

# **Strategies to Address Potential Medication Errors for EUA Products for COVID-19**

## **DIVISION OF MEDICATION ERROR PREVENTION AND ANALYSIS**

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Office of Medication Error Prevention and Risk Management

Office of Surveillance and Epidemiology

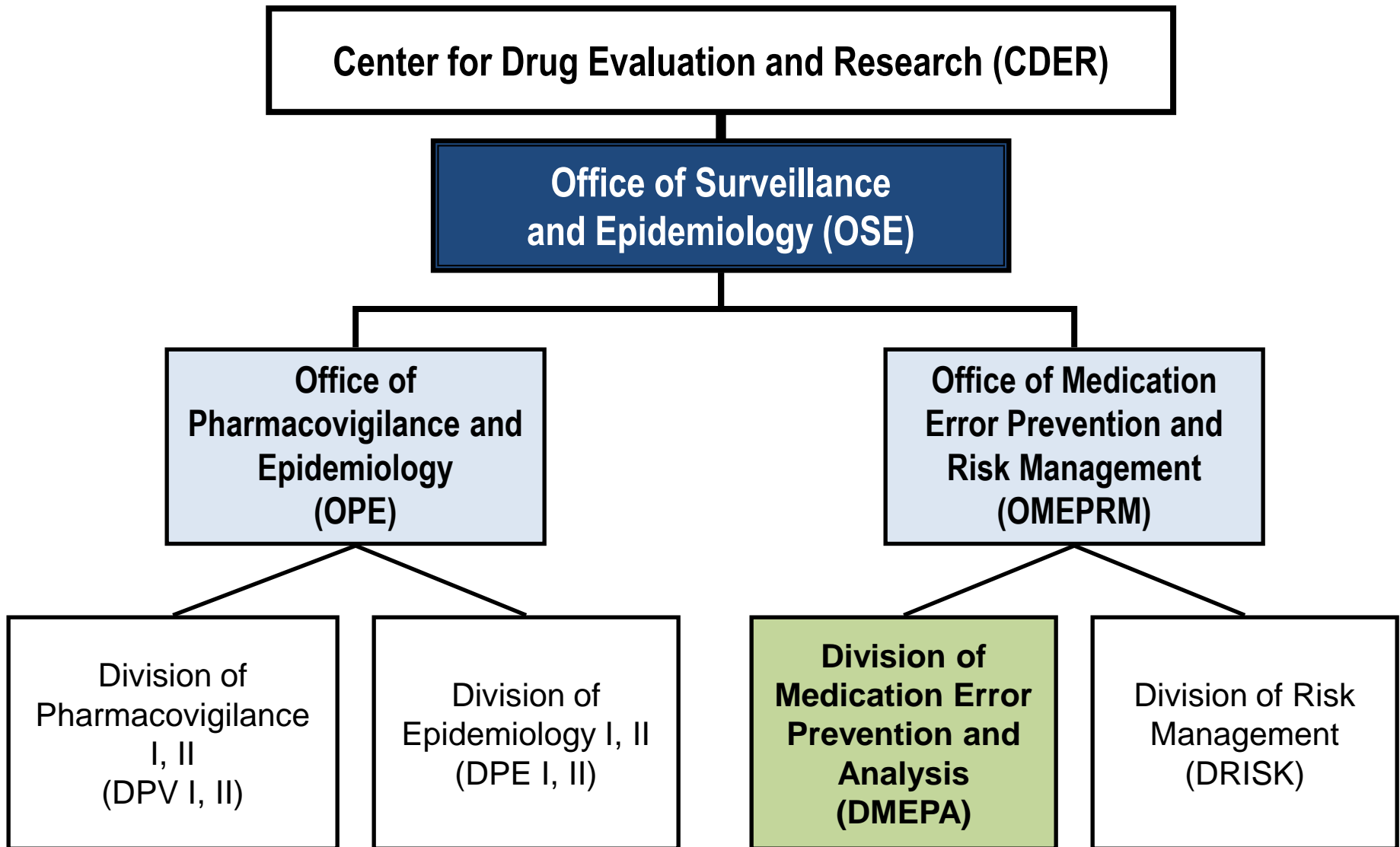


# Presentation Outline



- Overview and role of the Division of Medication Error Prevention and Analysis (DMEPA)
- Describe the medication safety considerations for EUA product design, container labels, carton labeling, and user interfaces to minimize medication errors
- Discuss examples of EUA product medication error case reports and approaches to medication error mitigation strategies







# **Division of Medication Error Prevention and Analysis (DMEPA)**

- Created in 1999
- Scientists and healthcare professionals with varied backgrounds
- 60 employees
- Aligned by therapeutic areas
- Leads CDER review pertaining to medication error prevention and analysis for drug and therapeutic biologics





## DMEPA Mission

To increase the *safe use* of  
drug products  
by minimizing use error  
that is related to the  
*naming, labeling, packaging,  
or design* of drug products





## DMEPA Mission

DMEPA is involved in conducting safety assessment of EUA products used to treat or prevent COVID 19.

- Conduct safety assessment of the EUA products labels, labeling, packaging, and product design
- Review medication error reports for EUA products and act when needed.
- Conduct safety assessment of the proposed proprietary names for the EUA products
- Review 'Dear Health Care Professional' letters for EUA products.



# What is a Medication error ?

“ any **preventable** event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. ”

Figure 1: Relationship between medication errors and ADEs



<sup>1</sup>Adapted from Figure 1 in Qual Saf Health Care 2004;13:306–314. doi: 10.1136/qshc.2004.010611



What to consider  
at early stage of  
drug product  
design to minimize  
medication errors?



# **Safety Considerations for Product Design to Minimize Medication Errors**

## **Guidance for Industry**

*Additional copies are available from:*

*Office of Communications*

*Division of Drug Information*

*Center for Drug Evaluation and Research*

*Food and Drug Administration*

*10001 New Hampshire Ave., Hillandale Bldg., 4<sup>th</sup> Floor*

*Silver Spring, MD 20993-0002*

*Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353*

*Email: [druginfo@fda.hhs.gov](mailto:druginfo@fda.hhs.gov)*

*<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>*

**U.S. Department of Health and Human Services**

**Food and Drug Administration**

**Center for Drug Evaluation and Research**

**April 2016**

**Drug Safety**





## What to consider at early stage of drug product design to minimize medication errors?

- Understanding product **medication use process** is crucial to minimize medication errors.
- Labeling, packaging, product design, and nomenclature are key elements that influence medication use.
- To identify how a medication error might occur, a complete understanding of how the drug will be used is necessary.



# Medication Use Process

Prescribing

Procurement

Preparation

Dispensing

Administration

## Who?

**Who** will prepare and administer the EUA product

## Where?

**The Environments of use**

## How?

**How the end users will interact** with the drug product (e.g., the product, container closure, container label, and accompanying labeling)



# Who?

- Who are the EUA product end users?
- Are there multiple user groups?
- What critical tasks must the end user perform?
- Is extensive manipulation or cognitive processes required to use the product?





# Where?

## *Environments of use*

- In what environment will product be used?
- What environmental factors need to be considered?
- How are drugs stored and obtained in the environment?
- Are there similar products used in the environment?







## Where? *Environments of use*

- *Environmental factors influence medication use within setting of use*
  - Distractions/workplace interruptions
  - Noise, tools, lighting
  - Other pandemic related considerations such as “Pandemic Nursing” care.

### PHARMACY PRACTICE NEWS

NOVEMBER 4, 2020

**‘Pandemic Nursing’ Is a Lethal Problem; ISMP Cites ‘Blame and Shame’ Culture**

Overworked staff, lax medication handling among risk factors seen

By Gina Shaw

Add “pandemic nursing” to the list of COVID-19 threats to medication safety. The practice pressure has led to at least one lethal drug error in a hospital scrambling to cope with a surge in cases, according to a new report from the Institute for Safe Medication Practices (ISMP).





**How?**

***Drug Product User Interface***

**Drug Product User Interface**

refers to all components of a product with which the user interacts throughout the medication use process.



## How? User Interface

- Is the drug product **User Interface** optimized?
  - Are the critical information needed to prepare and administer the product clear
  - Is the information on the EUA fact sheet consistent with the EUA product container label and carton labeling information (e.g., route of administration).



# How? User Interface

- How the EUA product is prepared?
  - 2 step or multi step dilution.
  - Single product or multiple product needs to be administered together.
- How the EUA product is packaged?
  - e.g., multiple vials needed to prepare a single dose.
  - e.g., multiple packaging presentation for the same EUA product





# **EUA Product Medication Error Case Reports Discussion**





# Example # 1: EUA for remdesivir





## Example # 1: EUA for remdesivir



Error type	Description of error
Wrong formulation	A child weighing less than 40 kg received one dose of remdesivir injection (concentrated solution) instead of the recommended lyophilized powder (remdesivir for injection)
Wrong preparation	Several doses of remdesivir for injection (lyophilized powder) were incorrectly reconstituted with 0.9% sodium chloride instead of the recommended sterile water for injection; the doses were also incorrectly diluted in 5% dextrose and water instead of the recommended 0.9% sodium chloride; the doses were not administered to patients
Incorrect storage	Vials of remdesivir injection (concentrated solution) were left out of the refrigerator overnight for more than 12 hours (sealed vials can only be stored up to 12 hours at room temperature prior to dilution) and had to be discarded



# Example # 1: EUA for remdesivir



Which approach would you take to help mitigate these errors?

- A. Revise the ~~EUA~~ fact sheet
- B. Revise the EUA container label and the carton labeling
- C. No action indicated because this is EUA product.
- D. Issue a Dear Health Care Provider Letter



# Strategies Used to Mitigate Remdesivir Product Selection Errors

Refer to package insert for dosage, detailed preparation and administration instructions. Further dilute in 250 mL of 0.9% Sodium Chloride Injection, USP prior to intravenous infusion. Store refrigerated between 2 °C and 8 °C (36 °F and 46 °F) until required for use.

Pediatric patients must weigh at least 40 kg



Must be diluted prior to use.  
For Intravenous Infusion.

Store refrigerated

Refer to package insert for dosage, detailed preparation and administration instructions. Reconstitute with 19 mL Sterile Water for Injection. Further dilute in 100 mL or 250 mL of 0.9% Sodium Chloride Injection, USP prior to intravenous infusion.

Store below 30 °C (86 °F).

After reconstitution, use vials immediately to prepare diluted solution. The diluted Veklury solution in the infusion bags can be stored up to 24 hours at room temperature (20 °C to 25 °C [68 °F to 77 °F]) prior to administration or 48 hours at refrigerated temperature (2 °C to 8 °C [36 °F to 46 °F]).



## Example # 2: EUA for Bamlanivimab

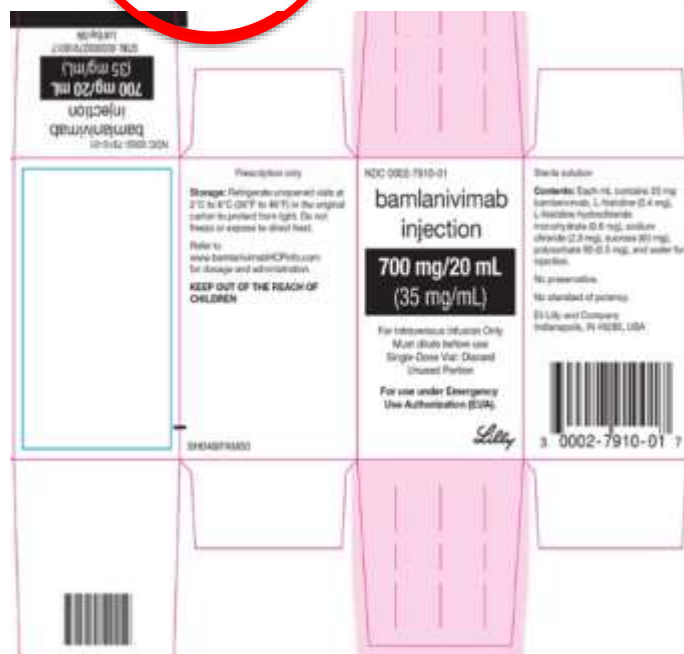
Error type	Description of error
Incorrect administration rate	“Bamlinivimab monoclonal antibody FACT SHEET FOR HEALTHCARE PROVIDERS contains an error in infusion rate information. Table 1: RECOMMENDED DILUTION AND ADMINISTRATION INSTRUCTIONS FOR BAMLANIVIMAB describes 200 mL/hr as the MINIMUM infusion rate, but states that the agent must be infused over at least 60 minutes. The specified rate of 200 mL/hr is actually the MAXIMUM infusion rate. Infusing it at a greater rate would result in the dose being given in less than 60 minutes”.
Incorrect preparation	Bamlanivimab treatment under Emergency use Authorization (EUA) Medication was diluted to 2.59mg/ml, instead of 3.5mg/ml. Pt received complete dose of 700 mg of Bamlanivimab in a total of 270 mL of 0.9% NaCl, instead of 700 mg of Bamlanivimab in a total of 200 mL of 0.9% NaCl.



# Example # 2: EUA for Bamlanivimab

**Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab**

Treatment	Dose/Volume of Bamlanivimab (# of vials)	Volume of 0.9% sodium chloride to Discard from a 250 mL IV bag	Total Final Volume for Infusion	Minimum Infusion Rate	Minimum Infusion Time
Bamlanivimab	700 mg/20 mL (1 vial)	70 mL	200 mL	200 mL/hr	60 minutes







Example # 2:  
EUA for  
Bamlanivimab

Which approach would you take to help mitigate these errors?

- A. Revise the EUA fact sheet
- B. Revise the container label and the carton labeling
- C. No action indicated because this is EUA product.
- D. Issue a Dear Health Care Provider Letter



# Strategies Used to Mitigate EUA for Bamlanivimab infusion rate confusion



**Revised Table 1**

<b>Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab</b>		
<b>Size of prefilled 0.9% Sodium Chloride infusion bag</b>	<b>Maximum Infusion Rate</b>	<b>Minimum Infusion Time</b>
50 mL	270 mL/hr	16 minutes
100 mL	270 mL/hr	27 minutes
150 mL	270 mL/hr	38 minutes
250 mL	270 mL/hr	60 minutes



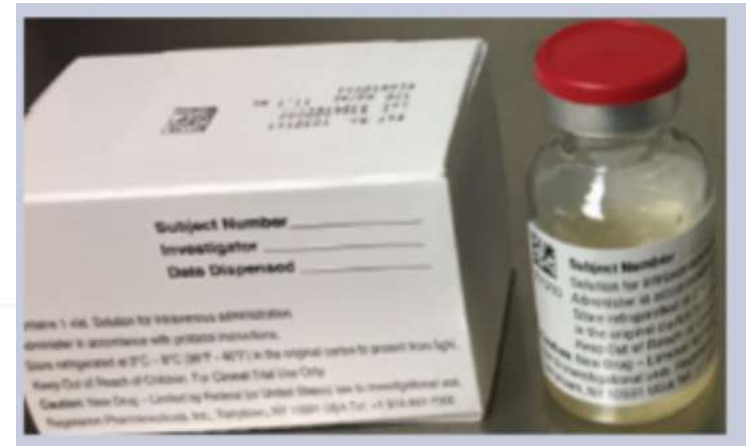
# Example # 3: EUA for Casirivimab and Imdevimab Product Label Confusion Errors

## The Washington Post

*Democracy Dies in Darkness*

Health

West Virginia clinic gave 44 people an antibody treatment instead of the coronavirus vaccine



“The packaging, the vials — there was nothing on them that said anything different.”





**FDA**





Example # 3:  
EUA for  
Casirivimab and  
Imdevimab  
Product Label  
Confusion  
Errors

Which approach would you take to help mitigate these errors?

- A. Revise the EUA fact sheet
- B. Revise the container label and the carton labeling
- C. No action indicated because this is EUA product.
- D. Issue a Dear Health Care Provider Letter



# Example # 3: EUA Casirivimab and Imdevimab Product Label Confusion Errors



Error Type	Description of Error
Wrong preparation	"...When compounding using the 300 mg/2.5 mL vials we drew up 2 x 2.5 mL of casirivimab and then 2 x 2.5 mL of imdevimab into the same syringe inadvertently prior to injecting into the diluent bag. This occurred due to the similarity in appearance of the packaging/vials of the EUA casirivimab and imdevimab products..."
Wrong dose	"...Patient received a higher dose of casirivimab (5,280 mg; 44 mL x 120 mg/mL) due to incorrect preparation. A total of #4 (11.1 mL) vials of casirivimab 120mg/mL were used instead of 2.5 mL vials due to similar looking containers (boxes). Patient received a total dose of casirivimab 5,280 mg and imdevimab 1,200 mg in 250 mL NS over 1 hours..."

EUA dose: 1200 mg casirivimab and 1200 mg imdevimab  
administered together as intravenous infusion



# Example # 3: EUA Casirivimab and Imdevimab Product Label Confusion Errors



Subject Number \_\_\_\_\_

701208

Solution for intravenous infusion or subcutaneous injection.  
Administer in accordance with protocol instructions.  
Store refrigerated at 2°C–8°C (36°F–46°F)  
in original carton to protect from light.

Keep Out of Reach of Children. For Clinical Trial Use Only.  
**Caution:** New Drug - Limited by Federal (or United States)  
law to investigational use. Regeneron Pharmaceuticals, Inc.  
Tarrytown, NY 10591 USA Tel: +1 914-847-7000

Lot

XXXXXXXXXX  
REGN10933  
300 MG/2.5ML  
(120 MG/ML)



Subject Number \_\_\_\_\_

701210

Solution for intravenous administration.  
Administer in accordance with protocol instructions.  
Store refrigerated at 2°C–8°C (36°F–46°F)  
in the original carton to protect from light.  
Keep Out of Reach of Children. For Clinical Trial Use Only.

**Caution:** New Drug – Limited by Federal (or United States)  
law to investigational use. Regeneron Pharmaceuticals, Inc.  
Tarrytown, NY 10591 USA Tel: +1 914-847-7000

Lot

XXXXXXXXXX  
REGN10933  
120 mg/mL  
11.1 mL

casirivimab



Subject Number \_\_\_\_\_

701208

Solution for intravenous infusion or subcutaneous injection.  
Administer in accordance with protocol instructions.  
Store refrigerated at 2°C–8°C (36°F–46°F)  
in original carton to protect from light.

Keep Out of Reach of Children. For Clinical Trial Use Only.  
**Caution:** New Drug - Limited by Federal (or United States)  
law to investigational use. Regeneron Pharmaceuticals, Inc.  
Tarrytown, NY 10591 USA Tel: +1 914-847-7000

Lot

XXXXXXXXXX  
REGN10987  
300 MG/2.5ML  
(120 MG/ML)



Subject Number \_\_\_\_\_

701210

Solution for intravenous administration.  
Administer in accordance with protocol instructions.  
Store refrigerated at 2°C–8°C (36°F–46°F)  
in original carton to protect from light.  
Keep Out of Reach of Children. For Clinical Trial Use Only.

**Caution:** New Drug - Limited by Federal (or United States) law  
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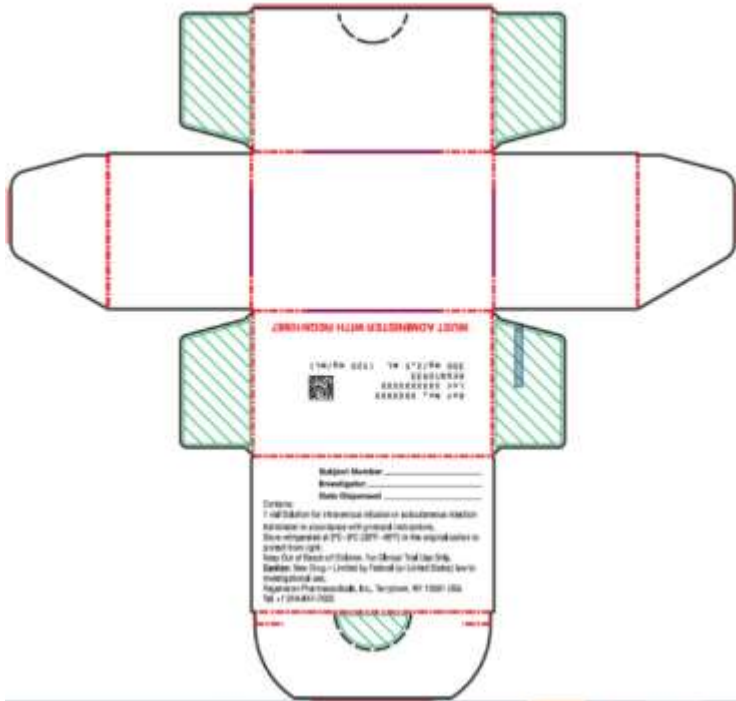
Lot

XXXXXXXXXX  
REGN10987  
120 MG/ML  
11.1 ML

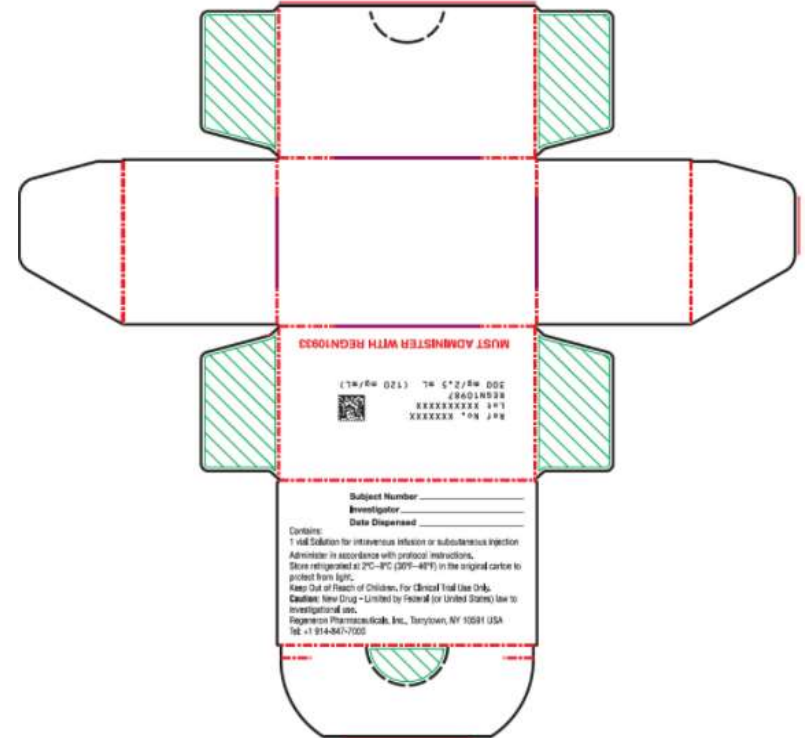
imdevimab



# Example # 3: EUA Casirivimab and Imdevimab Product Label Confusion Errors



casirivimab



imdevimab



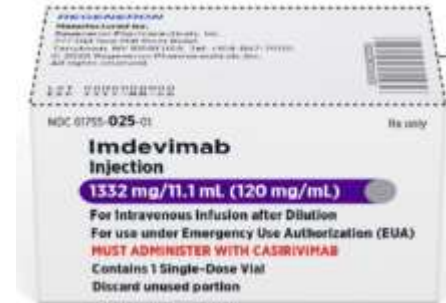
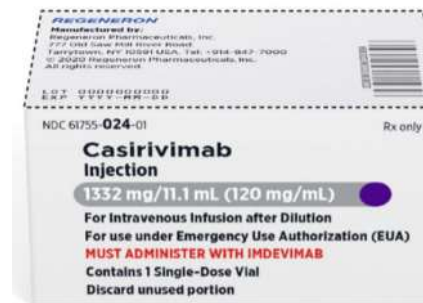
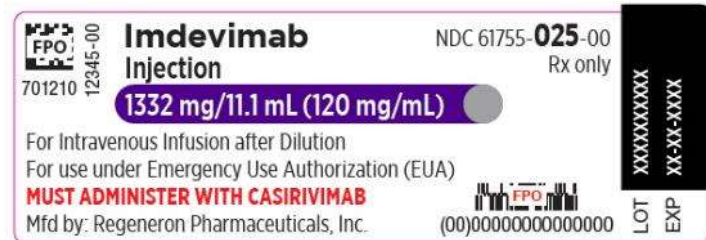
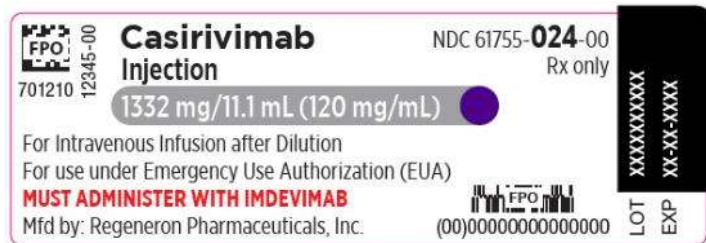
# Strategies Used to Mitigate Product Selection Errors with Casirivimab





# Strategies Used to Mitigate EUA for Casirivimab and Imdevimab Product Label Confusion Errors

- Revised EUA labels





Example # 3:  
EUA for  
Casirivimab and  
Imdevimab  
Product Label  
Confusion  
Errors

Which approach would you take to help mitigate wrong dose errors?

- A. Revise the EUA fact sheet
- B. Issue a Dear Health Care Provider Letter
- C. Revise the product packaging
- D. Revise container label and carton labeling



# Strategies Used to Mitigate EUA for Casirivimab and Imdevimab Product Label Confusion Errors





- Understanding the EUA medication use process is crucial to mitigate potential medication errors.
  - Consider **end users, environments of use, and user interface** for your EUA product.
- Use analytical methods from early stages of product design to help:
  - **Anticipate** potential use-related medication errors,
  - **Identify** need for packaging design modifications, and
  - **Ensure** such modifications do not introduce unintended consequences
- EUA Product container labels, carton labeling, and packaging should communicate information that is **critical to the safe use of EUA product throughout the medication use process.**



The Division of Medication Error Prevention and Analysis' role in EUA products:

- A. DMEPA reviews container labels and carton labeling for EUA products for COVID 19.
- B. DMEPA reviews the medication error reports for EUA products for COVID 19.
- C. DMEPA reviews the proposed proprietary name for EUA products for COVID 19.
- D. All of the above.



**The most effective strategies to address use-related medication errors should focus on end users and environment of use.**

☐ **True**

☐ **False**



