EXPLANATORY STATEMENT

Therapeutic Goods Act 1989

Medical Device Standards Order (Endotoxin Requirements for Medical Devices) 2018

The Therapeutic Goods Act 1989 (the Act) provides for the establishment and maintenance of a national system of controls for the quality, safety, efficacy and timely availability of therapeutic goods that are used in, or exported from, Australia.

Medical Device Standards Order (Endotoxin Requirements for Medical Devices) 2018 (the MDSO) is an order made by the delegate of the Minister for Health under subsection 41CB(1) of the Act.

The MDSO commences on the day after it is registered.

BACKGROUND

Under section 41C of the Act, the regulations (being, the *Therapeutic Goods (Medical Devices) Regulations 2002*) (the MD Regulations) may set out requirements for medical devices, to be known as the essential principles. The essential principles are important mandatory requirements or standards that apply to medical devices, and provide minimum benchmarks relating to the safety and performance characteristics of medical devices.

Sponsors applying to include their kinds of medical devices in the Australian Register of Therapeutic Goods (the Register) (i.e. to seek marketing approval) must certify that their kinds of devices comply with the essential principles, and that they have sufficient information available to substantiate that compliance or procedures in place with the device manufacturer to obtain such information (paragraph 41FD(e) of the Act refers). It is also a condition of inclusion in the Register for medical devices that at all times while a kind of device remains in the Register, the sponsor has sufficient information available to substantiate their product's compliance with the essential principles (paragraph 41FN(3)(a) refers).

A kind of device may also be cancelled from the Register if the Secretary of the Department of Health is satisfied that the certification made in relation to the kind of device's compliance with the essential principles was not, or is no longer, correct (paragraph 41GN(1)(f) refers). Division 1 of Part 4-11 of the Act also sets out criminal offences and civil penalty provisions relating to the importation, supply or export of kinds of medical devices that do not comply with the essential principles.

Section 41CB of the Act authorises the Minister to, by legislative instrument, determine that matters specified in the instrument constitute a medical device standard for the kinds of medical devices identified in the Order, and that medical devices of those kinds that comply with instrument are to be treated as complying with those parts of the essential principles specified in the instrument.

Orders made under section 41CB are not mandatory for sponsors or manufacturers of medical devices, but are designed to assist sponsors and manufacturers by providing a flexible and efficient mechanism, that they may elect to use for the purposes of demonstrating that their products comply with the essential principles.

If medical devices comply with such an order, they are treated, under paragraph 41CB(1)(b) of the Act, as complying with those parts of the essential principles specified in the order. So if a device sponsor elects to comply with an order, then compliance with the order, addressing a particular aspect of an essential principle, would satisfy the Secretary that the relevant essential principle applying to the device in question had been met.

The MDSO relates to endotoxin requirements for medical devices and, if applied correctly, has the effect of demonstrating that the kinds of medical devices identified in the order comply with essential principle 7.2, in relation to minimising the risks associated with endotoxin contaminants and residues in or on medical devices. This order does not apply to risks arising from other sources of pyrogenicity or risks associated with any other contaminants and residues in or on medical devices. Such risks should be separately addressed in order to demonstrate compliance with the essential principle 7.2 of the MD Regulations, if applicable.

Essential principle 7.2 is set out in Schedule 2 to the MD Regulations, and states that:

- a medical device must be designed, produced and packed in a way that ensures that any risks associated with contaminants and residues that may affect a person who is involved in transporting, storing or using the device, or a patient, are minimised, having regard to the intended purpose of the device; and
- in minimising risks, particular consideration must be given to the likely duration and frequency of any tissue exposure associated with the transportation, storage or use of the device.

The MDSO applies to any of the following kinds of medical devices:

- implantable medical devices;
- devices in direct or indirect contact with a person's cardiovascular system, lymphatic system, or cerebrospinal fluid that are labelled sterile and non-pyrogenic (e.g. intravenous catheters, and dialysis tubing);
- devices in direct or indirect contact with a person's intraocular environment (e.g. intraocular lenses, and ophthalmic viscosurgical devices); or
- any other devices that are labelled sterile and non-pyrogenic.

Endotoxins are the high molecular weight lipopolysaccharide component of the outer cell wall of gram-negative bacteria, which is usually a fever-inducing contaminant in the manufacturing process of medical devices.

If present in or on a medical device of the kind identified in the MDSO (e.g. an implantable medical device) endotoxin contaminants can be introduced into the blood stream or tissues of the human body and can induce strong biological effects such as fever, meningitis, and a rapid fall in blood pressure. Essential principles 7.2, and the MDSO, are therefore designed to address these concerns and to ensure patient safety in relation to these risks.

The MDSO principally addresses these risks by specifying endotoxin limits for the kinds of medical devices to which it applies, and by specifying bacterial endotoxin testing requirements for identifying bacterial endotoxin levels in or on a medical device.

The endotoxin requirements for medical devices included in the MDSO correspond with the current international opinion and requirements, where such exist. This MDSO will be subject to ongoing review, and the requirements included in the Order may be changed in the future when more information is accumulated and becomes available.

CONSULTATION

As compliance with the MDSO is not mandatory but is rather a voluntary standard for sponsors and manufacturers, it would appear to be of minor or machinery nature and provides clarity to the industry stakeholders in setting out the expectations of the TGA for demonstrating compliance with the essential principles with respect to the endotoxin requirements of medical devices, and on this basis was not the subject of consultation. Further, as a voluntary standard, MDSOs are covered by the advice of the Office of Best Practice that a carve-out is provided for such instruments (OBPR reference 14416).

Details of the MDSO are set out in Attachment A.

The MDSO is compatible with the human rights and freedoms recognised or declared under section 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*. A full statement of compatibility is set out in Attachment B.

This Order is a disallowable legislative instrument, and commences on the day after it is registered.

ATTACHMENT A

DETAILS OF MEDICAL DEVICE STANDARDS ORDER (ENDOTOXIN REQUIREMENTS FOR MEDICAL DEVICES) 2018

Section 1 Name
This section provides that the name of this instrument is the *Medical Device Standards Order (Endotoxin Requirements for Medical Devices) 2018* (the MDSO).

Section 2 Commencement
This section provides that the MDSO commences on the day after it is registered on the Federal Register of Legislation.

Section 3 Authority
This section makes it clear that the MDSO is made under subsection 41CB(1) of the *Therapeutic Goods Act 1989* (the Act).

Section 4 Definitions
This section sets out a number of definitions for key terms used in the MDSO, including for example 'default standard, 'label' and 'medical device'. In particular, this section would define 'endotoxin' as the high molecular weight lipopolysaccharide component of the outer cell wall of gram-negative bacteria, which is usually a fever-inducing contaminant in the manufacturing process of medical devices.

Section 5 Application
This section identifies the kinds of medical devices for which the MDSO constitutes a medical device standard. Principally these are any of the following:

- implantable medical devices;
- devices in direct or indirect contact with a person's cardiovascular system, lymphatic system or cerebrospinal fluid, and that are labelled as sterile and non-pyrogenic(e.g. intravenous catheters, and dialysis tubing);
- devices in direct or indirect contact with a person's intraocular environment (e.g. intraocular lenses, and ophthalmic viscosurgical devices); or
- any other devices that are labelled sterile and non-pyrogenic.

Section 6 Bacterial endotoxin content
This section specifies endotoxin limits for the kinds of medical devices identified in section 5 as kinds of devices to which the order applies, including a requirement that for most such devices the endotoxin limit must be not more than 20 endotoxin units per device, or not more than 2.15 endotoxin units per device for a device that is in contact with a person's cerebrospinal fluid.

For the kind of medical devices in direct or indirect contact with a person's intraocular environment, the endotoxin limits must, unless a higher number endotoxin units is justified, be not more than 0.2 endotoxin units per device for an anterior segment solid device, and not more 0.2 endotoxin units per millilitre for an ophthalmic viscosurgical device.

Section 7 Bacterial endotoxin testing
This section requires that a kind of medical device to which this MDSO applies and for which a sponsor or manufacturer is seeking to demonstrate compliance with must be tested using a bacterial endotoxin test methodology set out in a default standard or, if applicable, an alternative method that is validated. 'Default standard' has the same meaning in the MDSO as in the Act –

relevantly, this term is defined in subsection 3(1) of the Act as, in effect, any of the British Pharmacopoeia, European Pharmacopoeia or United States Pharmacopeia-National Formulary.

Subsection 7(2) requires that if an alternative test method is used, the device manufacturer must provide a scientifically sound justification for doing so, and also provide validation evidence for the suitability of the use of that alternative test method.

Subsections 7(3) and (4) require that, unless practical, bacterial endotoxin testing must be conducted on every batch and that where this is not practical, the device manufacturer must establish an appropriate sampling plan and test for incoming raw materials, in-process materials and representative products to ensure that the manufacturing process is capable of producing every batch of the final product in such a manner so as to comply with endotoxin limits (as well as providing a scientifically sound justification that addresses the risks of not testing every batch).

ATTACHMENT B

SUPPLEMENTARY MATERIAL - STATEMENT OF COMPATIBILITY WITH HUMAN RIGHTS FOR A LEGISLATIVE INSTRUMENT THAT DOES NOT RAISE ANY HUMAN RIGHTS ISSUES

Statement of Compatibility with Human Rights

Prepared in accordance with Part 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*.

Medical Device Standards Order (Endotoxin Requirements for Medical Devices) 2018

This legislative instrument is compatible with the human rights and freedoms recognised or declared in the international instruments listed in section 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*.

Overview of the Legislative Instrument

Medical Device Standards Order (Endotoxin Requirements for Medical Devices) 2018 (the MDSO) is an order made by the delegate of the Minister for Health under subsection 41CB(1) of the Act, and is designed to provide a voluntary option for sponsors and manufacturers of specified kinds of medical devices to demonstrate the compliance of their devices with essential principle 7.2 in relation to minimising the risks associated with endotoxin contaminants and residues in or on medical devices.

The kinds of medical devices for which the MDSO constitutes a medical device standard are any of the following:

- implantable medical devices;
- devices in direct or indirect contact with a person's cardiovascular system, lymphatic system or cerebrospinal fluid, and that are labelled as sterile and non-pyrogenic (e.g. intravenous catheters, and dialysis tubing);
- devices in direct or indirect contact with a person's intraocular environment (e.g. intraocular lenses, and ophthalmic viscosurgical devices); or
- any other devices that are labelled sterile and non-pyrogenic.

The essential principles are set out in Schedule 2 to the *Therapeutic Goods (Medical Devices) Regulations 2002*, and are important mandatory requirements or standards that apply to medical devices, and provide minimum benchmarks relating to the safety and performance characteristics of medical devices.

Sponsors applying for marketing approval must certify that their kinds of devices comply with the essential principles, and devices may have their marketing approval cancelled if the Secretary of the Department of Health is satisfied that the certification made in relation to the device's compliance with the essential principles was not, or is no longer, correct. The Act also sets out criminal offences and civil penalty provisions relating to the importation, supply or export of kinds of medical devices that do not comply with the essential principles.

Essential principle 7.2 is set out in Schedule 2 to the MD Regulations, and states that:

- a medical device must be designed, produced and packed in a way that ensures that any risks associated with contaminants and residues that may affect a person who is involved in transporting, storing or using the device, or a patient, are minimised, having regard to the intended purpose of the device; and

- in minimising risks, particular consideration must be given to the likely duration and frequency of any tissue exposure associated with the transportation, storage or use of the device.

Orders made under section 41CB are not mandatory for sponsors or manufacturers of medical devices, but are designed to assist sponsors and manufacturers by providing a flexible and efficient mechanism, that they may elect to use for the purposes of demonstrating that their products comply with the essential principles.

For this purpose, the MDSO specifies endotoxin limits for the kinds of medical devices identified above (e.g. that for the kind of medical devices in direct or indirect contact with a person's intraocular environment, the endotoxin limits must, unless a higher number endotoxin units is justified, be not more than 0.2 endotoxin units per device for an anterior segment solid device, and not more 0.2 endotoxin units per millilitre for an ophthalmic viscosurgical device), and specifies test methods for bacterial endotoxin testing.

Human rights implications

As this legislative instrument does not introduce any measures other than those outlined above (and is principally designed to provide a voluntary standard for sponsors and manufacturers of specified kinds of medical devices to demonstrate the compliance of their products with requirements relating to minimising the risks associated with endotoxin contaminants and residues), it does not engage any of the applicable rights or freedoms.

Conclusion

This legislative instrument is compatible with human rights as it does not raise any human rights issues.

Elizabeth McGrath

Delegate of the Minister for Health