986, 0.1896)	3.5%
Oral/enteral delivery of a drug with a narrow margin of safety	93.0% (0.8971, 0.9631)	6.6% (0.0335, 0.0975)	0.4%
Oral/enteral delivery of a drug with a wide margin of safety	74.2% (0.6857, 0.7990)	21.4% (0.1609, 0.2671)	4.4%
Oral/enteral delivery of nutrition	69.9% (0.6393, 0.7581)	24.0% (0.1848, 0.2955)	6.1%



Figure 4: Pediatric patient population - Dose accuracy variability per scenario

### Adult Patient Population Results

The results of all six questions regarding acceptable dose accuracy variability in the pediatric patient population for the 232 respondents that answered these questions is presented in Figure 5. Again, graphical visualization of the results allowed the researcher to easily see the differences in the results for intravenous injection compared to oral/enteral delivery, as well as visually compare narrow margin of safety drugs compared to wide margin of safety drugs compared to nutrition. The graphs again showed the respondents understood the differences of the three types of syringe contents, as the results show the participants clearly expect the smallest level of dose accuracy variability to be when administering a narrow margin of safety drug intravenously. The same conclusions can be made regarding the participant's expectations of dose accuracy variability for oral/enteral delivery of nutrition. Since the questions were not formatted in the survey to be mutually exclusive, inferential statistics were not able to be performed. This was a flaw in the survey design identified after the survey launched. However, SAS® Version 9.4, PROC FREQ was used to determine either the Wald or binomial confidence intervals for each of the six scenarios for neonatal patients with 95% confidence. Binomial confidence intervals were used when  $(np < 5)$  and  $(n(1-p) < 5)$ . The results of this analysis are presented in Table 8.

The 95% confidence intervals calculated show that for intravenous injection of a drug with a narrow margin of safety, 87.3% to 94.6% of healthcare professionals would expect the dose accuracy variability of a single use plastic syringe to be less than  $\pm 5\%$ , whereas only 5.4% to 12.8% of healthcare professionals would expect the same syringe to have no more than  $\pm 10\%$  variability. Confidence intervals were not calculated for dose accuracy variability results of

greater than 10% due to the low number of respondents that chose this dose accuracy variability for each of the scenarios. As one can see from the results presented in Table 11, the data also shows that the participants allowed their dose accuracy variability expectations to increase based on the risk of the route of administration (intravenous injection poses a higher risk than oral/enteral delivery), as well as the contents of the syringe (narrow margin of safety drugs pose a higher risk than wide margin of safety drugs which pose a higher risk than nutrition). However, even though inferential statistics could not be performed, the tabular and graphical representations of the results showed the participants relaxed their expectations of dose accuracy variability for the adult patient population as these results are slightly skewed to a higher expectation of dose accuracy variability. These results support the researcher's hypothesis that for each patient population, the expectation of the acceptable dose accuracy variability of single-use plastic syringes, regardless of the participant's sub-population, will be generally smaller for medications versus nutrition, smaller for medications with narrow therapeutic margins versus medications with wide therapeutic margins, and smaller for intravenous injection versus oral/enteral delivery.

Table 11: Adult patient population - Dose accuracy variability percentages per scenario			
Dose Accuracy Variability	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$
Scenario	$\hat{p}$ (95% CI)	$\hat{p}$ (95% CI)	$\hat{p}$
Intravenous injection of a drug with a narrow margin of safety	90.1% (0.8726, 0.9464)	9.1% (0.0536, 0.1274)	0.8%
Intravenous injection of a drug with a wide margin of safety	73.7% (0.6804, 0.7937)	22.0% (0.1665, 0.2731)	4.3%
Intravenous injection of parenteral nutrition	72.0% (0.6620, 0.7776)	22.4% (0.1705, 0.2778)	5.6%
Oral/enteral delivery of a drug with a narrow margin of safety	87.9% (0.8374, 0.9212)	11.6% (0.0751, 0.1576)	0.5%
Oral/enteral delivery of a drug with a wide margin of safety	66.0% (0.5985, 0.7205)	26.7% (0.2103, 0.3242)	7.3%
Oral/enteral delivery of nutrition	59.1% (0.5272, 0.6538)	30.6% (0.2467, 0.3653)	10.3%



Figure 5: Adult patient population - Dose accuracy variability per scenario

## General Results

Data was also analyzed by use scenario, again comparing the results in tabular form since performing inferential statistics was not possible due to the six different use scenarios not being presented in the survey as mutually exclusive. Tables 12, 13 and 14 below denote the results of the survey per patient population by the contents of the syringe (narrow margin of safety drug, wide margin of safety drug and nutrition, respectively) and route of administration. In this representation, the researcher can conclude, generally, the expectations of dose accuracy variability are associated with the what is being delivered to the patient, the route in which it's being delivered and if the patient is a child (neonatal and pediatric patients) or an adult. Figure 6 summaries all the results in Subpart 5 in one figure.

As stated above, the researcher has acknowledged that the design of survey questions for Subpart 5 was flawed. The objective of Subpart 5 was originally designed to be able to detect differences within each patient population related to the syringe contents (wide margin of safety drug versus narrow margin of safety drug versus nutrition) as well as the route of administration. However, based on the way the researcher structured the questions in Subpart 5, this statistical analysis could not be performed, as each question for each patient population were not designed to be mutually exclusive. This means the results of each of the six questions per patient population could not be compared to each other with any statistical significance. Since qualifier questions were added for each patient population, each patient population set of questions resulted in a different number of responses, therefore Subpart 5 results could not be statistically compared from one patient population to another, nor could the data be combined. Of significant note, the major flaws of Subpart 5 were the choices provided to the participants, without having a clear understanding of the level of knowledge the participants had for how syringes are designed

and mass produced. There is inherent variability with all medical devices that is controlled during manufacturing using pre-determined acceptable tolerance ranges. The researcher provided participants with response choices (i.e. 0% and  $\pm 3\%$  dose accuracy variability) that were not reasonable based on mass manufacturing limitations. Based on current science, it is impossible to mass produce single use plastic syringe with 0% or  $\pm 3\%$  dose accuracy variability. Since these choices are not actually achievable when mass manufacturing single use plastic syringes, the researcher should not have included them as choices in Subpart 5. For this reason, the researcher combined 0%,  $\pm 3\%$ , and  $\pm 5\%$  dose accuracy variability choices when analyzing the results. The researcher was surprised to review the number of participants that chose 0% variability. Based on the results of this study, one could conclude that the dose accuracy variability expectations of healthcare professionals far exceed the production capabilities of the syringe manufacturing industry. The participant's expectations of dose accuracy variability of single use plastic syringes are extremely unrealistic.

Table 12: Narrow margin of safety drug by patient type and route of administration						
Patient Type	Expected Dose Accuracy Variability ( $\hat{p}$ )					
	Intravenous Injection			Oral/enteral Delivery		
	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$
Neonatal patient	96.6%	3.4%	0.0%	92.1%	7.1%	0.8%
Pediatric patient	96.5%	3.5%	0.0%	93.0%	6.6%	0.4%
Adult patient	90.1%	9.1%	0.8%	87.9%	11.6%	0.5%

Table 13: Wide margin of safety drug by patient type and route of administration						
Patient Type	Expected Dose Accuracy Variability ( $\hat{p}$ )					
	Intravenous Injection			Oral/enteral Delivery		
	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$
Neonatal patient	85.0%	12.7%	2.3%	78.3%	17.2%	4.5%
Pediatric patient	80.8%	17.9%	1.3%	80.8%	17.9%	1.3%
Adult patient	73.7%	22.0%	4.3%	66.0%	26.7%	7.3%

Table 14: Nutrition by patient type and route of administration						
Patient Type	Expected Dose Accuracy Variability ( $\hat{p}$ )					
	Intravenous Injection			Oral/enteral Delivery		
	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$	$\leq \pm 5\%$	$\pm 10\%$	$> 10\%$
Neonatal patient	85.4%	12.0%	2.6%	71.9%	22.5%	5.6%
Pediatric patient	82.1%	14.4%	3.5%	69.9%	24.0%	6.1%
Adult patient	72.0%	22.4%	5.6%	59.1%	30.6%	10.3%

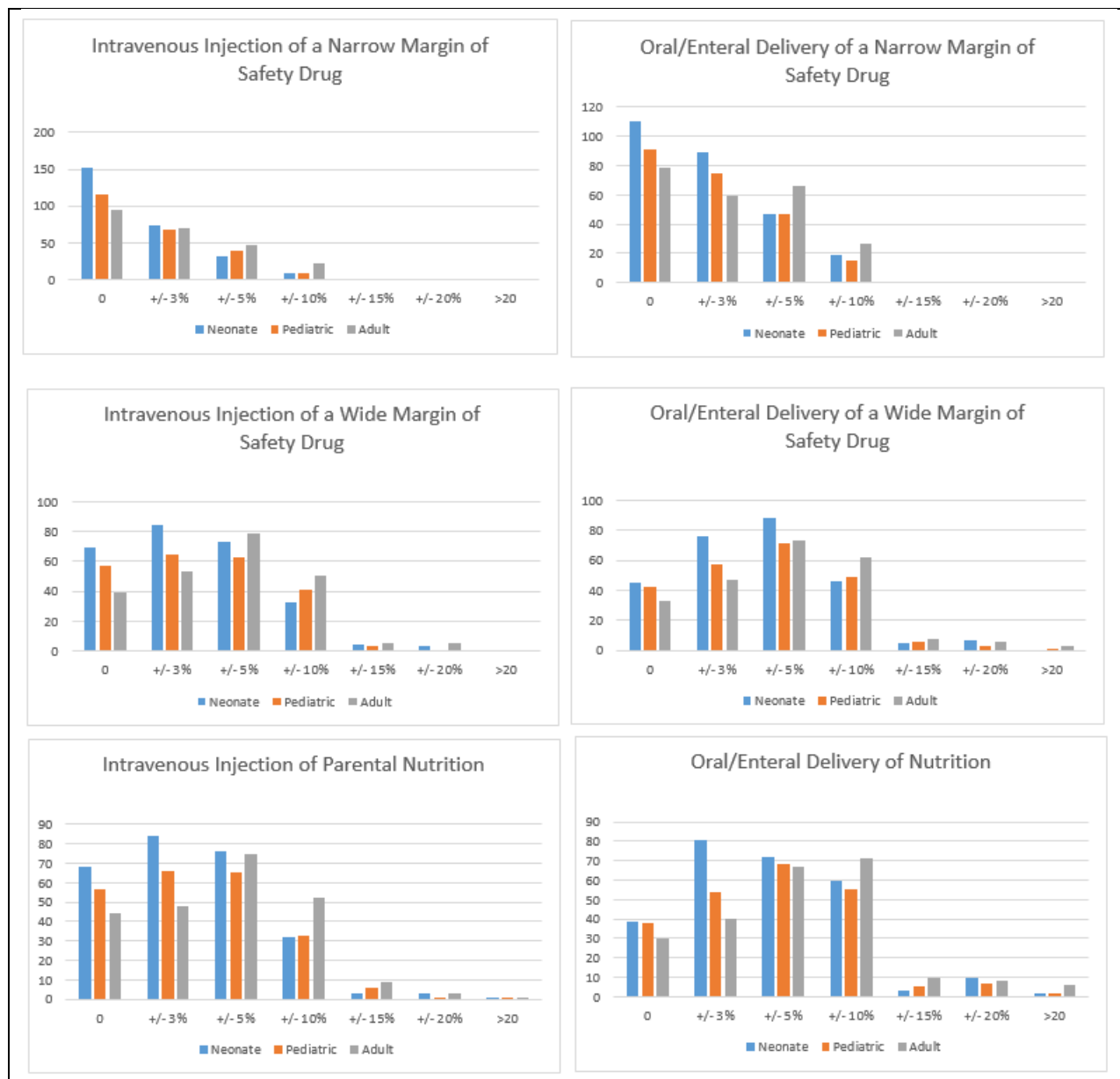


Figure 6: Summary of all results of Subpart 5

### *Analysis of Subpart 6*

Subpart 6 of the survey pertains to the general purpose of the research. The survey questions were designed to answer the researcher's hypothesis related to whether end users of syringes (healthcare professionals) think dose accuracy variability of single use plastics syringes should be standardized with a common test method and dose accuracy variability specification. The specific tolerance expectations of a dose accuracy variability specification were discussed in Subpart 5, however in general, Subpart 6 is asking the participant if they think this is even necessary.

This subpart considered two yes/no questions related to the healthcare professional's opinion regarding the need to standardize a common test method and define a dose accuracy variability specification of single use plastic syringes. The survey asked the following question for both intravenous injection and oral/enteral delivery separately: Do you think the dose accuracy of the single-use plastic syringes used for [route of administration] should be standardized by using a common test method and dose accuracy variability specification. Since there were not any qualifying questions related to Subpart 6, all 357 participant's responses were analyzed.

To analysis the results of Subpart 6, the researcher reviewed the two questions separately. The first question posed was related to the participant's current thinking regarding requirements for standardization of single use plastic syringes used for intravenous injection. Of the 357 completed responses, 356 (99.7%) agreed that there should be a standardized dose accuracy specification defined by using a common test method for syringe manufacturers to follow. The second question posed was related to the participant's current thinking regarding requirements for standardization of single use plastic syringes used for oral/enteral delivery. Of the 357

completed responses, 351 (98.3%) agreed that there should be a standardized dose accuracy specification defined by using a common test method for syringe manufacturers to follow.

The researcher hypothesized that at least the majority of healthcare professionals would agree that there should be a standardized dose accuracy specification defined by using a common test method regardless of the route of administration. To estimate the true proportion of healthcare professionals that think standardization of dose accuracy variability should be required, for each route of administration, an exact binomial proportion confidence interval was constructed using SAS<sup>®</sup> 9.4, PROC FREQ. These 95% confidence limits for intravenous injection were (0.9845, 0.9999) and were (0.9638, .9938) for oral/enteral delivery. This indicates that the true proportion of healthcare professionals who agree that there should be a standardized dose accuracy specification defined by using a common test method for single use plastic syringes used for intravenous injection is between 98.5% and 100% and is between 96.4% and 99.4% for single use plastic syringes used for oral/enteral delivery. Clearly the data shows, regardless of the route of administration, the syringe industry should standardize the variability of dose accuracy of single use plastic syringes using a common test method.

If the participant responded no to either of the questions of Subpart 6, they were required to document why they responded this way. There were only seven respondents (one for intravenous injection and six for oral/enteral delivery) that responded no to either question. The documented explanations for these are show in Table 14. The researcher reviewed these responses and did not determine them to be significant in nature, as the explanations listed in Table 14 are not based on scientific evidence or rationales, but are statements of opinion. Of the seven explanations in Table 14, two were provided by the same nurse (one for intravenous injection and one for oral/enteral delivery). The other five explanations were provided by three

nurses and two pharmacists. There were no physicians that responded no to either questions in Subpart 6.

Table 15: Responses provided by participant that chose no for questions of Subpart 6

1	(Intravenous Injection) I feel the variability of dose accuracy in most disposable syringes is low enough to not make a difference in treatment. Especially in my field of prehospital emergency medicine.
2	(Oral/enteral delivery) Does not need to be 100% accurate in the adult patient.
3	(Oral/enteral delivery) Parenteral nutrition can be a bit off. I just always give the exact amount, no matter what. I work mostly with neonates, so that may be why. I see no exception to giving the exact amount ordered every time.
4	(Oral/enteral delivery) I don't feel that oral medication dosages need to be that specific.
5	(Oral/enteral delivery) Oral goes thru gut and absorption is unpredictable anyway
6	(Oral/enteral delivery) I don't believe oral dosing has to be as exact as IV.
7	(Oral/enteral delivery) Variable emptying and absorption via the gut. "Consider it not deeply". Shakespeare

## CHAPTER 5

### CONCLUSION

#### *Conclusions*

The purpose of the research was to assess USA healthcare professionals' current thinking regarding dose accuracy variability of single use plastic syringes based on their experience using these type syringes. The primary objective was to determine if healthcare professionals think the dose accuracy variability of single use plastic syringes should require a standardized test method and specification for the syringe industry to use when mass production these medical devices. The results of the research confirmed that healthcare professionals in the USA do in fact believe that single use plastic syringes should follow a standardized test method and dose accuracy variability specification so manufacturers of single use plastic syringes will all abide by the same requirements regardless of route of administration. Several additional questions were asked of each of the participants to ascertain some current syringe end users thinking of the usage and capability of single use plastic syringes. Although the risk of misconnection (wrong route administration) is a known risk in acute care facilities, the results showed that there is still a high level of Luer Lock and Luer Slip syringes used for enteral feeding applications. It should be noted that the low level of physician responses (N=30) could have altered the results of the research potentially skewing the overall results more to the current thinking of nurses and pharmacist.

Only one of the results regarding the general usage of single use plastic syringe questions were as expected. The research showed that the majority of healthcare professionals agreed that

medication requires a higher level of dose accuracy than nutrition, regardless of the route of administration. However, the research did not show the same results for intravenous injection versus oral/enteral delivery, neonatal patients versus pediatric patients versus adult patients, or small volume doses versus larger than 2mL doses. The research showed that the majority of USA healthcare professionals do not think intravenous injection requires a higher level of dose accuracy than oral/enteral delivery, regardless of the contents of the syringe or the patient type. The research also showed that the majority of USA healthcare professionals do not think a neonatal patient requires a higher level of dose accuracy than a pediatric or adult patient. The research also showed that the majority of USA healthcare professionals do not think doses smaller than 2mL do not require a higher level of dose accuracy than doses larger than 2mL.

The results demonstrated that there was not enough statistical evidence to conclude that more than 50% of healthcare professionals think the neonatal patient population requires a higher level of dose accuracy than the pediatric or adult patient populations, regardless of route of administration or the contents of the syringe. This was not as the researcher hypothesized. However, there was a statistically significant difference between the responses of nurse and pharmacists, as pharmacist thought the neonatal population should require a higher level of dose accuracy than the other patients and nurses did not. The potential reasons for this were discussed in Chapter 4, Analysis of Subpart 4. The most interesting result of Subpart 4 was the responses related to the dose accuracy of small volume doses versus large volume doses. The research showed that overall, healthcare professionals do not think a smaller dose requires higher accuracy. The results of the sub-population analysis showed that there was no significant difference in the current thinking of physicians and pharmacists, as they both feel smaller volume doses warrant higher dose accuracy, however, nurses did not feel the same, therefore

lending to the overall result of the full target population. Conclusions regarding these results was also discussed in Chapter 4, Analysis of Subpart 4.

Statistically valid conclusions were difficult to draw from the results of Subpart 5 due to flaws in the design of the questions, however, descriptive statistics, tabular and graphical analysis allowed some conclusions to be extrapolated. The results for each patient population showed exactly what one would expect. Intravenous injection resulted in lower dose accuracy variability choices from the respondents when compared to oral/enteral delivery of the same syringe contents, just as narrow margin of safety drugs did when compared to wide margin of safety drugs and nutrition. The highest allowable dose accuracy variability was also as expected, with oral/enteral delivery of nutrition. Adults were also considered to have a higher level of dose accuracy variability than neonatal and pediatric patients.

Overall, the researcher can conclude that based on the results of this study, it is very evident that generally, healthcare professionals do not have a good understand of the dose accuracy variability of the single use plastic syringes currently on the market and used today.

For the past 60+ years single use plastic syringes have been considered a simple, standard, medical device that does not contribute to the success or decline of a patient. They are considered medication and nutrition delivery devices without question. However, they are medical devices with a measuring function, of which, could be the root cause of a serious adverse event if not manufactured and used properly. The research showed that many healthcare professionals in acute-care settings think or expect single use plastic syringes to be 100% accurate 100% of the time. The fact that the participants in this study frequently chose a dose accuracy variability of 0% suggests that the healthcare professionals in the United States do not understand that this expectation is unreasonable.

### *Limitations of the study*

Securing an adequate response rate for dissemination to enough demographics of the target population to make inferences to all healthcare professionals in acute care settings in the United States was shown to be challenging. The survey was deployed on several dates over a five-and-a-half-week period (in accordance with IRB approval) as well as posted on or distributed to organizational websites that focus on healthcare professionals. Based on the minimal response rates that could be tracked, the researcher estimates that the survey invitation email was distributed to over 120,000 healthcare professionals in the United States, which resulted in only 407 completed surveys in a 5½ week period.

The study survey instructed the participants to respond to the questions based on their experience. It was not possible to ascertain if participants responded based on their opinion instead of their experience, however the results showed that more than 60% of respondents were healthcare professionals with over 20 years of experience. Qualifying questions were added to certain subparts of the survey to limit these type responses based on feedback from the survey design validation. However, these qualifying questions made it difficult to compare certain aspects of the study, as the qualifying questions changed the number of respondents for each subpart.

More research should be performed to determine if the small number of physicians is skewing the data one way or the other. Meaning, the numbers could be different if we removed physicians?

A biostatistician was not consulted prior to survey deployment. This was an error of the researcher that resulted in the inability to use inferential statistics for certain subparts of the study; which in turn resulted in the inability to analyze two of the researcher's original

hypotheses. A biostatistician should have been consulted during survey design to ensure the questions were designed to adequately address the pre-determined hypotheses.

### *Recommendations*

The researcher has already pointed out several flaws and limitations of the study throughout this report which lead to several recommendations for future research. This study was specifically focused on USA based healthcare professionals. To further this work, the study should be conducted globally, as the primary purpose of the research was to determine if the end users of single use plastic syringes think the dose accuracy variability of these syringes should be controlled by a standardized common test method and specification. To adequately address the problem statement to obtain overwhelming supporting evidence that these syringes should in fact be controlled by an international standard, global results would be required.

Prior to any future research regarding this matter, the survey questions should be assessed further, as the results of the research indicate several imperfections in the survey design. These flaws could have been avoided with the aid of a biostatistician during the survey design process. The researcher also provided unrealistic choices to some of the survey questions that may have skewed the data. At least two of the choices provided in Subpart 5 of the survey were unreasonable (0% and  $\pm 3\%$ ), yet the respondents chose these answers based on their current thinking. This tells the researcher that further education may be warranted for healthcare professionals (particularly nurses) regarding the actual dose accuracy variability capability of single use plastic syringes. The survey design could have also collected more demographic information to potentially determine if the significant differences between nurses, physicians and pharmacists observed in Subpart 5 would have been different if the responses were grouped in

smaller sub-populations based on their level of education. In future research, dose accuracy variability choices that are not possible based on engineering, manufacturability, human error and usability challenges that accompany the use of a single use plastic syringe should not be presented as a viable option in the research.

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## APPENDIX A

### INITIAL RECRUITMENT EMAIL CONTENT

Email Subject Line: Syringe Survey - Dose Accuracy of Single Use Plastic Syringes - Be a part of an important survey!

Dear Sir or Madam,

You have been randomly selected to participate in an online survey that will assess your expectations (based on your experience) of the accuracy variability of single use plastic syringes commonly used to deliver fluids through intravenous injection and oral/enteral delivery. You have been chosen because of your expertise related to patient care. Your email address was provided by reputable organizations within the United States that focus on patient care initiatives.

Participation in this survey is voluntary and will take approximately 5-10 minutes of your time. The survey does not require you to provide any personal information. You may refuse to participate or withdraw your participation at any time by not fully completing the survey and submitting your responses. Submission of all your responses is performed at the end of the survey when you click the "SUBMIT" button. If you do not wish to be contacted again regarding this survey, please click the Unsubscribe button below.

If you would like to be entered into a random drawing for a chance to win a \$200 VISA gift card, please click the link below and enter a valid email address. Providing your email address is voluntary and will only be used for the drawing. Your email address will not be associated or linked to the study responses you provide. Survey participation is not required to be entered in the drawing.

Enter the drawing for a chance to win a \$200 VISA gift card click [here](#).

(Embedded link: <https://goo.gl/forms/a5fMzQTn6hwGGBvr1>)

The results of this survey will be utilized for my graduate studies thesis. Your participation is vital for accurate and meaningful survey results. For any questions or concerns, please contact me at the contact information listed below.

Thank you in advance for your help with this important study!

To participate in this online survey, please click the link below:

**[TAKE THE SURVEY NOW!!](#)**

Embedded Link:

[https://docs.google.com/forms/d/e/1FAIpQLSdec8\\_aRpVOzzgpWkFljZ7xohzJbS35H2YHtE\\_mu1wDu9bvA/viewform](https://docs.google.com/forms/d/e/1FAIpQLSdec8_aRpVOzzgpWkFljZ7xohzJbS35H2YHtE_mu1wDu9bvA/viewform)

Sincerely,



Melinda Harrison Smith, RAC, CBA  
Primary Study Researcher  
University of Georgia Graduate Student  
[syringesurvey@gmail.com](mailto:syringesurvey@gmail.com)  
770-905-5371

## APPENDIX B

### FOLLOW-UP RECRUITMENT EMAIL CONTENT

Email Subject Line: Syringe Survey - Dose Accuracy of Single Use Plastic Syringes - Be a part of an important survey!

Dear Sir or Madam,

The *Single Use Plastic Syringes: Variability of Dose Accuracy Survey* is in its final [weeks] [days] [hours]. If you have already taken the survey, thank you for your time! If you have not, don't miss your chance to make your voice heard!

You have been randomly selected to participate in an online survey that will assess your expectations (based on your experience) of the accuracy variability of single use plastic syringes commonly used to deliver fluids through intravenous injection and oral/enteral delivery. You have been chosen because of your expertise related to patient care. Your email address was provided by reputable organizations within the United States that focus on patient care initiatives.

Participation in this survey is voluntary and will take approximately 5-10 minutes of your time. The survey does not require you to provide any personal information. You may refuse to participate or withdraw your participation at any time by not fully completing the survey and submitting your responses. Submission of all your responses is performed at the end of the survey when you click the "SUBMIT" button. If you do not wish to be contacted again regarding this survey, please click the Unsubscribe button below.

If you would like to be entered into a random drawing for a chance to win a \$200 VISA gift card, please click the link below and enter a valid email address. Providing your email address is voluntary and will only be used for the drawing. Your email address will not be associated or linked to the study responses you provide. Survey participation is not required to be entered in the drawing.

Enter the drawing for a chance to win a \$200 VISA gift card click [here](#).  
(Embedded link: <https://goo.gl/forms/a5fMzQTn6hwGGBvr1>)

The results of this survey will be utilized for my graduate studies thesis. Your participation is vital for accurate and meaningful survey results. For any questions or concerns, please contact me at the contact information listed below.

Thank you in advance for your help with this important study!

To participate in this online survey, please click on the link below:

[TAKE THE SURVEY NOW!!](#)

Embedded Link:

[https://docs.google.com/forms/d/e/1FAIpQLSdec8\\_aRpVOzzgpWkFljZ7xohzJbS35H2YHtE\\_mu1wDu9bvA/viewform](https://docs.google.com/forms/d/e/1FAIpQLSdec8_aRpVOzzgpWkFljZ7xohzJbS35H2YHtE_mu1wDu9bvA/viewform)

Sincerely,



Melinda Harrison Smith, RAC, CBA  
Primary Study Researcher  
University of Georgia Graduate Student  
[syringesurvey@gmail.com](mailto:syringesurvey@gmail.com)  
770-905-5371

## APPENDIX C

### SURVEY QUESTIONS

Survey: [https://docs.google.com/forms/d/e/1FAIpQLSdec8\\_aRpVOzzgpWkFljZ7xohzJbS35H2YHtE\\_mu1wDu9bvA/viewform](https://docs.google.com/forms/d/e/1FAIpQLSdec8_aRpVOzzgpWkFljZ7xohzJbS35H2YHtE_mu1wDu9bvA/viewform)

#### **Subpart 1:**

Single-Use Plastic Syringes: Variability of Dose Accuracy

Study Title: Acceptable Dose Accuracy Variability of Single Use Plastic Syringes used in Intravenous and Oral/Enteral Medical Applications – Users’ Perspective

I, Melinda Smith, graduate student under the direction of Associate Professor David W Mullis, Jr., Ph.D., R.A.C., FRAP in the College of Pharmacy at The University of Georgia, invite you to participate in a research study entitled Acceptable Dose Accuracy Variability of Single Use Plastic Syringes used in Intravenous and Oral/Enteral Medical Applications – Users’ Perspective. The purpose of this study is to examine and document the current thinking of healthcare professional based on their experience as it relates to the most common single-use plastic syringes used for intravenous and oral/enteral medical applications. The questions will ask your opinion of the acceptable dose accuracy variability of a single-use plastic syringe as it relates to the patient’s age (neonate, pediatric, adult), the contents of the syringe and the route of administration. Please answer each question based on your experience.

You have been chosen for this survey because of your expertise related to patient care. Your participation in this survey is voluntary and will take approximately 5-10 minutes of your time. There are no foreseeable risks associated with your participation in this survey. You may refuse to participate or withdraw your participation at any time by not fully completing the survey and submitting your responses. Submission of all your responses is performed at the end of the survey when you click the “SUBMIT” button.

Since the survey is internet based, it is important to understand that internet communications are not always secure and there is a limit to the confidentiality that can be guaranteed due to the technology itself. However, once the survey responses are received, you will remain anonymous. The survey does not require you to provide any direct or indirect personal information.

The results of this study may be published or utilized to support the development of future International Organization of Standardization (ISO) medical device standards regarding single-use plastic syringes but your name or any identifying information will not be used.

If at any time you would like to go back to a previous page or question, utilize the "BACK" button within the survey (bottom of each survey page). Please note the internet back arrow will not navigate to previously viewed survey questions.

If you have any questions or concerns about this research study, please feel free to contact me via phone at (+1) 770-905-5371 or via email at [syringesurvey@gmail.com](mailto:syringesurvey@gmail.com). Questions or concerns about your rights as a research participant should be directed to The Chairperson, University of Georgia Institutional Review Board, 629 Boyd GSRC, Athens, Georgia 30602; telephone (706) 542-3199; email address [irb@uga.edu](mailto:irb@uga.edu).

By clicking YES (I agree to participate in this survey) below, you are agreeing to participate in the above described survey.

As stated in the participation email request you received, completion of this survey is not required into \$200 VISA gift card drawing.

Thank you for your consideration.  
Melinda Smith, RAC, CBA

I agree to participate in this survey.

- YES
- NO (software goes directly to submission page)

## Subpart 2: Participant Information

Which of the following choices best describes your occupation? (Only choose one)?

- Nurse (i.e. RN, LPN, BSN, MSN)
- Physician, Nurse Practitioner, Physician Assistant (i.e. MD, DO, NP, PA)
- Pharmacist (i.e. Pharm. D., RPh.)
- Pharmacy Technician (i.e. CPhT)
- Other, Specify \_\_\_\_\_

How many years have you been in the occupation you selected in the above question?

- less than 5 years
- 5 to 10 years
- 10 to 15 years
- 15 to 20 years
- more than 20 years

Where do you live and work?

- United States
- Outside the United States

### Subpart 3: Syringe Type Usage

Do you have experience filling syringes and/or administering syringe contents to patients?

- Yes (software continues to remaining questions in Subpart 3)
- No (software goes to Subpart 4)

Subpart 3 (continued)

Pictured below are five (5) single-use plastic syringes commonly used in medical applications. Please utilize the pictures to aid you with answering the two questions below.

Luer Lock



Luer Slip



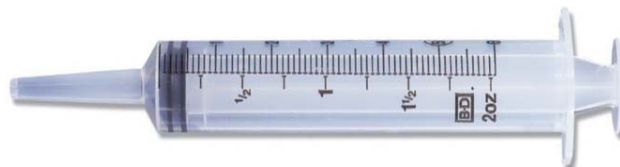
Reverse Luer



Oral/Enteral



Catheter



Subpart 3 (continued)

Question 1 – INTRAVENOUS INJECTION

Based on your experience, select the answer for each syringe type that best describes the frequency with which you fill and/or administer medication or parenteral nutrition INTRAVENOUSLY.

	Most Common	2 <sup>nd</sup> Most Common	3 <sup>rd</sup> Most common	4 <sup>th</sup> Most Common	5 <sup>th</sup> Most Common	I have never filled or administered this type syringe for eventual intravenous injection
Luer Lock	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Luer Slip	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Female Luer (Reverse Luer)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Oral/Enteral	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Catheter	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

(survey software requires only one response per row)

Question 2 – ORAL/ENTERAL DELIVERY

Based on your experience, select the answer for each syringe type that best describes the frequency with which you fill and/or administer medication or nutrition ORALLY or ENTERALLY.

	Most Common	2 <sup>nd</sup> Most Common	3 <sup>rd</sup> Most common	4 <sup>th</sup> Most Common	5 <sup>th</sup> Most Common	I have never filled or administered this type syringe for eventual intravenous injection
Luer Lock	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Luer Slip	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Female Luer (Reverse Luer)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Oral/Enteral	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Catheter	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

(survey software requires only one response per row)

#### Subpart 4: General Syringe Variability of Dose Accuracy Questions

##### Question 1:

Of the choices below, which do you think requires a higher level of dose accuracy regardless of the route of administration?

- Medication (drug)
- Nutrition (parenteral or enteral)
- I think medication and nutrition require the same level of accuracy

##### Question 2:

Of the administration routes listed below, which do you think requires a higher level of dose accuracy regardless of what (drug or nutrition) is being administered?

- Intravenous Injection
- Oral/enteral delivery
- I think intravenous injection and oral/enteral delivery require the same level of accuracy

##### Question 3:

Of the choices below, which patient type do you think requires the highest level of dose accuracy regardless of what (drug or nutrition) is being administered or route of administration?

- a neonatal patient
- a pediatric patient
- an adult patient
- I think a neonate, a pediatric patient and an adult all require the same level of dose accuracy

##### Question 4:

Of the choices below, which do you think requires a higher level of dose accuracy?

- Small volume dose (less than 2 mL)
- Dose over 2 mL
- I think all doses regardless of dose size should have the same level of accuracy.

## Subpart 5: Syringe Dose Accuracy Variability Specific Patient Population Questions

Below are definitions that may be beneficial when responding to Subpart 5 questions.

### VARIABILITY OF SYRINGE DOSE ACCURACY

The ratio of the actual volume delivered to the patient in relation to the intended volume (prescribed dose) and is defined as a percentage. For example, an intended dose is 1.0 mL, the syringe is filled to the 1.0 mL graduation mark and the syringe contents are administered to the patient. If the administered volume is 0.9 mL, the variability of syringe dose accuracy would be -10%. If this same scenario is repeated and the administered volume is 1.1 mL, then the variability of syringe dose accuracy would be +10%. If this was repeated multiple times with accuracy ranges from -10% to +10%, it could be inferred that the variability of syringe dose accuracy of that syringe is +/- 10%.

### MARGIN OF SAFETY

The range between the minimum therapeutic dose and the minimum toxic dose. This is also known as the therapeutic window or therapeutic index. The below table lists a few narrow margin of safety (therapeutic index) drugs.

Examples of Narrow Therapeutic Index Drugs (NTIDs) include:

5-fluorouracil, amphotericin B, carbamazepine, cyclosporine phenytoin, digoxin, flecainide, gentamicin, lithium, phenobarbital, theophylline, warfarin

Subpart 5 (continued)

Qualifier question 1 (neonatal patients):

Do you have experience with any of the following: filling syringes that will be administered to neonatal patients, administration of syringe contents to neonatal patients, and/or treatment of neonatal patients?

- Yes (software continues to neonatal patient population question)
- No (software goes to pediatric patient population qualifier question)

Neonatal patient population specific question:

Understanding that syringe dose accuracy variability does exist, what is the MAXIMUM variability of syringe dose accuracy you deem acceptable for a NEONATAL patient for each of the scenarios below?

Scenarios	Variability of Syringe Dose Accuracy (%)						
	0	+/- 3	+/- 5	+/- 10	+/- 15	+/- 20	More than +/- 20
Intravenous injection of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of nutrition (TPN)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of nutrition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(survey software requires only one response per row)

Subpart 5 (continued)

Qualifier question 2 (pediatric patients):

Do you have experience with any of the following: filling syringes that will be administered to neonatal patients, administration of syringe contents to pediatric patients, and/or treatment of pediatric patients?

- Yes (software continues to pediatric patient population question)
- No (software goes to adult patient population qualifier question)

Pediatric patient population specific question:

Understanding that syringe dose accuracy variability does exist, what is the MAXIMUM variability of syringe dose accuracy you deem acceptable for a PEDIATRIC patient for each of the scenarios below?

Scenarios	Variability of Syringe Dose Accuracy (%)						
	0	+/- 3	+/- 5	+/- 10	+/- 15	+/- 20	More than +/- 20
Intravenous injection of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of nutrition (TPN)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of nutrition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(survey software requires only one response per row)

Subpart 5 (continued)

Qualifier question 3 (adult patients):

Do you have experience with any of the following: filling syringes that will be administered to neonatal patients, administration of syringe contents to adult patients, and/or treatment of adult patients?

- Yes (software continues to adult patient population specific question)
- No (software goes to Subpart 6)

Adult patient population specific question:

Understanding that syringe dose accuracy variability does exist, what is the MAXIMUM variability of syringe dose accuracy you deem acceptable for an ADULT patient for each of the scenarios below?

Scenarios	Variability of Syringe Dose Accuracy (%)						
	0	+/- 3	+/- 5	+/- 10	+/- 15	+/- 20	More than +/- 20
Intravenous injection of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intravenous injection of nutrition (TPN)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a wide margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of a drug with a narrow margin of safety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oral/enteral delivery of nutrition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(survey software requires only one response per row)

## Subpart 6: Syringe Standardization Questions

### Question 1:

Do you think the dose accuracy of all single-use plastic syringes used for intravenous injection should be standardized by using a common test method and dose accuracy variability specification?

- Yes (software goes Subpart 6, question 2)
- No (software required response to the below question)

In the space provided below, please document why you selected "No" in the previous question.

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### Question 2:

Do you think the dose accuracy of all single-use plastic syringes used for oral/enteral delivery should be standardized by using a common test method and dose accuracy variability specification?

- Yes (software goes to submission page)
- No (software required response to the below question)

In the space provided below, please document why you selected "No" in the previous question.

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