



Australian Government

Department of Health

Therapeutic Goods Administration

Consultation: Proposed regulatory options for medical devices containing nanomaterials

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TGA Health Safety
Regulation

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Contents

Introduction	5
Background	5
European changes in medical device regulation of nanomaterials	5
Regulatory concerns on nanotechnology and nanomaterials	6
Previous consultation	8
This consultation	8
Options for regulatory amendments	8
Options	9
Effect	11
Your feedback	12
Issues and discussion	12
Nanomaterials	12
Is there a need for regulatory change?	14
Examples of medical devices containing nanomaterials	14
International regulation of nanotechnology and nanomaterials	16
Option 1 - No change	19
What would change for sponsors and manufacturers?	19
Option 2 - Make requirements explicit – add definitions and amend essential principles	19
Add definitions	19
Amend essential principles	19
What would change for sponsors and manufacturers?	20
Option 3 - Add new classification rules	20
Current classification applicable to these devices in Europe	20
Current classification applicable to these devices in Australia	21
Possible classification changes	21
What would change for sponsors and manufacturers?	22
Proposed regulatory amendment package	23
Transitional arrangements	23
Option 1	23
Option 2	24
Option 3	24
Engagement	25

Feedback notes _____	25
What we invite you to do _____	26
Questions _____	26
How to submit _____	27
Enquiries _____	27
Appendix A – Definitions and other provisions related to medical devices containing nanomaterial _____	28

Introduction

In 2015, the Report of the *Expert Panel Review of Medicines and Medical Devices Regulation* (MMDR) made 58 recommendations for reform of the regulatory framework for medicines and medical devices in Australia. The [Australian Government Response to the Review of Medicines and Medical Devices Regulation](#) was released in September 2016. The Government accepted 56 MMDR recommendations including Recommendation Twenty¹. This Recommendation provided that the regulation of medical devices, wherever possible and appropriate, align with the European Union (EU) framework including the classification of medical devices.

As part of the Australian Government Department of Health, the Therapeutic Goods Administration (TGA) regulates medicines and medical devices in Australia and is responsible for implementing the Government's reforms.

The EU introduced a new [medical device regulatory framework](#) from 2017, which included new requirements around nanomaterials. This paper examines whether the Australian medical device regulatory framework should be aligned to the EU framework, and how this could occur.

Background

The TGA regulates therapeutic goods in Australia, including medical devices, having regard to the risks and benefits (to the individual or public health) considered in the context of the goods' intended use.

All therapeutic goods carry some level of potential risk, and the TGA applies scientific and clinical expertise to ensure assessments and decisions are based on the balance between the benefits and the risks.

The risk classifications of medical devices take into account factors such as potential harm, level of invasiveness, reliance on power, where in the human body the device is used, intended use, the intended user, etc. Class I products are medical devices with the lowest level of risk-classification, while Class III medical devices carry the highest risks.²

The Government periodically reviews regulatory requirements for therapeutic goods to ensure the regulations continue to be appropriate and that the level of regulation for therapeutic goods is commensurate with the potential risk these products pose to public health and safety.

European changes in medical device regulation of nanomaterials

European regulatory changes on nanomaterials in medical devices has prompted consideration of nanomaterials in the context of the Australian regulatory framework. The [EU Regulation on medical devices \(2017/745\)](#) (EU MD Regulation) included several changes to:

¹ Sansom L, Delaat W, Horvath J. Review of Medicines and Medical Devices Regulation: Recommendations to the Minister for Health on the Regulatory Frameworks for Medicines, Medical Devices, Complementary Medicines and Advertising of Therapeutic Goods, July 2015, p. 10.

² [Therapeutic Goods Act 1989](#), s. 41DB, and [Therapeutic Goods \(Medical Devices\) Regulations 2002](#), Part 3, Div. 3.1, Schedule 2 and Schedule 2A – Classification rules for medical devices (other than an IVD) and IVD medical devices respectively

- **definitions:** introduce a 'nanomaterial' definition: "*particles with one or more external dimensions in the size range 1-100 nm*"; and some related definitions (particles, agglomerates, aggregates)
- **essential principles:** specify consideration of risks linked to the size of particles, with special attention given to nanomaterials in the essential principles (or equivalent)
- **classification rules:** reclassify some categories of medical devices to higher risk classes for "*all devices incorporating or consisting of nanomaterials*", based on the degree of potential invasiveness within the body.

The EU MD Regulation explains that the new requirements increase the robustness of the assessment process, and that the classification rules take into account the potential risks associated with the technical design and manufacture of the devices. The rules also take into account the level of invasiveness and potential toxicity of certain devices introduced into the human body as well as the place where the device performs its action in or on the human body.

The Australian Government's reforms aim to improve the scope, clarity and appropriateness of operation of regulations governing medical devices. This paper considers the EU regulatory framework and other work undertaken, internationally and in Australia, as an input into the review of Australian regulatory requirements for medical devices.

More detail on the regulation of nanomaterials in Europe, as well as other jurisdictions, is included in the *International activities related to nanotechnology and nanomaterials* section below (from page 16). As outlined below, various countries are managing the regulatory requirements around nanomaterials, with the European reclassification being the most systematic regulatory change being implemented this time.

Regulatory concerns on nanotechnology and nanomaterials

Consideration of changes for medical device nanomaterials regulation are being prompted at this time due to recent changes to the European regulatory framework. However, any proposed changes need to address the scientific evidence.

Nanotechnology is a term used to describe a wide range of methods involved in the production and engineering of structures and systems by controlling size and shape at the nanometre scale, and is an important tool that can be used in a broad range of products and applications. Nanotechnology is comprised of **nanomaterials**, which are generally defined as materials where at least half of the particles under consideration have at least one (or more) external dimensions that are in the size range between 1-100 nm (a nanometre is one-billionth of a metre or 1×10^{-9} m).

The need to manage any potential impacts associated with the use of nanomaterials has been acknowledged in Australia for some time.^{3,4,5} In 2007, the Australian Government established the National Nanotechnology Strategy (NNS) to capture the benefits of nanotechnologies, while addressing any potential health, safety and environmental risks. The key initiatives of the NNS were to review the capacity of current regulatory frameworks to manage risks associated with products derived from nanotechnologies, to raise public awareness and to establish metrology capabilities.

Within Australia and internationally, research in nanomaterials has highlighted wide-ranging applications that can benefit the community. Nanoscale particles “can be highly beneficial considering that many biological significant molecules such as water, antibodies, proteins, glucose, enzymes, haemoglobin and receptors all fit within this range”⁶. Materials at the nanoscale can also have quite different properties than in their bulk form, opening new avenues for medical treatment.

However, nanotechnology has also raised awareness of possible concerns about potential health, safety and adverse environmental impacts due to some nanotechnology applications. For example, the novel physicochemical properties that nanomaterials display compared to the parent material, the overuse of the biocide nanosilver reducing its medical usefulness and affecting agriculture, and biological scale of the material providing for the movement of nanomaterials throughout the body, are all concerns in this area. It also highlighted the need to ensure appropriate regulatory oversight.

Concerns associated with nanotechnology in the context of the regulatory framework for therapeutic goods, including for prescription medicines and sunscreens,⁷ were reviewed in 2007 – 2009. The TGA is responsible for regulating the range of therapeutic goods including medicines and medical devices. The Monash Review⁵ noted that TGA’s regulatory frameworks apply to and are generally well suited to the task of regulating nanotechnologies. For both medical devices and medicines, nanomaterials are regulated consistently with international jurisdictions, without specific definitions or requirements in the current regulations.

The risks posed by nanomaterials are unclear, and further work is being undertaken in this field of study. Even though the potential risks of nanomaterials have been under active scientific

³ *Nanotechnology: enabling technologies for Australian innovative industries*, Prime Minister's Science, Engineering and Innovation Council (PMSEIC), March 2005
webarchive.nla.gov.au/awa/20060125060513/http://pandora.nla.gov.au/pan/54380/20060125-0000/www.dest.gov.au/NR/rdonlyres/1E1B501A-727A-4153-85EF-134B2DAF0925/4112/nanotechnology_pmseic110305.pdf

⁴ Options for a national nanotechnology strategy: report to Minister Industry, Tourism and Resources / by National Nanotechnology Strategy Taskforce, 2006, Canberra.
webarchive.nla.gov.au/awa/20080220033531/http://pandora.nla.gov.au/pan/66740/20080220-1427/www.innovation.gov.au/Documents/taskforcereport20070215100254.pdf

⁵ Ludlow, K., Bowman, D., Hodge, G., (2007), *A Review of Possible Impacts of Nanotechnology on Australia's Regulatory Framework*, Monash Centre for Regulatory Studies & Institute for Environmental and Energy Law.
https://www.researchgate.net/publication/265997359_A_Review_of_Possible_Impacts_of_Nanotechnology_on_Australia's_Regulatory_Framework

⁶ Foulkes, R., Man, E., Thind, J., Yeung, S., Joy, A., Hoskins, C., (2020), *The regulation of nanomaterials and nanomedicines for clinical application: current and future perspectives*, *Biomaterials Science*, 2020, 8, 4653-4664, DOI: [10.1039/DOBM00558D](https://doi.org/10.1039/DOBM00558D), page 4653

⁷ TGA, *Literature Review on the safety of titanium dioxide and zinc oxide nanoparticles in sunscreens*, 2017, www.tga.gov.au/literature-review-safety-titanium-dioxide-and-zinc-oxide-nanoparticles-sunscreens

investigation for decades, a systemic understanding of the risks and benefits of nanomaterials in the context of medical devices has not yet emerged.⁸ The balance of risk and benefit are central to the regulation of medical devices. The TGA continues to monitor scientific literature in this area and work with international regulatory agencies to ensure that appropriate regulatory action is undertaken when required. A more detailed discussion on nanomaterials, including emerging scientific evidence and examples of medical devices incorporating nanomaterials, is included in the *Issues and discussion* section below (from page 12).

Previous consultation

A recent consultation⁹ on proposed changes to medical device essential principles for safety and performance has been conducted. It was noted in this consultation that the new requirements for both the EU general safety and performance requirements (GSPR) and the International Medical Device Regulators Forms (IMDRF) Essential Principles¹⁰ contained specific information stating that special attention should be given to nanomaterials when considering reduction of risks linked to size of particles released into patient's body.

This consultation

This consultation seeks feedback on possible options for amending the [Therapeutic Goods \(Medical Devices\) Regulations 2002](#) (Australian MD Regulations) to include new definitions, changes to essential principles and additional classification rules which provide specific requirements for medical devices containing nanomaterials, in alignment with the EU MDR.

Options for regulatory amendments

The purpose of this paper is to seek feedback on options for potentially introducing new regulatory requirements, including definitions and classification rules, for medical devices containing nanomaterials. The overall objective of any change is primarily to promote health and safety with the use of nanomaterials in medical devices. Any change may also seek to promote international alignment of regulatory requirements (in particular the European Union), and to provide clarity on the regulatory requirements. It will be important that any amendments for medical devices containing nanomaterials are appropriately tailored for the Australian regulatory context.

In the EU MD Regulation these devices are referred to as: "*All devices incorporating or consisting of nanomaterial.*"

⁸ Karakus, C. O., Bilgi, E., & Winkler, D. A., (2020), *Biomedical nanomaterials: applications, toxicological concerns, and regulatory needs*, Nanotechnology, DOI: [10.1080/17435390.2020.1860265](https://doi.org/10.1080/17435390.2020.1860265)

⁹ Consultation: *Proposed changes to medical device essential principles for safety and performance* www.tga.gov.au/consultation/consultation-proposed-changes-medical-device-essential-principles-safety-and-performance

¹⁰ IMDRF, *Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices*, 31 October 2018 www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grpp-essential-principles-n47.pdf

Options

Three options are proposed for Australia's medical device regulatory framework for nanomaterials:

Option 1 – No change

Under this option there would be no change to the existing medical device regulatory framework in Australia in respect of nanomaterials.

The existing Australian MD Regulations essential principle 7—Chemical, physical and biological properties, sub-essential principle 7.1 Choice of materials, requires that:

particular attention must be given to the chemical and physical properties of the materials used in the device, and the compatibility between the materials used and biological tissues, cells, body fluids and specimens.

This provision already implicitly includes any nanomaterials used in the device. The medical device regulatory framework requires manufacturers to implement a comprehensive risk-management system for their medical devices. Where nanomaterials are present this would need to include explicit consideration of the uncertainty associated with the potential hazards posed by nanomaterials and the limits of current scientific knowledge.

Option 2 – Make requirements explicit – add definitions and amend essential principles (EPs)

Under this option a definition of nanomaterials (and related terms) would be added to the regulations, and the essential principles amended to include the need to assess and manage the risks and benefits of nanomaterials included in medical devices. This option would not change the classification (and required regulatory oversight) of medical devices incorporating nanomaterials.

Add definitions

A new definition of nanomaterial could be included in the dictionary of the Australian MD Regulations, to align with that in the EU MD Regulation:

‘nanomaterial’ means a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm

Fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm shall also be deemed to be nanomaterials ¹¹

Additional related definitions may also be included:

‘particle’, for the purposes of the definition of nanomaterial, means a minute piece of matter with defined physical boundaries¹²

¹¹ EU MD Regulation, Article 2 Definitions (18)

¹² EU MD Regulation, Article 2 Definitions (19)

‘agglomerate’, for the purposes of the definition of nanomaterial, means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components¹³

‘aggregate’, for the purposes of the definition of nanomaterial, means a particle comprising of strongly bound or fused particles.¹⁴

The EU MD Regulation also specifically provides for delegation to amend these definitions ‘in the light of technical and scientific progress and taking into account definitions agreed at Union and international level.’¹⁵

There are currently no definitions of these items in the Australian MD Regulations.

Amend EPs

The EU MD Regulation general safety and performance requirement (GSPR) on chemical, physical and biological properties provides:

Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention shall be given to nanomaterials.¹⁶

The equivalent section of the Australian MD Regulations is EP 7 – Chemical, physical and biological properties. This EP does not currently include an equivalent provision, but does address ‘substances’ incorporated in, or ingressing, egressing or leaching from the device. On this basis it is noted that nanomaterials are covered by the existing EPs, but not explicitly so.

Other elements of EU GSPR 10.4 on Substances, also includes elements which may be relevant to nanomaterials:

- GSPR 10.4.1 address exposure to particles, from wear, degradation and processing residues;
- GSPR 10.4.5 provides for labelling of substances referred to in 10.4.1
- GSPR 10.5 provides for reducing risk from unintentional ingress of substances into the device

The international requirements and guidance for principles regarding safety and performance of medical devices have since been expanded, and this is reflected in the EU MD Regulation. As such, while there is consistency between the EU GSPR and Australian EPs, there is not direct alignment.

Broader alignment of the EPs with the GSPR is being considered, as outlined the previous consultation on *Proposed changes to medical device essential principles for safety and performance*.¹⁷ Any amendment to incorporate nanomaterials into the EPs would be progressed as part of the broader EP changes. For this purposes of this consultation, feedback is sought on whether these changes relating to nanomaterials ought to be included in the EPs.

¹³ EU MD Regulation, Article 2 Definitions (20)

¹⁴ EU MD Regulation, Article 2 Definitions (21)

¹⁵ EU MD Regulation, Article 3

¹⁶ EU MD Regulation GSPR Chapter 2 Requirements Regarding Design and Manufacture, Part 10 Chemical, physical and biological properties, clause 10.6

¹⁷ Consultation: Proposed changes to medical device essential principles for safety and performance, www.tga.gov.au/consultation/consultation-proposed-changes-medical-device-essential-principles-safety-and-performance

Option 3 – Add new classification rules

This option would introduce new classification rules for medical devices incorporating nanomaterials. This would potentially increase the classification (and so regulatory requirements) for those medical devices incorporating nanomaterials.

New classification rules could be included in Schedule 2, Part 5 (Special rules for particular kinds of medical devices) of the Australian MD Regulations, setting out the classification of medical devices containing nanomaterials depending on potential level of internal exposure in or on the human body. This would bring alignment with Rule 19 of the EU MD Regulation (Regulation (EU) [2017/745](#)), which provides:

All devices incorporating or consisting of nanomaterial are classified as:

- class III if they present a high or medium potential for internal exposure;
- class IIb if they present a low potential for internal exposure; and
- class IIa if they present a negligible potential for internal exposure.

These classification rules would operate in conjunction with existing rules. Where two or more classification rules apply to a medical device, the device has the highest level of classification applying under the applicable classification rules.¹⁸

Effect

Option 1 would mean that existing requirements continue to apply.

Under Option 2 a definition of nanomaterials, and possibly related definitions, would be included in the dictionary of the Australian MD Regulations. EPs would also be amended to specify the requirement to consider and manage risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, particularly nanomaterials (in line with current regulatory practice,¹⁹ but not explicitly required).

The Australian EPs already include broad requirements to consider materials in the design and construction of medical devices, and this includes nanomaterials where these are present or relevant. However Option 2 would make explicit the requirement to consider risks associated with size and the properties of particles, including nanomaterials.

Under Option 3 medical devices containing nanomaterials would be classified as Class IIa (low-medium risk), Class IIb (medium-high risk), or Class III (high risk), depending on the potential level of exposure the device has in or on the human body by any means.

Introducing new classification rules would potentially raise the classification of medical devices which include nanomaterials, based on the degree of internal exposure of the user. Increasing the classification of a medical device means a corresponding increase in the onerousness of the conformity assessment procedure required to be applied (outlined in more detail under *Option 3 – Add new classification rules below* – at page 20).

¹⁸ [Therapeutic Goods \(Medical Devices\) Regulations 2002](#), 3.3(7)

¹⁹ For example, see Matthew O'Donnell, *BSI: Nanomaterials and medical device regulations*, 2016 (presentation), available at www.medical-device-regulation.eu/wp-content/uploads/2021/01/2016-11-30_BSI_md-Nanomaterials-presentation.pdf

Options 2 and 3 can each be applied separately, but it makes most sense if selecting Option 3 to also apply Option 2. At a minimum, if applying Option 3, definitions of nanomaterials may also need to be included in the regulations to support the new classification rules.

Further discussion of the options is included under *Issues and discussion* below (from page 12). *Appendix A – Definitions and other provisions related to medical devices containing nanomaterials* (from page 28) has also been provided as a reference tool. It provides an overview and comparison between the EU MD Regulation and Australian MD Regulations of the relevant definitions, classification rules and other provisions applicable to medical devices containing nanomaterials and provides a summary of the proposed amendments in the Australian MD Regulations. Appendix A may help you to address definitions and other provisions in your feedback.

Your feedback

Are you a consumer, industry stakeholder, healthcare provider, patient, industry representative body, consumer advocacy group or other interested party?

We seek your views on the proposed amendments and implementation strategy. Your input will assist us to address any unintended consequences and inform the proposal and the regulatory amendment process.

On page 26 is a [list of questions](#) to help you address the proposal in your feedback.

Please refer to page 27 on [How to submit](#) your feedback to the TGA.



Please note

This consultation closes **Friday 9 April 2021**. Before providing feedback, it is important to read the explanatory material in the following *Issues and discussion* section.

Issues and discussion

Nanomaterials

Nanotechnology encompasses science, engineering, and technology conducted at the nanoscale. Nanotechnology can be presented in a wide range of forms and used in a broad range of products and applications.

The increasing number of products produced by nanotechnology or containing nanomaterials entering the market includes those used in healthcare (e.g. drug delivery, regenerative medicine, medical devices and diagnostics), electronics, cosmetics, textiles, information technology, and environmental protection.

There is a broad variety of nanomaterials which includes carbon-based materials (e.g. films and coating); metal-based materials (e.g. nanogold, nanosilver, metal oxides); nanosized polymers (e.g. dendrimers); and composites (nanoparticles combined with other nanoparticles or with larger, bulk-type materials), and they may be presented in the form of particles, tubes, rods or fibres.

Generally, referring to nanomaterials means referring to materials containing a significant proportion of particles with at least one dimension between 1-100 nm (a nanometre is one-billionth of a metre). Nanomaterials can be engineered or produced naturally (e.g. by combustion of fossil fuels and fragmentation of microplastics). Nanomaterials that have the same composition as known materials in bulk form may have different physicochemical properties than those same bulk form materials and may behave differently if they enter the body. The proposal classification rules focus on the 'potential for internal exposure'. To date a wide range of parameters have been shown to impact the behaviour of nanomaterials in the body, including:²⁰

- Physical properties: particle size (mean and distribution), shape (dimensions and aspect ratio), surface area, density, porosity, roughness and viscosity
- Chemical properties: composition (core, surface and overall), Surface properties (charge, coating, affinity), functionalisation, purity/impurities, chemical structure, crystallinity/defects and redox activity
- Behavioural properties: solubility, dispersibility, corrosivity, dissolution rate, degradation rate, dustiness, hydrophobicity, surface reactivity, aggregation/agglomeration.

In addition, the way nanomaterials interact with the human body varies greatly and there is not yet sufficient systematic understanding to allow prediction of the effects, even where the above parameters are known. As a result, in practice different nanomaterials may pose quite varied potential hazards when used in therapeutic goods such as medical devices.²¹ The hazard (ie as a source of potential harm) has raised concern around nanomaterials, and the risk (the chance that the hazard will actually cause harm) to date has been ascertained for many individual nanomaterials. However the interaction of the various characteristics of nanomaterials (including but not limited to the 'potential for internal exposure') is not sufficiently understood for risk for a nanomaterial to be accurately anticipated.

Users can be exposed to nanomaterials through inhalation (e.g. intubation, dental procedures); dermal applications; mucosal, oral, or parenteral exposure (e.g. by injection into the bloodstream or a muscle); surgical procedures (including continuing exposure through implanted medical devices); ocular exposure, etc.

While significant data on the hazards associated with particular nanomaterials has been generated, modelling of risk associated with the use of and exposure to nanomaterials continues to be less well developed.

Therapeutic goods containing nanomaterial metal oxides, liposomes, polymer protein conjugates, polymeric substances and suspensions have been marketed in Australia and overseas for some time.

While the Australian therapeutic goods framework has been adequately identifying, assessing and managing the risks associated with nanotechnologies, the TGA recognises that the developments in this area, as well as other technologies, will continue to pose challenges to regulators into the future.

²⁰ List from Karakus, C. O., Bilgi, E., & Winkler, D. A., (2020), *Biomedical nanomaterials: applications, toxicological concerns, and regulatory needs*, Nanotechnology, DOI: [10.1080/17435390.2020.1860265](https://doi.org/10.1080/17435390.2020.1860265), Table 1

²¹ Ibid, p 10

Is there a need for regulatory change?

A threshold issue is whether there is a need to change Australia's existing regulatory framework for nanomaterials in medical devices at all. Medical devices are regulated based on risk - the first essential principle requires that "any risks associated with the use of the device are ... acceptable risks when weighed against the intended benefit to the patient".²² In the context of medical devices, risk is the "combination of the probability of occurrence of harm and the severity of that harm"²³ and this is assessed based on scientific evidence. Broadly speaking, while there has been significant scientific research into the risk of particular nanomaterials to human health over the past several decades, there continues to be insufficient systemic understanding of nanomaterials to enable modelling and prediction of risks for nanomaterials.²⁴

Medical devices are regulated in Australia under a principles-based framework. The essential principles²⁵ set out the requirements relating to the safety and performance of medical devices. Nanomaterials are already in use in a broad range of medical devices and associated nanomaterial risks are being managed through the existing regulatory framework.

It is critical for regulators to ensure the best available evidence is used in regulating the risks associated with medical devices incorporating nanomaterials. However over-regulation relative to risk can stifle innovation which benefits patients through the emergence of new technologies.

The existing regulatory framework already requires manufacturers of medical devices to assess the safety of their product, both at initial approval and on an ongoing basis. Significant nanomaterial related adverse events have not broadly occurred. From this it may be inferred that the existing framework has, to date, been sufficient in managing the risks associated with nanomaterials in medical devices.

Examples of medical devices containing nanomaterials

The use of nanotechnology and nanomaterials in medical devices has been increasing with many such devices now used in clinical practice. These devices include catheters with a nanosilver coating for bladder drainage, haemodialysis or local administering of anaesthesia; catheters with nanotopographical morphology imprinted onto the exposed surface; bone fillers with hydroxyapatite and tricalcium phosphate nanoparticles which facilitate integration with the bone of the patient; implants modified with the aid of nanotechnologies to enable them to integrate better in the body, and in some cases for their antibacterial activity; injectable medical devices, for example, iron-oxide nanoparticles injected into tumour cells to be heated-up by radiation or an external magnetic field.

Some further examples are considered in more detail below.

Wound dressings incorporating nanosilver

Silver is included in many dressings for its antibacterial effect. If used separately, silver has an ancillary antibacterial action to that of the device.

²² [Therapeutic Goods \(Medical Device\) Regulations 2002, Schedule 1-Essential Principles, 1. Use of medical devices not to compromise health and safety](#)

²³ AS ISO 13485:2017, *Medical devices – Quality management systems – Requirements for regulatory processes*, 3.17

²⁴ Günter Oberdörster, Vicki Stone & Ken Donaldson (2007) Toxicology of nanoparticles: A historical perspective, *Nanotoxicology*, 1:1, 2-25, DOI: [10.1080/17435390701314761](https://doi.org/10.1080/17435390701314761). Provides a useful review of the evidence in the field of nanotoxicology.

²⁵ [Therapeutic Goods \(Medical Device\) Regulations 2002, Schedule 1-Essential Principles](#)

Due to its antibacterial action on the human body in Australia, silver, if used separately, is considered to be a medicine. Any medical device that incorporates or is intended to incorporate, as an integral part, a substance that if used separately, would be a medicine, and is liable to act on a patient's body with action ancillary to that of the device, is classified as Class III.²⁶ Also such medical devices require manufacturers to obtain a *conformity assessment certificate*²⁷ issued by the TGA before sponsors may apply for inclusion of such a device in the [Australian Register of Therapeutic Goods](#) (ARTG).

Therefore, because these devices are already required to be included in the ARTG as Class III medical devices, any classification change would not impact the classification of such devices. However, the manufacturers' technical and clinical data would be required to cover any potential risks associated with the use of silver as a nanoparticle in a device.

Dental fillings or dental implants incorporating nanomaterials

Presently, surgically invasive medical devices intended for long-term use (i.e. the device is to be used continuously for more than 30 days) and implantable medical devices are classified as Class IIb, unless specifically classified otherwise (e.g. devices used in direct contact with the heart, the central circulatory system or the central nervous system of a patient; or wholly, or mostly, absorbed by a patient's body; and joint replacements or surgical meshes are Class III medical devices, while long term invasive devices intended for use in the oral cavity or ear canal are classified as Class IIa).²⁸

For invasive devices, the released nanoparticles will have a direct port of entry into the body depending on the location the device is used in the body. For dental fillings containing nanomaterials, short exposure (during application to transform them from a paste to a solid form) may occur during the treatment procedures.

Nanomaterials from medical devices may also be released into the blood stream due to the release/loosening of nanomaterials present as coatings on medical devices or via chemical breakdown or wear-and-tear processes due to degradation of medical devices which may or may not contain nanomaterials. Additionally, in case of dental fillings, these devices must be ground, polished or shaped during application, which may be a source for the release of free nanoparticles, resulting in the possibility of respiratory tract/lung exposure.²⁹ This specific potential internal exposure should be considered in the risk evaluation of such materials.

Consistent with the above, under Option 3, implantable medical devices containing nanomaterials will be considered as presenting a *high potential for internal exposure* (compared, with, for example, non-invasive products used in contact with intact skin, in which case released nanosized components have a low potential to penetrate into the body)³⁰ and therefore will be classified as a Class III medical device.

As a further example, currently the metal or plastic dental fillings (medical devices intended to be placed in the teeth of a patient for more than 30 days) are classified as Class IIa³¹ and dental implants (metal posts or frames surgically positioned into the jawbone beneath the gums) are

²⁶ Therapeutic Goods (Medical Devices) Regulations 2002, Schedule 2, Cl. 5.1.

²⁷ Therapeutic Goods Act 1989, s.3

²⁸ Therapeutic Goods (Medical Devices) Regulations 2002, Schedule 2, Cl. 3.4.

²⁹ Guidance on the determination of potential health effects of nanomaterials used in medical devices, SCENIHR, January 2015, 3.6.4 (p.30), 3.8.5(p.45)

³⁰ Guidance on the determination of potential health effects of nanomaterials used in medical devices, SCENIHR, January 2015, 3.5.2.1 (p.24)

³¹ *Therapeutic Goods (Medical Devices) Regulations 2002*, Schedule 2, Cl. 3.4(3).

classified as Class IIb.³² According to Option 3, if dental fillings contain, for example, metal based nanomaterials, they should be classified as Class IIb (a low potential for internal exposure), and dental implants positioned into the jawbone beneath the gums containing nanomaterials should be a Class III medical device (a medium or high potential for internal exposure).

Examination gloves or surgical gloves containing nanomaterials

Currently, medical gloves may be classified as Class I medical devices (e.g. gloves intended to be used for patient examination – invasive medical devices intended to be used to penetrate a patient’s body orifice for transient use)³³ or as Class IIa (gloves intended to be used in surgical procedures for transient use)³⁴.

Under Option 3, if any of these devices contained nanomaterials (for example, powdered gloves) they could be classified as Class IIb (a short duration/low potential for release/loosening of nanomaterials contained in the powder covering the gloves) or Class III (a medium or high potential for internal exposure with the potential for nanomaterials to get into the blood stream during the surgical procedure) respectively.

International regulation of nanotechnology and nanomaterials

There is broad international acknowledgement that there are challenges and scientific uncertainty related to the risks and benefits associated with the application of nanotechnology in medical devices. It is also acknowledged that there is a need to ensure that these are adequately addressed when evaluating the safety and performance of such devices.

European Commission Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

The SCENIHR³⁵ published the ‘*Guidance on the determination of potential health effects of nanomaterials used in medical devices*’³⁶ which recognises that the use of nanomaterials in medical devices can vary considerably, and that it poses a challenge for the safety and risk assessment of these medical devices as the specific character of the nanomaterial used should be taken into consideration. The guidance considers different hazards which may be associated with the use of nanomaterials, and recognises that wear-and-tear of medical devices may result in the generation of nanosized particles even when the medical device itself does not contain nanomaterials.

Some examples provided include the use of free nanomaterials being a medical device and administered to the patient (e.g. iron oxide or gold nanomaterials for heat therapy against cancer), free nanomaterials in a paste-like formulation (e.g. dental filling composites), free nanomaterials added to a medical device (e.g. nanosilver as antibacterial agent in wound dressings), fixed nanomaterials forming a coating on implants to increase biocompatibility (e.g.

³² Ibid, Cl. 3.4(2).

³³ Ibid, Cl. 3.1(2)(a).

³⁴ Ibid, Cl. 3.2(2).

³⁵ SCENIHR is one of the European Commission independent non-food Scientific Committees that provide scientific advice relating to consumer safety, public health and the environment, and draw attention to the new or emerging problems which may pose an actual or potential threat.

³⁶ *Guidance on the determination of potential health effects of nanomaterials used in medical devices*, SCENIHR, January 2015, <https://publications.europa.eu/en/publication-detail/-/publication/e9899821-e4d4-4ceb-aada-0c62ce6cfc3>

nano-hydroxyapatite) or to prevent infection (e.g. nanosilver), or embedded nanomaterials to strengthen biomaterials (e.g. carbon nanotubes in a catheter wall).

The guidance recommends a phased approach for evaluating the risks of the use of nanomaterials in medical devices based on the potential release and characteristics of the nanomaterials. The phases cover particle release (phase 1), particle distribution and persistence (phase 2), hazard assessment (toxicological evaluations) (phase 3), and risk characterisation/risk assessment (phase 4). The guidance concludes that any potential risk from the use of nanomaterials in medical devices is mainly associated with the possibility for release of free nanoparticles from the device and the duration of exposure.

Section 3.5 of the guidance specifically discusses questions related to the **exposure to nanomaterials from medical devices**.³⁷ Depending on the relevant exposure route the nanomaterials will encounter various barriers before they are taken up by the body. Patients and users may be exposed, although the potential of exposure of patients and/or users will differ depending on the particular device and the way it is used. In general, the highest potential for exposure is associated with devices that consist of 'free' nanomaterials or that are subject to the release/loosening of nanomaterials present as coatings on the surface of medical devices. In addition, exposure to nanomaterials from medical devices may also result from degradation or wear processes, when nanomaterials are fixed on the surface (e.g. as coating on implants) or are embedded within the material of the medical device.

It was acknowledged that there are challenges related to the great variety of nanomaterials used and that certain kinds of devices, such as sensors/diagnostics for in vivo use, regenerative medicine, and implants result in high exposure potential for patients. For professional users, exposure potential is low. When the nanomaterial is used in an unbound state, it can potentially spread through the body.

Based on these findings of the SCENIHR and in order to ensure a high level of health protection and certainty, the EU MD Regulation introduced new definitions, classifications and general safety and performance requirements for devices with nanomaterials. These underpin the requirements that in the design and manufacture of such devices, manufacturers should take special care when using nanoparticles for which there is a high or medium potential for internal exposure and that such devices should be subject to the most stringent conformity assessment procedures.³⁸

International Standard

ISO 10993 is a series of standards for evaluating the biocompatibility of medical devices to manage biological risk. ISO 10993-22:2017³⁹ provides guidance on nanomaterials, including for medical devices composed of or containing nanomaterials, but also where nano-objects are generated as products of degradation, wear, or from mechanical treatment processes (e.g. *in situ* grinding, polishing of medical devices) from (components of) medical devices that are not manufactured using nanomaterials.

Under the Australian regulatory framework there are no mandatory standards, with the medical device required to comply with the EPs. Nevertheless compliance with relevant standard is encouraged because, where these standards exist, their use is the best method to demonstrate compliance with the EPs.

³⁷ *ibid*, p.21

³⁸ [Regulation \(EU\) 2017/745](#) of the European Parliament and of the Council of 5 April 2017 on medical devices, (OJ L 117, 5.5.2017, (15) p. 3).

³⁹ [ISO/TR 10993-22:2017](#) - Biological evaluation of medical devices — Part 22: Guidance on nanomaterials

U.S. Food and Drug Administration (U.S. FDA)

The U.S. FDA has not established regulatory definitions of “nanotechnology,” “nanomaterial,” “nanoscale,” or other related terms.

The U.S. FDA does not consider products containing nanomaterials or otherwise involving the application of nanotechnology as either intrinsically benign or harmful, instead it regulates nanotechnology products under its existing statutory authorities, in accordance with the specific legal standards applicable to each type of product. This means that medical devices containing nanomaterials are regulated under the current medical device framework, with the [FDA website](#) stating

Where premarket review authority exists, attention to nanomaterials is being incorporated into standing procedures. Premarket review processes for these products require applicants to submit data to answer questions related to the safety, effectiveness (where applicable), or regulatory status of the product. Individual premarket review procedures include attention to whether the use of nanomaterials suggests the need for additional data on safety or effectiveness, as applicable.

While the U.S. FDA has not published specific guidance on nanomaterials for the medical devices sector, it has published guidance on “[Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology](#)” which includes medical devices. The guidance asks sponsors/ manufacturers to consider whether:

- a material or end product is engineered to have at least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1 nm to 100 nm); and
- a material or end product is engineered to exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer (1,000 nm).

It has also published several [guidance and draft guidance documents](#) on topics relating to the application of nanotechnology in other FDA-regulated products such as drug products and liposome drug products, foods and cosmetics.

The U.S. FDA also runs focussed training for its assessors on matters specific to nanomaterials in therapeutic goods.

Health Canada

Health Canada has a [working definition](#) of nanomaterial which states that any manufactured substance or product and any component material, ingredient, device, or structure is considered to be a nanomaterial if:

- It is at or within the nanoscale (i.e., 1 to 100 nanometres) in at least one external dimension, or has internal or surface structure at the nanoscale, or;
- It is smaller or larger than the nanoscale in all dimensions and exhibits one or more nanoscale properties/phenomena.

Health Canada’s [guidance](#) on how to complete a medical device licence application outlines a number of specific requirements which relate to making an application for medical devices containing nanomaterials. These include requiring information on nanomaterials with a particle size of smaller than 1000 nanometres; identifying the specific type of nanomaterial present in the device, and providing detailed information about it including the intended purpose of the nanomaterial, manufacturing methods, chemical and physical characteristics, and any relevant

toxicological data specific to the nanomaterial. A risk assessment report of the nanomaterial in relation to the human body must also be provided.

Singapore Health Sciences Agency

The Health Sciences Agency (HSA) of Singapore states in both its "[GN-17: Guidance on Preparation of a Product Registration Submission for General Medical Devices](#)" and "[GN-18: Guidance on Preparation of a Product Registration Submission for In-Vitro Diagnostic Medical Devices](#)" that if a medical device has any unique/ novel features or characteristics (e.g., nanotechnology, incorporates animal or microbial cells or tissues) then a description of that feature must be provided.

Option 1 – No change

As outlined above, Australia's existing regulatory framework does provide for the regulation of nanomaterials in medical devices, although this is not explicit. Australia relies heavily on conformity assessment certification from comparable overseas regulators (including Europe, USA, Canada, Japan) and the existing provisions allow for this, including where medical devices include nanomaterials.

What would change for sponsors and manufacturers?

There would be no change for sponsors and manufacturers.

Option 2 - Make requirements explicit – add definitions and amend essential principles

Add definitions

As outlined in the discussion above, the definitions in use internationally by regulators and the relevant standards are generally consistent, all based around the 100 nanometres threshold. However definitions are described in guidance rather than prescribed in the regulatory framework in the USA, Canada and Singapore.

Amend essential principles

Any medical device supplied in Australia must comply with the requirements set out in the Australian MD Regulations, including relevant provisions of the EPs. The essential principles set out the requirements relating to the safety and performance of medical devices. There are six EPs that apply to all devices; and nine EPs about design and construction that apply to devices on a case-by-case basis.

In order to demonstrate compliance with the essential principles, a manufacturer and sponsor of a medical device that contains any substance/material, must be able to demonstrate that any risks associated with that substance/material, are acceptable risks when weighed against the intended benefit of the medical device to the patient/user.

The TGA position has always been that manufacturers of medical devices containing nanomaterials must implement a comprehensive risk-management system addressing any

hazard potentially posed by nanomaterials.⁴⁰ Until now however this requirement has not been explicitly formalised in the Australian regulatory framework.

What would change for sponsors and manufacturers?

In and of itself, the inclusion of a definition of nanomaterials (and associated definitions) would not change the requirements for medical devices. These definitions would operate to clarify obligations under amendments to the EPs (and/or adding new classification rules under Option 3)

If the EPs are amended as outlined, these requirements will be prescribed in the regulatory framework. As outlined above, manufacturers should already be addressing issues and risks associated with nanomaterials in their medical devices under the existing EPs. Sponsors who supply, or plan to supply, medical devices in Australia may be required to demonstrate compliance with the revised (and now explicit) EP for medical devices containing nanomaterials. Sponsors should also, in a practical sense, be able to identify all medical devices which include nanomaterials, or work with the manufacturers to do so, and they may not currently have an awareness of this as the existing requirements are not explicit.

Option 3 – Add new classification rules

Current classification applicable to these devices in Europe

The EU MD Classification Rule 19 classifies medical devices incorporating or consisting of nanomaterials based on the duration of use and degree of potential invasiveness within the body (e.g. is it used during a surgical procedure, or by application through the skin, or does exposure occur when the patient or other user breathes).

The potential for nanomaterials to be in contact with membranes inside the body is considered a critical factor in determining the level of internal exposure. Those devices presenting a high or medium potential for such contact will fall under the highest risk class and thus be subject to the most stringent conformity assessment procedures.⁴¹

It should be noted that any classification rule must be considered in the context of the *Implementing Rules* that guide the application of classification to a medical device. Relevant references are provided below.

Application of the classification rules shall be governed by the intended purpose of the devices.⁴²

If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. Accessories are classified in their own right separately from the device with which they are used.⁴³

⁴⁰ Australian Regulatory Guidelines for Medical Devices, s. 8-Differences between the Australian and European Union medical device regulatory requirements, p.157

⁴¹ European Commission - Fact Sheet, New EU rules to ensure safety of medical devices, Brussels, 5 April 2017 (http://europa.eu/rapid/press-release_MEMO-17-848_en.htm)

⁴² [Regulation \(EU\) 2017/745](#) of the European Parliament and of the Council of 5 April 2017 on medical devices, Annex VIII, Chapter II – Implementing Rules, 3.1, p. 140.

⁴³ OJ L 117, 5.5.2017, 3.2, p. 140.

If the device is not intended to be used solely or principally in a specific part of the body, it shall be considered and classified on the basis of the most critical specified use.⁴⁴

If several rules or several sub-rules apply to the same device based on the device's intended purpose, the strictest rule and sub-rule resulting in the higher classification shall apply.⁴⁵

Current classification applicable to these devices in Australia

There are currently no specific definitions and/or classification rules related to medical devices containing nanomaterials, and therefore any of the current classification rules set out in Schedule 2 of the Australian MD Regulations may be relevant to these devices.

Parts of Schedule 2 apply to these devices depending on their intended use, duration of use, level of invasiveness and functionality

Part 1—Transient, short-term and long-term use

Part 2—Rules for non-invasive medical devices

Part 3—Rules for invasive medical devices and implantable medical devices

Part 4—Special rules for active medical devices

Part 5—Special rules for particular kinds of medical devices

Introducing the nanomaterial classification rules would result in up-classification for a number of medical devices containing nanomaterials, which would align Australia with European requirements, but may put us out of step with other comparable international regulators.

Possible classification changes

Manufacturers of all medical devices must apply conformity assessment procedures and have appropriate technical documentation demonstrating compliance of the device with the relevant regulatory requirements. Further, manufacturers of all devices (except Class I (low-risk) medical devices) must be assessed by the TGA or an acceptable independent assessment body/overseas regulator and have a *conformity assessment document*⁴⁶ issued by that assessment body/regulator demonstrating that the manufacturer has applied appropriate conformity assessment procedures or requirements comparable to the conformity assessment procedures, to the device. High-risk Class III medical devices also require assessment of technical documentation related to each device, rather than that of a representative device from a group of similar devices.⁴⁷ Manufacturers of Class I medical devices self-declare compliance.

If the amendments proposed under Option 3 come into force some medical devices containing nanomaterials will be reclassified and the information to be assessed by the TGA will need to include clinical and technical data related to the respective nanomaterials. Such information may include physicochemical characterisations of nanomaterials, estimation of exposure to

⁴⁴ OJ L 117, 5.5.2017, 3.4, p.141.

⁴⁵ OJ L 117, 5.5.2017, 3.5, p.141.

⁴⁶ [Therapeutic Goods Act 1989](#), s.3

⁴⁷ [Therapeutic Goods \(Medical Devices\) Regulations 2002](#), r.3.6 and Schedule 3 – Conformity assessment procedures

nanomaterials from medical devices (e.g. release studies of nanomaterials from medical devices, degradation of medical devices), toxicity data, etc.

Sponsors of reclassified medical devices will be required to include their devices in the [Australian Register of Therapeutic Goods](#) (ARTG) with the correct classification. Sponsors of Class III (high-risk) medical devices will be required to include each device in ARTG separately, with an individual unique product identifier (UPI) to improve their traceability. Also sponsors are required to obtain manufacturer's *conformity assessment documents* relevant to the classification of the medical device, and provide such documents to the TGA to demonstrate procedures appropriate for their device when submitting applications for inclusion of a medical device in the ARTG.

What would change for sponsors and manufacturers?

If the regulatory changes proposed under Option 3 take effect, applicants would need to provide manufacturer's *conformity assessment documents* appropriate to devices of the respective classification.⁴⁸ For manufacturers this would mean they would need to seek conformity assessment certification appropriate to the class of the medical device.

Sponsors will be required either to apply for inclusion of their medical devices containing nanomaterials in the ARTG with the correct classification (where the new rules will change current classification of the medical device), or, where the classification remains the same, the sponsor will be required to submit a request for variation of the current ARTG entry to include information on the ARTG concerning the nanomaterial.

Where the manufacturer has conformity assessment documents from the EU or is seeking conformity assessment certification from the TGA, the medical device will have been assessed at the applicable classification. Where using conformity assessment documents from other comparable overseas regulators the manufacturer may not have the appropriate documentation to support the Australian application for inclusion at the Australian classification. For example, a medical device which is a Class III in Australia can be supported by an FDA PMA approval. However if the device has been approved in the USA under the premarket notification scheme (510(k)) this approval will be insufficient to support inclusion in Australia.⁴⁹

⁴⁸ Therapeutic Goods (Medical Devices—Information that Must Accompany Application for Inclusion) Determination 2018 (F2018L01410) (<https://www.legislation.gov.au/Details/F2018L01410>)

⁴⁹ Further explanation of comparable overseas regulator conformity assessment documents required for various classes of medical device see *Use of market authorisation evidence from comparable overseas regulators / assessment bodies for medical devices (including IVDs)*, Table 2, www.tga.gov.au/publication/use-market-authorisation-evidence-comparable-overseas-regulators-assessment-bodies-medical-devices-including-ivds#table2

Proposed regulatory amendment package

TGA's preferred option is Option 2 (add definitions and amend EPs), but not Option 3 (classification rules).

Input from stakeholders is being sought to inform advice to Government on this element of the proposed reforms to align with the European medical devices regulatory framework.

Introducing the definitions and EP amendments would increase the explicit oversight of nanomaterials in medical devices, without the consequent increase the regulatory burden associated with up-classifying medical devices with nanomaterials. There is general consensus on the definition of nanomaterials, internationally and across different types of therapeutic goods regulation (ie also for medicines).

Introducing the classification rules would result in up-classification for a number of medical devices containing nanomaterials, which would align Australia with European requirements, but would add regulatory burden and may put us out of step with other comparable international regulators.



In practice many applicants will already hold conformity assessment certification from the EU for the higher classification. However those seeking Australian market entry who do not hold European certification may need to seek additional conformity assessment certification from the TGA, as conformity assessment documentation from other comparable overseas regulators may be insufficient where the classification of the medical device has increased. As all medical devices must comply with the EPs, irrespective of classification, the changes to the EPs (and related definitions) are sufficient to address the relevant risks of nanomaterial, while not creating a barrier to entry to the Australian market.

In complying with the EPs manufacturers need to assess and manage risks associated with nanomaterials, and would need to provide evidence of this to the TGA (through the Australian sponsor) on request. This would usually be demonstrated with evidence of compliance with the international standard ISO 10933 (including ISO/TR 10993-22:2017 Biological evaluation of medical devices Part 22: Guidance on nanomaterials).

This approach would not preclude introducing the additional classification rules in future, as greater international convergence of regulatory requirements emerges.

Transitional arrangements

Option 1

No changes would be made and no transitional arrangements would be required.

Option 2

The introduction of new definitions can come into effect immediately on making the regulatory amendments, as this will have no impact in the absence of other options.

Amendments to the EPs would be aligned to other changes to the EPs being progressed as part of the European alignment, as outlined in the previous consultation on the EPs, [Consultation: Proposed changes to medical device essential principles for safety and performance](#). Delays due to the COVID-19 emergency mean that regulatory changes to the EPs are not in place. Sufficient time would be allowed between passage of the regulatory amendments and commencement of the changes. After this commencement date new devices would need to comply with the revised EPs, with existing devices generally needing to demonstrate compliance as their certification is renewed.

Option 3

In Europe, under the transitional arrangements, medical devices lawfully placed on the market that have pre-market authorisation in the form of a valid EC Certificate⁵⁰ can remain on the market until the expiry date of that EC Certificate or until 27 May 2024 (when these certificates become void), whichever is the earliest. Devices lawfully placed on the market may continue to be made available on the market or put into service until 27 May 2025.

If Option 3 is implemented, we propose that the new classification for **new medical devices in Australia**—that is, a device included in the ARTG following successful completion of applications submitted to the TGA on or after the commencement date of the amended regulations—would start from 12 months following the regulatory amendments being made. This would provide sufficient notice of the pending change, and allow for supporting guidance to be published.

Transitional arrangements would be available for existing ARTG entries for medical devices with nanomaterials, as outlined below. The end of the transition period would be 31 October 2024,⁵¹ matched with other reclassifications currently in progress under the changes to align with the European regulatory framework. This transition period is six months after the end of European transitional arrangements (May 2024), and provides for applicants having European certification in place to support applications.

Applications

At the date that the proposed amendment takes effect:

- **All new applications for marketing approval** (ARTG inclusion) for medical devices containing a nanomaterial submitted to the TGA, on or after the date when amendments to the regulations take effect, must be made in accordance with the new classification rules (consistent with EU MD Classification Rule 19) that will be provided in Part 5, Schedule 2 of the Australian MD Regulations.
- **Sponsors of devices already included in the ARTG**, or those for which applications have been submitted before regulatory amendments take effect, must apply to have their device/s re-entered in ARTG with the correct classification. Those devices, classification of which has

⁵⁰ EC certificates issued in accordance with EU Directive 93/42/EEC and which comply with the requirements in para. (2) of Article 120 of the EU MD Regulation.

⁵¹ Further information on timeframes for medical device regulatory changes is available on the TGA website at www.tga.gov.au/delays-commencement-certain-medical-device-regulatory-changes

not changed, may remain in the ARTG but sponsors **will be required to submit a variation request** and provide relevant information concerning the nanomaterial.

- **All applications must be submitted to the TGA by the end of the transition period.** Where an application to reclassify has been submitted to the TGA but has not been determined (i.e. is still under assessment), the device can continue to be supplied under the existing ARTG entry until an application for the new Class of medical device is finalised (including applications not finalised at the end of the transition period).
- For those **devices for which transitional provisions apply**, sponsors must notify the TGA of all such devices presently supplied under the existing ARTG entry within six (6) months of the amended regulations taking effect. These devices can continue to be supplied for the duration of the transition. If the sponsor has not notified the TGA within this period, they will no longer be eligible for the transitional arrangements. (This will apply to any device required to be reclassified or not.)
- If any **application for ARTG inclusion for a device with the current classification is in progress** on the date the regulations come into effect, it may continue. If the application is successful, the device will be included with the current classification. The sponsor must then reapply to include their device in ARTG with the correct classification (if applicable), as per requirements set out under the transitional arrangements.

Fees and charges

Normal application fees and audit assessment fees will apply (where applicable) for applications for inclusion of these devices in the ARTG.

It is proposed that a new assessment form will be introduced for devices requiring sponsors to submit a request of variation of their current ARTG entry/entries to enable assessment of information relating to nanomaterials.

Normal annual charges will also apply.

Engagement

Wherever practicable, the TGA will:

- Liaise with the healthcare sector, patient associations and industry peak bodies to inform and raise awareness about this proposal; and
- Provide relevant material on the TGA website.

Feedback notes

It is important to note that while we intend to take the European medical device framework and a broader international regulatory practice into account, the Australian legislative instruments are structured differently and there is variation in the legal terminology acceptable in each jurisdiction. We acknowledge that legislation cannot always be successfully replicated across jurisdictions. Therefore, your views on the impacts of the proposed regulatory changes related to medical devices containing nanomaterials are very important to us.

When considering the proposed measures, assume that the EU MD Regulation definitions and terminology, and classification Rule 19 apply to medical devices containing nanomaterials in the context of the Australian MD Regulations.

Please also keep in mind that current and future technological developments may potentially bring more categories and groups of medical devices under these classification rules.

What we invite you to do

In your submission, we ask you to consider the questions below and provide comments related to any other matter outlined in this consultation paper.

Questions

1. Should specific requirements for medical devices containing nanomaterials, be introduced in the Australian MD Regulations?
2. If so, what option/s should be adopted?:
 - a. Option 1 – no change
 - b. Option 2 – add definitions and amend essential principles
 - c. Options 3 – add new classification rules
3. What impacts—including any that we may not have anticipated and are therefore unintended—do you anticipate the new definitions, essential principles and/or classification rules may have for yourself and other stakeholders (such as consumers, healthcare professionals, health organisations, industry etc.)?
4. Are there any further issues and questions we should consider when implementing these changes (including areas that can/should be clarified in our guidance)?
5. If Option 3 – add new classification rules proceeds, what criteria should be used to decide whether a device has a negligible, low, medium and high potential for internal exposure? Should the term ‘potential for internal exposure’ be clarified in our guidance or defined in the Australian MD Regulations? If yes, what definition do you propose for the meaning of this term?
6. Are there any groups of medical devices containing nanomaterial that should be given particular consideration or treatment?
7. Nanoparticles may be generated as a consequence of the degradation of medical devices not containing nanomaterials or abrasive wear or grinding of a material. Should we clarify whether such devices will be affected by the proposed new rules?
8. Do you have any comments regarding the transitional arrangements proposed in this paper?



How to submit

Complete the online consultation submission form [webteam to add link and radio button] to upload your submission in either pdf or word format.

You can also submit your feedback directly to the TGA by email at: devicereforms@tga.gov.au. If you do so, **please ensure your submission is accompanied by a coversheet** (refer [webteam to add link]).

This consultation closes on **Friday 9 April 2021**.

Enquiries

If you have any questions relating to submissions please direct them to: devicereforms@tga.gov.au.

Appendix A – Definitions and other provisions related to medical devices containing nanomaterial

There are a number of differences between the definitions and other provisions in the Regulation (EU) 2017/745 and *the Therapeutic Goods (Medical Devices) Regulations 2002*.

Table A below provides overview of provisions related to medical devices with nanomaterials.

EU MD Regulation	Australian MD Regulations	Proposed amendments
Introductory part		
<p>(15) There is scientific uncertainty about the risks and benefits of nanomaterials used for devices. In order to ensure a high level of health protection, free movement of goods and legal certainty for manufacturers, it is necessary to introduce a uniform definition for nanomaterials based on Commission Recommendation 2011/696/EU (4), with the necessary flexibility to adapt that definition to scientific and technical progress and subsequent regulatory development at Union and international level. In the design and manufacture of devices, manufacturers should take special care when using nanoparticles for which there is a high or medium potential for internal exposure. Such devices should be subject to the most stringent conformity assessment procedures. In preparation of implementing acts regulating the practical and uniform application of the corresponding requirements laid down in this Regulation, the relevant scientific opinions of the relevant scientific committees should be taken into account.</p>	<p>No equivalent explanation.</p>	<p>N/A</p> <p>This paragraph of the EU MD Regulation provides the rationale supporting the regulatory changes concerning medical devices containing or consisting of nanomaterials.</p> <p>In Australia, such information is generally included in Explanatory Statements.</p>

EU MD Regulation	Australian MD Regulations	Proposed amendments
Article 2 Definitions		
<p>(18) 'nanomaterial' means a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm;</p> <p>Fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm shall also be deemed to be nanomaterials;</p>	<p>Dictionary (regulation 1.3). No equivalent definition.</p>	<p>This definition is subject of this consultation paper. The TGA proposes to incorporate this definition into the Australian MD Regulations.</p> <p>Currently, 'nanomaterial' is not defined in the Australian therapeutic goods legislation.</p> <p>However improving clarity and understanding of the regulatory requirements for such medical devices should facilitate better regulatory compliance and consequently the safety and performance of medical devices.</p> <p>Further such approach is consistent with the TGA's interpretation of the requirements applied to devices containing nanomaterials, and a broad international regulatory practice and Australian work undertaken in the field of nanotechnology.</p>
<p>(19) 'particle', for the purposes of the definition of nanomaterial in point (18), means a minute piece of matter with defined physical boundaries;</p>	<p>Dictionary (regulation 1.3). No equivalent definition.</p>	<p>As above, the TGA proposes to incorporate this definition into the Australian MD Regulations.</p> <p>This definition clarifies and complements the definition of 'nanomaterial'. Therefore if the definition of 'nanomaterial' is included in the Australian MD Regulations, this definition of 'particle' will be required as well.</p>

EU MD Regulation	Australian MD Regulations	Proposed amendments
<p>(20) 'agglomerate', for the purposes of the definition of nanomaterial in point (18), means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components;</p>	<p>Dictionary (regulation 1.3). No equivalent definition.</p>	<p>As above, the TGA proposes to incorporate this definition into the Australian MD Regulations.</p> <p>This definition clarifies and complements the definition of 'nanomaterial'. Therefore if the definition of 'nanomaterial' is included in the Australian MD Regulations, this definition of 'agglomerate' will be required as well.</p>
<p>(21) 'aggregate', for the purposes of the definition of nanomaterial in point (18), means a particle comprising of strongly bound or fused particles.</p>	<p>Dictionary (regulation 1.3). No equivalent definition.</p>	<p>As above, the TGA proposes to incorporate this definition into the Australian MD Regulations.</p> <p>This definition clarifies and complements the definition of 'nanomaterial'. Therefore if the definition of 'nanomaterial' is included in the Australian MD Regulations, this definition of 'aggregate' will be required as well.</p>
<p>Article 3 Amendment of certain definitions</p>		
<p>The Commission is empowered to adopt delegated acts in accordance with Article 115 in order to amend the definition of nanomaterial set out in point (18) and the related definitions in points (19), (20) and (21) of Article 2 in the light of technical and scientific progress and taking into account definitions agreed at Union and international level.</p>		<p>N/A</p> <p>Replication of this Article of the EU MD Regulation (that at any future point in time, the definition of nanomaterial and other related provisions may be amended) is not necessary. Any decision to amend our legislation is made in accordance with the Australian law.</p>

EU MD Regulation	Australian MD Regulations	Proposed amendments
<p>ANNEX I - GENERAL SAFETY AND PERFORMANCE REQUIREMENTS</p> <p>CHAPTER II REQUIREMENTS REGARDING DESIGN AND MANUFACTURE</p>		
<p>Page 96</p> <p>10.4.1. Design and manufacture of devices</p> <p>Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including wear debris, degradation products and processing residues that may be released from the device.</p>		<p>TGA has consulted on the essential principles, and also plans to consult on conformity assessment procedures. The specifics of how the EPs are updated (e.g. structure and scope, wording) will also be informed by those processes.</p> <p>This GSPR is subject of this consultation paper.</p> <p>If supported, this GSPR element would be incorporated into the essential principles (Australian MD Regulations, Schedule 1).</p>
<p>Page 97</p> <p>10.6. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention shall be given to nanomaterials.</p>		<p>As above.</p>

EU MD Regulation	Australian MD Regulations	Proposed amendments
ANNEX VIII CLASSIFICATION RULES CHAPTER III CLASSIFICATION RULES	Schedule 2—Classification rules for medical devices other than IVD medical devices	
<p>7. SPECIAL RULES</p> <p>7.6. Rule 19</p> <p>All devices incorporating or consisting of nanomaterial are classified as:</p> <ul style="list-style-type: none"> — class III if they present a high or medium potential for internal exposure; — class IIb if they present a low potential for internal exposure; and — class IIa if they present a negligible potential for internal exposure. 	No equivalent classification rules.	<p>This classification rule is subject of this consultation paper.</p> <p>If supported, this classification rule would be incorporated into the classification rules in the Australian MD Regulations, Schedule 2, Part 5 (Special rules for particular kinds of medical devices)</p>

Version history

Version	Description of change	Author	Effective date
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