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Medical Devices Safety Update

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Be alert to standards to prevent risk of misconnections

Health professionals are reminded of the risks associated with intravenous and epidural misconnections and are advised to take note of the relevant standards that have been developed to mitigate the risks.

The January 2014 edition of *Medical Devices Safety Update* described strategies to minimise intravenous and epidural misconnections and foreshadowed the development of international standards to address the issue. These standards have now been developed.

Many of the reported cases in 2014 had resulted in serious adverse events and in some instances were fatal.

In one reported case, confusion between lines resulted in a medicine intended for epidural infusion being inadvertently connected to a catheter for intravenous administration. This error was identified quickly and corrected, so the patient suffered minimal harm and discomfort. Had the error not been identified early or the situation had been reversed (if an intravenous infusion had been connected to an epidural port), the consequences could have been more serious.

The TGA's reviews of adverse event reports found that user error was a major contributing factor in many cases.

The standards

The standards developed to assist with decreasing reports of misconnection are:

- Standard ISO 80369-1 Small-bore connectors for liquids and gases in healthcare applications – Part 1: General requirements (15/12/2010)
- Standard ISO 80369-2 Breathing systems and driving gases
- Standard ISO 80369-3 Enteral (feeding tube) applications
- Standard ISO 80369-4 Urethra and urinary tubing
- Standard ISO 80369-5 Limb cuff inflation or non-invasive blood pressure
- Standard ISO 80369-6 Neuraxial applications used to deliver medications to spinal fluid
- Standard ISO 80369-7 Luer fittings.

The Australian Commission on Safety and Quality in Health Care (ACSQHC) and the Australian and New Zealand College of Anaesthetists (ANZCA) have published a joint position statement supporting the introduction of the sixth standard.

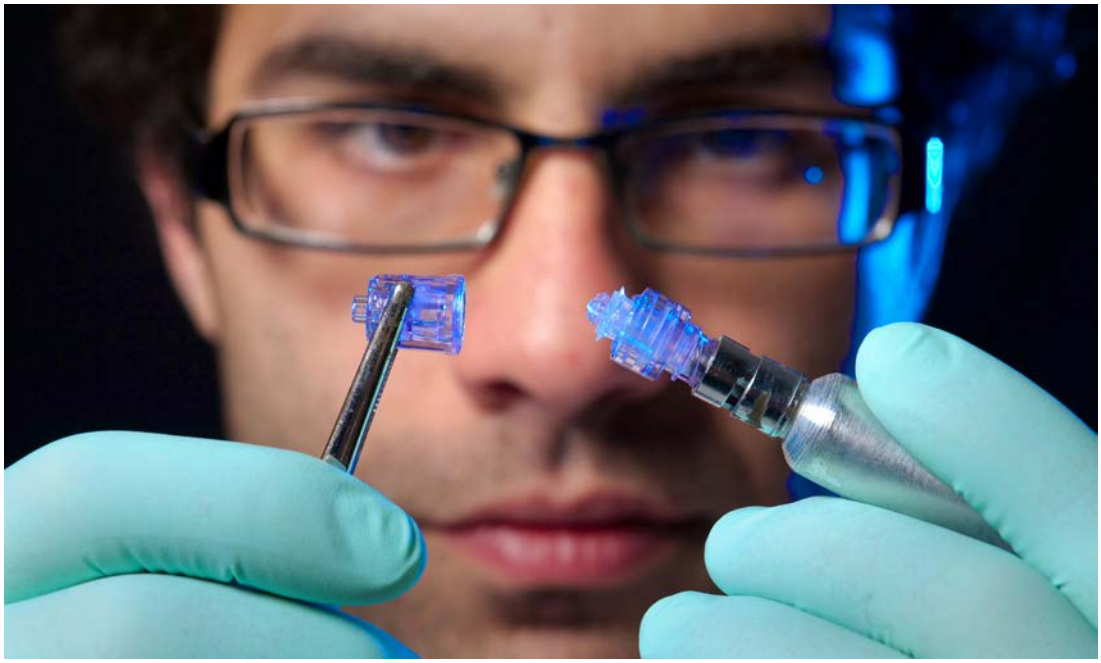
Advice for health facilities

To help prevent misconnection issues, the TGA recommends the following for health facilities:

- Ensure relevant staff are aware of the different standards and can adopt them in the workplace.
- Be alert to the new standards when purchasing new equipment.
- Follow any hospital or national recommendations for decreasing misconnections such as those published by the ACSQHC (for example, the national user-applied labelling standard).

Medical Devices Safety Update is the medical devices safety bulletin of the Therapeutic Goods Administration (TGA)

TGA Health Safety Regulation



Centers for Disease Control and Prevention laboratory technician Mustafa Mazher with a disassembled, needleless connection. Photo: James Gathany.

- Ensure adequate training of all staff members who are responsible for patient lines and connectors. Ensure this training includes misconnection prevention.
- Ensure staff members are aware that they must trace all lines from the device or solution back to the access point to ensure the correct fluid is being delivered via the correct route.
- When transporting a patient with multiple lines, ensure that handover includes a description of what each line/device is for and where they connect.
- Develop polices/procedures aimed at preventing misconnection of lines and strategies to deal with the issue should it occur.

Reporting problems

The TGA is concerned that incidents involving misconnections may be under-reported and reminds health professionals of the importance of reporting all adverse events or near misses involving medical devices.

Reporting adverse events assists the TGA in effectively identifying and responding to safety issues.

Reports can be made via the TGA website.

Eltrombopag: reports of interference with bilirubin and creatinine test results

Use of eltrombopag can lead to bilirubin and/or creatinine test results being inconsistent with clinical observations due to the highly coloured substance causing chromatogenic interference in analysing equipment.

Eltrombopag is an oral thrombopoitin receptor agonist, marketed in Australia under the brand name Revolade.

It is indicated for use in adults with aplastic anaemia and both adults and children with refractory idiopathic thrombocytopenia purpura, as well as thrombocytopenia in adults with chronic hepatitis C to allow interferon therapy.

Eltrombopag can be hepatotoxic and monitoring of ALT, AST and bilirubin is advised by the manufacturer. Creatinine monitoring is also advised in patients with renal disease.

However the drug has been found to interfere with the latter two assays. Serum discoloration

and interference with total bilirubin and creatinine testing have been reported in patients taking eltrombopag.

The issue is noted in the Product Information which also advises: 'If the laboratory results and clinical observations are inconsistent, evaluation of contemporaneous aminotransferase values may help in determining the validity of low total bilirubin levels in the presence of clinical jaundice and blood urea should be evaluated in the event of an unexpectedly high serum creatinine. Re-testing using another method may also help in determining the validity of the result.'

The UK government has issued a warning regarding potential drug interference in test results.

What is happening?

Eltrombopag is red, and it shows a pH dependant colour shift to yellow or orange. Many chemistry assays are chromatogenic, and the analyser measures the increase in absorbance at certain wavelengths.

The colour shift is the key to the interference, as many analysers can compensate for a certain degree of haemolysis or icterus. In circumstances involving the addition of acidic or basic reagent, the plasma colour can shift from red to yellow or orange, even as the reaction increases the colour level, giving an overall reduction in colour intensity and thus a reduction in absorbance, leading to a false negative result for bilirubins, while the increase in yellow pigment yields a falsely elevated creatinine result.

Not all methods are affected, and this may be dependent on the nature of the reagents or whether the analyser blanks on reagent alone or initial reagent + sample.

Doses of greater than 100 mg per day have been found to cause a reversible yellowing of the skin.

Other drugs which may cause this problem include 'Rose Bengal', being trialled in a formulation called PV-10 for use in melanoma and breast cancer, and phenazopyridine hydrochloride, used to treat urinary pain.

The TGA recommends that creatinine and bilirubin results for patients on eltrombopag be interpreted in combination with other liver and kidney relevant results and, where discrepant, alternative or confirmatory testing be undertaken, using alternative testing methods if available.

Amniotic fluid tests should be used in conjunction with a clinical assessment

Amniotic fluid detection in vitro diagnostic devices should be used as an adjunct when clinical assessment is not conclusive rather than a stand-alone diagnostic test.

Amniotic fluid/rupture of membrane (ROM) in vitro diagnostic devices (IVDs) are point-of-care tests used in the assessment of pregnant women who present with symptoms or signs suggesting rupture of membranes.

Prelabour rupture of membranes (PROM, >37 weeks gestation), premature prelabour rupture of membranes (PPROM, <37 weeks gestation) and midtrimester prelabour rupture of membranes (16-26 weeks gestation) can increase fetal morbidity, due to risk of infection and prematurity, thus requiring prompt diagnosis to enable optimal management.

The US Food and Drug Administration (FDA) has reported on several deaths associated with false-negative test results in relation to amniotic fluid detection IVDs and has distributed a letter to health care providers alerting them to the risks associated with these devices.

TGA staff have reviewed related Australian adverse event reports and have not encountered the same issues described the FDA. There is a single Australian report for a false negative report which resulted in the woman being discharged from hospital and then subsequently giving birth at home. No harm to child or mother was reported.

The FDA report is consistent with the recognised guidelines and publically available literature[1,2,3,4] that use of point of care ROM tests should be done in conjunction with a clinical assessment, including history and examination with a sterile speculum. Use of lab tests (nitrazine or ferning) or ROM IVDs

should be used when there is clinical uncertainty regarding the initial assessment. It is consistently stated in the literature that they should not be used as a sole source of information to make critical management decisions.

The negative predictive value of these tests is unlikely to be 100% for use in cohorts other than those recommended in the IFU, especially if not used as per the IFU. There are limitations outlined in the IFUs, for example in one IFU it is stated the test is not accurate 12 hours after the leaking has occurred, significant amounts of blood interfere with the accuracy and removal of any disinfectant or medicines in the vagina interferes with the accuracy.

The gravity of a false negative that influences a critical management decision (for example, a patient being sent home when PROM/PPROM is incorrectly ruled out due to a negative on the ROM IVD) is likely to be maximal at the end of second trimester/first half of third trimester when a home delivery of a premature baby will have adverse implications for long term outcome. A home delivery of an unviable fetus (<24 weeks) may have poor psychological outcomes for the mother, but is unlikely to change the outcome for the baby. A home delivery for a term baby will usually not affect maternal or fetal outcome, but may if there is a complication such as post-partum haemorrhage or the baby is compromised in some way.

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2. Duff P et al. 'Preterm pre labour rupture of membranes'. UpToDate September 2018.
3. Scroza et al 'Management of prelabour rupture of the fetal memrbanes at term'. UpToDate January 2018.
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What to report? Please report adverse events, as well as near misses

The TGA encourages the reporting of any suspected adverse event or potential adverse event relating to a medical device. Adverse events can involve actual harm to a patient or caregiver, or a near miss that may have resulted in harm.

Some issues relating to medical devices that may lead to adverse events and prompt you to report include:

- mechanical or material failure
- design issues
- labelling, packaging or manufacturing deficiencies
- software deficiencies
- device interactions
- user/systemic errors

Suspected adverse events or near misses can be reported directly to the TGA:

- **online** at www.tga.gov.au (click 'Report a problem')
- **by emailing** iris@tga.gov.au
- **by mail** to IRIS, TGA, PO Box 100, Woden ACT 2606
- **by fax** to 02 6203 1713

For more information about reporting, visit www.tga.gov.au or contact the TGA's Medical Devices Branch on 1800 809 361.

For the latest information from the TGA, subscribe to the TGA Safety Information email list via the TGA website

For correspondence or further information about Medical Devices Safety Update, contact the TGA's Medical Devices Branch at iris@tga.gov.au or 1800 809 361

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