

EXPLANATORY STATEMENT

Therapeutic Goods Act 1989

Therapeutic Goods (Permissible Ingredients) Determination (No. 2) 2024

The *Therapeutic Goods Act 1989* (the Act) provides for the establishment and maintenance of a national system of controls for the quality, safety, efficacy or performance, and timely availability of therapeutic goods that are used in, or exported from, Australia. The Act is administered by the Therapeutic Goods Administration (the TGA) within the Australian Government Department of Health and Aged Care.

Subsection 26BB(1) of the Act relevantly provides that the Minister may, by legislative instrument, make a determination specifying ingredients and, for some or all of those ingredients, requirements in relation to those ingredients being contained in a medicine. Under subsections 26BB(2), (2A) and (3) of the Act, such requirements may relate to particular ingredients not being contained in particular medicines or being contained in particular medicines only in specified circumstances or within permitted concentrations or total amounts of an ingredient in a medicine.

The purpose of a legislative instrument made under section 26BB of the Act is to specify those ingredients that may be contained in a medicine that is listed in the Australian Register of Therapeutic Goods (the Register) under section 26A or 26AE of the Act, and specify requirements in relation to the inclusion of those ingredients in such medicines. Listed medicines can only use ingredients specified in an instrument under section 26BB.

The *Therapeutic Goods (Permissible Ingredients) Determination (No. 2) 2024* (the Determination) repeals and replaces the *Therapeutic Goods (Permissible Ingredients) Determination (No. 1) 2024* (the former Determination), and specifies those ingredients that may be contained in a medicine that is listed in the Register and requirements in relation to the inclusion of those ingredients in such medicines.

Background

Medicines that are listed in the Register under section 26A of the Act are considered to be low risk and are not individually evaluated before those medicines are listed. Medicines that are listed in the Register under section 26AE of the Act are also considered to be low risk, but are evaluated in relation to whether the efficacy of the medicine for the purposes for which it is to be used has been satisfactorily established (these purposes are specific efficacy claims for which the sponsor of the medicine holds supporting evidence). When listed under section 26AE, these listed medicines are commonly referred to as ‘assessed listed medicines’.

As the safety and quality of medicines listed under sections 26A and 26AE are not evaluated by the TGA before being given marketing approval, the Act contains mechanisms to help ensure that those medicines are of appropriate quality and able to be used safely by consumers. In particular, medicines listed under sections 26A and 26AE may only contain ingredients from an approved list of ingredients that have been evaluated in relation to their quality, safety and suitability for use in such medicines. Sponsors of such medicines may also only use indications (statements of therapeutic use) from a list of pre-approved, low-level indications to ensure that these products do not overstate their therapeutic benefits.

Under paragraphs 26A(2)(ca) and (cb) of the Act, persons applying to list a medicine in the Register under section 26A of the Act must certify that the medicine does not contain an ingredient that is not specified in a determination under paragraph 26BB(1)(a) of the Act; and does not contravene a requirement in relation to such an ingredient that is specified in such a determination. Paragraphs 26AB(2)(d) and (e) contain equivalent certification requirements for applicants seeking marketing

approval in relation to assessed listed medicines. A listed (or assessed listed) medicine may be cancelled from the Register if it appears to the Secretary that such a certification is incorrect.

Separately, items 3, 4A, 5, 7 and 8 of Schedule 4 to the *Therapeutic Goods Regulations 1990* (the Regulations), which identifies those therapeutic goods that are eligible for listing in the Register, require that, in order for the goods mentioned in each of those items to be eligible for listing, the goods must only contain ingredients that are specified in a determination under paragraph 26BB(1)(a) of the Act, and must not contravene a requirement in such a determination.

Purpose

The Determination, made under section 26BB of the Act, provides a comprehensive list of ingredients which have been assessed or otherwise considered to be safe for use in listed medicines (including assessed listed medicines), and associated requirements to be followed when using particular ingredients in such medicines.

The requirements imposed under the Determination are principally designed to ensure or support the quality and safety of listed medicines that contain permitted ingredients. The requirements may relate, for example, to:

- how a permitted ingredient is to be used in the medicine, that is, as an active, homoeopathic or excipient ingredient;
- the intended method of ingestion or application of the medicine, for example, oral or topical use;
- the source of the ingredient, or procedures to be followed in its manufacture;
- appropriate limits on the volume or concentration of an ingredient; and
- the inclusion of relevant safety information on product labels, for example, allergen advice or advice about the use of medicine containing the ingredient for susceptible members of the population such as children and pregnant women.

The Determination incorporates a number of changes in comparison to the former Determination, including in particular:

- the addition of the following four new ingredients for use in listed and assessed listed medicines, and requirements for including the ingredients in medicines:
 - *Bacillus subtilis*;
 - *behentrimonium metilsulfate*;
 - *D-glucose, polymer with xylitol*;
 - *polyglyceryl-2 isostearate*;
- the addition of the ingredient *1,8,12-bisabolatriene*, following evaluation for its use in flavour proprietary excipient formulations;
- amendments to introduce specific requirements for the ingredient *Litchi chinensis*, in relation to its use in flavour proprietary excipient formulations;
- amendments to the specific requirements for the ingredient *nonivamide*, in relation to its use in fragrance proprietary excipient formulations, and minor formatting changes for the purposes of improving the internal consistency of the Determination; and
- the removal of requirements for the following ingredients to reflect the expiry of periods of exclusive use for the applicant, and minor formatting changes for the purpose of improving the internal consistency of the Determination:
 - *Euglena gracilis whole cell dry*;
 - *beeswax alcohols*.

Consultation

Between January 2023 and March 2024, the TGA engaged directly with the applicant who applied for the approval of the ingredient *Bacillus subtilis*, in connection with the application.

Between June 2022 and May 2024, the TGA engaged directly with the applicant who applied for the approval of the ingredient *behentrimonium metilsulfate*, in connection with the application.

Between April 2023 and May 2024, the TGA engaged directly with the applicant who applied for the approval of the ingredient *D-glucose, polymer with xylitol*, in connection with the application.

Between April 2022 and December 2023, the TGA engaged directly with the applicant who applied for the approval of the ingredient *polyglyceryl-2 isostearate*, in connection with the application.

Between September 2023 and May 2024, the TGA engaged directly with flavour, fragrance, or printing ink suppliers who notified they had products containing *1,8,12-bisabolatriene*, *Litchi chinensis*, and *nonivamide*. The suppliers requested these products to be made available for inclusion in listed medicine and assessed listed medicine applications.

Prior to June 2022, the TGA engaged with the applicants for *Euglena gracilis whole cell dry* and *beeswax alcohols* to be included in the Determination. The amendments reflect the conclusion of periods of exclusive use consulted at that time, and do not require additional consultation.

Incorporation by reference

Pharmacopoeia and FCC

The Determination references the British Pharmacopoeia, European Pharmacopoeia and United States Pharmacopoeia-National Formulary, and the note in section 4 of the Determination makes it clear that each is defined in subsection 3(1) of the Act.

The definitions of the pharmacopoeia in subsection 3(1) of the Act refer to the publications of each as in force from time to time. The intention in this Determination is therefore to adopt the defined meaning of the pharmacopoeia as set out in subsection 3(1) of the Act (an approach permitted by subsection 26BB(8) of the Act). These pharmacopoeia are incorporated in the Determination as in force or existing from time to time, in accordance with these provisions, and may be accessed from www.pharmacopoeia.com/, <https://pheur.edqm.eu/home> and www.uspnf.com/.

The Determination also adopts specified applicable monographs in the Food Chemicals Codex (the FCC) published by the United States Pharmacopoeial Convention (available at www.foodchemicalscodex.org/) in relation to the following ingredients:

- Glycerol Ester of Partially Hydrogenated Gum Rosin;
- Glyceryl Rosinate; and
- Polyisobutylene.

The intended manner of adoption of the FCC is also as it is in force or existing from time to time, as permitted by subsection 26BB(8) of the Act.

While unfortunately the pharmacopoeia and the FCC are not available for free, it is anticipated that the persons most affected by their adoption in this Determination (sponsors of medicines included in the Register and other interested persons in the medicines industry using the Determination), would be in possession of these documents in order to manufacture medicines or ingredients. As important international benchmarks for the safety and quality of therapeutic goods, it would be infeasible from a regulatory perspective (particularly in relation to the safety of listed medicines that are not, for the most part, evaluated before being given marketing approval) to not adopt such benchmarks on the basis that the publications are not available for free.

However, by prior written arrangement with the TGA, members of the public may arrange to view the pharmacopoeia and the FCC without charge at the TGA office in Fairbairn, ACT.

It should also be noted, in relation to the pharmacopoeia, that the National Library's Trove online system (www.trove.nla.gov.au/) allows users to identify libraries in Australia that are open to the public where editions (in most cases, earlier editions) of the pharmacopoeia may be viewed (for example, the University of Tasmania or the University of Western Australia in relation to the British Pharmacopoeia).

Members of the public may also approach any library that participates in inter-library loans with those university libraries to request an inter-library loan, or to obtain a photocopy of a particular part or monograph for personal study or research (but not for commercial purposes). Fees apply in relation to the making of such a request. Enquiries should be made with local libraries, State libraries and the National Library.

Other documents incorporated by reference

The Determination also incorporates the following documents:

- the *Animal Products Act 1999* and the *Animal Welfare Act 1999* of New Zealand, and regulations made under these Acts, in relation to two ingredients (Deer Velvet Antler Powder and Deer Velvet Antler Slice), which are incorporated as in force or existing from time to time (as permitted by subsection 26BB(8) of the Act) and are available for free from www.legislation.govt.nz/;
- the World Health Organization publication '*Expert consultation on oral rehydration salts formulation*', which is incorporated as at 18 July 2001 and which is available for free from www.rehydrate.org/ors/expert-consultation.html;
- the 'code tables' in 'TGA eBusiness Services', which are incorporated by reference as in force or existing from time to time (as permitted by subsection 26BB(8) of the Act) and may be accessed for free at www.ebs.tga.gov.au.

Other details

Details of the Determination are set out in **Attachment A**.

The Determination 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**.

The Office of Impact Analysis (OIA) has previously advised that an impact analysis is not required for updates to determinations made under section 26BB of the Act that are minor or machinery in nature, including the introduction of new permitted ingredients, corrections of errors, clarifications of requirements and ingredient names, changes to reflect scheduling decisions in the Poisons Standard and the outcomes of TGA safety evaluations where the regulatory impacts are minor or machinery in nature (OIA references 14416, 20999 and 21645).

This Determination is a disallowable legislative instrument for the purposes of the *Legislation Act 2003*, and commences on 14 June 2024.

Details of the *Therapeutic Goods (Permissible Ingredients) Determination (No. 2) 2024*

Section 1 – Name

This section provides that the name of the instrument is the *Therapeutic Goods (Permissible Ingredients) Determination (No. 2) 2024* (the Determination).

Section 2 – Commencement

This section provides that the Determination commences on 14 June 2024.

Section 3 – Authority

This section provides that the legislative authority for making the Determination is subsection 26BB(1) of the *Therapeutic Goods Act 1989* (the Act).

Section 4 – Interpretation

Subsection 4(1) provides definitions for a number of terms used in the Determination. These include ‘code tables’, ‘excipient’, ‘homoeopathic preparation ingredient’ and ‘TGA eBusiness Services’.

The note to this section also makes it clear that a number of expressions used in the Determination have the same meaning as in the Act, including ‘British Pharmacopoeia’, ‘European Pharmacopoeia’ and ‘United States Pharmacopoeia-National Formulary’.

Subsection 4(2) provides that the terms set out in closed brackets in column 4 of the table in Schedule 1 to the Determination that are associated with warning statements in relation to particular ingredients, are terms from the code tables under the heading ‘Product Warning’, and are not required to be included on the label of the medicine.

Section 5 – Permissible ingredients

This section provides that the ingredients specified in column 2 of the table in Schedule 1 to the Determination are specified for the purposes of paragraph 26BB(1)(a) of the Act.

Section 6 – Requirements in relation to permissible ingredients being contained in medicine

This section provides that for an ingredient mentioned in column 2 of an item in the table in Schedule 1 to the Determination, the requirements in paragraphs 6(a) to (c) are specified for the purposes of paragraph 26BB(1)(b) of the Act. These include, for example, that the ingredient must only be used in a medicine for a purpose specified in relation to the ingredient in column 3 of that item and the ingredient must comply with the requirements specified in column 4.

Section 7 – Repeals

This section provides that the *Therapeutic Goods (Permissible Ingredients) Determination (No. 1) 2024* is repealed.

Schedule 1 – Specified permissible ingredients and requirements applying to these ingredients when contained in a medicine.

This Schedule specifies ingredients and related requirements for the purposes of sections 5 and 6 of the Determination.

Statement of Compatibility with Human Rights

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

Therapeutic Goods (Permissible Ingredients) Determination (No. 2) 2024

This disallowable 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

Subsection 26BB(1) of the Act relevantly provides that the Minister may, by legislative instrument, make a determination specifying ingredients and, for some or all of those ingredients, requirements in relation to those ingredients being contained in a medicine. Under subsections 26BB(2), (2A) and (3) of the Act, such requirements may relate to particular ingredients not being contained in particular medicines or being contained in particular medicines only in specified circumstances or within permitted concentrations or total amounts of an ingredient in a medicine.

The purpose of a legislative instruments made under section 26BB of the Act is to specify those ingredients that may be contained in a medicine that is listed in the Australian Register of Therapeutic Goods (the Register) under section 26A or 26AE of the Act, and specify requirements in relation to the inclusion of those ingredients in such medicines. Listed medicines can only use ingredients specified in an instrument under section 26BB.

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Background

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Under paragraphs 26A(2)(ca) and (cb) of the Act, persons applying to list a medicine in the Register under section 26A of the Act must certify that the medicine does not contain an ingredient that is not specified in a determination under paragraph 26BB(1)(a) of the Act; and does not contravene a requirement in relation to such an ingredient that is specified in such a determination. Paragraphs

26AB(2)(d) and (e) contain equivalent certification requirements for applicants seeking marketing approval in relation to assessed listed medicines. A listed (or assessed listed) medicine may be cancelled from the Register if it appears to the Secretary that such a certification is incorrect.

Separately, items 3, 4A, 5, 7 and 8 of Schedule 4 to the *Therapeutic Goods Regulations 1990* (the Regulations), which identifies those therapeutic goods that are eligible for listing in the Register, require that, in order for the goods mentioned in each of those items to be eligible for listing, the goods must only contain ingredients that are specified in a determination under paragraph 26BB(1)(a) of the Act, and must not contravene a requirement in such a determination.

Purpose

The Determination, made under section 26BB of the Act, provides a comprehensive list of ingredients which have been assessed or otherwise considered to be safe for use in listed medicines (including assessed listed medicines), and associated requirements to be followed when using particular ingredients in such products.

The requirements imposed under the Determination are principally designed to ensure or support the quality and safety of listed medicines that contain permitted ingredients. The requirements may relate, for example, to:

- how a permitted ingredient is to be used in the medicine, that is, as an active, homoeopathic or excipient ingredient;
- the intended method of ingestion or application of the medicine, for example, oral or topical use;
- the source of the ingredient, or procedures to be followed in its manufacture;
- appropriate limits on the volume or concentration of an ingredient; and
- the inclusion of relevant safety information on product labels, for example, allergen advice or advice about the use of medicine containing the ingredient for susceptible members of the population such as children and pregnant women.

The Determination incorporates a number of changes in comparison to the former Determination, including in particular:

- the addition of the following four new ingredients for use in listed and assessed listed medicines, and requirements for including the ingredients in medicines:
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- the removal of requirements for the following ingredients to reflect the expiry of periods of exclusive use for the applicant, and minor formatting changes for the purpose of improving the internal consistency of the Determination:
 - *Euglena gracilis whole cell dry*;
 - *beeswax alcohols*.

Human rights implications

The Determination engages the right to health in Article 12 of the International Covenant on Economic, Social and Cultural Rights (the ICESCR). Article 12 of the ICESCR promotes the right of all individuals to enjoy the highest attainable standard of physical and mental health, and includes an obligation to take reasonable measures within available resources to progressively secure broader enjoyment of the right.

In *General Comment No. 14: The Right to the Highest Attainable Standard of Health (Art. 12)* (2000), the United Nations Committee on Economic, Social and Cultural Rights states that health is a ‘fundamental human right indispensable for the exercise of other human rights’, and that the right to health is not to be understood as the right to be healthy, but includes the right to a system of health protection which provides equal opportunity for people to enjoy the highest attainable level of health.

The instrument takes positive steps to promote the right to health by ensuring the safety and quality of therapeutic goods that are listed medicines. The Determination prescribes those ingredients that are considered to be safe for use in listed medicines. The Determination also sets out important requirements relating to the use of those ingredients in such medicines. Such requirements may relate, for example, to maximum concentrations of such ingredients in listed medicines, or to the inclusion of warning statements on medicine labels (such as ‘Keep out of reach of children’ for relevant ingredients). Through the Determination, the safety of Australian consumers will be better protected, and they will be better able to make informed decisions about such medicines.

This is particularly important for listed medicines, given that those medicines are not evaluated for safety and quality by the TGA prior to listing in the Register. Further, those medicines are usually available for self-selection by consumers without a requirement to first obtain the advice or prescription of a registered medical practitioner or the advice of a pharmacist.

Conclusion

This legislative instrument is compatible with human rights because it promotes the right to health in Article 12 of the ICESCR and does not raise any other human rights issues.