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ISMP An ECRI Affiliate

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

A comprehensive, proactive plan is needed to mitigate risk when changing drug concentrations

Problem: Errors related to a medication's concentration have been reported to ISMP, particularly when multiple concentrations exist. These errors are more prevalent during transitions in patient care and when switching to an alternative product with a different concentration, including during a drug shortage. We have previously published many of these errors, as well as the risks associated with concentration changes in commercially available products. For example, in our last newsletter, we wrote about the risk of errors as healthcare providers transition patients to the recently approved **EPRONTIA** (topiramate) 25 mg/mL oral solution, which differs from common pharmacy compounded topiramate concentrations of 20 mg/mL for adults and 6 mg/mL for children (www.ismp.org/node/32061). We also warned practitioners about a new formulation of baclofen oral suspension, **FLEQSUVY** (25 mg/5 mL), which differs in strength from another brand of baclofen oral solution, **OZOBAX** (5 mg/5 mL), used for the same purpose (www.ismp.org/node/32062). We recommended standardizing to a single concentration, when possible, and establishing a comprehensive, proactive concentration change plan to prevent undesirable consequences, including errors, during the conversion.

The American Society of Health-System Pharmacists (ASHP) *Standardize 4 Safety* initiative (www.ismp.org/ext/923) is a national, interprofessional initiative that has created several standardized concentration lists. To date, the initiative has provided lists of standard concentrations for many adult and pediatric continuous medication infusions, and oral liquid medications. Additional lists are coming soon. Healthcare providers are encouraged to adopt these standardized concentrations to decrease the risk of medication errors, increase provider efficiency, and improve patient outcomes.

Recent Errors During Concentration Changes

Medication errors, including serious under- and overdoses, can happen if organizations overlook even the smallest details when converting to a new concentration. Two recently reported errors illustrate this risk.

Case 1

A hospital pharmacy that had been compounding intravenous (IV) milrinone (100 mcg/mL) infusions for heart failure patients decided to switch to commercially available, ready-to-use premixed bags with a different concentration (200 mcg/mL) to reduce the risk of a pharmacy preparation error, improve efficiency, and differentiate the standard milrinone concentration from a much stronger concentration (1 mg/mL) that the pharmacy also compounded for fluid-restricted patients. The pharmacy coordinated the conversion in various computer systems, including the electronic health record (EHR), pharmacy technologies and IV workflow systems, and the smart pump drug library. Soon after switching to the 200 mcg/mL concentration, an intensive care unit (ICU) nurse received a patient from the operating room (OR) with a milrinone infusion. When she tried to put the milrinone infusion on a smart infusion pump, she realized that the infusion must have been prepared using the old concentration, 100 mcg/mL. Investigation of the event identified that anesthesia staff used a separate anesthesia-specific documentation system that had not been updated to the 200 mcg/mL concentration.

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SAFETY briefs

HIGH-ALERT

US name and International Nonproprietary Name (INN) are different. A clinical pharmacist reported confusion when pharmacy staff initially tried to locate **ANDEXXA** (coagulation factor Xa [recombinant], inactivated-zhzo), manufactured by Alexion Pharmaceuticals for AstraZeneca. This product is a reversal agent for patients taking **ELIQUIS** (apixaban) or **XARELTO** (rivaroxaban) who are experiencing life-threatening or uncontrolled bleeding. Andexxa is also used off-label to reverse anticoagulation with **SAVAYSA** (edoxaban) and **LOVENOX** (enoxaparin).

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Figure 1. Andexxa is labeled as "coagulation factor Xa (recombinant), inactivated-zhzo" and is not referred to as its commonly known International Nonproprietary Name (INN), andexanet alfa.

Nominations open for CHEERS AWARDS

Each year, ISMP honors individuals, organizations, and groups from various healthcare disciplines that have demonstrated an exemplary commitment to medication safety through innovative projects with an **ISMP CHEERS AWARD**. The **AWARDS** will be presented in December—more to follow on the celebration! Nominations for this year's **CHEERS AWARDS** will be accepted through **September 9, 2022**. ISMP accepts external nominations, including self-nominations. Please refer to **page 6** for a checklist of **DOs and DON'Ts** when submitting a nomination for a **CHEERS AWARD**. For details and to submit a nomination, visit: www.ismp.org/node/123.

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Case 2

A wholesaler notified a hospital pharmacy that an over-the-counter (OTC) antidiarrheal medication, loperamide 1 mg/5 mL (0.2 mg/mL) oral solution, was being discontinued. So, the pharmacy purchased another loperamide oral solution with a different concentration of 1 mg/7.5 mL (0.13 mg/mL). Communication about the change was shared with staff, computer systems were updated, and patients were switched to the new concentration. Staff thought that all bottles containing the discontinued concentration had been removed from the pharmacy and discarded. While checking an oral solution batch of loperamide a few weeks later, a pharmacist discovered that a bottle of the discontinued loperamide concentration (1 mg/5 mL) had been used to fill oral syringes that were labeled with the new loperamide concentration (1 mg/7.5 mL). Barcode scanning was not available in the pharmacy to detect the error, and because only one concentration was typically available, pharmacy staff had not noticed the concentration difference. Doses from a batch of oral syringes had already been dispensed from the bottle the previous day, resulting in several patients receiving almost twice the intended dose. These patients were monitored, and no harm was noted. Investigation of the event determined that a bottle of the 1 mg/5 mL oral solution in the overstock area had not been discarded and was used.

SAFE PRACTICE RECOMMENDATIONS: Whether adopting the standard concentrations promoted by *Standardize 4 Safety* or exploring a change that requires a different medication concentration, consider the following elements of a comprehensive, proactive concentration change plan to prevent confusion and medication errors.

Select a Conversion Team

- Commission a small, dedicated team with representation from inpatient pharmacy, informatics, nursing, medical staff, and other disciplines (e.g., anesthesia staff, outpatient pharmacy, respiratory therapy, clinical nutrition, emergency medical services) as needed when a concentration change is necessary in your organization. Have the team plan, implement, monitor, and sustain each change. Involving an interdisciplinary team enhances collaboration across disciplines; improves the readiness of health systems to make a change; results in more efficient, higher-quality implementations; and sustains the change through mentoring and prompt problem-solving.[1]

Determine Feasibility

- Assess the ease of procuring or compounding the new concentration, considering the cost, required resources, and whether this will be a temporary or long-term change.

- Have the team review the medication's normal dose range as well as outliers (patients on higher or lower than typical doses) to ensure the new concentration is feasible for your organization. For example:
  - ☐ If you are considering a more concentrated infusion, will there be any smart infusion pump low-rate limitations that would prevent the practitioner from being able to program and administer the dose as patients are being weaned off the medication?
  - ☐ If you are considering a more diluted concentration, could this result in any patients receiving too much fluid volume?
  - ☐ You may be required to make a product change with a different concentration during a drug shortage, despite limitations; in that case, the team can determine whether it is feasible to sustain the concentration change after the drug shortage has been resolved.

- If your organization plans to transition to the standard concentrations in *Standardize 4 Safety*, use a phased approach to make the conversions due to the numerous systems involved and various actions needed to prevent an error during the transition. Have the team prioritize the medication concentrations that require updates, managing just one product change at a time.

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Andexxa has an International Nonproprietary Name (INN), andexanet alfa, which is widely cited in professional references, including *Lexicomp,* but not included on the vial label or product labeling. In one case, a clinical pharmacist called the main pharmacy to confirm the availability of andexanet alfa in anticipation of a patient who was potentially at high risk of bleeding. After searching the pharmacy inventory, a pharmacy technician reported that the pharmacy did not have the medication, which caused concern. However, the pharmacy procurement staff notified the clinical pharmacist the following morning that the pharmacy had 35 vials on hand.

The next month, a hematologist contacted the same clinical pharmacist to ensure the pharmacy had andexanet alfa on hand in case it was needed if protamine failed to reverse active bleeding for a patient who had a supratherapeutic dose of enoxaparin. The clinical pharmacist requested andexanet alfa, and again, a pharmacy technician informed him the pharmacy did not have the drug. Remembering he had been told that the pharmacy had 35 vials of Andexxa on hand, the clinical pharmacist followed up with the sterile compounding supervisor, who mentioned that the nonproprietary name on the actual container label is coagulation factor Xa (recombinant), inactivated-zhzo (**Figure 1**, page 1). With this information, the pharmacy technician was then able to locate the medication.

Confusion caused by the various nonproprietary naming conventions are troubling and could lead to treatment delays or lack of access to the needed reversal agent. We spoke to the manufacturer and the US Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) and learned that the US nonproprietary naming convention uses the blood factor name rather than the INN. Organizations should review how this medication is ordered and displayed in their electronic health record (EHR) and ensure consistent naming across all systems, labels, and storage areas. Including the brand name with the generic name in search fields and order

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Plan the Change

- Involve frontline staff to identify which systems will be impacted by the concentration change and anticipate the necessary modifications. For example:
  - ☐ Review standard concentration references, related policies and procedures, master formulation records for extemporaneously compounded products, and patient teaching materials, to determine any necessary modifications.
  - ☐ If the medication is on your automated dispensing cabinet (ADC) override list, does a safety review show that the new concentration may warrant removal from the list? Will the new formulation fit into the allotted ADC compartment?
  - ☐ Do prescribing systems/EHRs, medication administration records (MARs), and/or smart infusion pump drug libraries require modifications? Depending on your organization, there may be certain electronic systems (e.g., stand-alone prescribing systems) and unique devices (e.g., smart pump drug libraries) used in perioperative areas, the emergency department, radiology, catheterization laboratory, dialysis department, and other specialized areas that will need to be updated separately.
  - ☐ Evaluate areas and technologies in the pharmacy where the concentration will need to be modified, including inventory system software, automated compounding devices, IV workflow management systems, master formulation records, robotics, radio frequency identification (RFID) systems, unit dose packaging templates, the controlled substance safe, and ADCs.
  - ☐ Do any emergency or critical care reference guides (e.g., critical care tables, code binders) used during rapid responses or other emergencies need to be modified?
  - ☐ For concentration changes of stock medications or infusions, where is the current supply of the older concentration stored, how can you coordinate the swapping out of all stock, and where should the new product exist outside the pharmacy?
- Prepare and validate conversion charts (electronic or manual) for each concentration change.
- Plan for and test the barcode for each new medication concentration that will be needed with pharmacy inventory, preparation and dispensing software, and bedside barcoding technology.
- If the concentration change involves a new, commercially available product, review the product for potential look-alike and sound-alike drug names (www.ismp.org/node/31981), and whenever possible, review the packaging for potential look-alike hazards that will require additional safeguards, such as a modified storage location.
- For each concentration modification, determine the key practitioner types that should be involved in the decision-making process, along with required committee approvals.
- Determine a go-live date for the concentration change in advance, if possible. Changing a concentration due to a drug shortage may require a hurried go-live date; however, other concentration changes should allow for a scheduled go-live date. Avoid go-live dates just prior to a weekend or holiday.
- Establish a communication and staff education plan to alert all involved practitioners about the concentration change and go-live date.
- Establish a plan to identify all patients with current, held, or future inpatient orders for the medication that will need to be converted to the new concentration.
  - ☐ If your organization has an outpatient pharmacy, identify in the computer system all outpatients who currently receive the old concentration of the medication to ensure all active outpatients are converted to the new concentration within a defined period of time.

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sets may help reduce confusion. Alert staff to the INN and US naming convention differences to ensure the medication can be located when needed. Until systems can be aligned, if practitioners are unfamiliar with the medication's blood factor name, consider affixing a temporary auxiliary label to notify staff that this product is also known as andexanet alfa.

List of COVID-19 vaccine resources. Immunize.org (formerly the Immunization Action Coalition) has compiled a tool for healthcare professionals that organizes information about coronavirus disease 2019 (COVID-19) vaccines currently available in the US. The *Checklist of Current Versions of US COVID-19 Vaccination Guidance and Clinic Support Tools* (www.ismp.org/ext/933) provides links to dosing guidance for various ages, *Fact Sheets*, package inserts, storage and handling summaries, as well as preparation and administration information, all in one place. This resource is updated at least monthly.

Lot number or expiration date? A vial of droperidol (5 mg/2 mL, American Regent) appears to have expired on January 24, 2020 (**Figure 1**). However, 2020 is actually the lot number, as noted by the small words printed just below the barcode. Thus, the last day of January 2024 is the actual expiration date. Displaying a 4-digit lot number that is similar to a recent year, and listing it right next to the expiration date, contributes to confusion. This could lead to unnecessarily discarding what is thought to be an expired medication, a situation made worse because the medication has been on the drug shortage list.

The practitioner who reported this to ISMP contacted the manufacturer about this issue, as did we. If the lot number needs to be numerical, manufacturers

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Figure 1. The lot number, 2020, on the 5 mg/2 mL droperidol vial can be mistaken for the year the vial expires.

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- Before a patient transitions from inpatient to outpatient, develop a patient education plan if there is a change in the required volume of their medication taken at home.
  - ☐ In outpatient pharmacies, consider tagging prescriptions for medications with a concentration change for mandatory patient education.

Implement the Change

- Initiate the communication and staff education plan.
- Coordinate the removal of old stock located in areas identified during planning (e.g., central pharmacy, satellite pharmacies, overstock areas; patient care unit storage locations such as patient-specific bins or drawers, ADCs, code carts).
- Provide the medication in the new concentration to locations identified during planning.
- Activate the new concentration and deactivate the previous concentration in all electronic systems as anticipated during planning.
- Run a report of all active, held, and future orders to identify patients currently prescribed the medication.
- Work closely with nursing staff prior to converting all active patients to the new concentration and coordinate any required modifications to administration times.
- Require new orders that discontinue the old concentration and start the new concentration so the MAR reflects the new concentration. (The timing of this should be coordinated with the distribution of the new concentration and removal of the old concentration.)
- Using the teach-back method, communicate with patients and/or caregivers about the new concentration, the corresponding volumetric dose, and how to measure each dose of an oral liquid medication with an oral syringe. Also, teach home infusion patients or their caregivers about programming changes for their infusion pumps.
- As applicable, collect information on the strength of concentrations during medication reconciliation when a patient is admitted.
- Validate that discharge paperwork and prescriptions reflect the new concentration.

Sustain the Change

- Run a follow-up report to check that patients who have been prescribed medications in the previous concentration have been updated to the new concentration.
- Engage in safety walkarounds in the pharmacy and all affected patient care units to gather feedback, answer questions, troubleshoot any issues, and mentor practitioners through the concentration change.

Reference

1) National Implementation Research Network. Framework 4: implementation teams. In: NIRN. *Module 1: An Overview of Active Implementation Frameworks*. The University of North Carolina at Chapel Hill; 2021. www.ismp.org/ext/929

Newsletter readers act upon ISMP recommendations

ISMP would like to extend its sincere appreciation to 172 readers who completed our ***ISMP Medication Safety Alert! Acute Care Readership Survey*** between March and May 2022. It had been almost a decade since we last surveyed newsletter readers about their overall satisfaction with this newsletter (www.ismp.org/node/633). Please know that your recent input is highly valued and will be used to improve the newsletter. A brief description of the survey results follows.

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should consider using at least 5 numbers, and perhaps incorporating letters at the beginning and/or end of the lot number to differentiate it from the expiration date. USP General Chapter <7> *Labeling* will be requiring manufacturers to use a 4-digit year on their products by 2023. In May 2022 (see Your *Reports* at *Work*), the US Food and Drug Administration (FDA) released a labeling guidance document, *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (www.ismp.org/ext/930), which also includes a 4-digit recommendation for the expiration date year.

Your *Reports* at *Work*

On May 18, 2022, the US Food and Drug Administration (FDA) published final guidance for industry, *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (www.ismp.org/ext/930). As explained in the document, its purpose is to help prescription drug and biologic product manufacturers minimize medication errors associated with their products. The guidance provides principles and recommendations for ensuring that critical elements of a product's container and carton labeling are designed to promote safe dispensing, administration, and use of the product. Although it is not binding for FDA or manufacturers to use the approaches suggested, in most cases, both FDA and manufacturers follow this guidance.

We have reviewed the document and believe that FDA has done a thorough job in addressing labeling and packaging issues that have led to confusion and medication errors through the years. It's hats off to you, the error reporters, because the document would not have been possible without your active reporting of errors and hazardous conditions to the ***ISMP National Medication Errors Reporting Program*** (ISMP MERP) and the FDA Adverse Event Reporting System (FAERS). Thank you, and keep the reports coming!

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Respondent Profile

Most survey respondents were pharmacists (61%) and nurses (21%); however, we also received responses from pharmacy technicians (9%); quality, risk, or safety practitioners (7%); and others (2%). Respondents reported their position as frontline staff (30%), medication safety specialists (30%), managers or directors (28%), educators (5%), administrators or executives (1%), or other varied positions (6%).

When and How the Newsletter is Read

More than four out of five respondents read the newsletter immediately when received (35%) or within a week of publication (48%). Most respondents (81%) typically read the PDF newsletter or the online newsletter version, which is available on the ISMP website. Most read the newsletter from a computer screen (92%) and/or from a printed copy (25%). Few respondents read the newsletter from a phone (4%) or a tablet (3%) screen.

Sharing the Newsletter with Others

Three-quarters of respondents (75%) reported that the newsletter is shared with them and others in the organization as a PDF file. Respondents reported sharing the newsletter with all pharmacy staff (46%) or all pharmacists (38%), and all nurses (21%). Another 13% share the newsletter with select pharmacy staff or pharmacists, and 40% share it with select nurses. Fewer share the newsletter with all physicians (9%) or select physicians (25%).

Newsletter Length and Format

Most respondents agreed or strongly agreed that the newsletter information was presented in an easy-to-read, organized manner (88%) and at an appropriate academic level (97%). They felt that the content stimulated discussion among colleagues, and 86% of respondents reported using the newsletter to educate staff and/or students. Ninety-four percent of respondents found the length of the newsletter and the number of pages to be just right. Several respondents provided suggestions for improving the layout of the newsletter, such as using more bullet points, providing the text in a larger font size, and presenting each article in a linear fashion so the material flows in a continuous format. These suggestions will be considered for future issues.

Implementing Recommendations

Most respondents strongly agreed (56%) or agreed (33%) that the newsletter has helped to reduce or prevent harmful medication events. Most reported that they have used information from the newsletter to make improvements in their personal practice habits (98%), in their unit or department (91%), or system-wide (85%). Additionally, 71% of respondents reported visiting the ISMP website for more information. Two-thirds (67%) of respondents agreed or strongly agreed that their organization uses the ISMP ***Action Agenda*** to assess risk and reduce the frequency of medication errors.

Overall Satisfaction

Nearly all respondents (96%) agreed that the newsletter increases their understanding of medication errors and how to prevent errors. Most (93%) felt the recommendations presented in the newsletter were practical, helpful, and relevant to their practice. Almost all respondents (99%) strongly agreed or agreed that the newsletter serves as a credible, respected, and reliable source of information on medication safety.

Conclusion

ISMP recommendations are built upon the learning that accompanies a thorough analysis of medication errors reported to the ***ISMP National Medication Errors Reporting Program*** (www.ismp.org/MERP), literature review, and our peer review process. Thank you to those who report medication safety issues to ISMP so that we can share the lessons learned with the healthcare community. And kudos for putting the newsletter to good use and adopting many of the published error-prevention strategies! We look forward to our continued service to you and encourage your ongoing comments about the newsletter via: ismpinfo@ismp.org.

Special Announcements

Apply for a Just Culture scholarship

The Just Culture Company, in cooperation with ISMP, will award three ***Judy Smetzer Just Culture Champion Scholarships*** annually to honor Judy Smetzer, BSN, RN, FISMP, a retired ISMP vice president. Applications for next year's scholarships are due by **July 31, 2022**, after which ISMP will select the scholarship awardees. For details and to apply, visit: www.ismp.org/node/30840.

Virtual MSI workshops

Don't miss the opportunity to register for one of our unique 2-day, virtual ***ISMP Medication Safety Intensive (MSI)*** workshops offered in 2022. Our next workshop is scheduled for **August 4 & 5, 2022**. To register, visit: www.ismp.org/node/127.

Free FDA webinar series

The US Food and Drug Administration's (FDA) Division of Drug Information is presenting a **FREE** webinar, ***FDA Drug Topics: Drug Shortages: Root Causes and Potential Solutions***, on **June 28, 2022**. For details, visit: www.ismp.org/ext/30, and to register for the program, visit: www.ismp.org/ext/31.

FREE webinar from ASPEN

On **June 22, 2022**, the American Society for Parenteral and Enteral Nutrition (ASPEN) will be hosting a **FREE** webinar, ***Incorporating Multi-Chamber Bag (MCB) Parenteral Nutrition Formulations into Practice***, in light of the automated compounding device valve shortage. For details and to register, visit: www.ismp.org/ext/925.

To subscribe: www.ismp.org/node/10

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Report medication and vaccine errors to ISMP: Call 1-800-FAIL-SAF(E) or visit our website at: www.ismp.org/report-medication-error. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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DOs and DON'Ts for submitting an ISMP CHEERS AWARD Nomination

Do you know an individual or an organization/group collaborative that you want to nominate for an **ISMP CHEERS AWARD**? Here are some helpful tips to make sure your nomination meets the criteria. **Nominations that are incomplete or do not meet the criteria outlined below will not be considered.**

DO

Nominate an Individual or Organization/Group Collaborative that:

- Clearly identifies a high-risk, error-prone medication safety initiative
- Demonstrates successful implementation of the initiative
- Provides measurable outcomes
- Utilizes innovative, proactive medication error-reduction strategies based on ISMP's philosophy and recommendations in ISMP newsletters, ISMP ***Action Agendas***, ISMP guidelines, and other ISMP resources
- Participates in medication safety committees, teams, and/or does advocacy work
- Will share the initiative with others (at no cost)
- Exemplifies a commitment to the promotion of medication safety

Complete the nomination form:

- Ensure all fields are filled in accurately and completely.
- Provide your information as the submitter.
- Provide information about the nominee (self nominations are accepted).
- Provide a paragraph summarizing why you believe this nominee should receive an award.
  - In your own words, please highlight the project/nominee description, the impact of the initiative, and/or the nominee's commitment to medication safety (five to ten sentences).
- After submitting the nomination, upload documentation to support the nomination (e.g., a full description of the nomination and safety initiative, slides, data tables, diagrams, figures, meeting minutes, pamphlets, curriculum vitae [CV]).
- Additional forms and information required for **Organizations**:
  - An Interdisciplinary Commitment Declaration
  - Proof of accreditation by an appropriate professional body (e.g., The Joint Commission)
  - Proof of executive leadership commitment by completing a Leadership Declaration

Submit your nomination, along with supporting documents and forms, by September 9, 2022.

DON'T

Don't submit a nomination that does not clearly identify a high-risk, error-prone medication safety initiative.

Don't submit only one or two sentences about the nominee without supporting documentation.

Don't forget to complete all the information on the nomination form before submitting.

Don't enter pages of information into the summary text box (summarize the project/nominee in only five to ten sentences).

Don't forget to upload a full description of the nomination, medication safety initiative, and additional documentation to support your nomination after completing the initial form (after you submit the nomination).

Don't forget to submit all your information by September 9, 2022.

For a list of past **ISMP CHEERS AWARD** winners, click here.