U.S. FOOD & DRUG ADMINISTRATION

FDA DRUG TOPICS: HOW FDA AND ISMP UTILIZE MEDICATION ERROR REPORTS TO IMPROVE DRUG SAFETY

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Learning Objectives

- Describe FDA's role in pre-marketing and post-marketing activities to prevent and address medication errors.
- Provide a brief overview of strategies aimed to increase the safe use of drug products by minimizing use error that is related to the design, naming, labeling, and/or packaging of drug products.
- Provide examples of recent medication errors.
- Describe how you can help identify, prevent, and mitigate medication errors.

A Lot Happens When You Report A Medication Error or Hazard to FDA and ISMP

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(www.ismp.org)

U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Page 1 of 3

Form Approved: OMB No. 0910-0291, Expires: 6/30/2015
See PRA statement on reverse.

FDA USE ONLY
Triage unit
sequence #

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event or Date of Birth:	3. Sex	4. Weight
In confidence		☐ Female ☐ Male	_____ lb or _____ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☐ **Adverse Event** ☐ **Product Problem** *(e.g., defects/malfunctions)*
   ☐ **Product Use Error** ☐ **Problem with Different Manufacturer of Same Medicine**

2. **Outcomes Attributed to Adverse Event** *(Check all that apply)*
   ☐ Death: _____ *(mm/dd/yyyy)*
   ☐ Life-threatening
   ☐ Hospitalization - initial or prolonged
   ☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)
   ☐ Disability or Permanent Damage
   ☐ Congenital Anomaly/Birth Defect
   ☐ Other Serious (Important Medical Events)

3. Date of Event *(mm/dd/yyyy)*	4. Date of this Report *(mm/dd/yyyy)*

5. **Describe Event, Problem or Product Use Error**

6. **Relevant Tests/Laboratory Data, Including Dates**

7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

C. PRODUCT AVAILABILITY

Product Available for Evaluation? *(Do not send product to FDA)*

☐ Yes ☐ No ☐ Returned to Manufacturer on: _____ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S)

1. **Name, Strength, Manufacturer** *(from product label)*

#1 Name:
Strength:
Manufacturer:

#2 Name:
Strength:
Manufacturer:

2.	Dose or Amount	Frequency	Route
#1			
#2			

3. **Dates of Use** *(If unknown, give duration) from/to (or best estimate)*
#1
#2

4. **Diagnosis or Reason for Use** *(Indication)*
#1
#2

6. Lot #	7. Expiration Date
#1	#1
#2	#2

5. **Event Abated After Use Stopped or Dose Reduced?**
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

8. **Event Reappeared After Reintroduction?**
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

9. **NDC # or Unique ID**

E. SUSPECT MEDICAL DEVICE

1. **Brand Name**

2. Common Device Name	2b. Procode

3. **Manufacturer Name, City and State**

4. Model #	Lot #	5. Operator of Device
Catalog #	Expiration Date *(mm/dd/yyyy)*	☐ Health Professional ☐ Lay User/Patient ☐ Other:
Serial #	Unique Identifier (UDI) #	

6. If Implanted, Give Date *(mm/dd/yyyy)*	7. If Explanted, Give Date *(mm/dd/yyyy)*

8. **Is this a Single-use Device that was Reprocessed and Reused on a Patient?**
☐ Yes ☐ No

9. **If Yes to Item No. 8, Enter Name and Address of Reprocessor**

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates *(exclude treatment of event)*

G. REPORTER *(See confidentiality section on back)*

1. **Name and Address**
Name:
Address:
City: State: ZIP:

Phone #	E-mail

2. Health Professional?	3. Occupation	4. Also Reported to:
☐ Yes ☐ No		☐ Manufacturer ☐ User Facility ☐ Distributor/Importer

5. **If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box:** ☐

FORM FDA 3500 (2/13) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ISMP
Institute for Safe Medication Practices

ABOUT NEWS EVENTS SUPPORT ISMP

Information for consumers ›

ISMP National Medication Errors Reporting Program

Thank you for for submitting a report to the ISMP National Medication Errors Reporting Program (MERP).

- Please provide as much detail as possible when telling us the story of what went wrong or could go wrong, the causes or contributing factors, how the event or condition was discovered or intercepted, and the actual or potential outcome of the involved patient(s).
- Be sure to include the names, dosage forms, and dose/strength of all involved products. For product-specific concerns (e.g., labeling and packaging risks), please include the manufacturer.
- Share your recommendations for error prevention.
- If possible, submit associated materials (e.g., photographs of products, containers, labels, de-identified prescription orders) that help support the report being submitted.

Please complete the form below and click on the "Submit" button to report the error or hazard to the ISMP National Medication Errors Reporting Program.

Name: (optional)

Email:

Confirm email:

Error Description: Please **describe** the incident as best you can. This information will be handled in confidence.

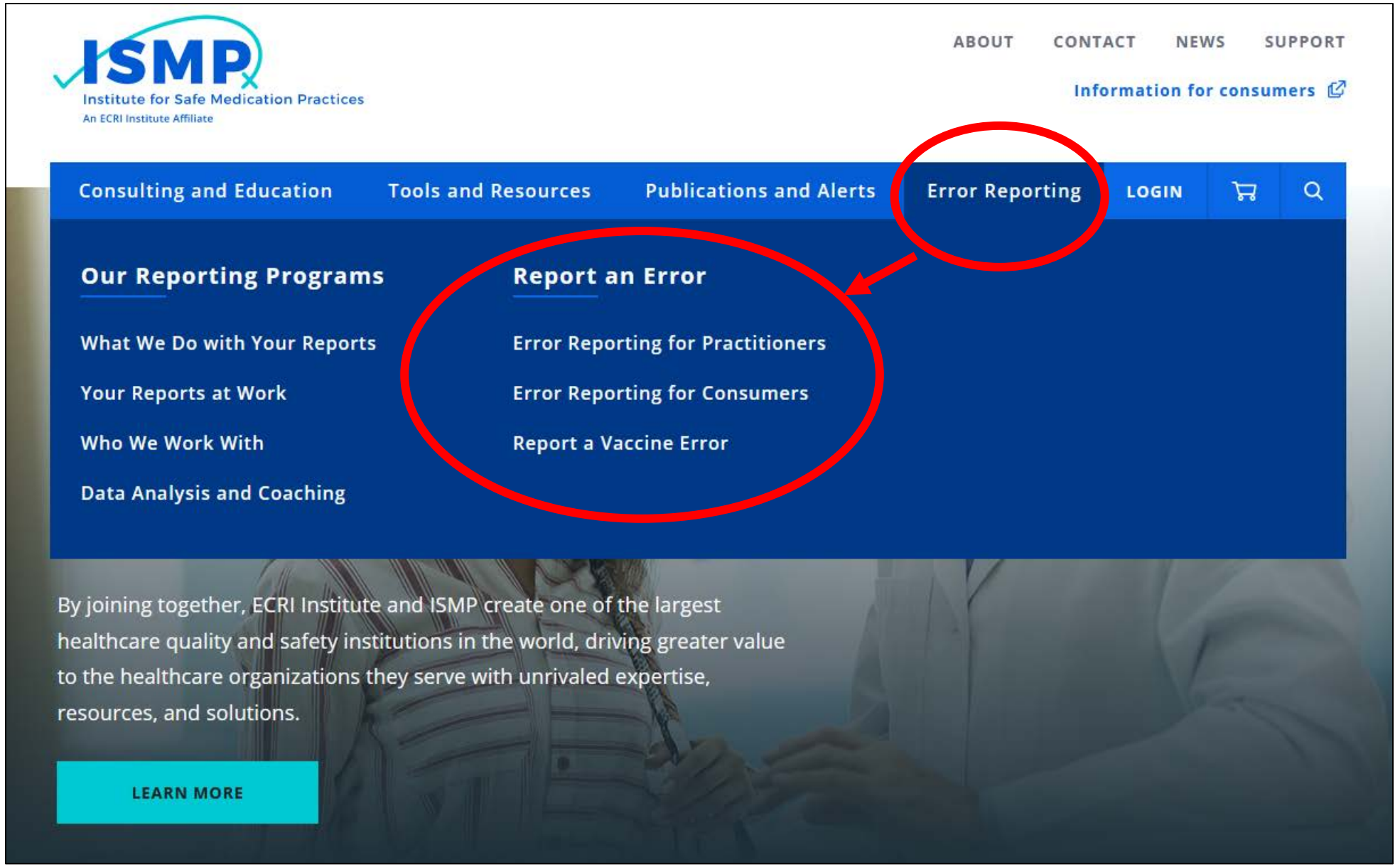
Upload Images (optional) Select

Up to three images can be uploaded, Input area will appear after each image is selected up to 3.

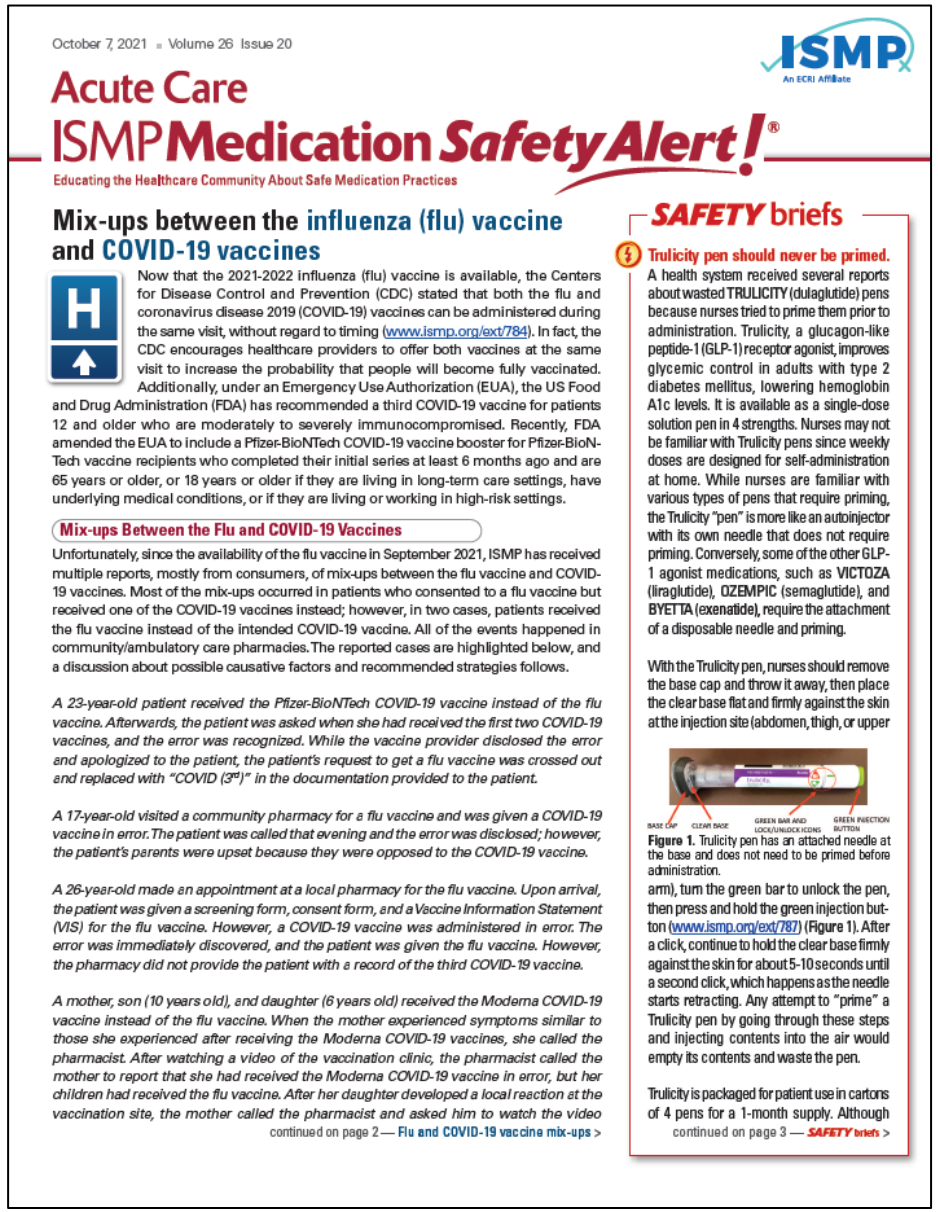
Submit

Reporting to a Patient Safety Organization (PSO)

ECRI Institute for Safe Medication Practices PSO


ISMP
Institute for Safe Medication Practices
An ECRI Institute Affiliate
ABOUT
CONTACT
NEWS
SUPPORT
Information for consumers
Consulting and Education
Tools and Resources
Publications and Alerts
Error Reporting
LOGIN
Our Reporting Programs
What We Do with Your Reports
Your Reports at Work
Who We Work With
Data Analysis and Coaching
Report an Error
Error Reporting for Practitioners
Error Reporting for Consumers
Report a Vaccine Error
By joining together, ECRI Institute and ISMP create one of the largest healthcare quality and safety institutions in the world, driving greater value to the healthcare organizations they serve with unrivaled expertise, resources, and solutions.
LEARN MORE

ISMP National Medication Error Reporting System



October 7, 2021 ▪ Volume 26 Issue 20

ISMP An ECRI Affiliate

Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Mix-ups between the influenza (flu) vaccine and COVID-19 vaccines

Now that the 2021-2022 influenza (flu) vaccine is available, the Centers for Disease Control and Prevention (CDC) stated that both the flu and coronavirus disease 2019 (COVID-19) vaccines can be administered during the same visit, without regard to timing (www.ismp.org/ext/784). In fact, the CDC encourages healthcare providers to offer both vaccines at the same visit to increase the probability that people will become fully vaccinated. Additionally, under an Emergency Use Authorization (EUA), the US Food and Drug Administration (FDA) has recommended a third COVID-19 vaccine for patients 12 and older who are moderately to severely immunocompromised. Recently, FDA amended the EUA to include a Pfizer-BioNTech COVID-19 vaccine booster for Pfizer-BioNTech vaccine recipients who completed their initial series at least 6 months ago and are 65 years or older, or 18 years or older if they are living in long-term care settings, have underlying medical conditions, or if they are living or working in high-risk settings.

Mix-ups Between the Flu and COVID-19 Vaccines

Unfortunately, since the availability of the flu vaccine in September 2021, ISMP has received multiple reports, mostly from consumers, of mix-ups between the flu vaccine and COVID-19 vaccines. Most of the mix-ups occurred in patients who consented to a flu vaccine but received one of the COVID-19 vaccines instead; however, in two cases, patients received the flu vaccine instead of the intended COVID-19 vaccine. All of the events happened in community/ambulatory care pharmacies. The reported cases are highlighted below, and a discussion about possible causative factors and recommended strategies follows.

A 23-year-old patient received the Pfizer-BioNTech COVID-19 vaccine instead of the flu vaccine. Afterwards, the patient was asked when she had received the first two COVID-19 vaccines, and the error was recognized. While the vaccine provider disclosed the error and apologized to the patient, the patient's request to get a flu vaccine was crossed out and replaced with "COVID (3rd)" in the documentation provided to the patient.

A 17-year-old visited a community pharmacy for a flu vaccine and was given a COVID-19 vaccine in error. The patient was called that evening and the error was disclosed; however, the patient's parents were upset because they were opposed to the COVID-19 vaccine.

A 26-year-old made an appointment at a local pharmacy for the flu vaccine. Upon arrival, the patient was given a screening form, consent form, and a Vaccine Information Statement (VIS) for the flu vaccine. However, a COVID-19 vaccine was administered in error. The error was immediately discovered, and the patient was given the flu vaccine. However, the pharmacy did not provide the patient with a record of the third COVID-19 vaccine.

A mother, son (10 years old), and daughter (6 years old) received the Moderna COVID-19 vaccine instead of the flu vaccine. When the mother experienced symptoms similar to those she experienced after receiving the Moderna COVID-19 vaccines, she called the pharmacist. After watching a video of the vaccination clinic, the pharmacist called the mother to report that she had received the Moderna COVID-19 vaccine in error, but her children had received the flu vaccine. After her daughter developed a local reaction at the vaccination site, the mother called the pharmacist and asked him to watch the video

continued on page 2 — Flu and COVID-19 vaccine mix-ups >

SAFETY briefs

Trulicity pen should never be primed.

A health system received several reports about wasted TRULICITY (dulaglutide) pens because nurses tried to prime them prior to administration. Trulicity, a glucagon-like peptide-1 (GLP-1) receptor agonist, improves glycemic control in adults with type 2 diabetes mellitus, lowering hemoglobin A1c levels. It is available as a single-dose solution pen in 4 strengths. Nurses may not be familiar with Trulicity pens since weekly doses are designed for self-administration at home. While nurses are familiar with various types of pens that require priming, the Trulicity "pen" is more like an autoinjector with its own needle that does not require priming. Conversely, some of the other GLP-1 agonist medications, such as VICTOZA (liraglutide), OZEMPIC (semaglutide), and BYETTA (exenatide), require the attachment of a disposable needle and priming.

With the Trulicity pen, nurses should remove the base cap and throw it away, then place the clear base flat and firmly against the skin at the injection site (abdomen, thigh, or upper

Figure 1. Trulicity pen has an attached needle at the base and does not need to be primed before administration.

arm), turn the green bar to unlock the pen, then press and hold the green injection button (www.ismp.org/ext/787) (**Figure 1**). After a click, continue to hold the clear base firmly against the skin for about 5-10 seconds until a second click, which happens as the needle starts retracting. Any attempt to "prime" a Trulicity pen by going through these steps and injecting contents into the air would empty its contents and waste the pen.

Trulicity is packaged for patient use in cartons of 4 pens for a 1-month supply. Although

continued on page 3 — SAFETY briefs >

- Early warning system
  - Issue nationwide hazard alerts and press releases
- Learning
  - Dissemination of information and tools
- Change
  - Product nomenclature, labeling, and packaging changes, device design, practice issues
- Standards and Guidelines
  - Advocates for national standards and guidelines

Where does ISMP get its information? Where does it go?

ISMP MERP and VERP

Providers, Consumers

FDA MedWatch

News media, other sources

ISMP

An ECRI Affiliate

ISMP Canada
ISMP Spain
ISMP Brazil
IMSN

Healthcare providers

Healthcare organizations

Consumers

Regulatory

Industry


Acute Care
ISMP Medication Safety Alert!

Errors associated with oxytocin use: A multi-organization analysis by ISMP and ISMP Canada

SAFETY briefs

Process when you report a hazard or error to ISMP – Every report is indispensable!

Report received and entered into ISMP database

- Report entered into one of our databases and initially reviewed by ISMP nurse or pharmacy technician analyst
- ISMP sends an email to reporter to confirm receipt of the report and thank him or her for reporting

ISMP professional staff review every report and gather additional information if necessary

- Report redacted of identifying provider and/or facility information
- Nurse or analyst distributes reports and accompanying photographs, screen shots or attachments through secure portal to ISMP interdisciplinary professional staff
- Professional staff reviews every report, shares comments on topic with one another via the portal

ISMP professional staff review every report and gather additional information if necessary

- Similar hazards, errors identified
- Suggest questions to ask reporter to better understand the report, make recommendations for mitigating the risk
- Reports incite conversation among professional staff
- Gain understanding of the reported risks and underlying causes

Report identified as requiring further investigation for sharing the lessons learned

- Significant factor - is report actionable? Leads to further investigation and sharing of lessons learned
- Can patients, vendors, standards organizations and regulators take specific actions to prevent or reduce risk of similar error, or mitigate potential patient harm?
- Is hazard or error new? Has it caused or could it cause harm? Does it require action by FDA or manufacturer, state professional board, standards organizations such as USP or The Joint Commission?

Further investigation conducted, with additional resources accessed

<u>Steps ISMP may take to investigate hazards or errors:</u>

- Reach out to reporter to ask clarifying questions, seek out additional information, graphics or examples
- Conduct professional literature, drug information and error-reporting database searches
- Seek out expert advice from established advisory groups or organizations with extensive knowledge in key subject areas

Further investigation conducted, with additional resources accessed

- Interact with other federally listed patient safety organizations (PSOs), such as our ECRI affiliate
- Interact with FDA Division of Medication Error Prevention and Analysis and others within the agency.
- Memorandum of Understanding with CDER

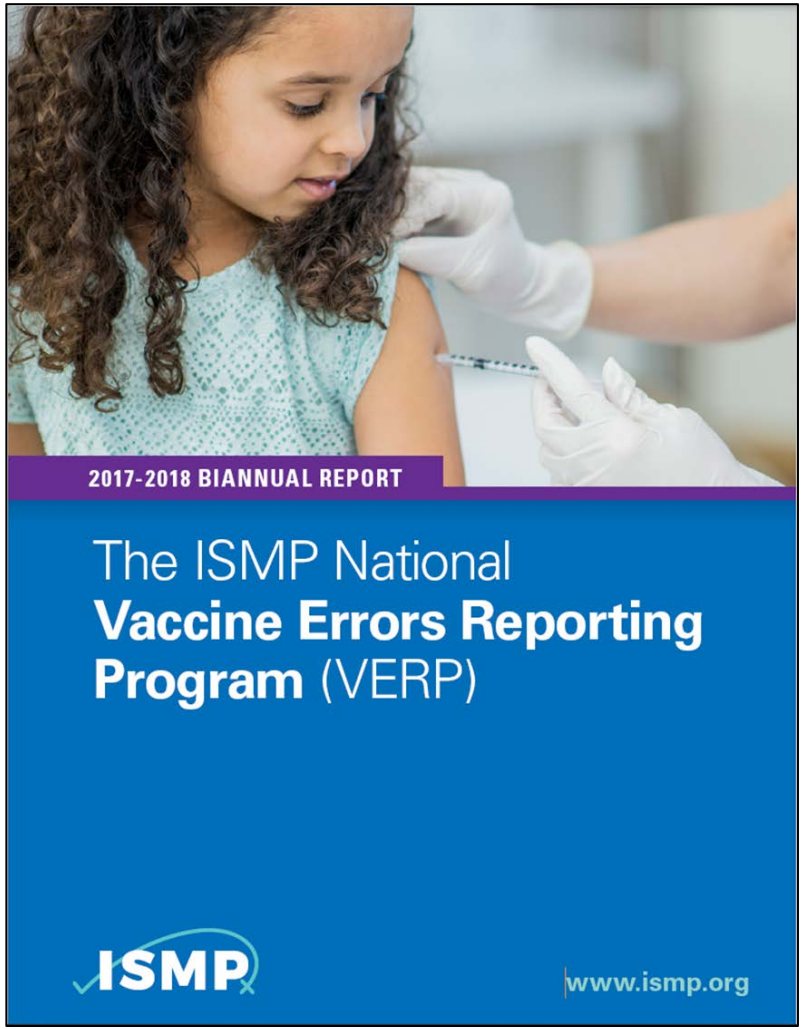
Further investigation conducted, with additional resources accessed

- Formal monthly calls and two face to face meetings annually
- Contact the pharmaceutical product manufacturer, device and technology vendors, drug information vendors and other service providers
- Conduct surveys to learn more about specific types of errors

Recommendations identified to drive further improvements

- Primary focus is on a few well-thought-out, high-leverage, long-term recommendations that are realistic, measurable, and attainable with reasonable resources
- Because ISMP is not a standards-setting organization, we sometimes make ambitious recommendations to drive practice, process, and technology improvements
- Many reports trigger FDA, manufacturer, device/technology vendors to further investigate and respond

Aggregate data from error databases analyzed and published periodically



https://www.ismp.org/resources/2017-2018-vaccine-bi-annual-report

https://www.ismp.org/node/14240

Hazard/error story & recommendations shared with FDA and via newsletters, interaction with manufacturers, vendors, other key stakeholders

- ISMP's primary vehicles are publication in one or more of our 5 subscription-based newsletters
- Urgent medication advisories requiring immediate notification of healthcare providers published first in a National Alert Network (NAN) bulletin to both ISMP email lists, ASHP members, ISMP website and member organizations of National Coordinating Council Medication Error Reporting and Prevention (NCCMERP)
- Error information contextually deidentified as necessary. Stories make information memorable

January/February 2020 ▪ Volume 8 Issue 1

ISMP

Long-Term Care AdviseERR™

Educating the Healthcare Community About Safe Medication Practices

A lot happens when you report a hazard or error to ISMP—there's no "black hole" here!

ECRI Institute – ISMP affiliation creates one of the largest nonprofit

January 2020 ▪ Volume 18 Issue 1

ISMP

Nurse AdviseERR®

Educating the Healthcare Community About Safe Medication Practices

A lot happens when you report a hazard or error to ISMP—there's no "black hole" here!

SAFETY wires

Abbreviations to avoid. Angiotensin II (GIAPREZA) injection for intravenous

In 2019, ISMP celebrated its 25th anniversary as the nation's or zation devoted entirely to medication error prevention. As accomplishments over the years, we recognize that you, too to our successes because you have reported medication hazar bringing attention to significant medication safety issues. Every sable to us, and we want to assure you that the reports you submit never fall into a "black hole," irretrievably lost and never to be seen again. To demonstrate this, we want to share with you all that happens when you report a hazard or error to ISMP (summarized in **Figure 1**), whether it is face-to-face, via email or a phone call, or through one of our three error-reporting programs—the ISMP National Medication Errors Reporting Program (ISMP MERP), the ISMP National Vaccine Errors Reporting Program (ISMP VERP), and the ISMP Consumer Medication Errors Reporting Program (ISMP C-MERP).

Initial Review of Reports

When ISMP receives a hazard or error report, it is entered into one of our databases and initially reviewed by an ISMP nurse or pharmacy technician analyst. Since most reports submitted to ISMP include the reporter's email address, ISMP sends an email to the reporter to confirm receipt of the report and to thank them for reporting.

After redacting any identifying patient and/or facility information, our nurse or analyst distributes all reports and any accompanying pictures or attachments through a secure portal to all ISMP interdisciplinary professional staff. The professional staff review every report and often share comments on the topic with each other through the portal; identify similar hazards, errors, or related resources; suggest questions to ask the reporter to better understand the report; and make recommendations for mitigating the risk. Many reports incite conversation among ISMP professional staff so we can all understand the reported risks and underlying causes.

Depending on the level of detail provided in the original report, our nurse or analyst (or another ISMP professional) sends specific questions to the reporter so we can learn as much as possible about the event and its causes. In addition, each report is shared with the US Food and Drug Administration (FDA) and, if known, the manufacturer(s)

continued on page 2 — No "black hole" >

Supported by educational grants from Novartis and Fresenius Kabi

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ISMP

Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Medical abbreviations that have contradictory or ambiguous meanings

ISMP would like to thank Neil M. Davis, PharmD, MS, FASHP, for authoring this article. The author can be reached at: neil@medabbrev.com for any comments or questions.

Introduction

Abbreviations are a convenience, a time saver, and a way of fitting a word or phrase into a restricted space or avoiding the possibility of misspelling words. However, a high price can be paid for their use. Abbreviations are sometimes not understood, misread, or interpreted incorrectly. Their use lengthens the time needed to train healthcare professionals; wastes time tracking down their meaning; sometimes delays the patient's care; and occasionally results in patient harm.

I published my first book of medical abbreviations, *Medical Abbreviations: 1,700 Conveniences at the Expense of Communication and Safety*, in 1983. To expand the list of abbreviations, I contacted hospitals and requested lists of abbreviations that were used at their facility, searched the literature, and solicited readers to send me abbreviations. Since then, I have published 16 editions of the book, which now contains 55,000 abbreviations.[1] A web version of the book is updated with more than 30 new entries per week.[2]

One of the problems I noticed was that one abbreviation could have two or more contradictory or ambiguous meanings, which can create dangerous communications. I collected these meanings, and a partial list of medical abbreviations with contradictory or ambiguous meanings is shown in **Table 1** (pages 3-5). It is obvious from an examination of this list that these abbreviations should not be used, as they fail to communicate with any certainty their intended meaning and present possible dangers to the health of patients.

The Joint Commission directs medical facilities to publish a Do Not Use List[3] of abbreviations that must not be used (see ISMP's list at: www.ismp.org/node/8). This list is a very important step in the right direction but does not solve the systemic problem of an abbreviation with contradictory or ambiguous meanings.[3] The Joint Commission standards also state, if multiple abbreviations exist for the same term, the organization must identify which one will be used to eliminate ambiguity.[4] This step is extremely difficult to achieve.

Two Possible Solutions That May Not Be Feasible

① **Create a national list of standard abbreviations.** A simplistic approach to this problem is to create a national list of approved abbreviations, with each abbreviation having only one meaning. The problem with this approach is that all medical specialties, allied health professionals, health-related organizations, and government agencies would have to agree on one meaning for each abbreviation.

A recognized health-related organization, such as USP, the American Medical Association, the Council of Science Editors, ISMP, or ECRI Institute, would have to be funded to take responsibility for creating and maintaining such a list. The organization would have to reach out to all the health-related organizations to suggest abbreviations that should be on this list. Then, arbitration would be required between organizations if there is conflict with a suggested abbreviation that has more than one submitted meaning, such as PT

continued on page 2 — Abbreviations >

SAFETY briefs

Waste and error risk tied to Stivarga packaging. The oral kinase inhibitor STIVARGA (regorafenib) is approved for treatment of metastatic colorectal cancer, metastatic gastrointestinal stromal tumor, and hepatocellular carcinoma. The drug, which is available through specialty pharmacies, is formulated as 40 mg tablets and supplied in a carton containing three 28-count bottles, totaling 84 tablets (Figure 1). Current labeling states, "Store tablets in the original bottle," and "Discard any unused tablets 7 weeks after opening the bottle." The recommended dose is 160 mg daily (4 x 40 mg tablets) for the first 21 days of each 28-day cycle, which totals 84 tablets per cycle. Treatment is continued until disease progression or unacceptable toxicity.

Product labeling mentions various drug-related toxicities that require reduced

continued on page 2 — SAFETY briefs >

Figure 1. Stivarga carton holds three 28-tablet bottles.

Become an ISMP Fellow

ISMP fellowships can help you grow in your career and make major contributions to medication safety worldwide. ISMP is now accepting applications for three unique programs that begin this summer/fall—the ISMP Safe Medication Management Fellowship, the ISMP International Medication Safety Management Fellowship, and the FDA (US Food and Drug Administration)/ISMP Safe Medication Management Fellowship. The deadline for applications is March 31, 2020. For information, program descriptions, and application, visit: www.ismp.org/node/871.

January 2020 ▪ Volume 19 Issue 1

ISMP

Community/Ambulatory Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Speaking up about patient safety requires an observant questioner and a high index of suspicion

SAFETY briefs

Mix-ups between Almovig strengths

November/December 2019 ▪ Volume 17 Issue 6

ISMP 25 ADVANCING MEDICATION SAFETY

SAFEMedicine®

Protect Yourself from Medication Errors

As approval of medical marijuana spreads state by state, labeling problems have led to errors

f Columbia (Washington, DC) have legalized s plus DC have legalized recreational use of different than the street product. With medical oducts' contents, so this information can be However, each state has its own regulations in a wide variety of medical marijuana prodth the labeling of these products.

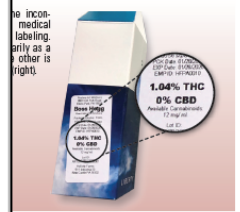
a

a is *Cannabis sativa*. Much like the different marijuana comes in many different strains lled cannabinoids. These cannabinoids are art on the growing conditions.

medical marijuana are tetrahydrocannabinol cts the mind, behavior, and coordination, n such as euphoria (happiness), relaxation, e intensity of these effects tends to be dosearijuana with high levels of THC may make Even when taken in small doses, symptoms headedness, increasing the risk of falls. THC cannabis use disorder).

tudies suggest it may help reduce inflamma-, and seizures from epilepsy. Unfortunately, feel the effects of CBD, they may take higher ects include headache, diarrhea, restlessness, l to marijuana addiction.

continued on page 2—Medical marijuana >



Sidebar:
Labeling issue with medical marijuana

A patient in the hospital told a nurse she takes medical marijuana at home for pain and to help her sleep. She showed the bottle of medical marijuana to the nurse. The dropper bottle had a wrap-around label on it (Figure 1). The label said it was a 330 mg tincture and listed the contents as a "hybrid" with a 1:10 ratio. Instructions for use were not on the label. The patient stated the bottle contained a 30-day supply and that she takes half a dropperful at bedtime. The dropper had 0.5 mL and 1 mL markings on it.

Brand X	
Medical Marijuana	
330 MG TINCTURE	Hybrid 1:10

Figure 1. Wrap-around label on a dropper bottle of medical marijuana liquid (with the product name replaced with "Brand X").

So how much THC and CBD did the patient take with each dose? The label does not show how much liquid (mL) equals 330 mg. Since the bottle contained a 30-day supply, the nurse calculated that the full bottle likely contained 15 mL (30 days times each daily dose of 0.5 mL). Thus, the strength of the product might have been 330 mg per 15 mL. But, this is an unreliable way to determine the product strength.

The label also does not say if the ratio of 1:10 is THC:CBD or CBD:THC. So how much THC and CBD are in each dose? When the patient's husband brought in the box that held the bottle, the label said there was no CBD at all in the product, even though the label said it was a 1:10 ratio of a "hybrid."

ISMP Publications

- Regular Journal and Newsletter Features:
  - *Pharmacy Practice News*
  - *Nursing 2021*
  - *Hospital Pharmacy*
  - *Pharmacy Times*
  - *Pharmacy Today*
  - *US Pharmacist*
  - *Journal of Emergency Nursing*
  - *Home Healthcare Now*

Error reporting outcomes

Reporter's Event Description

- "81 y.o. male admitted to hospital with slurred speech and gait change to R/O stroke. Blood glucose 57 mg/dL (Hgb A1C was 13.9% upon admission).
- **It was discovered that the patient had not been removing the inner cap of his pen needle for his insulin until the day prior to admission**.
- For over a year, the patient's physician was constantly increasing the patient's insulin dose to 150 units in the morning and 156 units at bedtime (plus 80 units insulin lispro before each meal).
- The patient described that when he injected his insulin, he would use a napkin to soak up the excess insulin that spilled when he injected himself.
- He confirmed he would use an entire pen per day. On day PTA **he realized he had not been removing the pen needle inner cap** as instructed during diabetes self-management education.
- Patient took off the inner cap and injected the prescribed amount of insulin resulting in hypoglycemia.
- The patient was treated and recovered. During hospital stay he required significantly less insulin (glargine 15 units subcutaneously hs and insulin lispro 4-6 units before meals)."

Hazard/Error Story & Recommendations Shared

February 26, 2009 Volume 14 Issue 4

SafetyBriefs continued from page 2

Vaccine abbreviations. The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) has provided a current list of standardized abbreviations for vaccines included in the immunization schedules for children, adolescents, and adults (www.cdc.gov/vaccines/recs/acip/downloads/vac-abbrev.pdf). These abbreviations are intended to provide a uniform approach to vaccine references used in ACIP Recommendations and Notices to Readers that are published in the *MMWR*, the *Pink Book*, the American Academy of Pediatrics *Red Book*, and other publications. However, ISMP discourages the use of vaccine abbreviations (or any drug name abbreviation) when communicating prescription information because some abbreviations on the CDC list have been confused with one another. For example, diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed (DTaP) have been confused with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, adsorbed (Tdap). These are age dependent and are not interchangeable. Also, DT (diphtheria and tetanus toxoids adsorbed [children]) has been confused with Td (tetanus and diphtheria toxoids adsorbed [adult]).

Special Announcement ...

ISMP teleconference. Join ISMP and our guest speakers from Brigham and Women's Hospital and the Cleveland Clinic for our next teleconference, ***Enhancing Medication Safety: The Role of Safe Labeling, Bar Coding, and Outsourcing of IV Products***, on March 12, 2009. You will learn how product labeling, bar-coding technology, and outsourcing IV products can reduce the risk of adverse drug events with IV products. For details, please visit: www.ismp.org/educational/teleconferences.asp.

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Inattentional blindness continued from page 2

enced by age and mental aptitude. From time to time, attention is also variable within an individual due to influences such as distractions, alcohol, drugs, and fatigue.

It is difficult to reduce the risk of inattentional blindness, as it is an involuntary and unnoticed consequence of our adaptive ability to defend against information overload. Error-reduction strategies such as education, training, and rules are of little value. Instead, efforts should center on increasing conspicuity of critical information, and decreasing diversions of attention and secondary tasks when carrying out complex tasks.

References: 1) Green M. "Inattentional blindness" and conspicuity. *Visual Expert* 2004 (www.visualexpert.com/Resources/inattentionalblindness.html). 2) Angier N. Blind to change, even as it stares us in the face. *The New York Times* April 1, 2008 (www.nytimes.com/2008/04/01/science/01angi.html?_r=2&ex=1207713600&en=204&conf=&oref=slogin). 3) Federal Aviation Administration (FAA). FAA human factors awareness course. (www.hf.faa.gov/webtraining/IntroN/Intro1.htm). 4) Arons B. A review of the cocktail party effect. MIT Media Lab; 1992. (www.media.mit.edu/speech/papers/1992/arons_AVIOSJ92_cocktail_party_effect.pdf).

Unusual explanation for hyperglycemia in patients on insulin

From a regulatory standpoint, hospitals are required by OSHA (CPL 2- 2.69) to "use engineering and work practice controls that eliminate occupational exposure or reduce it to the lowest feasible extent." Whenever possible, that means using such things as safety needles in the hospital (preferably a passive system) to protect against needle stick injuries.

One example of a safety needle for use with the **NOVOLOG** (insulin aspart) **FlexPen** is the **NovoFine Autocover** (Figure 1). The user holds the cover while the system is screwed onto the insulin pen. The cover is then removed, exposing a plastic needle shield that initially covers a 30-gauge needle. As the insulin is injected, the shield slides and allows the skin to be punctured, needle unseen (a demonstration can be viewed at: www.novonordisk.com/diabetes/public/needles/novofine_autocover/quickguide/view.asp?Id=intro). When the needle is removed, the shield retracts and locks over the needle, which remains hidden, so it can't be used again.

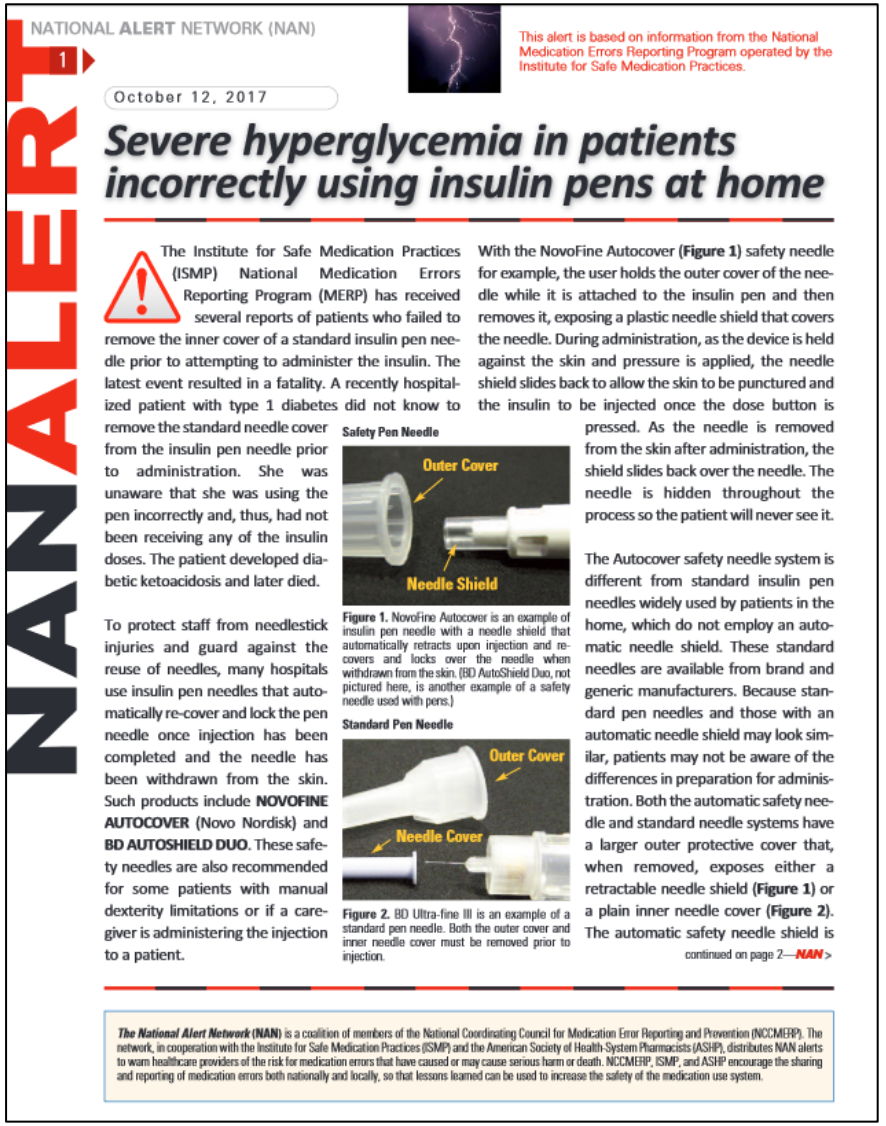
The Autocover system is quite different from standard insulin pen needles that patients purchase at their pharmacy, which may not employ a shielded system. A hospital pharmacist and a nurse recently reported that some patients who became familiar with the NovoFine Autocover while in the hospital were later confused as they began to use a standard BD pen needle (BD Ultra-Fine III) after discharge. This needle also has a cover that, when removed, exposes a needle shield. However, the shield is actually just a needle cap that must first be removed to expose the needle for injection of the insulin (Figure 2). Some patients were confused and thought the cap would expose the needle when it was pushed against the skin, just as the Autocover shield did. After realizing that some patients' blood sugars were high, clinic nurses investigated and learned that patients were misusing the standard pen needles and, thus, not getting any insulin.

Patients who use Autocover devices and then switch to standard pen needles must be educated about the need to remove both caps. Removing the gray cap is an extra step that is not required with the NovoFine Autocover needles. If blood glucose levels are elevated after injection, the patient should be reminded to consult with their diabetes educator or physician, who should review injection techniques with the patient. Community pharmacists dispensing pen device supplies should also educate patients regarding their proper use.

Figure 1. NovoFine Autocover has outer cover that must be removed, but the plastic needle shield slides back during injection.

Figure 2. BD Ultra-Fine III pen needle has clear outer cover and gray needle cover that must be removed prior to injection.

Please encourage your patients and staff to visit www.consumermedsafety.org often. **It may save a life!**



NATIONAL **ALERT** NETWORK (NAN)

This alert is based on information from the National Medication Errors Reporting Program operated by the Institute for Safe Medication Practices.

October 12, 2017

Severe hyperglycemia in patients incorrectly using insulin pens at home

The Institute for Safe Medication Practices (ISMP) National Medication Errors Reporting Program (MERP) has received several reports of patients who failed to remove the inner cover of a standard insulin pen needle prior to attempting to administer the insulin. The latest event resulted in a fatality. A recently hospitalized patient with type 1 diabetes did not know to remove the standard needle cover from the insulin pen needle prior to administration. She was unaware that she was using the pen incorrectly and, thus, had not been receiving any of the insulin doses. The patient developed diabetic ketoacidosis and later died.

To protect staff from needlestick injuries and guard against the reuse of needles, many hospitals use insulin pen needles that automatically re-cover and lock the pen needle once injection has been completed and the needle has been withdrawn from the skin. Such products include **NOVOFINE AUTOCOVER** (Novo Nordisk) and **BD AUTOSHIELD DUO**. These safety needles are also recommended for some patients with manual dexterity limitations or if a caregiver is administering the injection to a patient.

With the NovoFine Autocover **(Figure 1)** safety needle for example, the user holds the outer cover of the needle while it is attached to the insulin pen and then removes it, exposing a plastic needle shield that covers the needle. During administration, as the device is held against the skin and pressure is applied, the needle shield slides back to allow the skin to be punctured and the insulin to be injected once the dose button is pressed. As the needle is removed from the skin after administration, the shield slides back over the needle. The needle is hidden throughout the process so the patient will never see it.

The Autocover safety needle system is different from standard insulin pen needles widely used by patients in the home, which do not employ an automatic needle shield. These standard needles are available from brand and generic manufacturers. Because standard pen needles and those with an automatic needle shield may look similar, patients may not be aware of the differences in preparation for administration. Both the automatic safety needle and standard needle systems have a larger outer protective cover that, when removed, exposes either a retractable needle shield **(Figure 1)** or a plain inner needle cover **(Figure 2)**. The automatic safety needle shield is

continued on page 2—*NAN*>

Safety Pen Needle

Figure 1. NovoFine Autocover is an example of insulin pen needle with a needle shield that automatically retracts upon injection and recovers and locks over the needle when withdrawn from the skin. (BD AutoShield Duo, not pictured here, is another example of a safety needle used with pens.)

Standard Pen Needle

Figure 2. BD Ultra-fine III is an example of a standard pen needle. Both the outer cover and inner needle cover must be removed prior to injection.

***The National Alert Network* (NAN)** is a coalition of members of the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP). The network, in cooperation with the Institute for Safe Medication Practices (ISMP) and the American Society of Health-System Pharmacists (ASHP), distributes NAN alerts to warn healthcare providers of the risk for medication errors that have caused or may cause serious harm or death. NCCMERP, ISMP, and ASHP encourage the sharing and reporting of medication errors both nationally and locally, so that lessons learned can be used to increase the safety of the medication use system.

U.S. FOOD & DRUG ADMINISTRATION

September 26, 2018

LABELING CHANGE REQUEST

Dear Manufacturer,

The Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) is aware of a postmarket safety issue associated with the use of pen needles used with pen injectors. These needles are regulated under the classification regulation 21 CFR 880.5570[1] with product code FMI (Hypodermic Single Lumen Needle). Standard pen needles often have an outer cover and a removable inner needle cover, which are both removed before an injection. However, the FDA is aware that in some cases, the inner needle cover is not removed prior to use, resulting in non-delivery of the intended medication. The FDA has received some reports of hyperglycermia and diabetic ketoacidosis, including one death, associated with failure to remove the inner needle cover when a standard pen needle was used to inject insulin.

There are other safety pen needles which have an outer cover that is removed, and a fixed inner needle shield (sharps injury prevention feature) that is not removed before an injection. It is possible that patients could be taught using one type of pen needle, then receive the other type later. This could cause confusion about how to use the pen needle correctly, and may prevent the patient from getting the medicine they need. This issue was brought to our attention through the Institute for Safe Medication Practices[2] (ISMP), National Alert Network (NAN)[3], Medical Device Reports (MDRs), FDA Adverse Event Reporting Sytem (FAERS), and published literature[4].

FDA reviewed the device labeling across standard insulin pen needle manufacturers to assess whether the Instructions for Use (IFU) adequately contain the necessary directions on steps to remove both covers, if applicable. While some manufacturers provide clear IFU to remove both the outer cover and the inner needle cover, the FDA found that some manufacturers do not provide this information, or the information may be confusing. For example, some manufacturers provide both written and visual graphics, while others provide only written instructions. Additionally, FDA found instances where removal of the outer cover and the inner needle cover were listed under one step in the IFU. Furthermore, there may be limited graphics supporting all necessary steps for safe use (e.g., the written information provided both steps but the graphic only showed one step).

It is important that the IFU for each device clearly and completely convey important information to device users. Therefore, FDA is requesting manufacturers who currently market pen needles cleared under product code FMI to review your most recent labeling (i.e., IFU) and training materials to assess the need for updates to clearly convey how to safely use your pen needle. In addition, FDA requests that all applicable standard pen needle manufacturers consider adding a warning in the labeling, similar to the following:

[1] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=880.5570
[2] https://www.ismp.org/alerts/severe-hyperglycemia-patients-incorrectly-using-insulin-pens-home
[3] https://www.nccmerp.org/sites/default/files/nan-20171012.pdf
[4] Truong, T. H., Nguyen, T. T., Armor, B. L., & Farley, J. R. (2017). Errors in the Administration Technique of Insulin Pen Devices: A Result of Insufficient Education. *Diabetes Therapy*, *8*(2), 221–226. http://doi.org/10.1007/s13300-017-0242-y

Your *Reports* at *Work*

FDA tells pen injector needle manufacturers to improve patient instructions

Thanks to your reporting about patients who failed to remove the inner pen needle cover prior to administering insulin, the US Food and Drug Administration (FDA) has asked needle manufacturers to update labeling and improve patient instructions for use.

Standard pen needles have outer and inner needle covers, both of which must be removed prior to injection. However, hospitals often use safety needles for medication pens. These have an outer cover that must be removed, but there is no inner cover to remove. An inner shield over the needle automatically retracts during injection and covers the needle after injection to prevent needlestick injuries. After discharge, patients may receive standard pen needles from their pharmacy and not know that the inner needle cover must be removed, especially if they have not been taught this step while hospitalized. If the inner cover of a standard pen needle is not removed, patients may not receive the medication. ISMP and the American Society of Health-System Pharmacists (ASHP) published a National Alert Network (NAN) Alert about this issue (www.ismp.org/node/44) in October 2017.

In response to these concerns, FDA has asked needle manufacturers to review their labeling and educational materials and to update and clarify the need to remove the inner needle cover/cap before injection. The agency also requested manufacturers to add a warning in the labeling, such as: "Remove both the outer cover and the inner needle cover before an injection. If both the outer cover and the inner needle cover are not removed before use, the medication or dose may not be injected, which may result in serious injury or death." The FDA labeling request can be accessed at: www.ismp.org/ext/155.

ISMP Medication Safety Alert! January 31, 2019

Working with industry to improve products

#	Report Date	Description	Product
74092	10/22/2019	Udencya and Prolia have very similar packaging. A patient was dispensed Udencya instead of Prolia. Luckily the error was caught by the RN before it reached the patient, but I feel like a change of the packaging is necessary to prevent this from happening in the future.	PROLIA
73744	7/19/2019	This error is in regards to the medications Prolia and Udenyca. The packages for both medications, from different manufacturers are very similar. Because of this, the medications were placed in the same bin in the refrigerator at XXXXXXX XX XXXXXXXX Medical Center in XXXXX XXXXX, XXXXXXXXXXX. This could have potentially led to the wrong medication being given to a patient within the hospital.	PROLIA
73708	07/11/2019	Look alike packaging for Udenyca (biosimilar for Neulasta) made by Coherus and Prolia (Denosumab) made by Amgen. Undenyca is a newer biosimilar that has come to market. The box containing the product is, ironically, very similar looking to an AMGEN product, Prolia. Neulasta is also made by AMGEN. Both carry similar font and coloring including a green dot for the dosage/concentration. Undenyca is 6 mg and Prolia is 60 mg. If you contact me with an email address, I can attach a photo I took with them next to each other. Significant chance of staff grabbing 2 different medications with very different outcomes.	PROLIA
73678	6/28/2019	We encountered a look-alike packaging in our ambulatory clinics. Please see the attached photos of very similar packing of Prolia (denosumab) and Udenyca (pegfilgrastim-cbqv). These are both used in the same areas within in our clinics.	PROLIA
73674	6/28/2019	Our practice recently started purchasing pegfilgrastim-cbqv (Udenyca), a biosimilar product. When we received it, we noted that the packaging is very similar to denosumab (Prolia). The packages are of similar size, have similar coloring and other features. We are concerned that this is a potential safety issue and may lead to medication errors if the drug is incorrectly dispensed due to lookalike packaging.	PROLIA
73596	06/06/2019	I know ISMP often includes alerts in your newsletter regarding products with similar packaging. just found one that i haven't seen reported yet. Product packaging very similar on Prolia and Udenyca. Similarly sized box, same color scheme etc.	PROLIA
73550	5/22/2019	Medication safety issue with look-alike packaging between Udenyca and Prolia. Both are routinely use medications at an outpatient cancer center. See attached images.	PROLIA
73516	5/15/2019	While trying to obtain a Prolia injection from their unit's Omnicell they noticed that the wrong medication had be stock in the cabinet. Udenyca had been stocked in the wrong location. Upon review by the pharmacy staff it was noted that the packaging was VERY similar despite having different manufactures. Both medications have green and white packaging with the concentration of the medication listed in a green circle in the same location.	PROLIA
73490	5/6/2019	Prolia syringes were found stocked in place of Udenyca syringes at an infusion site at my institution. No patient harm occurred. Contributed to this medication error is likely that their boxes are very similar in appearance in color and word placement, as well as their supply as a single-dose pre-filled syringe for subcutaneous administration (see image of both products side-by-side). It was thought that both items may have also been delivered in the same bag from our supplier in our order since they both require refrigeration, and that may have also contributed to the error. The very similar labeling and supply of these two commonly utilized medications at outpatient infusion centers may contribute to medication errors with these agents.	PROLIA

Working with industry to improve products

Coherus BIOSCIENCES

October 2019

IMPORTANT DRUG WARNING

Subject: Potential of carton confusion between UDENYCA® and Prolia® packaging associated with the risk of administration or dispensing error and adverse events

Dear Health Care Provider,

The purpose of this letter is to make you aware of the potential of carton confusion between the UDENYCA® (pegfilgrastim-cbqv) and Prolia® (denosumab) packaging which could lead to a risk of product administration or dispensing error and adverse events.

Potential of carton confusion between UDENYCA® and Prolia®

UDENYCA® and Prolia® have a similar carton appearance (**Figure 1**) which has led to product administration or dispensing errors and adverse events.

1. Carton Appearance: Both cartons look similar with a green/white color scheme and green horizontal bands across the top (**Figure 1**).
2. Presentation and Strength: Both cartons hold one single-dose prefilled syringe, and both medications are intended for subcutaneous administration. The UDENYCA® syringe contains 6 mg and the Prolia® syringe contains 60 mg.
    a. The needle guard of UDENYCA® syringe is colorless while the Prolia® syringe is translucent green (**Figure 2**).
3. Storage: Both are refrigerated items and have the potential to be stored next to each other.

Figure 1: UDENYCA® (left) and Prolia® (right) Cartons

Figure 2: UDENYCA® (left) and Prolia® (right) Syringes

Coherus BioSciences, Inc. 333 Twin Dolphin Drive, Suite 600 Redwood City, CA 94065

July 18, 2019 ■ Volume 24 Issue 14

ISMP 25 ADVANCING MEDICATION SAFETY

Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

New recommendations to improve drug allergy capture and clinical decision support

The *Partnership for Health IT Patient Safety*, a national collaborat... convened by ECRI Institute, has released a new report on drug alle... interactions and how clinical decision support (CDS) and hea... information technology (IT) can be used to improve safety.[1] The rep... ***Safe Practices for Drug Allergies—Using CDS and Health*** ..., presents the findings of a multistakeholder workgroup composed ... members from the *Partnership*, including healthcare provide..., members from professional and patient safety organizations, safety and qua... advocates, health IT developers, and academic researchers. The workgroup w... co-chaired by ISMP President Michael Cohen and ISMP Medication Safety Specia... Christina Michalek and funded in part by the Gordon and Betty Moore Foundati... The report sets forth evidence-based safe practices and suggested implementat... strategies for using technology to standardize allergy documentation, enabling C... tools to provide more actionable allergy information, monitoring alerts ... effectiveness, and engaging patients. A summary of key highlights from the rep... follows.[1]

Importance of Drug Allergy Information and CDS Tools

Timely access to accurate, up-to-date drug allergy information is critical to av... potentially life-threatening adverse drug reactions that can delay the delivery of ... appropriate treatment, necessitate additional treatments, increase care costs, a... negatively impact patient outcomes. To facilitate the appropriate triggering of ale..., the information must be documented using the correct allergy terminology, cod... properly, and captured in a standard location. Outdated allergy information m... also be removed from the patient's list of active allergies.

continued on page 2—Drug aller...

22nd Annual ISMP Cheers Awards Nominations

In our ongoing effort to improve patient safety, ISMP takes great joy in recognizing ... others who share this same vision for the future. Each year, ISMP celebrates individuals, ... institutions, and groups that have demonstrated exemplary commitment to the continued ... science and study of medication safety through innovative and creative projects, ... educational efforts, standard setting, and/or research. The celebrated winners will ... receive an ISMP Cheers Award, which will be presented during an evening ceremony ... in early December of each year—more to follow on the gala!

Nominations for this year's Cheers Awards will be accepted through **September 6**... ISMP accepts external nominations, including self-nominations. The prestigious Awards ... spotlight efforts from all healthcare disciplines, and winners have included represent... atives from hospitals, health systems, long-term care, ambulatory care, community ... pharmacies, professional associations, federal and state agencies, as well as individual ... advocates. Cheers Award winners demonstrate a willingness to share learning beyond ... the organization (e.g., professional presentations; articles in peer-reviewed publications; ... tools shared on the internet; willingness to share learning in ISMP newsletters). To ... submit a nomination, visit: www.ismp.org/node/1036.

SAFETY briefs

Prolia-Udenyca look-alike update. We continue to receive reports about potential look-alike mix-ups between cartons of **PROLIA** (denosumab; Amgen), an osteoporosis drug, and **UDENYCA** (pegfilgrastim-cbqv; Coherus BioSciences), a biosimilar leukocyte growth factor associated with the reference pegfilgrastim product, **NEULASTA**. The US Food and Drug Administration (FDA) initially approved Prolia in 2010. Udenyca was approved in November 2018, and since its launch in January, we have received 12 reports of potential mix-ups. None of the reports have mentioned an actual error involving a patient. However, as reported in our May 23, 2019 issue, we have received reports of dispensing and drug storage errors. In several cases, a Prolia syringe carton was stocked in place of Udenyca, and vice versa, in automated dispensing cabinet refrigerators in outpatient infusion sites.

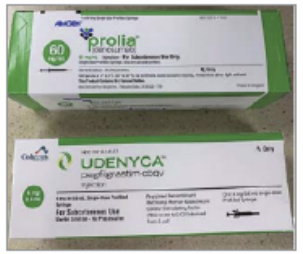


Figure 1. Package similarity has led to dispensing and storage errors.

The reports all indicate that the similar appearance of the outer cartons of these medications increases the risk of a medication error (**Figure 1**). Each carton holds a single syringe. Each outer carton has similar green and white coloring, and the packaging appears to be of similar size and dimension. Both medications are marked "for subcutaneous use." The concentration for each drug is listed in a green circle in the same location. Both concentrations include the numbers 6 and 0, which one

continued on page 2—SAFETY briefs >

Your Reports at Work

Thanks to your reporting, Coherus BioSciences submitted a revised carton label to the US Food and Drug Administration (FDA) for its product, **UDENYCA** (pegfilgrastim-cbqv), a biosimilar leukocyte growth factor associated with the reference pegfilgrastim product, **NEULASTA**. The revision was recently approved. ISMP had received several reports last year about the potential for confusion with **PROLIA** (denosumab; Amgen), an osteoporosis drug. Two actual errors were reported in which patients received the wrong drug. **Figure 1** shows the carton label similarities between Udenyca and Prolia while **Figure 2** shows the revised carton label. While the company works to implement the new packaging, cartons of Udenyca will be shipped with a bright orange-red warning sticker affixed to the carton (**Figure 3**).

Figure 1. Former green carton label for Udenyca (bottom) led to confusion with Prolia cartons (top).

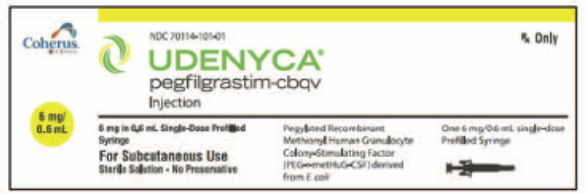


Figure 2. Recently approved color change for Udenyca contrasts with Prolia carton label above.

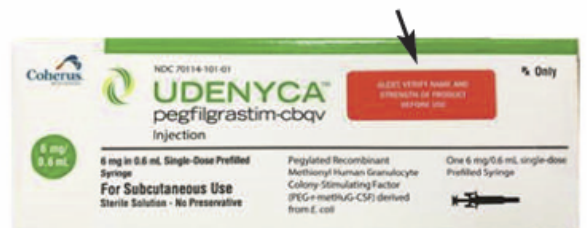


Figure 3. An orange-red sticker will be affixed to the original Udenyca carton until the new packaging is available. The sticker reminds practitioners to verify the product name and strength before use.

Error reporting outcomes

- Improvements in patient safety as a result of hundreds of specific product-related changes
  - Drug naming, labeling, packaging, medication-related device design, measuring devices, infusion pump safety issues.
- Some products withdrawn from market due to medication error issues
- Thousands of product label and labelling changes as a result of new FDA requirements or changes in USP standards (USP <7>) due to reported medication errors.
  - Dangerous abbreviations and dose designations, ratio expression, expression of drug concentration, certain new drug packaging requirements, etc.
- Practice-related standards (CMS, Joint Commission, etc.)

USP Standards

⟨7⟩ LABELING

INTRODUCTION

This general chapter provides definitions and standards for labeling of official articles. Labeling standards for an article recognized in *USP–NF* are expressed in the article's monograph and applicable general chapters. It is intended that all articles in *USP* or *NF* will be subject to the labeling requirements specified in this chapter by means of a provision in *General Notices, 10 Preservation, Packaging, Storage, and Labeling*, unless different requirements are provided in a specific monograph. As with compendial standards for naming, identity, strength, quality, and purity, compendial requirements for labeling have a role in the adulteration and misbranding provisions of federal law [see the Federal Food, Drug, and Cosmetic Act (FDCA) sections 501(b), 502(e)(3)(b), 502(g), and 502(h)]. Exceptions or additional requirements specific to animal drug products and compounded preparations are provided in separate sections. Vaccine labeling is not included in this general chapter.

DEFINITIONS

The term "labeling" includes all labels and other written, printed, or graphic matter on an article's immediate container or on, or in, any package or wrapper in which it is enclosed, except any outer shipping container. The term "label" is that part of the labeling on the immediate container.

A shipping container that contains a single article, unless the container also is essentially the immediate container or the outside of the consumer package, must be labeled with a minimum of product identification (except for controlled substances), lot number, expiration date, and conditions for storage and distribution.

Beyond-use dates (BUDs) and expiration dates are not the same. An expiration date identifies the time during which a conventionally manufactured product, active ingredient, or excipient can be expected to meet the requirements of a compendial monograph, if one exists, provided it is kept under the prescribed storage conditions. The expiration date limits the time during which the conventionally manufactured product, active pharmaceutical ingredient (API), or excipient may be dispensed or used. Expiration dates are assigned by manufacturers of conventionally manufactured products based on analytical and performance testing of the sterility, chemical and physical stability, and packaging integrity of the product. Expiration dates are specific for a particular formulation in its container and at stated exposure conditions of illumination and temperature.

The beyond-use date (BUD) is the date or time beyond which a compounded preparation must be discarded. The date or time is determined from the date the preparation was compounded.

LABELS AND LABELING FOR DRUG PRODUCTS AND COMPOUNDED PREPARATIONS EXPRESSED AS ACTIVE MOIETY IN NAME AND STRENGTH

The names and strengths of drug products and compounded preparations formulated with a salt of an acid or base are to be expressed in terms of the active moiety on the label (see *Nomenclature* ⟨1121⟩, *Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations*).

Labeling

The labeling clearly states the specific salt form of the active moiety that is present in the product or preparation because this information may be useful to practitioners and patients. The names and strengths of both the active moiety and specific salt form (when applicable) are provided in the labeling.

Exceptions

In rare cases in which the use of the specific salt form of the active moiety in the title provides vital information from a clinical perspective, an exception to this policy may be considered. In such cases, when the monograph title contains the specific salt form of the active moiety, the strength of the product or preparation is also expressed in terms of the specific salt form.

LABELS AND LABELING FOR INJECTABLE PRODUCTS

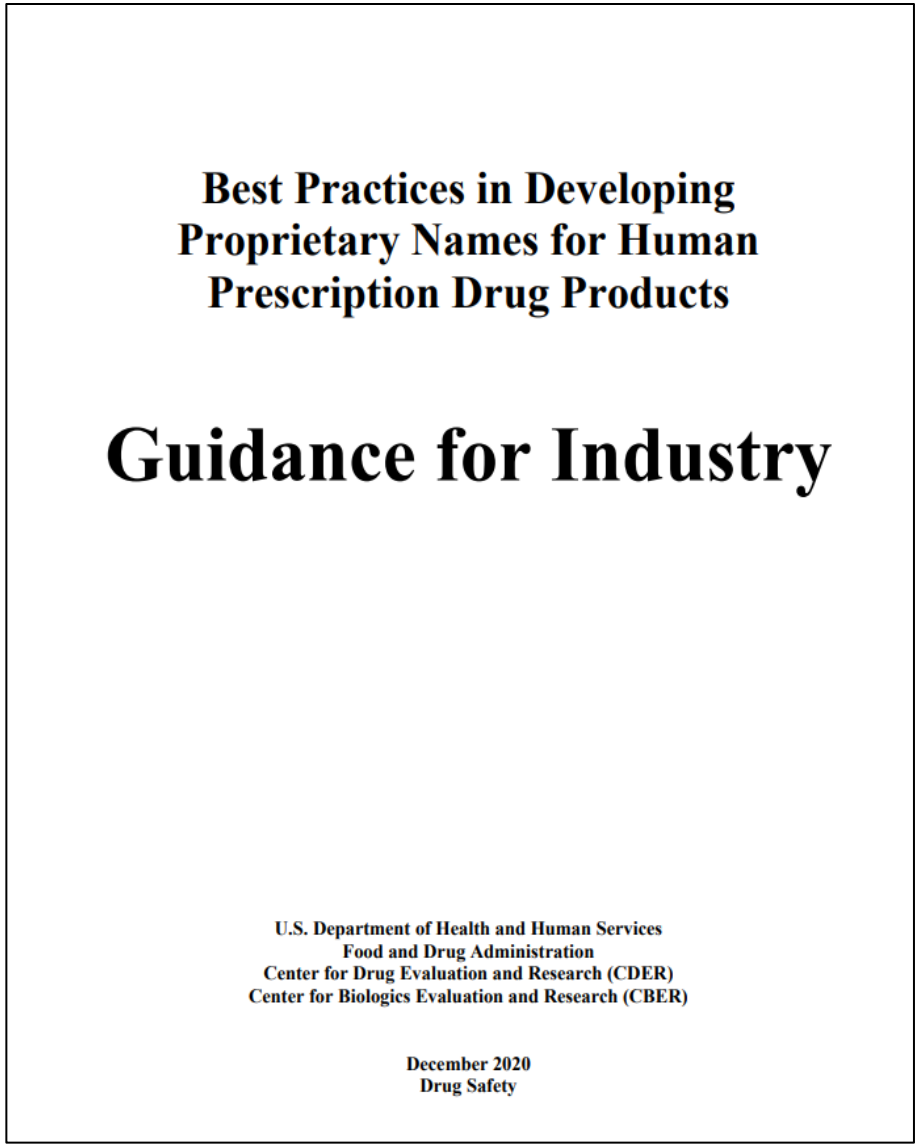
The labels[1] and the labeling state the following information:

- Name of the product
  - In the case of a liquid, the quantity or proportion of each active moiety or drug substance in a specified volume
  - In the case of any product to which a diluent must be added before use, the quantity or proportion of each active moiety or drug substance, name and volume of diluent to be added, the concentration after the diluent is added, directions for proper storage of the constituted solution, and a BUD (see *Expiration Date and Beyond-Use Date*)
- Route(s) of administration

[1] If there are space limitations, see 21 CFR§ 201.10(i), 21 CFR§ 201.105(b), 21 CFR§ 610.60.

C234255-M4908-NL2015, rev. 00 20190830

FDA Guidance

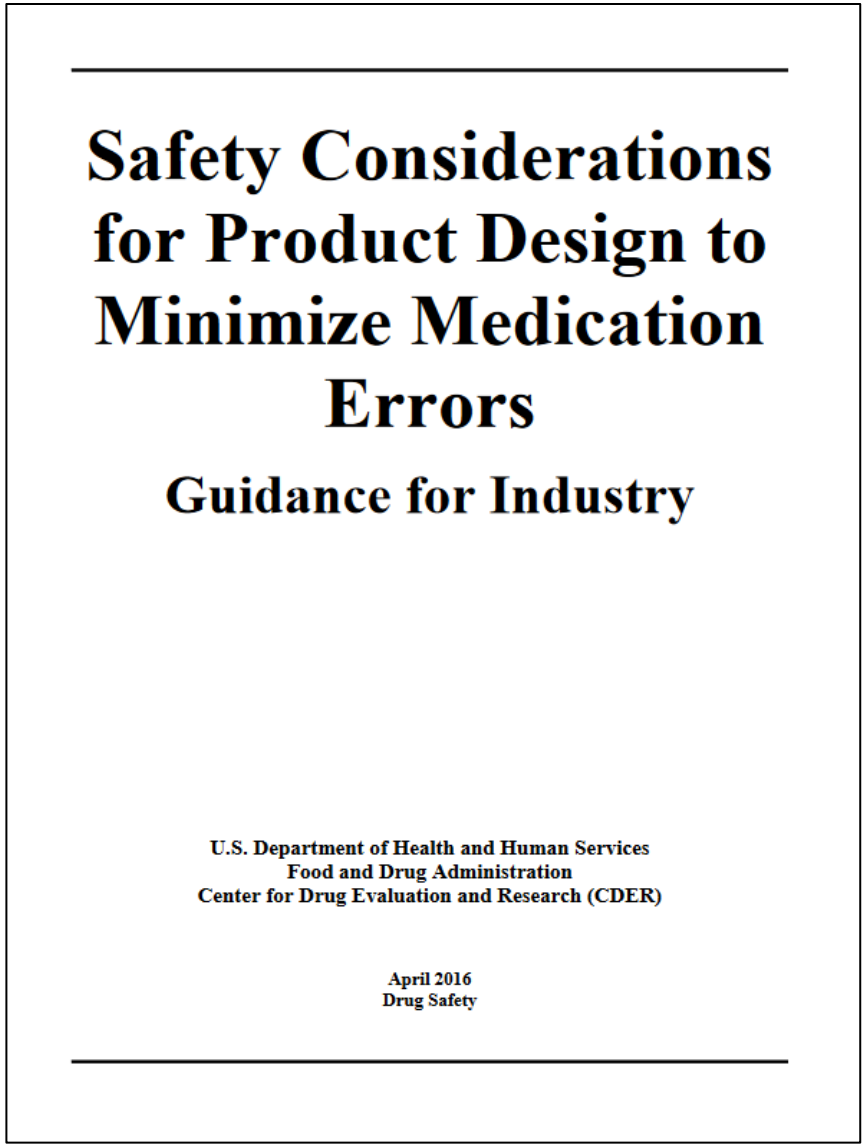


Best Practices in Developing Proprietary Names for Human Prescription Drug Products

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2020
Drug Safety



Safety Considerations for Product Design to Minimize Medication Errors

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2016
Drug Safety

Public Health Advisories

the New Year and our continued service to you as we work together to protect patients from medication errors.

Your Reports at Work

FDA Public Health Advisory.

Thanks to your reports, FDA published a Public Health Advisory late Wednesday to warn US citizens traveling abroad or buying prescription drugs via the Internet about risks when obtaining medications from foreign sources (www.fda.gov/oc/opacom/reports/confusingnames.html). The advisory noted that some FDA-approved products have the same brand names as foreign drug products with completely different ingredients. They also found that 105 US brand names are dangerously close to foreign brand names used for different products; patients who fill prescriptions abroad may get the wrong drugs. FDA noted that the advisory builds on recognition of the problem as published in our January 13, 2005 newsletter. The advisory was accompanied by tables to identify the involved products. continued on page 2 ▶

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FDA drug safety communications

FDA Drug Safety Communications for Drug Products Associated with Medication Errors

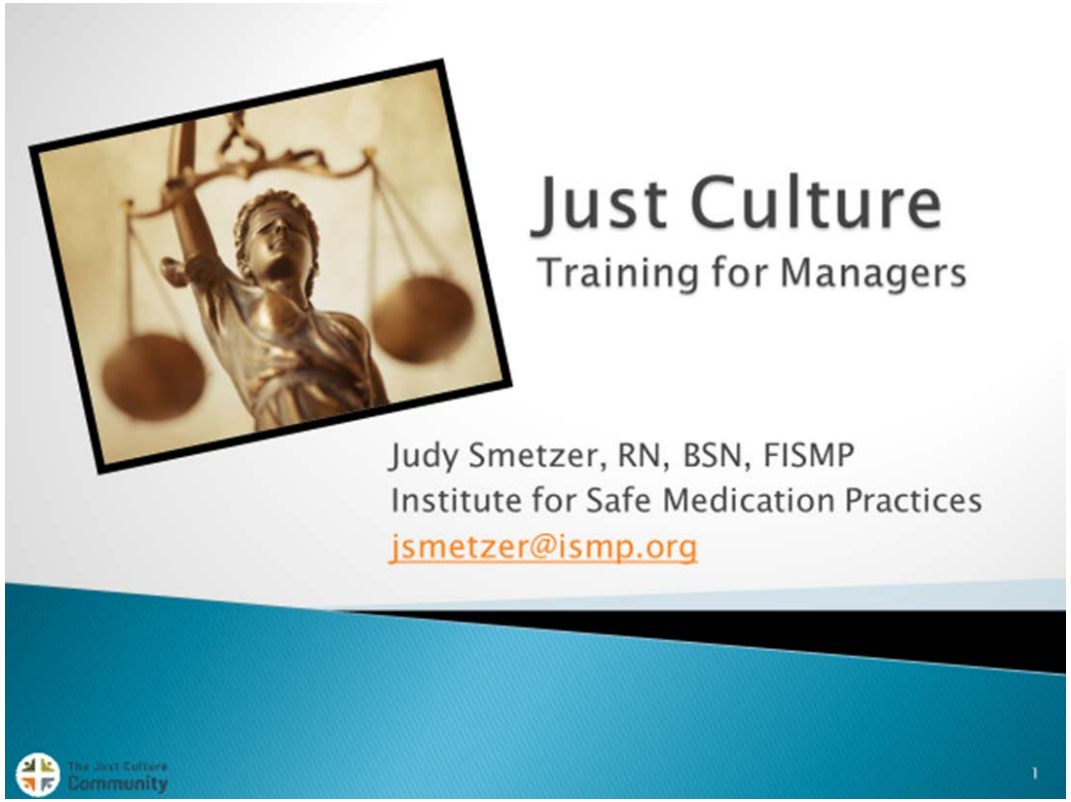
- FDA Drug Safety Communication: FDA approves brand name change for antidepressant drug Brintellix (vortioxetine) to avoid confusion with antiplatelet drug Brilinta (ticagrelor)
- FDA Drug Safety Communication: FDA cautions about dosing errors when switching between different oral formulations of antifungal Noxafil (posaconazole); label changes approved
- FDA Drug Safety Communication: FDA cautions about dose confusion and medication error with antibacterial drug Avycaz (ceftazidime and avibactam)
- FDA Drug Safety Communication: FDA cautions about dose confusion and medication errors for antibacterial drug Zerbaxa (ceftolozane and tazobactam)
- FDA Drug Safety Communication: FDA Alerts Pharmacists and Health Care Professionals to Potential for Injury when Dispensing the Similar-Sounding Drugs Durezol and Durasal
- FDA Drug Safety Communication: FDA requires label warnings to prohibit sharing of multi-dose diabetes pen devices among patients
- FDA Drug Safety Communication: FDA requiring color changes to Duragesic (fentanyl) pain patches to aid safetyâemphasizing that accidental exposure to used patches can cause death
- FDA Drug Safety Communication: FDA warns about potential medication errors resulting from confusion regarding nonproprietary name for breast cancer drug Kadcyla (ado-trastuzumab emtansine)

FDA Advise-ERR in ISMP Medication Safety Alert! publications and FDA website

ISMP FDA Advise-ERR Articles

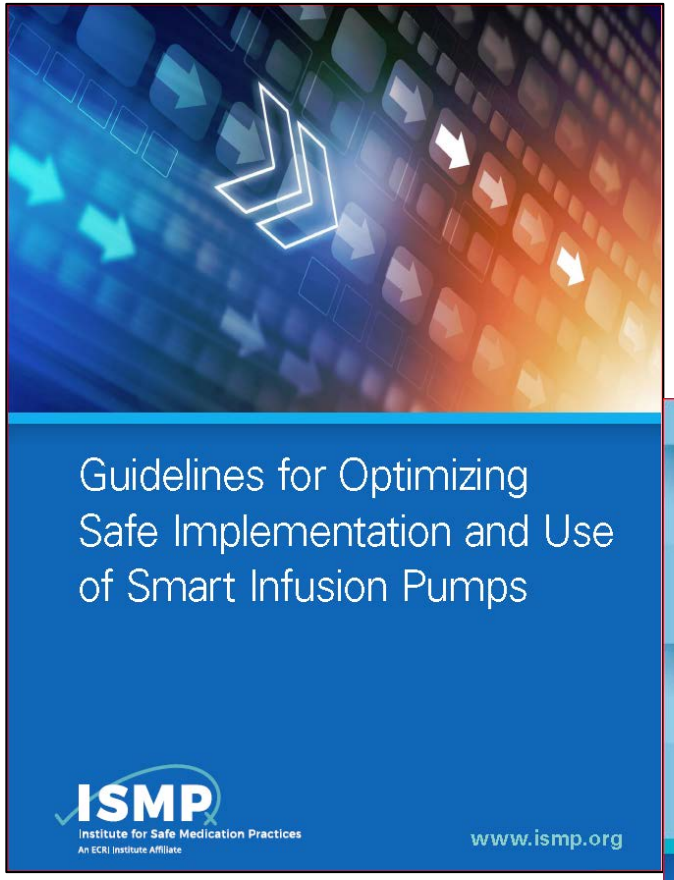
- FDA Advise-ERR: Taking Crysvita with active vitamin D analogs is contraindicated
- FDA Advise-ERR: Covers still being applied without the cloNIDine patch
- FDA Advise-ERR: Lumoxiti has unique preparation instructions!
- FDA Advise-ERR: Vyxeos: Verify Drug Name and Dose to Avoid Errors!
- FDA Advise-ERR: Concomitant use of Entresto and ACE inhibitors can lead to serious outcomes
- FDA Advise-ERR: Veterinary Drug and Human Drug â A Drug Name Mix-up
- FDA Advise-ERR: Avoid using the error-prone abbreviation, TPA
- FDA Advise-ERR: MefloquineâNot the same as Malarone!

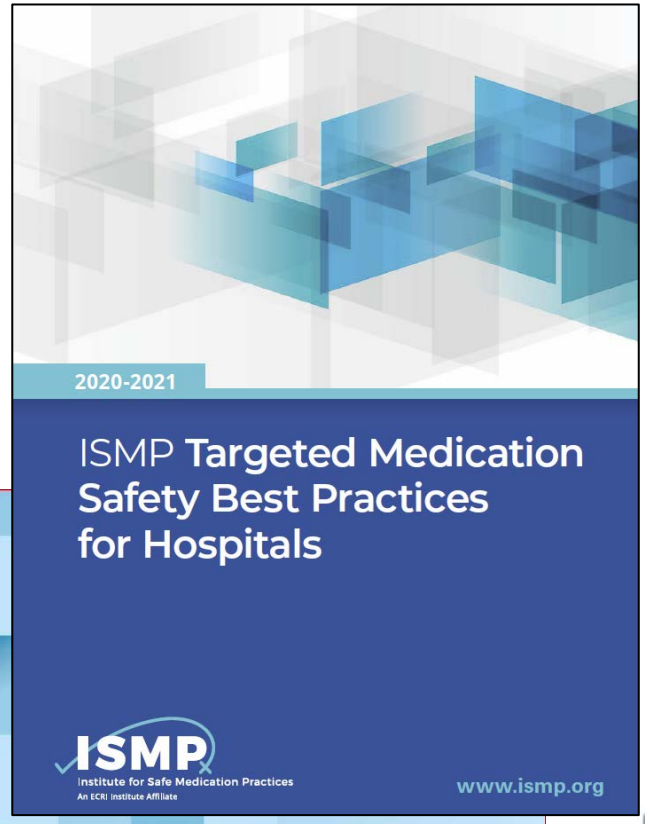
ISMP educational programs

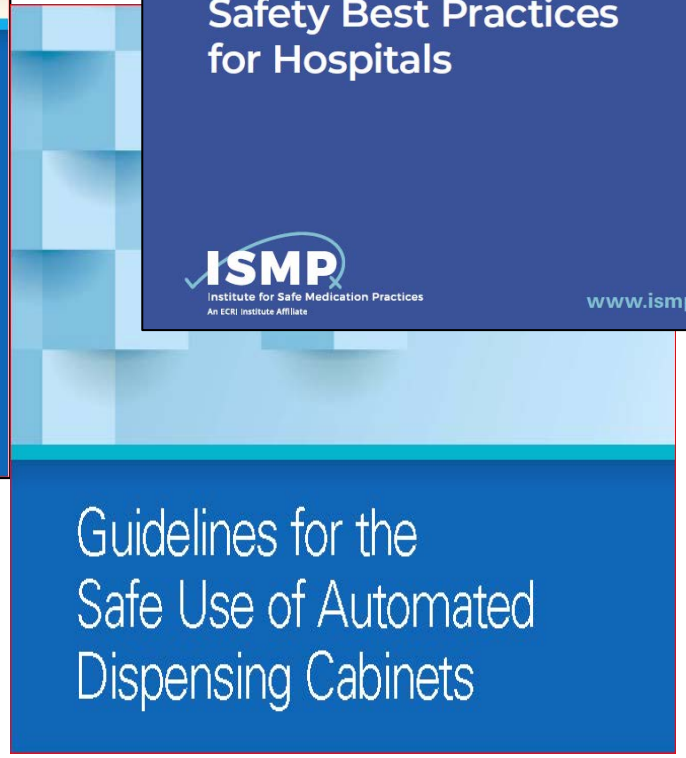


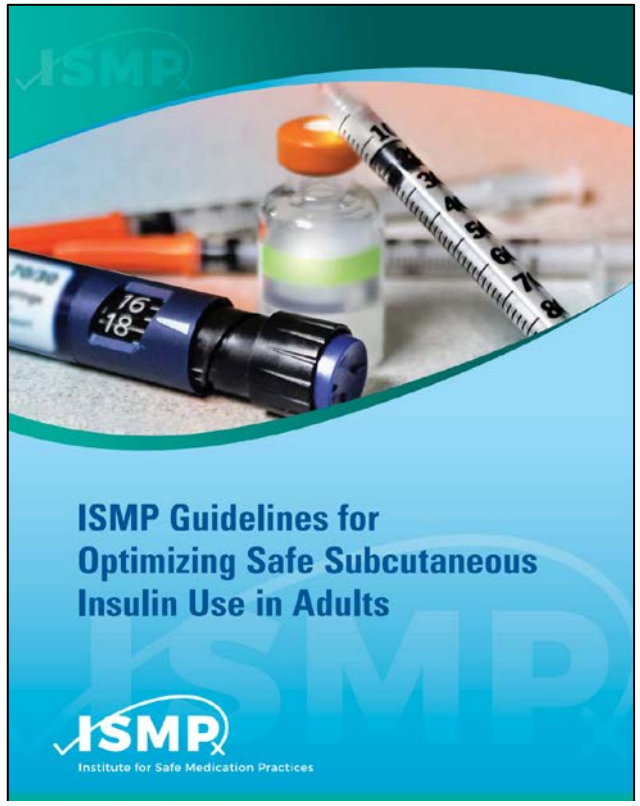
Safety Tools/Lists

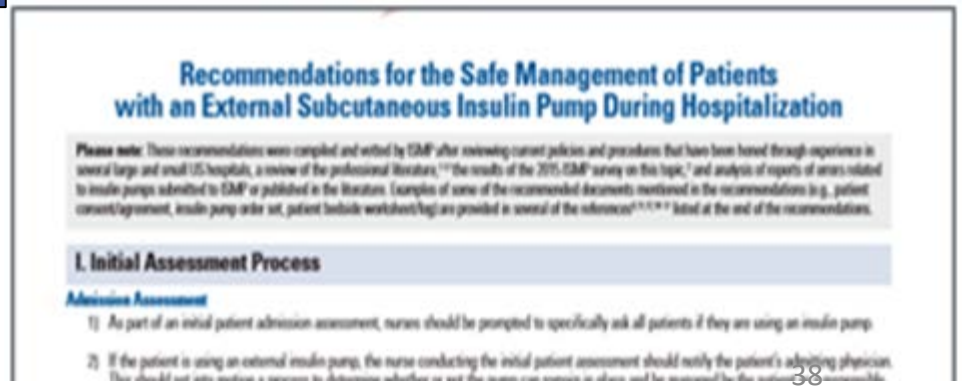
ISMP Practice Guidelines









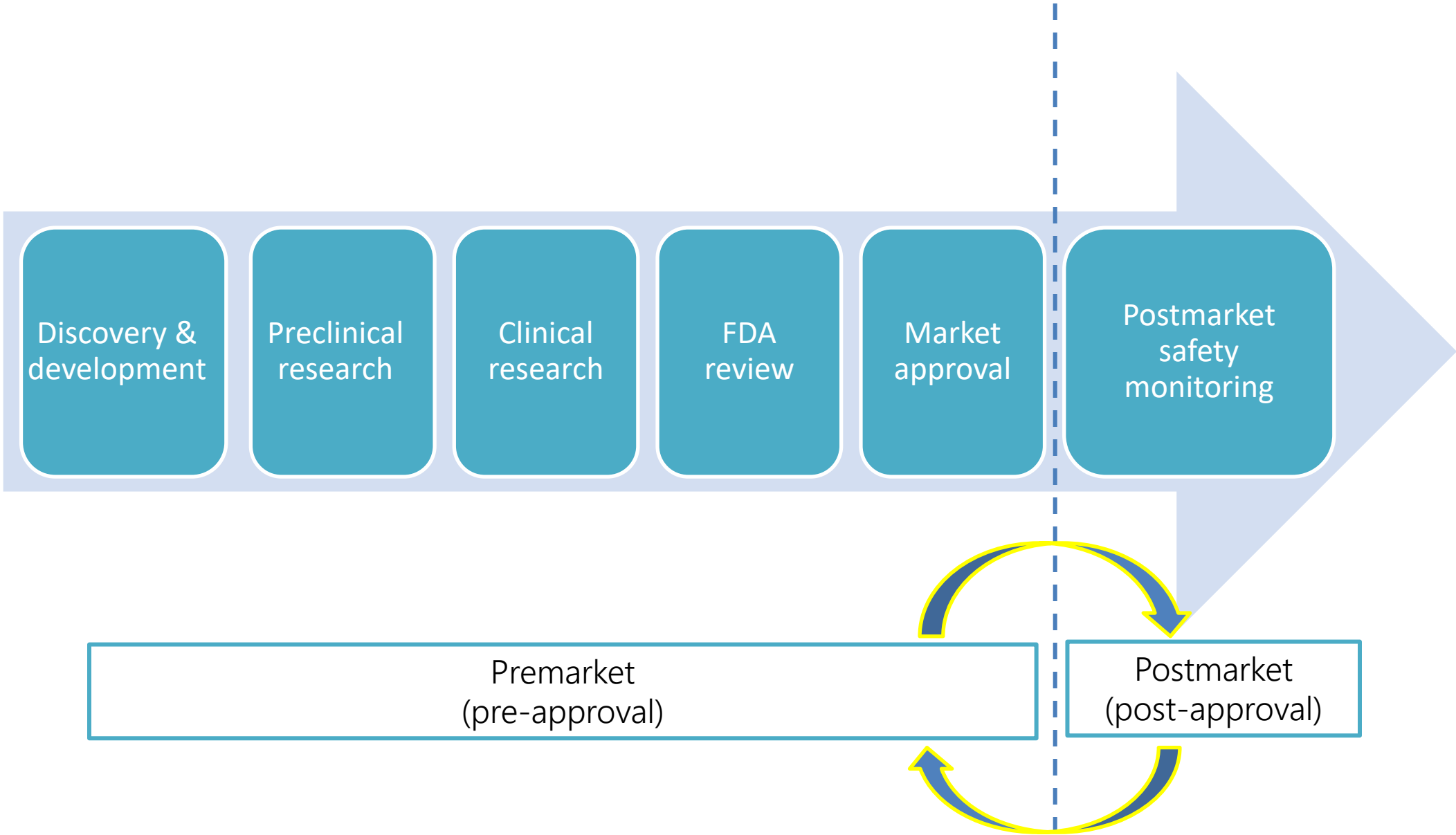

Recommendations for the Safe Management of Patients with an External Subcutaneous Insulin Pump During Hospitalization

I. Initial Assessment Process

OSE's Premarket and Postmarket Activities in Preventing Medication Errors

Valerie S. Vaughan, PharmD
LCDR, U.S. Public Health Service
Team Leader, FDA, CDER, OSE, OMEPRM, Division of Medication Error Prevention and Analysis I (DMEPA I)

Medication Errors and Product Life Cycle



Definition: Medication Error

- "A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer"
  - National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP)

- Intentional or deliberate uses (e.g., abuse, misuse, off label use) are generally not considered medication errors

FDA Medication Errors Related to CDER-Regulated Drug Products: https://www.fda.gov/drugs/drug-safety-and-availability/medication-errors-related-cder-regulated-drug-products

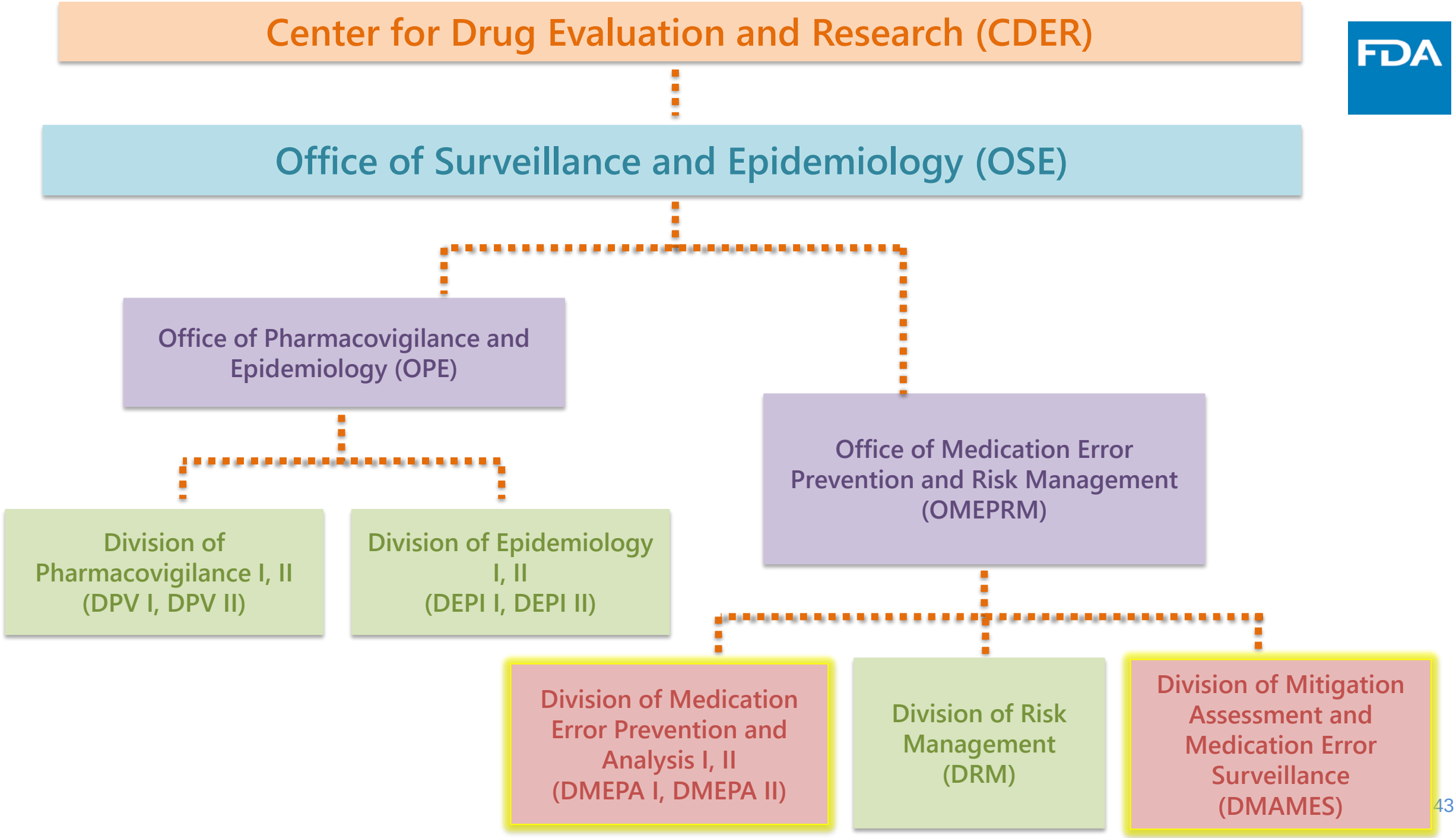
Medication Errors are a Global Public Health Burden

FDA

$21 BILLION	Estimated annual cost of U.S. outpatient and inpatient preventable medication errors
52%	Among adult outpatients…**52% (95% CI: 42–62%)** of adverse drug reactions were **preventable**
45%	Among inpatients…**45% (95% CI: 33–58%)** of adverse drug reactions were **preventable [errors]**

Network for Excellence in Health Innovation. Dec 2011. Available from: http://www.nehi.net/bendthecurve/sup/documents/Medication_Errors_%20Brief.pdf

Hakkarainen KM, et. al., Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions – a meta-analysis. PLoS One. 2012.


Center for Drug Evaluation and Research (CDER)
Office of Surveillance and Epidemiology (OSE)
Office of Pharmacovigilance and Epidemiology (OPE)
Division of Pharmacovigilance I, II (DPV I, DPV II)
Division of Epidemiology I, II (DEPI I, DEPI II)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Division of Medication Error Prevention and Analysis I, II (DMEPA I, DMEPA II)
Division of Risk Management (DRM)
Division of Mitigation Assessment and Medication Error Surveillance (DMAMES)

Overview of OSE's Medication Error Prevention and Surveillance

Division of Medication Error Prevention and Analysis I and II (DMEPA I and DMEPA II)

- CDER Lead for **premarket** medication error prevention and analysis for drug and therapeutic biological products

Division of Mitigation Assessment and Medication Error Surveillance (DMAMES)

- CDER lead for medication error pharmacovigilance, including signal management
- Postmarket research and innovation

Both DMEPA and DMAMES consist of scientists and healthcare professionals with varied backgrounds

WHAT DOES DMEPA DO?

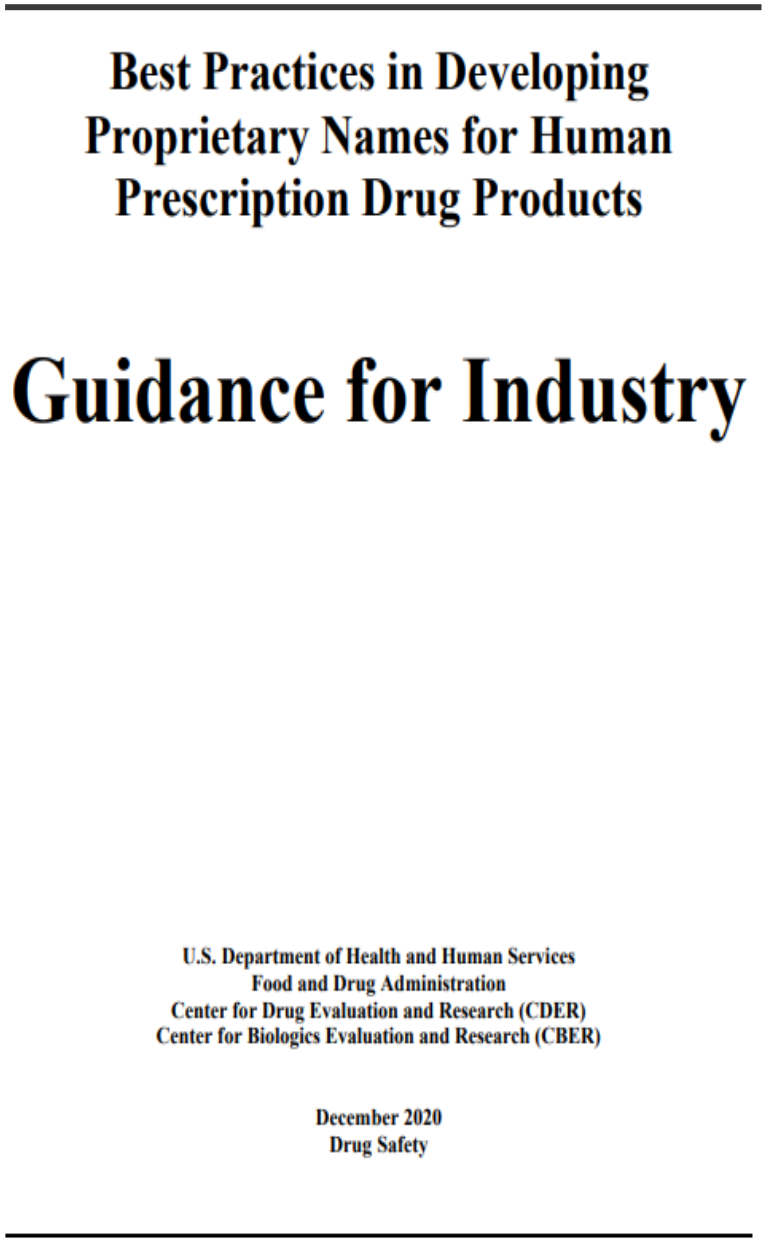
DMEPA Review Activities

Reviews take into account current federal regulations, applicable Guidance for Industry, USP Standards, and relevant postmarket experience.

- **PROPRIETARY NAMES**
  Primary/signatory authority on review of proprietary names.
- **NONPROPRIETARY NAME SUFFIX**
- **PRODUCT LABELING**
- **PRODUCT PACKAGING**
- **HUMAN FACTORS/ PRODUCT DESIGN**
  Primary/signatory authority on human factors protocols.
- **POSTMARKET PHARMACOVIGILANCE** (DMAMES)

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020


Best Practices in Developing Proprietary Names for Human Prescription Drug Products

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2020
Drug Safety

FDA

Safety assessment of proposed proprietary name for risk of drug name confusion that may lead to medication errors.

Considerations:

- **spelling** of the name
- **pronunciation** of the name when spoken
- **appearance** of the name when scripted throughout the medication use system

Look-Alike Sound-Alike Safety Assessment

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Institute for Safe Medication Practices. Durasal-Durezol mix-up illustrates how dangerous product problems persist long after recognition. ISMP Med Saf Alert Acute Care. 2011;16(19):1-3.

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Proprietary Name Review

OPDP* — Conducts **misbranding** assessment of the proposed proprietary name

*For OTC products, the misbranding review is conducted by the Office of Nonprescription Drugs (ONPD)

OND — Provides **misbranding** and **safety** concerns with the proposed proprietary name based on clinical, chemistry, and/or pharmacology data that may impact acceptability

DMEPA — Conducts **safety** assessment of the proposed proprietary name for risk of drug name confusion that may lead to medication errors.

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Proprietary Name Review
Misbranding Assessment

DMEPA will object to a proposed name if it may misbrand the product for the following reasons:

- The proprietary name suggests that the drug is safer or more effective than has been demonstrated by scientific evidence.
- The proprietary name is "fanciful" and suggests that it has some unique effectiveness or composition when it does not. (21 CFR 201.10(c)(3)).

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Proprietary Name Review
Safety Assessment

Focus: Prevent medication errors due to drug name confusion

21 CFR 201.10 (c.) The labeling of a drug may be **misleading** by reason (among other reasons) of:
(5) Designation of a drug or ingredient by a proprietary name that, because of ***similarity in spelling or pronunciation***, may be confused with the proprietary name or the established name of a different drug or ingredient.

Draft Guidance: Best Practices in Developing Proprietary Names for Drugs
http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm398997.pdf

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Proprietary Name Review
Safety Assessment

- Preliminary safety assessment:
  - United States Adopted Names (USAN) stems
  - other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors
- Similarity in printing, writing, and speech
- FDA Prescription Simulation Studies
  - handwritten prescriptions
  - verbal pronunciation of the drug name
  - computerized provider order entry
- Similarity of names by using FDA's Phonetic and Orthographic Computer Analysis (POCA) program and assessment of POCA scores

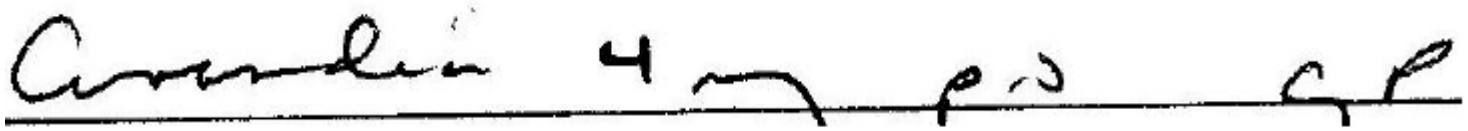
Phonetic and Orthographic Computer Analysis (POCA) Program. http://www.fda.gov/Drugs/ResourcesForYou/Industry/ucm400127.htm

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Proprietary Name Review
Safety Assessment

Role of product characteristics in proprietary name review



Coumadin 4 mg or Avandia 4 mg?

- Indications
- Strength
- Dose
- Dosage form
- Unit of measure, typical quantity or volume
- Route of administration
- Frequency of administration
- Instructions for Use
- Patient population
- Prescriber population
- Product Packaging
- Physical attributes
- Storage conditions
- Setting of use

BEST PRACTICES IN DEVELOPING **PROPRIETARY NAMES** FOR DRUGS.

GUIDANCE FOR INDUSTRY
DECEMBER 2020

Proprietary Name Review
Safety Assessment

FDA

Considerations for Computerized Provider Order Entry

"Starts with"
Provides choices after typing only a few letters

"Contains"
Provides all options that contain what was typed

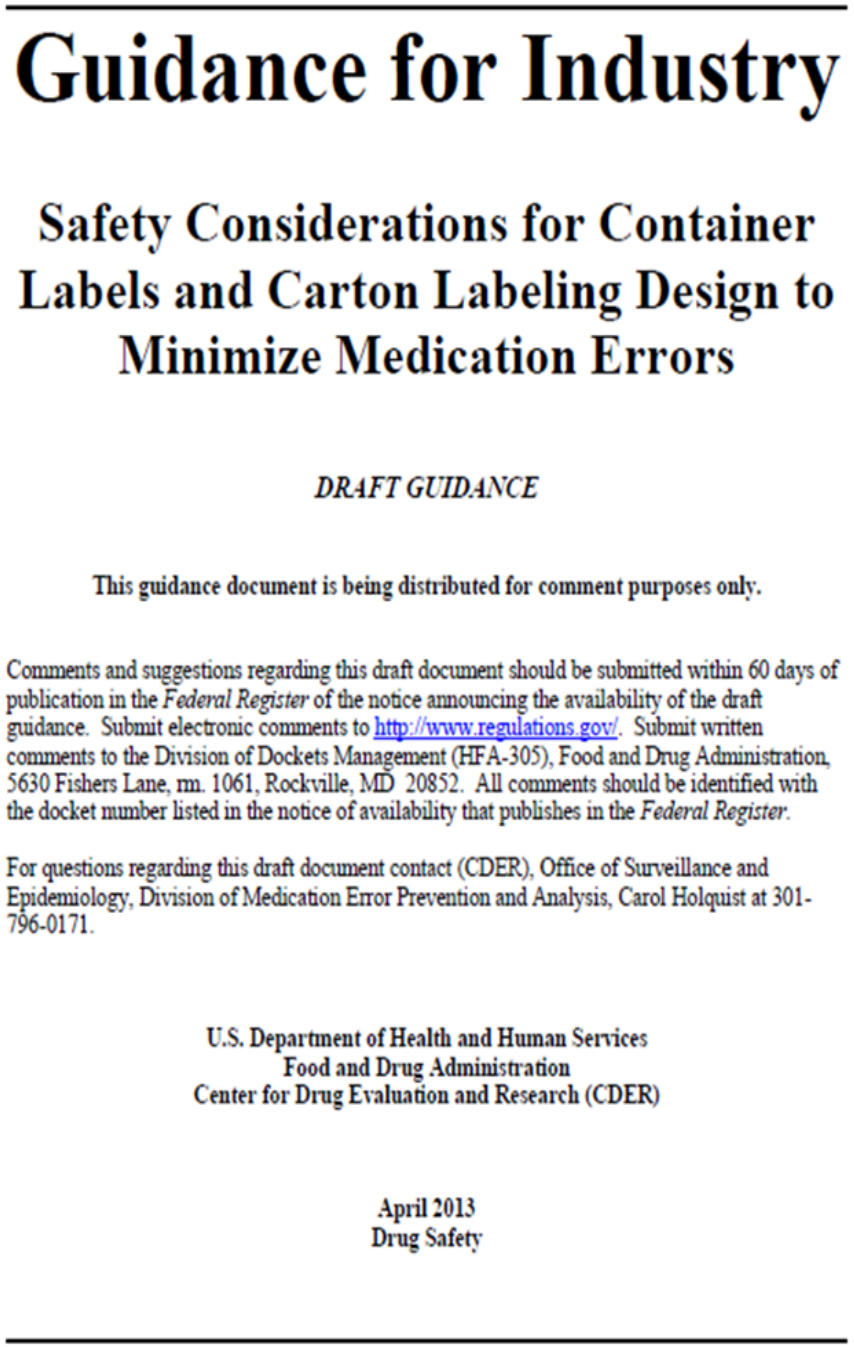
Brintellix
Brilinta

Ranexa
Tranexamic acid

Brintellix name changed to Trintellix in May 2016 http://www.fda.gov/Drugs/DrugSafety/ucm497942.htm

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013



Guidance for Industry

Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov/. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER), Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis, Carol Holquist at 301-796-0171.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

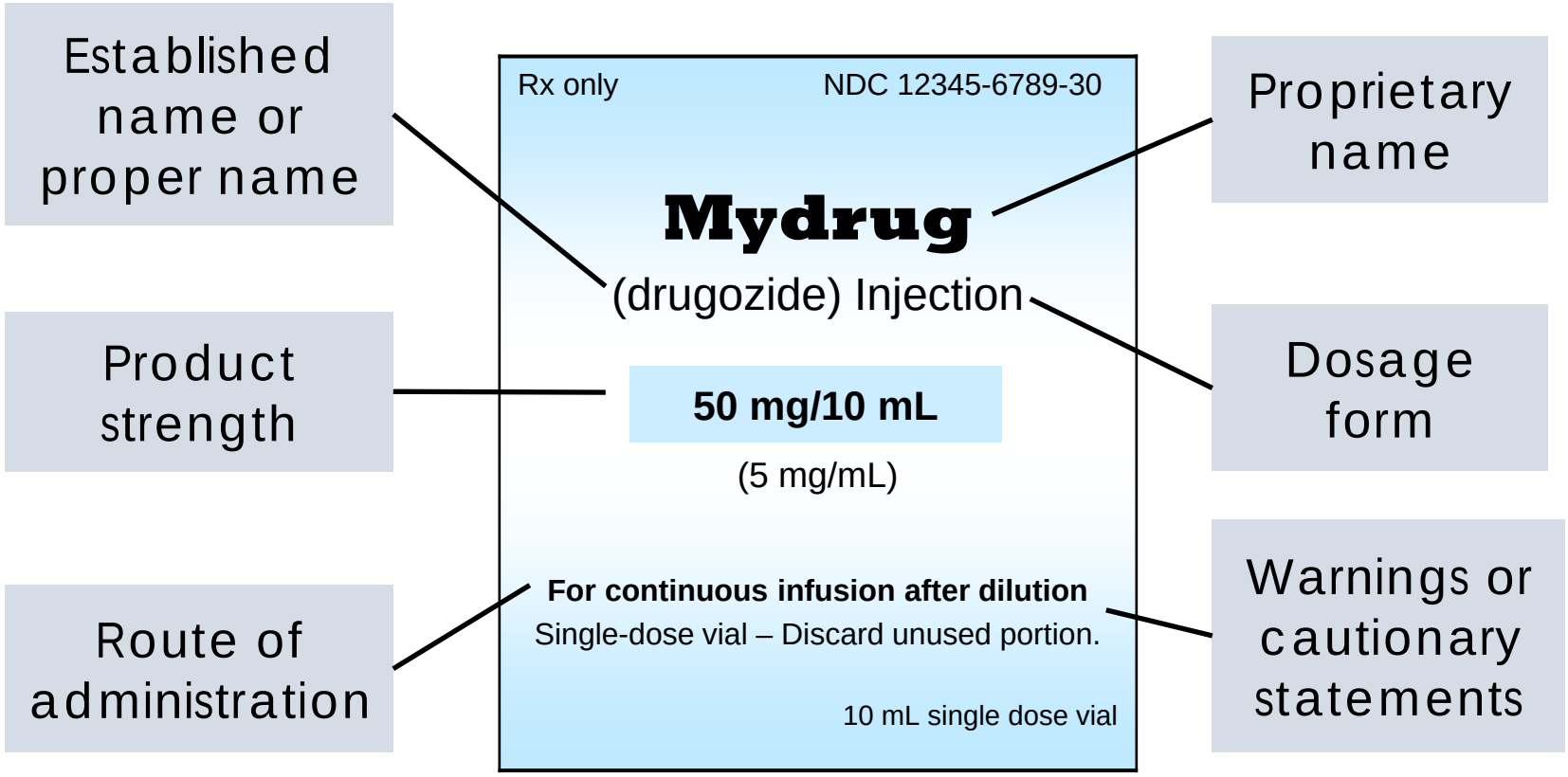
April 2013
Drug Safety

Product container labels and carton labeling should communicate information that is critical to the safe use of a medication throughout the medication use system.

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Critical product information should appear the most prominent on the Principal Display Panel (PDP)

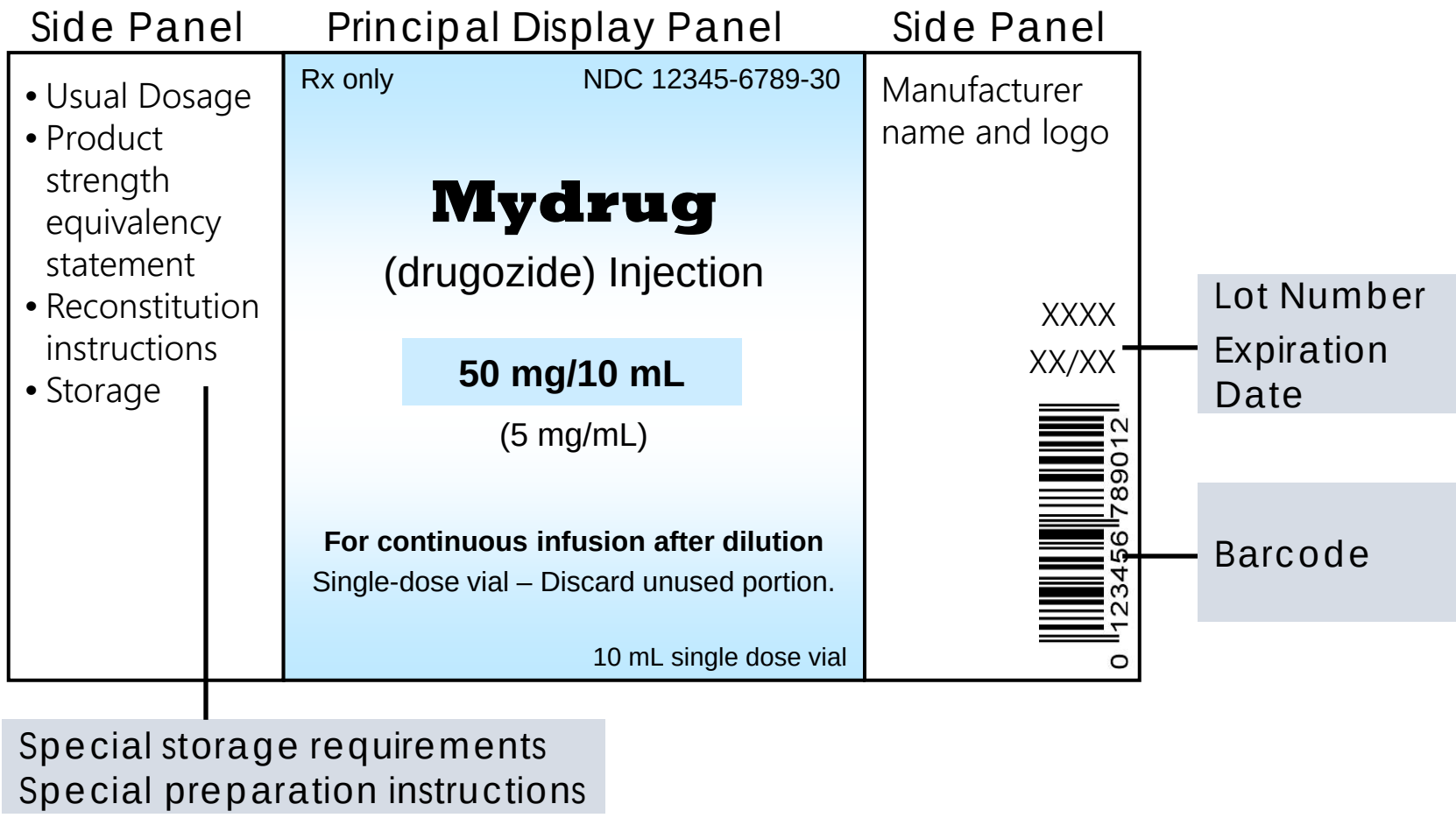


The Principal Display Panel is the portion of the container label or carton labeling that is most likely to be displayed, presented, shown, or examined by the user when the product is on a shelf

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Product information on side and back panels



Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Text Size, Font *Style*, and Color on the Principal Display Panel

- Use at least a 12-point sans-serif font (e.g., Arial)
- Choose text and background color to afford adequate legibility of text
- Avoid color combinations that do not afford maximum legibility of text

Proprietary Name
(Established name)

Proprietary Name
(Established name)

Proprietary Name
(Established name)

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Avoid Crowding, Visual Clutter, Dangerous Abbreviations, and Acronyms

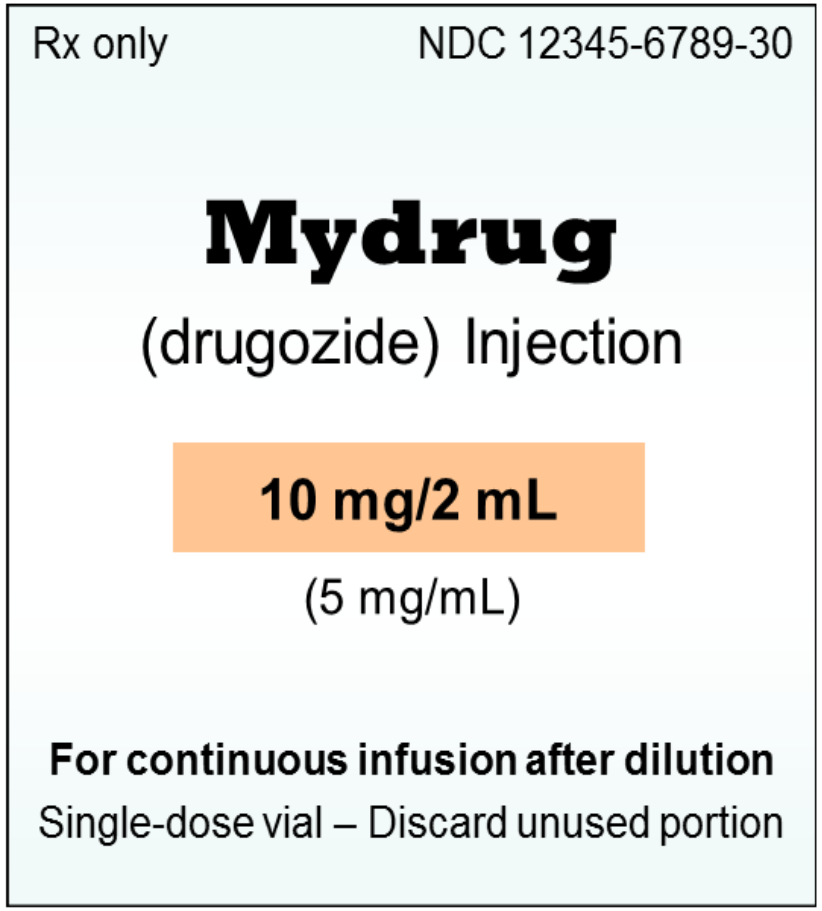
- Crowded labels/labeling may make important information difficult to read and/or easily overlooked
- Safety considerations:
  - Separate lines or blocks of text with sufficient blank space
  - Place non-critical information on side/back panels
  - Refer to ISMP's "List of Error Prone Abbreviations, Symbols, and Dose Designations"
  - Don't superimpose text over images or logos

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Product Name

- The proprietary and established or proper name should be the most prominent information on the label
- The established name should be at least ½ the size of the proprietary name
- The established name should include the dosage form

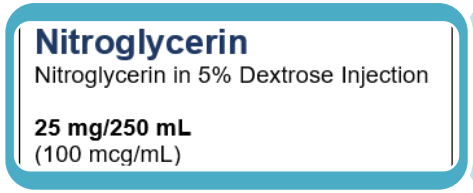


SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

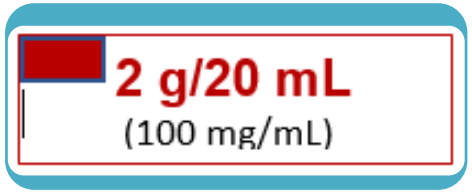
DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Product Strength Expression

Use metric units of measure (e.g., mg, mcg, mL)

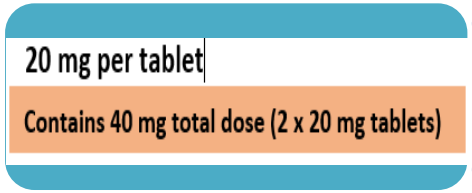


The strength should match the units of measure in the Dosage and Administration section of the Prescribing Information



Small volume parenteral products: Express strength as the quantity per total volume followed in close proximity by quantity per milliliter enclosed by parentheses

Dry powder parenteral products: Express strength as the amount per container



Blister packs: Express strength per unit; may also display the dose in certain instances

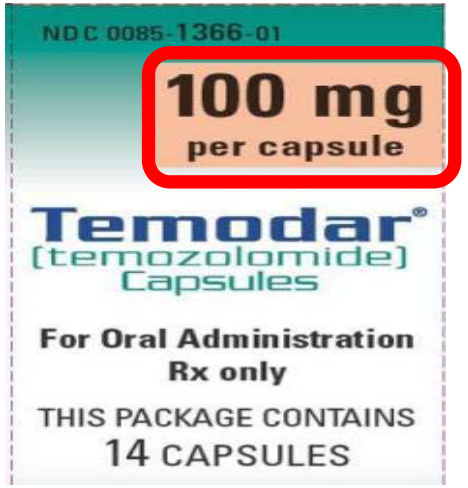
SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Product Strength and Net Quantity Statements

Note the placement of strength and net quantity

Note prominence of strength



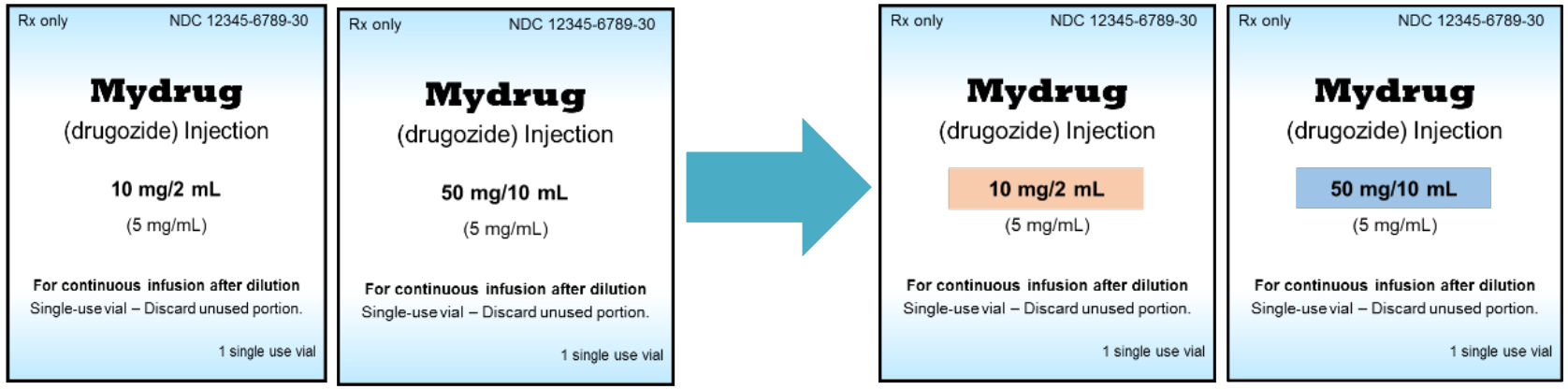
Product Strength Differentiation

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Ensure the product strength stands out on the container label and carton labeling

Techniques include:
- Boxing
- **Prominent** typeface or type weight
- Color differentiation



SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Route of Administration

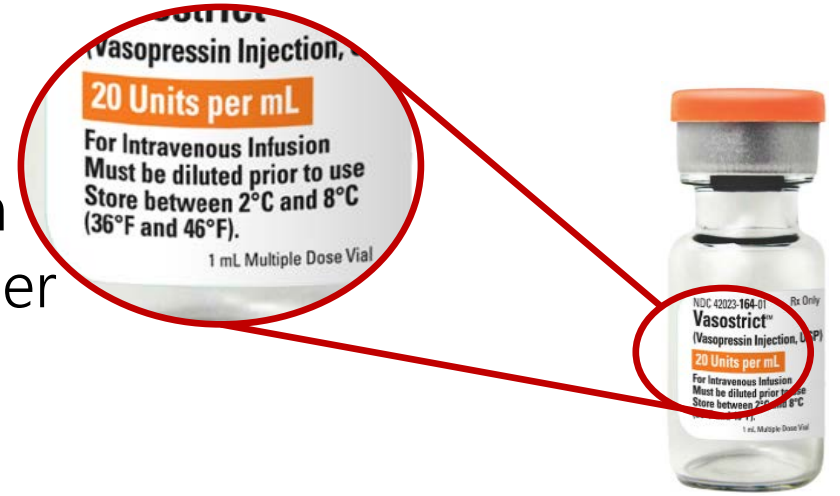
- Must be present on the PDP for non-oral products per 21 CFR 201.100 (b)(3)
- Avoid abbreviations
- Use affirmative statements (e.g., use "for irrigation" instead of "not for injection") because "not" can be obscured or overlooked

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Warnings for Critical Information

- Use affirmative statements
  - For intravenous infusion
  - Fatal if given by any other route
  - Must dilute before use



- Consider whether the statement is helpful to ensure safe use

Patient: Took 1 mg orally once daily.

Patient stated she was following directions on the bottle

Institute for Safe Medication Practices. Safety Briefs: Positive change, negative consequence. ISMP Med Saf Alert Acute Care. July 2014;19(15):1.

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Use of Color:
Color Differentiation vs. Color Coding

- **Color differentiation** is an effective tool that can:
  - —Differentiate products within a manufacturer's product line
  - —Differentiate strengths within a manufacturer's product line
  - —Highlight certain aspects of the label, such as important warning statements
- Most effective when the color used has no association with a particular feature and there is no pattern in application of the color scheme

- **Color coding** uses color to designate a specific meaning
- FDA generally recommends avoiding color coding in most instances (identifying products by color may discourage reading labels)
  - — Reserved for special circumstances after human factors testing and feedback on the prototype from all end users is received and evaluated by FDA prior to use

SAFETY CONSIDERATIONS FOR **CONTAINER LABELS and CARTON LABELING** TO MINIMIZE MEDICATION ERRORS.

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Use of Color: Color Coding

Certain applications of color coding may be appropriate

- Certain drug product strengths (e.g., warfarin, levothyroxine) are universally color coded across all manufacturers

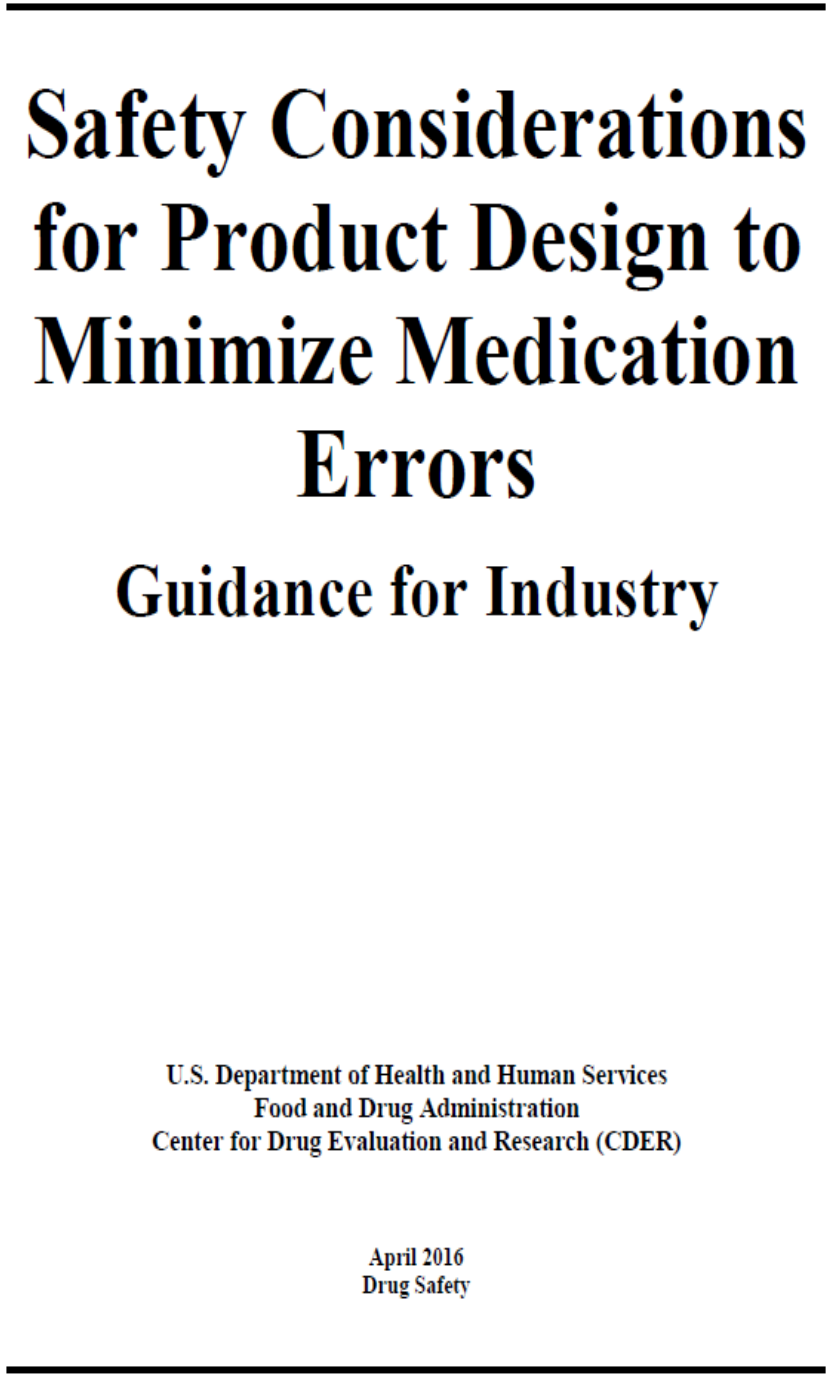
- In other cases, color coding can lead to confusion

Different strengths

Different products

SAFETY CONSIDERATIONS FOR PRODUCT DESIGN TO MINIMIZE MEDICATION ERRORS.

GUIDANCE FOR INDUSTRY
APRIL 2016



Safety Considerations for Product Design to Minimize Medication Errors

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2016
Drug Safety

FDA EXPECTS MANUFACTURERS TO:

1. Investigate, understand and correctly identified risks

   Use analytical methods to develop drug products

2. Build safety into the product design

   Apply these methods **early** in drug development and throughout the drug product's life cycle

3. Enable safe and correct use

   Eliminate or reduce design elements that can cause use-related hazards

SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

GUIDANCE FOR INDUSTRY
APRIL 2016

Drug product user interface

refers to **all parts of a product a user interacts (e.g., sees and touches)**

SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

GUIDANCE FOR INDUSTRY
APRIL 2016

Most effective strategies focus on improvements to design of drug product user interface.

- Consider **effect of each design choice** on end user
- Evaluate using **proactive risk assessments** before finalizing design
- Evaluate **how and why** problems have occurred with similar products
  - Identify error prone features and eliminate them from design
  - Prevent same errors from occurring
- Sponsors should consider **lessons learned** to minimize risks associated with their designs

SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

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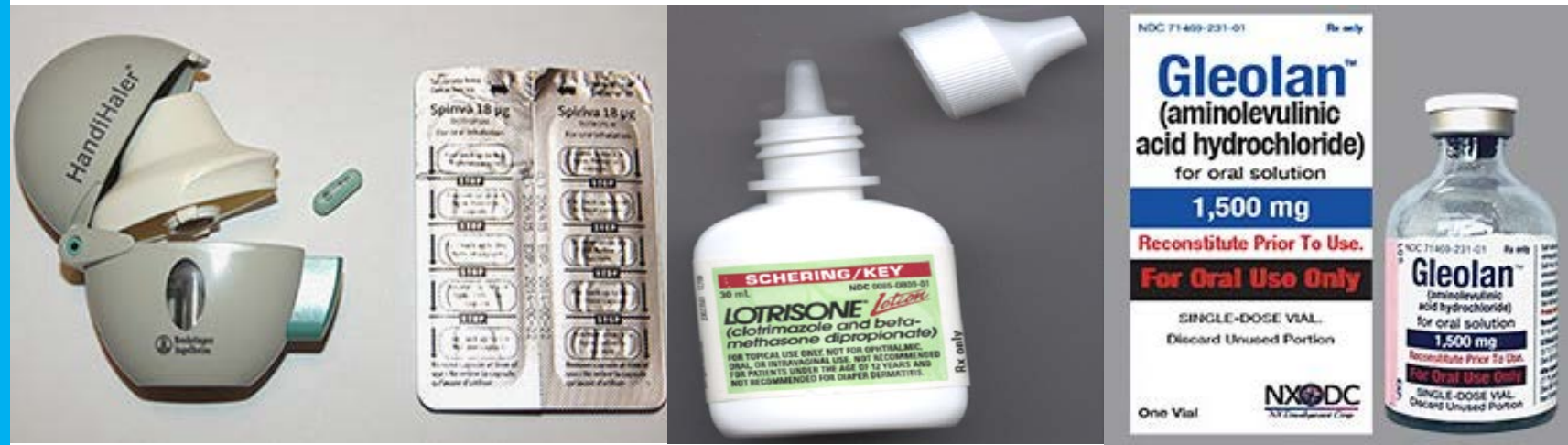
Container Closure Design

- Is the container closure design:
  - safe for the route of administration?
  - appropriate for the intended users?

- Avoid use of a container closure that implies a route of administration other than the route intended, unless there are no other options available



SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

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Product Strength

- Review for inconsistency between drug product strength and dosing
  - Multiple units (e.g. tablets, capsules, vials, syringes) required to achieve a usual single dose?
- Dosing errors due to:
  - miscalculations
  - forgetting how much has already been administered

SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

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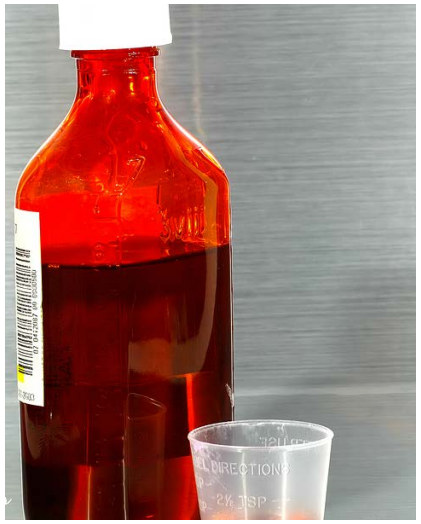
Product Strength



- Co-packaged dosage delivery device should be consistent with recommended dosing regimen/directions for use
- Printed matter appearing on dosage delivery device is considered labeling
  - Dose markings must be easy to read
- Dosing devices for oral solutions should use *metric unit markings*

SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

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Human Factors?

"…the application of knowledge about human capabilities (physical, sensory, emotional, and intellectual) and limitations to the design and development of tools, devices, systems, environments, and organizations…."

Human factors engineering – Design of medical devices. American National Standards Institute / Association for the Advancement of Medical Instrumentation (ANSI/AAMI) HE75:2009, Introduction. http://my.aami.org/aamiresources/previewfiles/HE75_1311_preview.pdf

SAFETY CONSIDERATIONS FOR **PRODUCT DESIGN** TO MINIMIZE MEDICATION ERRORS.

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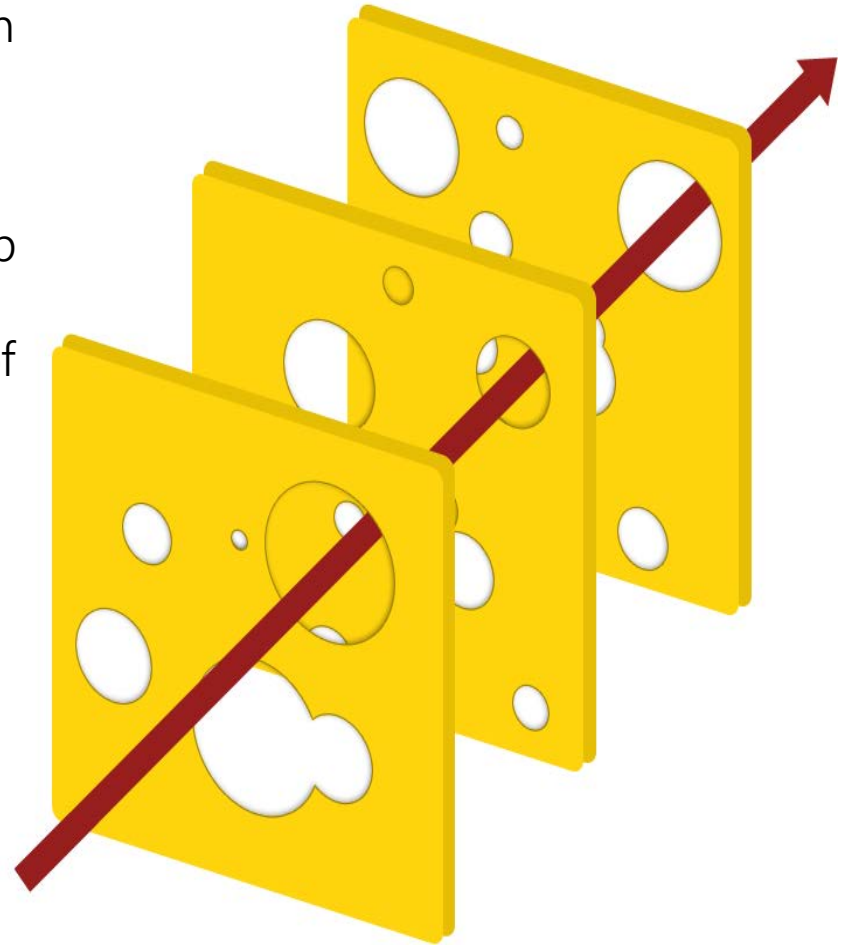
Failure Mode and Effects Analysis (FMEA)

- Analyze all steps involved in user interactions with the drug product in the anticipated use environments
- Identify potential use-related medication errors and system failures that could occur at each step of the medication use process
- Estimate probability of occurrence of identified potential medication errors and system failures
- Assess potential effects and severity of consequences of identified potential medication errors and system failures
- Identify mitigation strategies to address identified risks
- Evaluate success of mitigation strategies at reducing risk to acceptable level



Human Factors Considerations

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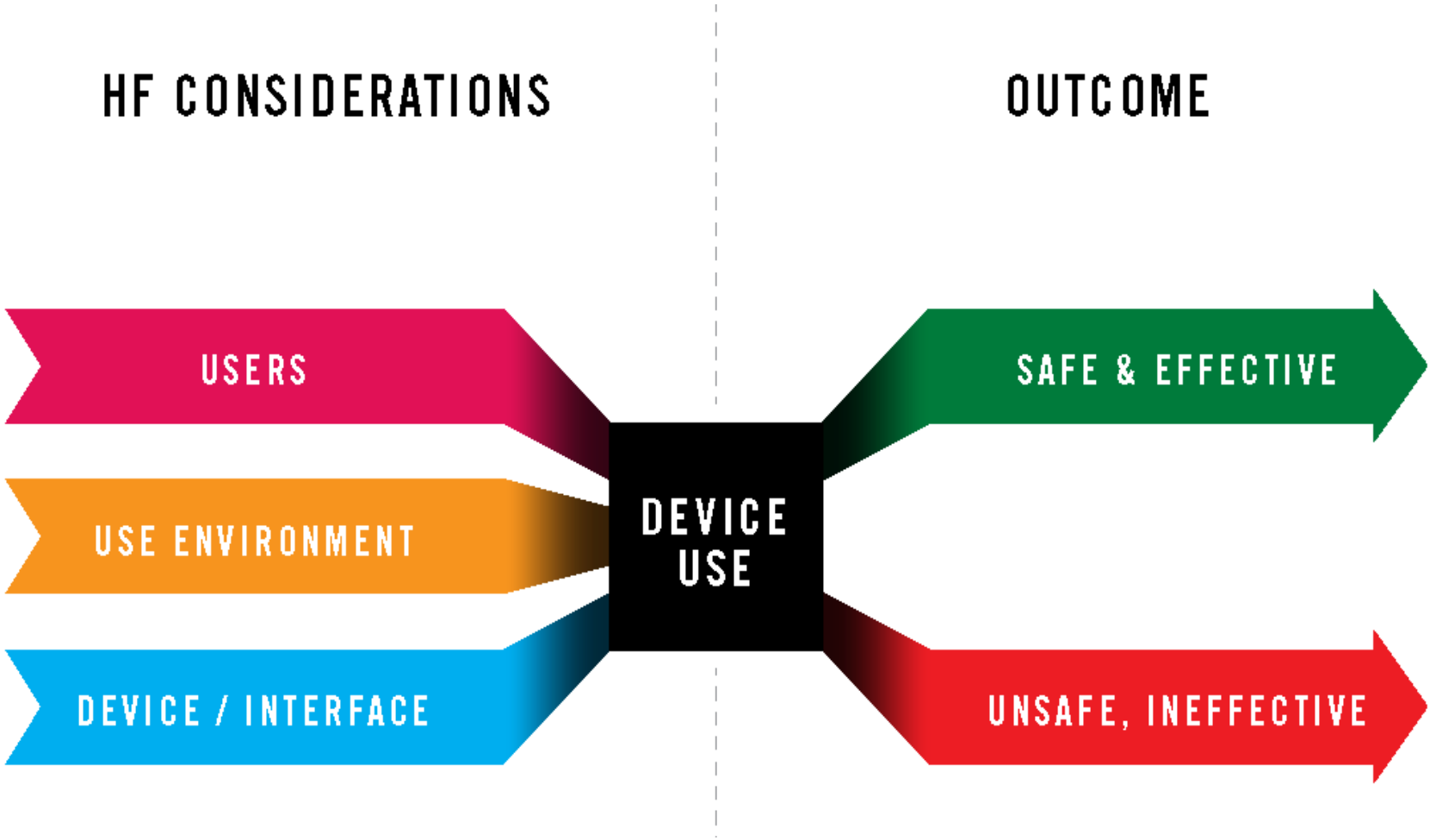

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Human Factors Validation Studies

- Systematic collection of data from representative participants in realistic situations
- Help determine whether users can safely and correctly perform critical tasks involved in using the product
- Seeks to assess actual use
- Results can be used to update the FMEA
- Should be conducted before product is submitted for approval, before any product modifications or additions to a product line
- Recommend that sponsors conduct human factors studies to characterize risks as well as develop mitigation strategies
  - Studies are generally small in size and short in duration (as compared to clinical studies that support drug approval)
  - Relatively small investment of resources early in product development can avoid the need to resolve issues post-approval

Postmarket Surveillance of Medication Errors

Why is postmarket surveillance necessary?

- Limitations of premarket clinical trials
  - Trials are conducted under controlled conditions, and may not use the final approved name, labels, labeling, and packaging
  - Numbers of patients tested is too small to detect serious but rare problems, and some errors may fall into this category
  - Trials are often of short duration
- FDA has a robust program to identify potential errors and address them prior to approval. However, medications errors remain a significant burden on public health*
- Allows us to monitor error reports and address the causes of errors that may be related to a drug's name, label, labeling, or packaging (before a product is widely distributed).

*Preventing Mediation Errors: A $21 Billion Opportunity. Network for Excellence in Health Innovation (NEHI); 2011. https://www.nehi.net/bendthecurve/sup/documents/Medication_Errors_%20Brief.pdf

Medication error case reports

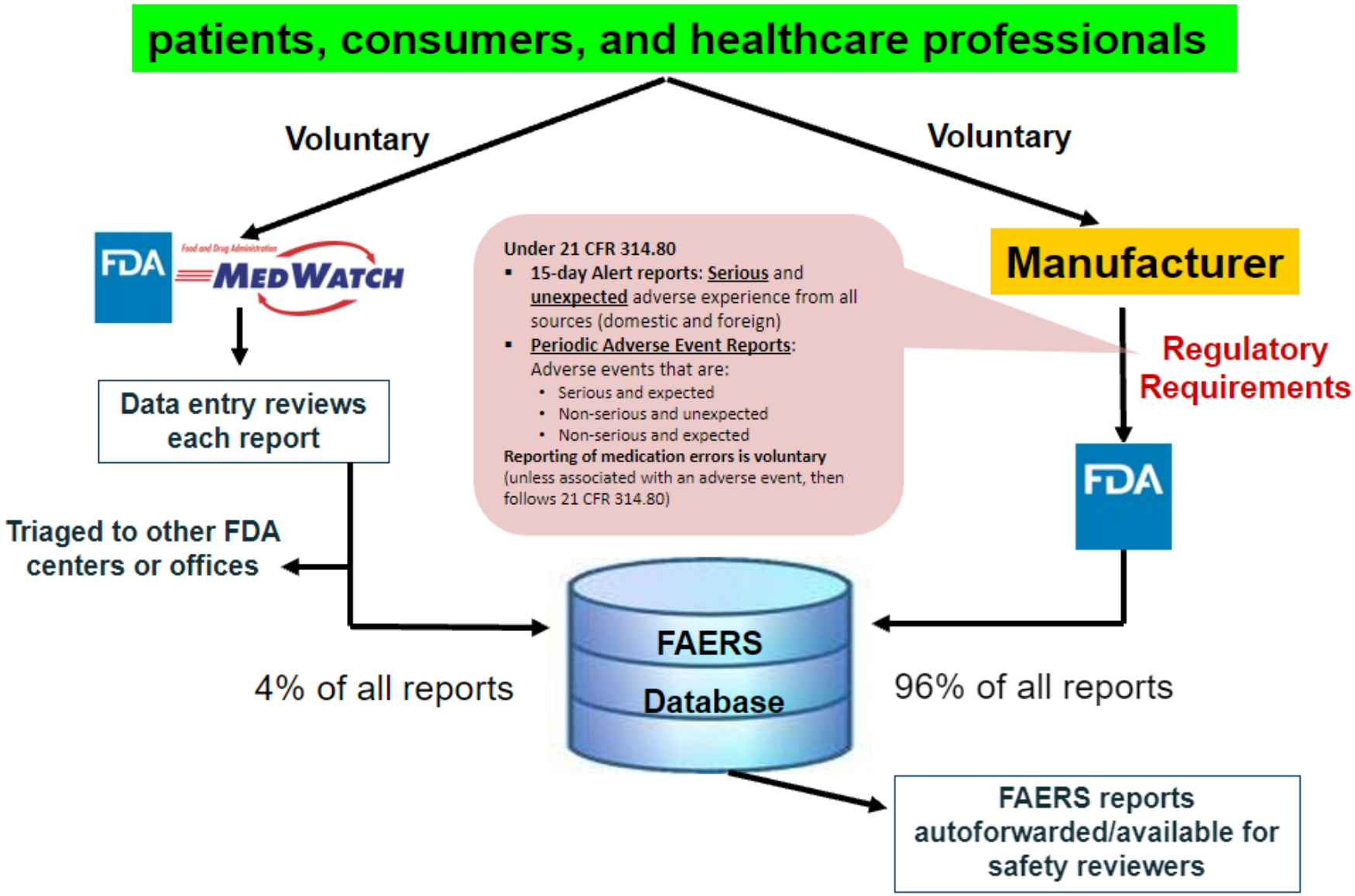
- The FDA Adverse Event Reporting System (FAERS) is FDA's primary source for monitoring medication errors, but we surveil other sources, including ISMP newsletters

- FDA has Memorandum of Understanding (MOU) agreements with ISMP and other organizations to share publicly available medication error information

ISMP
INSTITUTE FOR SAFE MEDICATION PRACTICES

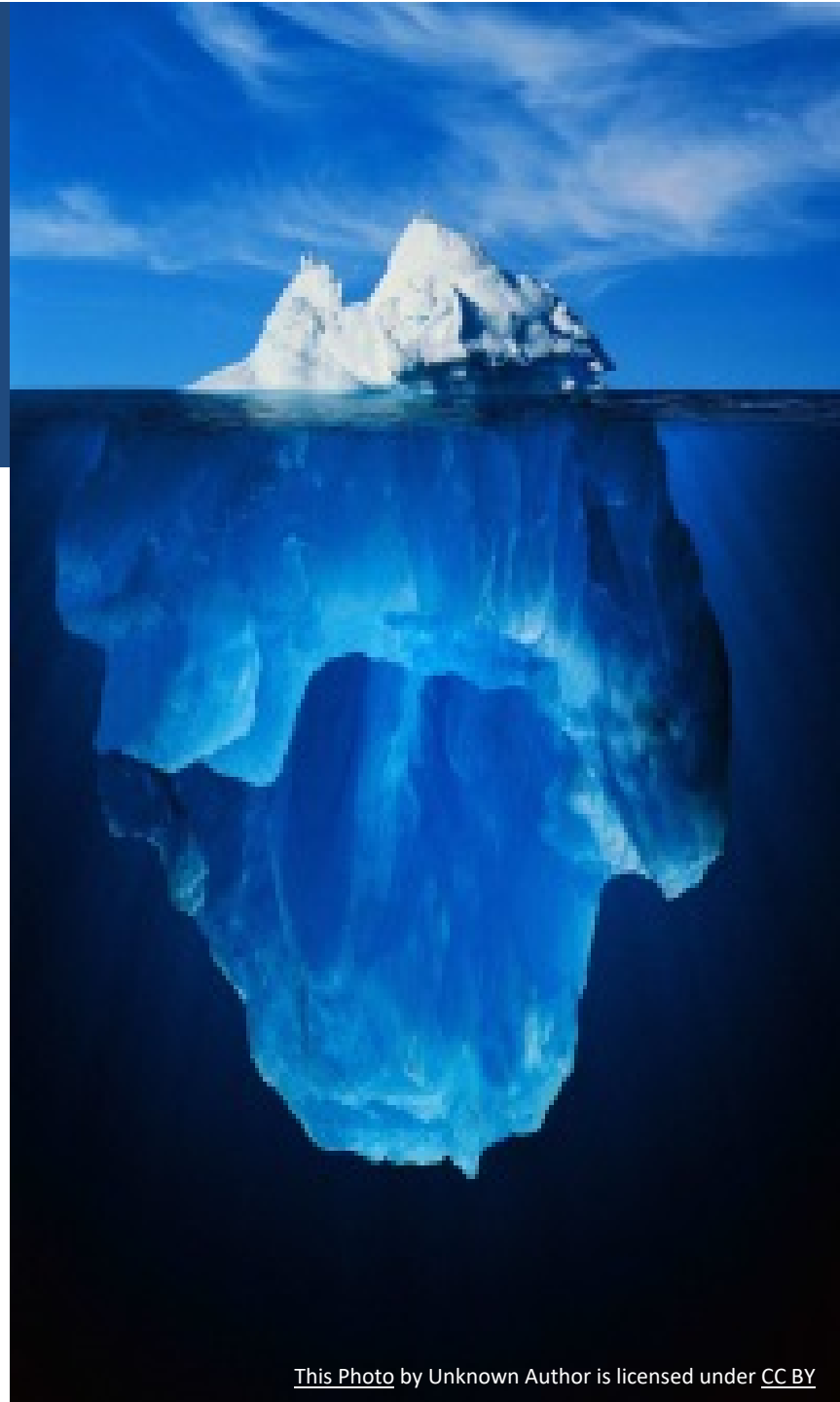
*Preventing Mediation Errors: A $21 Billion Opportunity. Network for Excellence in Health Innovation (NEHI); 2011. https://www.nehi.net/bendthecurve/sup/documents/Medication_Errors_%20Brief.pdf

How Postmarket Reports Get to FAERS



Medication errors are *underreported*

- Extent of underreporting is unknown
  - Elliott, et.al., "estimated that **237 million medication errors occur** at some point in the medication process in England per year"
    - Prevalence and Economic Burden of Medication Errors in The NHS in England. 2018 (http://www.eepru.org.uk/wp-content/uploads/2018/02/eepru-report-medication-error-feb-2018.pdf)
- No U.S. requirement to report medication errors to FDA
- Likelihood of reporting medication errors is lower *versus* adverse events



Barriers for reporting medication errors

- Fear of punishment or litigation
- Embarrassment of having been involved a medication error
- Different definitions for medication error
- Not knowing where, why, or what to report
- No allowance for anonymous reporting
- Organizational culture
- Workload/amount of time required for reporting

Original research

Identifying, understanding and overcoming barriers to medication error reporting in hospitals: a focus group study

Nicole Hartnell,[1] Neil MacKinnon,[2] Ingrid Sk

ABSTRACT

Objectives: The under-reporting of medication errors can compromise patient safety. A qualitative study was conducted to enhance the understanding of barriers to medication error reporting in healthcare organisations.

Methods: Focus groups (with physicians, pharmacists and nurses) and in-depth interviews (with risk managers) were used to identify medication error reporting beliefs and practices at four community hospitals in Nova Scotia, Canada. Audio tapes were transcribed verbatim and analysed for thematic content using the template style of analysis. The development and analysis of this study were guided by Safety Culture Theory.

Results: Incentives for medication error reporting were thematised into three categories: patient protection, provider protection and professional compliance. Barriers to medication error reporting were thematised into five categories: reporter burden, professional identity, information gap, organisational factors and fear. Facilitators to encourage medication error reporting were classified into three categories: reducing reporter burden, closing the communication gap and educating for success. Participants indicated they would report medication errors more frequently if reporting were made easier, if they were adequately educated about reporting, and if they received timely feedback.

Conclusions: Study results may lead to a better understanding of the barriers to medication error reporting, why these barriers exist and what can be done to successfully overcome them. These results could be used by hospitals to encourage reporting of medication errors and ultimately make organisational changes leading to a reduction in the incidence of medication errors and an improvement in patient safety.

BACKGROUND

Medication errors ('any preventable event that may cause or lead to inappropriate medication use or patient harm while the

BMJ Qual Saf 2012;21:361–368. doi:10.1136/bmjqs-2011-000299

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Student observations of medication error reporting practices in community pharmacy settings

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ARTICLE INFO

Keywords:
Medication safety
Community pharmacy
Medication error reporting

ABSTRACT

Background: Medication safety practices and methods for reporting errors in community pharmacies are relatively unknown.

Objective: (s): The primary objective of this study was to describe student-reported data on medication safety and error reporting practices in community pharmacies, and secondarily describe student learning from this assignment.

Methods: Second professional year pharmacy students enrolled at Purdue University College of Pharmacy in the United States observed and recorded medication safety and error reporting practices as part of an experiential assignment. Data were collected from 170 unique pharmacy settings between the years 2016–2018 and analyzed using descriptive statistics and a paired *t*-test to assess student learning.

Results: 51% of students reported documentation of 1–10 errors or near misses annually, with an additional 30% reporting 11–30. Near misses were only reported 26% of the time. Errors were most commonly reported to a pharmacy-specific reporting system (84%) and the Institute for Safe Medication Practices National Medication Errors Reporting Program (84%). The most frequently reported error types included wrong directions (34%), wrong drug (14%), wrong strength (13%), and wrong patient (12%). Pharmacists were observed to be interrupted approximately 19 times every hour. Anonymous error reporting was typically not allowed to the pharmacy's preferred error reporting system (71%). A policy requiring that the prescriber is contacted about errors was observed at 77% of the sites. The most common consequences of committing an error were education/training (72%) or progressive discipline (41%). Students reported a statistically significant increase in understanding of medication safety practices and methods for reporting errors in community pharmacies. ($p < 0.01$).

Conclusion: This data supplements existing literature on medication safety practices and error reporting in community pharmacy settings, as well as highlights knowledge gaps outside the scope of this study.

1. Introduction

There is no current international consensus regarding the definition of a medication error.[1] The United States National Coordinating

including workspace design, number of prescriptions filled, number of pharmacists on staff, or inadequate pharmacy technician training.[3,4]

Community pharmacies in the United States dispense over 4.1 billion prescriptions annually.[5,6] Using a dispensing error rate of 3.2%

Example of Progression from Nonserious Event to SERIOUS

Report warning of potential look-alike container and cartons

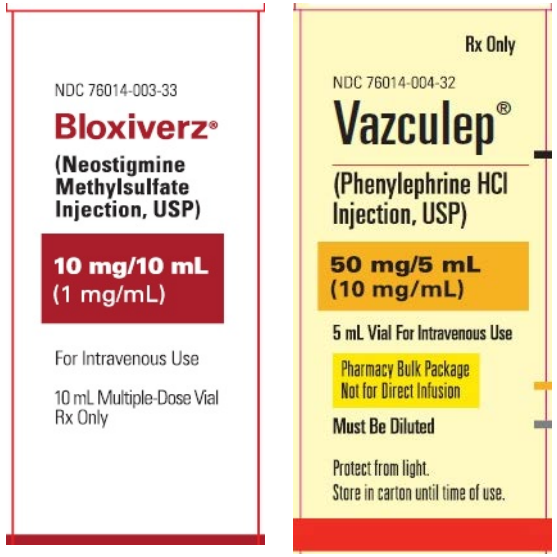
DMEPA performs risk assessment, notifies FDA review division and company

Multiple reports of "near miss"

Company issues safety alert, distributes stickers, prepares to revise labeling

First serious report received (patient received wrong drug)

Labels and labeling urgently revised



Summary

- We encourage healthcare providers to report all medication errors to MedWatch.
- If we are aware of potential problems, we can work to provide effective interventions that may help minimize further errors.
- Post marketing experience also helps us anticipate potential errors.
- We aim to identify and address the risk prior to marketing to help prevent medication errors.

Resources

Guidances for Industry:

- Best Practices in Developing Proprietary Names for Drugs – December 2020
- Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (*Draft*) – April 2013
- Safety Considerations for Product Design to Minimize Medication Errors – April 2016
- Applying Human Factors and Usability Engineering to Medical Devices – February 2016

We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Regulations*:

- 21 CFR 200s, 300s and 600s

*http://www.ecfr.gov/cgi-bin/text-idx?SID=c8497935ae0f040dfcfe06c6251ba507&mc=true&tpl=/ecfrbrowse/Title21/21tab_02.tpl