February 2023 | Volume 21 ■ Issue 2

ISMP
An ECRI Affiliate

Nurse AdviseERR®
Educating the Healthcare Community About Safe Medication Practices

ISMP updates its list of drug names with tall man (mixed case) letters based on survey results

Several design techniques have been explored for the purpose of differentiating look-alike drug names to prevent medication selection errors. Tall man (mixed case) lettering describes a method for differentiating the unique letter characters of similar drug names known to have been confused with one another. Starting with a generic drug name expressed in lowercase letters, tall man lettering highlights the differences between similar drug names by CAPITALIZING dissimilar letters. Occasionally, brand names, which always start with an UPPERCASE letter, may require the use of tall man letters to differentiate them from other brand or generic names. The use of tall man lettering to accentuate a unique portion of a drug name with UPPERCASE letters, along with other means such as color, **bolding**, or a contrasting background, can draw attention to the dissimilarities between look-alike drug names as well as alert healthcare providers that the drug name can be confused with another drug name.

Since 2008, ISMP has maintained a list of drug names with recommended UPPERCASE and **bolded** tall man letters. The list includes mostly generic-generic drug name pairs or larger groupings, although a few brand-brand or brand-generic name pairs are also included. Periodically, ISMP updates this list; it was last revised in 2016. Each time the list is updated, we analyze reported events from our error databases, survey practitioners on the topic, and conduct an internal review of drug names that would benefit from the application of UPPERCASE and **bolded** tall man lettering. The internal assessment includes an exploration of orthographic similarity; patterns of similarities in dosage, formulation, and use; and the potential for patient harm if the drugs are confused.

Standardization of Tall Man Letters

To promote standardization regarding which letters to present in **bold**/UPPERCASE, ISMP follows a tested methodology whenever possible, called the CD3 rule.[1] The rule suggests working from the left of the drug name first by CAPITALIZING all the characters to the right once two or more dissimilar letters are encountered. Then, working from the right of the word back, returning two or more letters common to both words to lowercase letters. When the rule cannot be applied because there are no common letters on the right side of the word, the methodology suggests CAPITALIZING the central part of the word only. When this rule fails to lead to the best tall man lettering option (e.g., makes names appear too similar or hard to read based on pronunciation), an alternative option is considered. ISMP suggests that the tall man lettering provided by the US Food and Drug Administration (FDA) and ISMP be followed to promote consistency.

ISMP Survey

ISMP conducted a survey between October and December 2022 to help update ISMP's current list of look-alike drug names with tall man (mixed case) letters. We believe healthcare practitioners should be involved in the process of identifying confusing drug names relevant to their respective practice settings, along with reviewing proposed tall man lettering for possible implementation. The CAPITALIZED and **bolded** letters should make the drug names distinguishable from the user's perspective.[2]

Respondent profile. ISMP extends our sincere appreciation to the 298 respondents who completed our survey on drug names with tall man letters. The respondents were mostly pharmacists (57%), nurses (24%), and pharmacy technicians (12%); however, we also received responses from physicians

continued on page 2 — Tall man (mixed case) letters >

Worth repeating...

Naloxone syringe and Clave/MicroClave connector incompatibility

In a recent case, a practitioner connected an Aurobindo Pharma (Eugia Pharma Specialties Limited) naloxone syringe, distributed by AuroMedics Pharma, to a MicroClave (ICU medical) needlefree syringe connector on the intravenous (IV) tubing access port to administer the drug. They could not push the medication out of the syringe. When the practitioner detached the naloxone syringe from the MicroClave connector, they noted a piece of glass or plastic stuck in the tip of the syringe, which blocked the flow of medication. The organization replicated this issue several times using various lots of Aurobindo naloxone syringes and MicroClave devices. This situation is quite serious since the timely administration of a reversal agent is critical in preventing patient harm or death.

We previously reported a similar issue with Dr. Reddy's Laboratories prefilled naloxone syringes and MicroClave needlefree syringe connectors. Details of the event, including photos, can be found here: www.ismp.org/node/25848. Evidently, the action of inserting the glass syringe tip can cause the pin in the MicroClave access system to break off in the syringe tip, preventing delivery of the medication. In some events, a piece of plastic was found lodged inside Dr. Reddy's naloxone syringe tip, also effectively blocking the flow of medication. This could also compromise the MicroClave port and increase the risk of IV line contamination and infection.

We have reached out to the US Food and Drug Administration (FDA) and the manufacturers again. Aurobindo told us that, according to their syringe vendor (BD), the syringe is not compatible with any external devices, and practitioners must use the needle provided with the kit. For now, organizations should refrain from using Aurobindo and Dr. Reddy's

continued on page 2 — *Worth* repeating >

Supported by an educational grant from Fresenius Kabi and Ivenix

FRESENIUS KABI IVENIX INFUSION SYSTEM

> Tall man (mixed case) letters — continued from page 1

and other prescribers (2%), and others (e.g., consultant, project manager, respiratory therapist) (5%). The findings from the survey and a discussion of how we updated the FDA and ISMP lists follow.

Scope of using tall man letters. A majority (94%) of respondents reported that their facility uses tall man letters. Almost three-quarters (74%) consistently use tall man letters for organization-defined drug names in all required contexts (e.g., computer screens for pharmacy and prescribers, smart infusion pump drug libraries, labels). Four out of five (80%) respondents use tall man letters in all settings (e.g., pharmacy, surgical suites) and across multihospital and/or multi-clinic settings.

Internal selection of drug names for tall man letters. Fewer than one out of five (18%) respondents use tall man letters for one or more drug names that do NOT comply with the configurations on the ***FDA and ISMP Lists of Look-Alike Drug Names with Recommended Tall Man (Mixed Case) Letters***. However, most of the examples provided by respondents were drug names that were NOT on the FDA or ISMP lists. Examples include dox**EP**in (confused with doxycycline), nitro**GLY**cerin and nitro**PRUS**side, and **ALTE**plase and **TENECTE**plase. One respondent notified us that internally selected tall man letters for drug name pairs created confusion because of differences in the tall man letters used in drug information references (which comply with the FDA and ISMP lists). Thus, the organization opted to use the configurations on the FDA and ISMP lists, and to eliminate the use of tall man letters for drug names not included on either list.

Reduction of errors. The vast majority of respondents felt that the use of tall man lettering helped reduce the risk of errors among medications with look-alike names. Specifically, 95% of respondents felt that the use of tall man letters by the pharmaceutical industry on product and carton labels helps to reduce drug selection errors. More compelling is the fact that 87% of survey respondents were able to recall one or more instances when tall man lettering had actually prevented them from prescribing, transcribing, dispensing, or administering the wrong medication. Respondents provided examples of look-alike name pairs involved in these potential events, including hydr**ALAZINE** and hydr**OXY**zine, lev**ETIRA**cetam and levo**FLOX**acin, and **SOLU**-Medrol and **DEPO**-Medrol. Many others reported a personal experience where tall man lettering has helped them avoid errors when selecting drugs during order entry, removing medications from an automated dispensing cabinet (ADC) via override, programming the smart pump using the drug library, and prior to administration when referencing the medication administration record (MAR). Others reported that the use of tall man lettering on preprinted paper order sets helps prevent errors during electronic health record (EHR) downtime when technological safeguards are unavailable.

Several respondents also told us that tall man lettering alerts them to the possibility of a drug mix-up, reminding them to be cautious. They said that tall man letters are an effective alert system that quickly captures their attention and causes them to pause, read the drug name more carefully a second or third time, and make sure the drug is appropriate for the patient. Respondents referred to the tall man letters as a "tool to highlight errors" that helps to "catch your eyes" and "slow down or stop the process" to ensure they have the correct drug and "to prevent confirmation bias" when handling drugs with similar names.

Updated Lists

FDA list. In 2001, FDA initiated the name differentiation project to continually evaluate postmarketing reports of name pair confusion and to determine if tall man lettering should be used to help differentiate similar generic names (www.ismp.org/ext/1072). Since our last update to the lists in 2016, FDA has added three drug name pairs to its list:

- **CIS**platin and **CARBO**platin
- mig**ALA**stat and mig**LU**stat
- tra**ZOD**one and tra**MAD**ol

continued on page 3 — Tall man (mixed case) letters >

>Worth repeating

continued from page 1

prefilled naloxone syringes with a MicroClave connector and consider purchasing naloxone syringes from an alternative manufacturer. If incompatible prefilled glass syringes remain on the market, FDA and device/drug manufacturers need to clearly communicate this potential problem and perhaps include prominent warnings on the packaging itself.

SAFETY wires

New ready-to-use vaccine is better, but may pose new hazard. We were pleased to see that the US Food and Drug Administration (FDA) recently approved two newly reformulated vaccine products that eliminate the need to mix two components together. GSK recently received approval for a ready-to-administer presentation of **ROTARIX** (rotavirus vaccine, live, oral). The new product will be available in early 2023 (www.ismp.org/ext/1031). Rotarix is administered orally to infants to prevent gastroenteritis caused by rotavirus.

Historically, Rotarix has only been available as a two-component product that requires reconstitution of lyophilized vaccine with the liquid contained in an oral dosing applicator, which looks like a prefilled syringe, using a supplied transfer device (**Figure 1**). However, there have been long-standing issues with practitioners inadvertently omitting reconstitution and

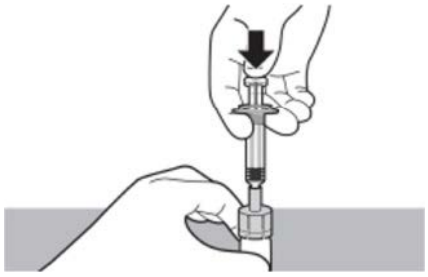

Figure 1. The older two-component Rotarix presentation requires reconstitution of the vial containing the lyophilized vaccine component with the liquid within the dosing applicator.

using the liquid in the syringe by itself. Or the vaccine was mixed, transferred to a parenteral syringe, and injected. To avoid the need for dilution and to facilitate the correct route of administration, the new, fully liquid formulation is provided in an oral

continued on page 3 — SAFETY wires >

> **Tall man (mixed case) letters** — continued from page 2

Two of these name pairs were already on the ISMP list: **CIS**platin and **CARBO**platin, and tra**ZOD**one and tra**MAD**ol. Also, aceto**HEXAMIDE**, sulfi**SOXAZOLE**, and **TOLBUT**amide have been discontinued and are not marketed in the United States. However, FDA does not want to remove these names from its list because the names might still be listed in electronic drug information sources. Unless a drug is removed from the market for safety or efficacy reasons, the drug could be marketed at a later date.

Table 1. Drug names tested for possible addition to the ***ISMP List of Look-Alike Drug Names with Recommended Tall Man Letters***

Drug Names	Aware of Confusion? (%)	Add to List? (%)
py**RID**ostigmine and **PHYS**ostigmine	49	91
cyclo**PHOS**phamide (confused with cyclo**SPORINE** and cyclo**SERINE**, already on FDA list)	50	83
dro**PER**idol and dro**NAB**inol	37	82
lina**GLIP**tin and lina**CLO**tide	27	79
le**NALID**omide and le**FLUN**omide	21	79
hydroxy**UREA** (confused with hydr**OXY**zine, already on FDA list)	43	77
dex**AMETH**asone and dexmede**TOMID**ine	44	75
DESMOpressin and **VASO**pressin	44	71
NIZatidine and nita**ZOX**anide	21	68
metho**TREX**ate (confused with met**OL**azone, meth**IMA**zole, and methazol**AMIDE**, already on ISMP list)	31	63

ISMP list. In the 2022 survey, we asked for feedback on 10 potential new drug name pairs or single drug names that may be confused with another drug name pair already on the list. Of these, 75% or more of the respondents felt that seven of these should be added to the ISMP list of drug names with tall man letters (**Table 1**). For these seven drug names or pairs, we evaluated the potential for overlap among indications, frequency of administration, storage, drug formulation, and available strengths, along with the potential for harm if a mix-up occurred. We also searched our error-reporting databases to see how often we received reports of mix-ups with a similar-looking drug name. Based on this assessment, the following drug names were added to the ISMP list:

- cyclo**PHOS**phamide (confused with cyclo**SPORINE** and cyclo**SERINE**, already on FDA list)
- dro**PER**idol and dro**NAB**inol
- dex**AMETH**asone and dexmede**TOMID**ine
- py**RID**ostigmine and **PHYS**ostigmine

Many respondents shared their thoughts regarding other drug names that were not tested in the survey. We reviewed each suggestion while considering all risk factors and the need to keep the list short enough to avoid diluting the effectiveness of tall man letters. Overuse of tall man letters may reduce effectiveness, as names would no longer appear novel.[2] More than 30 name pairs with tall man letters were suggested (many brand names, which we hesitate to include without FDA approval). There were drug name pairs or single drug names that may be confused with other drug names already on the list that were closely associated with a high risk of harm if a mix-up were to occur, therefore, the following were added to the ISMP list:

- **AL**fentanil (confused with **SUF**entanil and fenta**NYL**, already on the ISMP list)
- **BUP**ivacaine and **ROP**ivacaine
- oxy**BUTY**nin (confused with oxy**CODONE**, Oxy**CONTIN**, and oxy**MOR**phone, already on the ISMP list)

continued on page 4 — **Tall man (mixed case) letters** >

> **SAFETY**wires continued from page 2

dosing applicator (**Figure 2**), and the tip does not allow for a needle to be attached (www.ismp.org/ext/1032).

Figure 2. The new Rotarix oral dosing applicator-only presentation does not require reconstitution.

While the new ready-to-administer Rotarix will soon be available, keep in mind that the dosing applicator tip cap could present a choking hazard if used improperly. Practitioners administer the vaccine by placing the oral dosing applicator (which looks like a prefilled syringe) into the infant's mouth. But there is a protective cap on the tip of the syringe that practitioners must remove before administration. The GSK labeling emphasizes the need to remove the tip cap before administration (**Figure 3**). However, in rare circumstances it is possible that the person administering the vaccine may not be aware of this, as has happened when capped syringes are used orally. Also, leaving the empty dosing applicator or the removed tip cap within reach (e.g., on an examination table) of a baby or child might lead to it being put in their mouth.

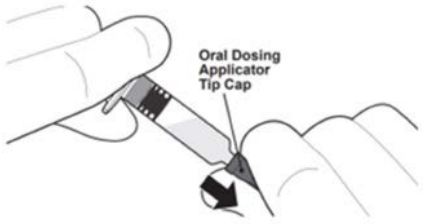

Figure 3. Remove and discard the oral dosing applicator tip cap on the Rotarix vaccine prior to administration.

We are unaware of any such reports with Rotarix vaccine, but one cannot be too cautious. Years ago, there were cases of asphyxiation after practitioners provided parents with parenteral syringes, which

continued on page 4 — **SAFETY**wires >

> **Tall man (mixed case) letters** — continued from page 3

ISMP has previously recommended NOT using brand names of drugs that have been discontinued (e.g., Versed); thus, three name pairs were removed from the ISMP list:

- **AVIN**za (discontinued) and **INV**anz
- **SINE**quan (discontinued) and **SERO**quel
- **TREN**tal (discontinued) and **TEG**retol

In addition, the list was updated to include a notation for a medication that is not currently available in the United States:

- ra**NITI**dine (not available) confused with ri**MANTA**dine

The ***FDA and ISMP Lists of Look-Alike Drug Names with Recommended Tall Man (Mixed Case) Letters*** has been updated on our website (www.ismp.org/node/136).

Ongoing Research

In 2016, ISMP published an up-to-date review of the research, ***Tall man letters: A review of the evidence; in Special Edition: Tall Man Lettering; ISMP Updates Its List of Drug Names with Tall Man Letters*** (www.ismp.org/node/250). Using tall man letters, alone or with other text enhancements, has been shown to reduce errors due to drug name similarity. However, the evidence is mixed, with some studies showing the method may not be effective. Interestingly, a 2021 meta-analysis (www.ismp.org/ext/1077) that looked at 11 articles representing 20 individual trials, showed a significant reduction in wrong medication selection errors caused by look-alike drug names when using tall man lettering or other forms of text enhancement.

ISMP is currently serving as a co-investigator in a 4-year Northwestern University (Chicago) research project, led by Bruce L. Lambert, PhD, to assess the comparative effectiveness of various methods of tall man lettering, text enhancements, and their ability to reduce errors during drug selection. This research project is being funded through a grant from FDA. We look forward to participating in the research project and learning more about the effectiveness of tall man lettering.

Although there are still questions to be answered, tall man lettering is done at little or no cost, has little or no downside, and is not known to be associated with any potential risk for patient harm. Considering past research showing it may be an effective way to prevent mix-ups, and the overwhelming support for tall man lettering shown by survey respondents, ISMP strongly encourages continued use by FDA, pharmaceutical manufacturers, outsourcers and compounders, hospitals, and other practice locations, while we conduct further research to answer questions about the most effective way to differentiate look-alike drug name pairs.

References

1) Gerrett D, Gale AG, Darker IT, Filik R, Purdy KJ. Tall man lettering. Final report of the use of tall man lettering to minimize selection errors of medicine names in computer prescribing and dispensing systems. Loughborough University Enterprises Ltd; 2009.
2) ISMP Canada. Principles for the application of tallman lettering in Canada. October 2015. www.ismp.org/ext/1083

what's in a Name?

The "-domide" drug stem name

Medications with the suffix "-domide" belong to a class of chemotherapy agents referred to as angiogenesis inhibitors. Angiogenesis inhibitors block the development of blood vessels that support tumor growth. There are three "-domides" approved for use in the United States:

continued on page 5 — what's in a Name? >

> SAFETY wires continued from page 3

at the time had a tip cap, to measure their child's oral liquid antibiotic dose. Not all parents realized they had to remove the syringe cap before using it. The cap was often loose enough so that the person preparing the dose could draw the oral liquid into the syringe without removing it. Then, when they placed the syringe tip into their child's mouth to administer the dose of medicine, the cap fell off into the child's mouth. As a result, BD eliminated caps from all parenteral syringes. It is interesting to note that Rotarix is available in a squeezable tube in some countries, Canada being one. The manufacturer told us the decision to use the oral applicator presentation in the United States was based on healthcare provider market research, which showed a clear preference for the oral applicator rather than a squeezable tube due to ease of delivery and controlled administration.

If your organization plans to purchase this product when it becomes available in 2023, ensure practitioners and clinic/office staff are aware of this potential choking hazard.

Inappropriate use of ADC overrides. One of the biggest challenges to the safe use of automated dispensing cabinets (ADCs) is the ease with which medications can be removed upon override, many times unnecessarily and with a lack of perceived risk. ISMP's affiliate, ECRI, recently released ***Top 10 Health Technology Hazards for 2023*** (www.ismp.org/ext/1079). Coming in at number three is the inappropriate use of ADC overrides and how they can result in medication errors. We encourage organizations to review the ***ISMP Targeted Medication Safety Best Practices for Hospitals***, *Best Practice* #16: www.ismp.org/ext/986, and implement the following recommendations:

- Limit the variety of medications that can be removed from an ADC using the override function.
- Require a medication order (e.g., electronic, written, telephone, verbal) prior to removing any medication from an ADC, including those removed using the override function.

continued on page 5 — SAFETY wires >

what's in a Name?

continued from page 4

thalidomide, lenalidomide, and pomalidomide. Brand names for these medications may be found in **Table 1**.

Table 1. Generic formulations of "-domides" available in the United States with associated brand names.

Generic Name	Brand Name
thalidomide	**THALOMID**
lenalidomide	**REVLIMID**
pomalidomide	**POMALYST**

Figure 1. Various strengths of Thalomid capsules with a symbol warning against the use of this medication during pregnancy.

Thalidomide was first released in the late 1950s in Germany under the brand name **CONTERGAN.** It was initially used to treat insomnia and morning sickness, and was thought to be safe to use during pregnancy. Following its widespread use in Europe, practitioners began to correlate thalidomide with birth defects such as phocomelia (underdeveloped or absent upper and lower limbs in children), urinary tract and heart problems in children, and miscarriages. Dr. Frances Kelsey, a physician, pharmacologist, and US Food and Drug Administration (FDA) scientist, was largely credited for keeping thalidomide off the US market at that time. Thalidomide was withdrawn from the worldwide market in 1961.

It wasn't until 1998 that thalidomide was approved for use in the United States. Since then, "-domides" have found their place in the treatment of leprosy and certain types of cancers, such as multiple myeloma. They are intended for oral administration and are available in various capsule strengths. Of note, thalidomide (**THALOMID**) capsules contain a logo of a pregnant woman with a strike-through symbol warning against use in this patient population (**Figure 1**). However, all three medications carry a US Boxed Warning for pregnancy (embryo-fetal toxicity) and thromboembolic events and are available under separate Risk Evaluation and Mitigation Strategy (REMS) programs. The drugs in this class of angiogenesis inhibitors are also considered hazardous according to the National Institute for Occupational Safety and Health (NIOSH) and require the use of personal protective equipment (PPE) when being handled.

Common side effects associated with "-domides" include, but are not limited to, fatigue, gastrointestinal issues, headache, weakness, and weight loss. Monitoring parameters include, but are not limited to, complete blood count with differential, liver function tests, pregnancy testing, and thyroid function tests. Monitor for signs and symptoms of thromboembolism (shortness of breath, chest pain, and arm/leg swelling) and tumor lysis syndrome (hyperuricemia, hyperphosphatemia, hyperkalemia, uremia, hypocalcemia) both of which are life-threatening and need to be identified and treated immediately. In addition, patients should be monitored for dermatologic reactions such as Stevens-Johnson syndrome (SJS) that can lead to toxic epidermal necrosis (TEN) which can be fatal. Patients should be instructed to seek immediate medical attention if they experience new onset of a fast or abnormal heartbeat; difficulty urinating; muscle weakness or cramps; nausea, vomiting, or diarrhea. Monitor patient's adherence to the dosing regimen.

>SAFETY wires

continued from page 4

- Monitor ADC overrides to verify appropriateness, and documentation of administration.
- Using a multidisciplinary team, periodically review for appropriateness and approve the list of medications available using the override function.

Special Announcements

Become an ISMP Fellow

ISMP is now accepting applications until **March 31, 2023**, for our unique Fellowship programs that will begin in the summer—the ***ISMP Safe Medication Management Fellowship*** and the ***FDA/ISMP Safe Medication Management Fellowship***. For a brief description of our Fellowship programs, candidate qualifications, program brochures, and directions for applying, please visit: www.ismp.org/node/871. See **page 5** of this newsletter for additional information.

FREE drug diversion 2-part webinar

Drug diversion is a serious problem that affects patients' and health professionals' safety. Patients may suffer from suboptimal therapy, substandard care, or be at risk for adverse reactions or infections. Join us on **February 15, 2023**, for ***Part I: The Pursuit of Prevention—Confronting Drug Diversion***, which will highlight how organizations can confront drug diversion. ***Part II: Reducing the Risk and Infection Outbreaks from Drug Diversion***, will be held on **March 15, 2023**, and will look at drug diversion from a risk management and an infection control perspective. For details and to register, visit: **Part I**, www.ismp.org/node/61019; and **Part II**, www.ismp.org/node/61022.

Editors: Ann Shastay, MSN, RN, AOCN; Jennifer Gold, MSN, RN; Shannon Bertagnoli, PharmD; Michael Cohen, RPh, MS, ScD (hon), DPS (hon), FASHP; Kelley Shultz, MD. ISMP, 5200 Butler Pike, Plymouth Meeting, PA 19462. Email: ismpinfo@ismp.org; Tel: 215-947-7797.

ISMP Safe Medication Management Fellowships

ISMP is now accepting applications for unique Fellowship programs commencing in 2023

ISMP Safe Medication Management Fellowship

Location and Term: This Fellowship commences in July 2023. The Fellow will spend 12 months with ISMP, a virtual-hybrid organization with its headquarters located in the suburbs of Philadelphia, PA. Relocation is not required; however, in-person meetings may be required as frequently as monthly, and the Fellow is responsible for their own travel expenses.

Description: This Fellowship offers a healthcare professional with at least 1 year of postgraduate experience in a healthcare setting an unparalleled opportunity to work collaboratively with the nation's experts in medication safety to assess and develop interdisciplinary medication error-prevention strategies.

FDA/ISMP Safe Medication Management Fellowship

Location and Term: This Fellowship commences in the summer of 2023. The Fellow will spend 6 months with ISMP, a virtual-hybrid organization with its headquarters located in the suburbs of Philadelphia, PA, and 6 months with the US Food and Drug Administration (FDA), which is located in Silver Spring, MD. Relocation is not required; however, in-person meetings may be required as frequently as monthly, and the Fellow is responsible for their own travel expenses.

Description: This Fellowship, open to a healthcare professional with at least 1 year of postgraduate experience in a healthcare setting, is a joint effort between ISMP and FDA's Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Divisions of Medication Error Prevention and Analysis I and II. The Fellowship allows the candidate to benefit from ISMP's years of medication safety experience along with FDA's valuable regulatory experience focused on medication error prevention.

Applicants for all Fellowship programs must be legally eligible to work in the US and have excellent written and verbal communication skills. A competitive stipend is provided with all Fellowship programs.

How to Apply

For a complete description of candidate qualifications and how to apply online, visit:
www.ismp.org/professional-development/fellowships

The application deadline for all Fellowship programs is **March 31, 2023**.

ISMP
An ECRI Affiliate

www.ismp.org