## Patient and User Centric Considerations on In-Use Study Design

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### What's 'in-use'?

What happens when our carefully manufactured vials and syringes leave our control?



Are they ready for the real world?

- Storage and storage errors at hospitals, pharmacies, and patient's homes
- Dose preparation; reconstitution and compatibility with diluents and pharmacy components
- Handling and storage stress shear, shaking, transport, dropping, light exposure



#### "In-Use" in the News

#### The New York Times

# Most Parents Give the Wrong Dose of Liquid Medication

Clinical Advisor

#### A Call for Mandatory Barcode Technology to Reduce Medication Errors

Barcode technology can reduce medication errors by ensuring that the right drug is administered to the right patient at the right time.

JUNE 8, 2018

# Is Drug Vial Optimization Set to Expire?

Joint Commission eyes CSTD-enabled practice

## USP : New Regulations to Protect Health Care Workers from Hazardous Drugs

April 15, 2015 Michael R. Page, PharmD, RPh Specialty Pharmacy Times, March/April 2015, Volume 6, Issue 2



More than 16,000 vaccine doses potentially spoiled in Maine and Michigan by temperature problems

🥂 NBC News

Morning Mix

#### Vaccine storage too often fails to meet standards

By correcting one potential error, the Ventura County Health Care Agency in California accidentally made another — and jeopardized vaccines...



Ants, spiders, and mold: Why a big compounding pharmacy recently recalled all its products

### Pneumatic tube system will provide secure method to move materials throughout future hospitals

By Larry Becker- August 17, 2020

## With robots dispensing medication, startup hopes to halt deadly errors

The second robot will dispense medications in powder and liquid forms into ready-to-use IV bags, cutting back on errors when pharmacists prepare...

Jul 1, 2021





### What is a Patient Centric In-Use Stability Profile?



Considers the *specific end user group* who will prepare the product



Considers *the environment the product will be used* in and the likely handling stresses



In-use studies are <u>robust</u> and anticipate real world scenarios



Simplifies storage and preparation as much as possible to prevent errors



### Health Care Professional (HCP) Users

HCPs are a highly varied population who work in dramatically different environments

- Educational range: 6 months to 10+ years higher ed.
- Community Pharmacy, Primary Care, Specialty Care, Outpatient Clinics, Oncology, Emergency, In-Patient, Central Pharmacy, Pediatrics, Home Health...
- Ability to understand complex preparations or product handling concerns *will differ* depending on specialty and education



### Home Users (non HCPs)

**Patients and Caregivers** 



- Users generally lack understanding of drug stability and may not be able to identify if drug quality could be at risk
- Able to perform simple drug preparation tasks with limited components
- Range of literacy levels should be considered when writing instructions









### Storage and Handling Reliability and Monitoring

Environment impacts the ability to maintain appropriate storage conditions, detect temperature excursions or other storage errors, and if the users can identify when mis-handling may impact drug quality



- Expiries tracked by automated system or barcode scanning
- Users more knowledgeable that mishandling may impact drug quality
- Able to prepare complex products



Users do not understand impact of

Simple preparation only

storage excursions or mis-handling

#### Home Storage Temperature Study

#### **Study Details**

- 225 patients; 756 dispensed medications (TNF-α inhibitor) with temperature monitors
- Told to store according to approved storage conditions
  - 2-8°C storage
  - Up to 48 hours total between 0 to 2°C, and 8 to 25°C



#### Total storage time per temperature

#### **Results**

- Products were between 2 and 8°C 54.8% of the time
  Between 8 and 15°C about ¼ of the time
- Only 6.7% of participants were able to store their medication completely within labeled requirements
- 24.3% of participants had a medication go below 0°C for longer than 2 hours
  - 5.9% of participants stored a medication below 0°C for longer than 24 hours
  - 13.7% had at least 3 cycles below 0°C with median duration of 4 days
  - 2.4% had 32 or more cycles below 0°C
- Only 2.0% of participants stored the medication above 25°C for more than 2 hours

Vlieland et al; Rheumatorology 2016;55:704-709 Vlieland et al; Pharm Res (2018) 35:42



#### Hospital Drug Handling Technology



Automated dispensing cabinets



Compounding Robotics











Pneumatic Tube Transport



### **In-Market Transportation**

- Applies to <u>all use environments</u>
- Transportation *outside* manufacturer control
  - Product may no longer be in tertiary packaging, and potentially without secondary (or even primary) packaging
- Prepared IV bags or syringes may be transported from central pharmacies to infusion centers or homes
- Home use products have an initial transportation to the user's home, and then may travel to school, work, or on trips
- Temperature control is limited, risk of freezing or high temp excursions
- Shock/drop/vibration stress also anticipated





# Most aspects of In-Use and Handling are already assessed as part of typical drug development programs

Small, targeted expansions of existing work builds a robust In-Use profile



- > Product labeling strategy determines study criteria (on-label or supportive robustness)
  - Critical handling risks should be addressed on product labeling
  - Provide supportive data to Medical Information to answer HCP queries



#### Preparation Instructions in Prescribing Information – HCP Use

- Work with a cross functional team (Pharmacy, Medical, CMC)
- Supportive studies should be robust enough to allow for flexibility and site practices wherever possible
- Prescriptive only on critical, unique, product specific steps or stability concerns
- Customize level of detail depending on HCP population
- Consider adding most common handling needs to label (ex. room temperature allowance)

Generation of Home/Patient use instructions should follow country specific regulatory guidance



#### Patient and User Centric Study Design



Understand your users, their environment, and the most likely storage and handling concerns



Build robustness into handling and stability studies that anticipates real-world use



Create a product labeling strategy that fits the user and storage profile



# Thank You

