Australian Government
Department of Health
Therapeutic Goods Administration

Medical Devices Safety Update

Volume 2, Number 2, March 2014

In this issue

TGA tests ultrasound transmission gels for bacterial contamination

Health professionals are advised that the labelling of ultrasound transmission gels has been updated to include additional warnings, information on storage requirements and detailed instructions to ensure safe multi-use of the products.

This follows a worldwide recall of an ultrasound transmission gel due to microbial contamination and subsequent testing by the TGA of all similar gels listed on the Australian Register of Therapeutic Goods (ARTG).

Two gels in Australia have been recalled.[1,2]

The TGA undertook a review of product labelling of the 27 ultrasound transmission gel products included on the ARTG.

Sponsors were required to update the labelling on 18 of the products (for example adding 'for external use only', 'not to be used on broken skin/mucosal surfaces', 'discard if contamination is suspected') after they were found to be non-compliant with Australian regulatory standards.

Health professionals are advised to always review the warnings on ultrasound transmission gel labels and to only use the products as per instructions.

Non-sterile transmission gels should not be used for invasive procedures (for example trans-vaginal, trans-rectal, trans-oesophageal).

Sterile gels are available for such procedures.

REFERENCES

1. L-Gel Ultrasound Transmission Gel recall (safety information). Therapeutic Goods Administration. [accessed 2014 Jan 30]
2. System for Australian Recall Actions. FIAB Ultrasound Transmission and IPL Transparent Gel. Therapeutic Goods Administration. [accessed 2014 Jan 30]

Searchable recall action database available online

The System for Australian Recall Actions (SARA) is a searchable database containing information on recall actions taken in Australia since 1 July 2012. SARA was launched as part of the TGA's commitment to improve transparency, trust and confidence in the safety and quality of therapeutic goods. In addition to SARA, the TGA website contains other valuable sources of information on medical devices safety.

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

TGA Health Safety Regulation

Remind patients of flame dangers while using oxygen concentrators

Analysis by the TGA has revealed an increasing number of adverse events relating to patient injuries sustained from fires involving oxygen concentrators.

Most of the cases reported to the TGA involved patients smoking while using oxygen concentrators.

In the five years to 23 January 2014 there were five reports of burns/fires directly attributed to patients smoking while using oxygen concentrators, including one that resulted in death. Another patient received facial burns after using an angle grinder while connected to an oxygen concentrator.

The TGA undertook a review of labelling and Instructions for Use (IFU) documents for all oxygen concentrators on the Australian Register of Therapeutic Goods to determine whether they included appropriate warnings for users regarding the risk of fire and injury from allowing naked flames and sparks near such devices.

The review found that all oxygen concentrators had appropriate warnings on both the devices and in the IFU.

Health professionals are advised to be aware of the dangers posed by flames and sparks near oxygen concentrators and to ensure patients are aware of the risks.

Adverse events lead to review of surgical gauze with X-ray detectable strips

An additional warning has been added to the product labelling of all surgical gauze products that are supplied with a thermally bonded X-ray strip. The warning identifies that these products are not intended to be unfolded and that the devices should be used as presented/supplied (i.e. folded).

The requirement for the updated labelling followed an adverse event report submitted to the TGA regarding the detachment of the X-ray detectable strip in a surgical gauze product.

The TGA undertook a review of all similar Australian Register of Therapeutic Goods entries. X-ray detectable strips are attached to surgical gauze products using either thermal bonding or by being woven into the fabric.

The review found X-ray detectable strips were more likely to detach in gauze that used the thermal bonding process, rather than woven bonding, if gauze that was intended to be used folded was unfolded.

The aim of the review was to ensure that if the risk of X-ray detectable strip detachment existed, appropriate mitigation strategies were in place. All affected thermally bonded surgical gauze products available in Australia now carry appropriate warning labels on the product packaging.

Health professionals are advised to be aware of this issue and to only use those surgical gauze products as they are intended to be used.

The TGA encourages the reporting of any suspected adverse event or potential adverse event relating to surgical gauze with X-ray detectable strips.

Adverse events can involve actual harm to a patient or caregiver, or a near miss that may have resulted in harm.

This information will assist the TGA to continue to monitor and manage this issue.

For further information about reporting adverse events, visit the 'Report a problem' webpage on the TGA website or phone the Office of Product Review on 1800 809 361.

Index of suspicion: assessing accuracy and predictive value in testing

The TGA has received many reports relating to inaccurate results from diagnostic tests, with the majority relating to issues with in vitro diagnostic devices.

It is important to note that even in perfectly functioning testing equipment, you will sometimes get false positives and negatives. This means health professionals need to use their clinical judgement and assess test results according individual circumstances.

Use of the troponin blood test is a good example where clinical observations, judgement and experience play an important part in assessing the significance of results.

Over the past five years the TGA Incident Reporting and Investigation Scheme (IRIS) has received 114 reports of false positive troponin results.

A major contributing factor in false positive results is the sensitivity of the test being used. Other factors include incorrect use, blood sample quality and poor device maintenance.

Given the large number of tests performed annually, the incidence of false positive troponin tests is low and within acceptable limits.

The predictive values of tests change depending on the circumstances of each case and you will need to assess the meaning of results, depending on the person being tested and the test being undertaken.

Some key concepts involved in diagnostic test accuracy, namely sensitivity, specificity, positive predictive value, negative predictive value, pre-test probability and post-test probability, are introduced below.

Reference tests: measuring against the gold standard

When thinking about diagnostic test accuracy it is important to understand two concepts, the reference standard and the index test.

The reference standard (sometimes referred to as gold standard) is the definitive test to decide whether an individual has a disease or not. For example, melanoma is diagnosed/defined using histopathology.

Testing someone with the reference standard is often invasive, expensive and time consuming.

For some diseases, it is impractical to apply the reference standard to everyone you suspect of having the disease. In this situation you might want to use a cheaper, easier, less invasive test. In diagnostic test accuracy, this is called the index test.

Examples of index/reference test combinations include ultrasound versus findings at surgery for appendicitis and exercise stress test versus angiogram for coronary artery disease.

Index tests: sensitivity and specificity

The index test will usually not be as accurate as the reference standard.

When we use an index test we want to know how it compares to the reference standard, in other words, how accurate it is. This is done by evaluating two measurements, the sensitivity and specificity.

The sensitivity is the proportion of people who have the disease in whom the index test is positive.

The specificity is the proportion of people who don't have the disease in whom the index test is negative. For example, a sensitivity of 80% can be thought of as follows.

If you have 100 people defined as disease positive by the reference standard, the index test will be positive in 80 of them. Conversely, 20 people will be told by the index test that they don't have the disease when they actually do.

A specificity of 90% can be thought of as follows. If you have 100 people defined as disease negative by the reference standard, the index test will be negative in 90 of them. Conversely, 10 people will be told by the index test that they have the disease when they actually don't. This is illustrated in Table 1 (see next page).

Table 1: Index test with sensitivity of 80% and specificity of 90%

	Disease positive (reference test positive)	Disease negative (reference test negative)
Index test positive	80 (true positive)	10 (false positive)
Index test negative	20 (false negative)	90 (true negative)
Total	100	100

Assessing predictive value

Just looking at sensitivity and specificity in isolation are not that helpful in clinical practice because in clinical practice we are interested in testing people we suspect of having a disease.

We want to know 'if my patient has a positive test, what is the probability that they have the disease?' Or 'if my patient has a negative test, what is the probability that they don't have the disease?' This is demonstrated in Table 2 (see below).

In the example in Table 2, 90 people had a positive index test and 80 of those actually had the disease so the positive predictive value ('if my patient has a positive test, what is the probability that they have the disease?') is 88%. Among the group 110 people had a negative index test and 90 of those were actually disease free so the negative predictive value ('if my patient has a negative test, what is the probability that they don't have the disease?') is 81%.

As seen in Table 2, 100 out of the 200 people tested had the disease. This is a population prevalence of 50%. This can be also thought of as the pre-test probability. This is the probability that a patient has the disease before you do any testing on them.

In Table 3 (see below) the sensitivity and specificity remain the same, 80% and 90% respectively. However, in this case, the pre-test probability has changed. Now, only 25% of the population has the disease.

Remember, the total number of patients remains the same and the accuracy of the test remains the same.

The positive predictive value is now 72%, down from 88% and the negative predictive value is now 93%, up from 81%. Both of these measures can also be thought of as the post-test probability.

The positive predictive value is the post-test probability of having the disease after a positive test and the negative predictive value

Table 2: Probabilities and predictive value

	Disease positive (reference test positive)	Disease negative (reference test negative)	Total	Predictive value
Index test positive	80 (true positive)	10 (false positive)	90	80/90 = 88%
Index test negative	20 (false negative)	90 (true negative)	110	90/110 = 81%
Total	100	100	200	

Table 3: Changed pre-test and post-test probabilities

	Disease positive (reference test positive)	Disease negative (reference test negative)	Total	Predictive value
Index test positive	40 (true positive)	15 (false positive)	55	40/55 = 72%
Index test negative	10 (false negative)	135 (true negative)	145	135/145 = 93%
Total	50	150	200	

is the post-test probability of not having the disease following a negative test.

It therefore evident that the post-test probability (the chance that a positive or negative test result is true) changes depending on how likely it is that the person has the disease in the first place.

There are no fixed cut off values of sensitivity and specificity to decide if a diagnostic test is going to be useful.

These values must be considered in parallel with the pre-test probability and the consequences of a false positive or a false negative test.

Conclusion

A reference standard is a definitive test to decide whether an individual has a disease or not, but in many circumstances it is impractical to apply it to everyone suspected of having the disease. In such situations a cheaper, easier, less invasive index test may be available.

When an index test is used it is important to know how it compares to the reference standard, that is how accurate it is. This is done by evaluating two measurements, the sensitivity and specificity.

The sensitivity is the proportion of people who have the disease in whom the index test is positive.

The specificity is the proportion of people who don't have the disease in whom the index test is negative.

It is important to note that the post-test probability (the chance that a positive or negative test result is true) changes depending on how likely it is that the person has the disease in the first place.

There are no fixed cut off values of sensitivity and specificity to decide if a diagnostic test is going to be useful. These values must be considered in parallel with the pre-test probability and the consequences of a false positive or a false negative test.

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 Office of Product Review 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 Office of Product Review at iris@tga.gov.au or 1800 809 361

Medical Devices Safety Update is written by staff from the Office of Product Review

Editor:
Dr Katherine Gray

Deputy Editor:
Mr Aaron Hall

TGA Principal Medical Adviser:
Dr Tony Hobbs

Contributors include:
Mr Trent Greentree
Dr Alex Stevenson