International approaches to Natural Health Product regulations

Regulatory scan

February 2024

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Executive summary

This report outlines and compares regulatory approaches to natural health products (NHPs) in Australia, Canada, the EU, UK, USA and China. For the purpose of this report, NHPs are a group of health and wellness products. They include nutritional supplements and products used in traditional healing practices. They are mostly derived from natural ingredients but can also contain synthetic equivalents (e.g. ascorbic acid for vitamin C and folic acid for the B vitamin, folate). They come in edible and inedible forms (e.g. tablets, powders, creams and inhalants). Examples include nutritional supplements (e.g. vitamin E, magnesium and sports supplements), herbal products (e.g. echinacea tablets, St John's Wort capsules, and kawakawa balm), and animal products (e.g. deer velvet and fish oil capsules).

It also covers regulation of homeopathy in Germany and Ayurveda in India. Information in this report was extracted from both peer-reviewed and grey literature. The overall findings are as follows:

	Cross-jurisdictional findings
Definitional interface	Deciding how an NHP (or equivalent term) is defined is a complicated matter across all jurisdictions. Most jurisdictions included in this review have published guidance or tools to help businesses determine whether their product is an NHP, a medicine, a food or a cosmetic. The approaches taken by the selected jurisdictions include considering: • the function or claims of the product. In the EU and UK this mainly determines whether a product is a medicine or a food supplement – EU and UK • if ingredients are contained in a database of approved ingredients for NHPs – Australia, EU, UK, Canada and US • whether the product requires a prescription – Canada. Due to the different definitions, a product could be classified differently in each jurisdiction: • In Australia and Canada, NHPs are classified as a therapeutic good or drug. • In the EU and UK, they are classified as either a food or medicine, depending on function and claim of the product. • In the US, they are classified as food.

	• In China, traditional Chinese medicines (TCMs) are regulated as drugs, while health foods (which are similar to dietary supplements[1] in New Zealand) are regulated as foods.
Getting a product on the market	The process for getting a product on the market varies widely across jurisdictions with regard to whether notification (i.e. listing a product) or authorisation (i.e. seeking assessment and approval by the Regulator) is required. • In Australia, most 'complementary medicines' are listed. This generally requires: providing information to the regulator, passing validation to be listed on the Australian Register for Therapeutic Goods and paying fees. Some higher-risk products require 'registration' (i.e. an assessment and approval from the regulator). • In the EU, only some Member States require notification prior to a 'food supplement' product with permitted ingredients being put on the market. In the UK, there is no requirement for 'food supplements' to be licensed or registered. In both the EU and the UK, products classified as 'traditional herbal medicines' need to be authorised. • In Canada, there are product licensing requirements for all NHPs. Class III applications require full screening, while Class I and II applications go through administrative and regulatory screening, with potential additional information requirements. • In the US, products with known ingredients do not require notification. However, a pre-market notification to the FDA must be made at least 75 days prior to entering the market if the 'dietary supplement' contains a 'new dietary ingredient'. • In China, approval is needed for both traditional Chinese medicines and health foods. Each jurisdiction also has controls on labelling (e.g. indications, contraindications and warnings).

[1] Dietary supplements are defined in the Dietary Supplements Regulations 1985 as:
"…
(2) It is an amino acid, edible substance, herb, mineral, synthetic nutrient, or vitamin.
(3) It is sold by itself or in a mixture.
(4) It is sold in a controlled dosage form as a liquid, powder, or tablet (which might be described on the label as a cachet, capsule, lozenge, or pastille instead of as a tablet).
(5) It is intended to be ingested orally.
(6) It is intended to supplement the amount of the amino acid, edible substance, herb, mineral, synthetic nutrient, or vitamin normally derived from food."

Permissible ingredients	All jurisdictions have published lists of permissible ingredients for use in NHPs (or equivalent). Most jurisdictions also publish ingredients that are prohibited for use in NHPs (or equivalent) (EU, UK, Canada). If a business wants to use an ingredient not in the lists, it generally has to go through an authorisation procedure to have the ingredients evaluated for safety and quality.
Health benefit claims	There are restrictions on the types of claims that are allowed. Requirements are principally based on making claims with lower-level therapeutic impacts (e.g. maintaining and promoting health, and nutrition supplementation). That is, some jurisdictions do not allow claims that a product can prevent, treat or cure diseases or other conditions. Jurisdictions that regulate NHPs (or equivalent) as a subset of medicines (e.g. Australia, Canada, and the EU and the UK for products classified as traditional herbal medicine), however, allow for higher-level claims to be made (e.g. treating a condition or disease) compared to jurisdictions where NHPs (or equivalent) are classified as food (e.g. the US, and the EU and UK for products classified as food supplements) because the claim must be approved by the regulator (Blaze, 2021). The EU and the UK have a set list of claims that are allowed to be made on food supplements. If a business wants to make a claim not on the list, this needs to be approved and substantiated by evidence (which includes the requirement of a comprehensive review of published studies). Uses or claims by NHPs in Canada are included in their respective monographs; if specific claims are made not contained in monographs, applicants must make a Class III application. Australia lists acceptable indications on health maintenance, health enhancement, or prevention of vitamin/mineral deficiencies, which sponsors can link to their product through an evidence-based process. The US and China do not have specific lists, but in the US, manufacturers must submit a notification with the text of the claim to the FDA within 30 days of marketing a dietary supplement with a claim.

Manufacturing requirements	Most jurisdictions require good manufacturing practice (GMP). For NHPs classified as food in the EU and UK, GMP is only required for materials that come in contact with the product (e.g. the packaging, printing inks, adhesives), but regulations require food supplement manufacturers to comply with other strict quality control standards under food law. The US requires GMP for the production of dietary supplements, although proof of GMP is not required for getting a product on the market. China has GMP in place for the production of all drugs, including TCMs. However, GMP for TCMs includes requirements for cultivation of Chinese medicinal materials. Manufacturing licences are generally also required for sites that manufacture products. These licences are obtained by applying to the competent authority in each jurisdiction and demonstrating how the site complies with GMP. There are extensive requirements to meet relevant GMP standards, including personnel, site specifications, documentation and record keeping, premises and equipment, quality control, and self-inspection. GMP requirements vary between jurisdictions, with the most highly regarded being the 56 Participating Authorities (i.e. regulators) who are members of the international Pharmaceutical Inspection Co-operation Scheme (PIC/S). PIC/S develops and promotes harmonised GMP standards and guidance documents; trains competent authorities, in particular Inspectors; assesses (and reassesses) inspectorates and facilitates the co-operation and networking for competent authorities and international organisations.
Exporting requirements	For the EU, an Economic Operators Registration and Identification (EORI) number is required for all exported EU goods. Other export requirements depend on the type of product. For example, exporting natural ingredients for health products requires a business to follow the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). For products classified as medicines, businesses must hold a wholesale distribution authorisation (noting that those who already hold a manufacturing authorisation do not require a separate authorisation). In the UK, depending on the ingredients of the product, an exporter may need an Export Health Certificate to confirm the exported product meets the health requirements of the destination country. Products that do not contain ingredients of animal origin generally do not require this. A Certificate of Free Sale may also be required, depending on the importing country's requirements. For Traditional Herbal Medicines, export certificates are required, of which there are five specific types (e.g. Certificate of a pharmaceutical product (licensed)), depending on the requirements of the importing country. In Canada, export certificates are required to be signed by exporters of NHPs. International Trade Certificates – which confirm the regulatory status of an NHP or site licence in Canada – may also be required by importing countries. This is similar to a Certificate of Free

	Sale in the UK and is the responsibility of third parties such as Food, Health & Consumer Products of Canada and Cosmetics Alliance Canada. Exporters generally require a site licence unless NHPs are manufactured for the sole purpose of export. In the EU and the UK, licences are required to export NHPs classified as medicines, for example, the manufacturer/importer licence in the UK, which allows for manufacture and/or assembly of licensed medicines, includes the ability to export to a country outside the European Economic Area. Some countries such as Australia and the US do not require licensing or certification for export, but this can be provided if it is required by an importing country. We were unable to find specific information on export requirements in China but understand certain TCMs may be prohibited from export.
Importing requirements	Generally, importers must ensure that the product complies with all applicable legislation in their jurisdiction (e.g. in relation to labelling, claims, manufacturing and permitted ingredients). Similar to exporting above, other importing requirements depend on the ingredients of the product. China has strict importing rules, particularly for first-time importers of TCMs. These rules generally include assurance from the exporting country's relevant agency on compliance with GMP, safety systems, and Chinese customs undertaking inspection and quarantine requirements. There are also separate requirements for health foods, although there are exemptions if certain processes are followed (e.g. processes for cross-border e-commerce).
Exemption requirements	Jurisdictions have exemptions to specific requirements, depending on the product or intended recipient. For example, in Canada, UK and Australia, practitioners that compound NHPs for sale solely to an individual who requests it are exempt from manufacturing licence requirements. In the UK and Australia, exemptions on the basis of compounding must be for specific therapeutic application for a person, i.e., resulting from a consultation.
Specific groups of products	Homeopathy is often singled out as an NHP (or equivalent) that requires special consideration. For example, the EU, UK and Australia classify homeopathic preparations as medicinal products and have established a simplified registration procedure outside the otherwise prescribed rules for marketing authorisation for medicines. Canada also regulates homeopathic products as NHPs but has additional restrictions on labelling where health claims are backed by traditional references rather than scientific evidence.

1. Background and approach

1.1 Purpose

This report outlines and compares regulatory approaches to natural health products (NHPs) in Australia, Canada, the EU, UK, USA and China. It includes specific coverage on the regulation of homeopathy in Germany and Ayurveda in India.

1.2 Approach

This review was undertaken in a six-week period between November and December 2023.

The information in this report was extracted from both peer-reviewed and grey literature. Grey literature was generally official government websites, however, on occasion other types of websites were used (e.g. consulting or industry association websites). The search strategy is set out in Appendix A. The following topics were covered:

- legislative definitions
- definitional interface between NHPs and other types of products, e.g. medicines, foods
- the process for getting a product on the market
- permissible ingredients that can be used, including the application process for permitting new ingredients
- health benefit claims, including the application process for making new claims
- manufacturing requirements, including licensing
- exporting requirements
- importing requirements
- identification of any exemptions to requirements
- specific consideration of groups of products, e.g. essential oils.

In addition, we consulted with a distinguished Australian professor on TCM regulations in China and Australia to gain more information on the insights we have gleaned. This consultation took place in January.

1.3 Structure of this document

This report is set out as follows:

- The executive summary contains an overview of each topic, looking across the jurisdictions.
- The main body of the report sets out the above topics under each jurisdiction.
- Appendix B of the report contains summary tables across each topic.

1.4 Limitations

There are a number of limitations to this review that need to be taken into account when reading the report.

The process

- This was not a systematic review and is instead intended to provide an overview of the international regulatory features for NHPs. Further detail can be obtained through the hyperlinks throughout this document.
- Due to the rapid nature of this review (six weeks), it is possible that relevant studies and websites were missed in the analysis.
- While the majority of sources were peer-reviewed or government websites, some information was sourced from consulting or industry association websites, which are at risk of bias.

The report

- For some topics, it was not possible to find any official information. This is clearly noted in the body of the report.
- As this was a rapid review, it did not cover individual countries within the EU, or individual states/territories within Australia, Canada or the US. These individual laws may differ, for example, where EU law is not fully harmonised and Member States take their own approach.
- Many jurisdictions are members of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) which is a non-binding informal agreement between regulatory authorities aimed at harmonising inspection procedures by having comparable good manufacturing practice (GMP). Some jurisdictions are not PIC/S members (such as China), and some jurisdictions do not follow all the requirements of PIC/S (e.g. in Australia, the manufacture of listed medicines is exempt from some PIC/S requirements). It can therefore be difficult to compare GMP for NHPs across jurisdictions.
- Some official documents, particularly from China and India, have been translated into English using online machine-based methods such as Google Translate; thus, we cannot guarantee the accuracy of our translations. Where applicable, we have indicated that the documents available are in Chinese or in Hindi.
- Three webpages that we refer to (Thomson Reuters – Life Sciences Regulation in China, Thomson Reuters – Commercialisation of Healthcare in China and Thomson Reuters – Life Sciences Regulation in Germany), may require institutional access or a free trial to access.
- This research is a snapshot of regulations at a point in time; regulations may change, therefore the findings in this report may not be accurate in the future.

1.5 High-level overview of government organisations

The information set out in Blaze (2021) provides the first port of call regarding each jurisdiction. This has been reproduced and added to in the table below.

Table 1: High-level overview of government organisations

Jurisdiction	Government body	Notes
Australia	Therapeutic Goods Administration – https://www.tga.gov.au/topics/complementary-medicines	Details of existing complementary medicine regulations, policies and guidelines.
European Union	**Herbal medicinal products** EU Parliament and Council – https://health.ec.europa.eu/medicinal-products/herbal-medicinal-products_en	Details on the traditional herbal medicine directive re: Member States.
	Herbal medicinal products European Medicines Agency, Committee on Herbal Medicinal Products – https://www.ema.europa.eu/en/committees/committee-herbal-medicinal-products-hmpc	Prepares the Agency's opinions on herbal substances and preparations, recommended uses and safe conditions.
	Food supplements European Food Safety Authority – https://www.efsa.europa.eu/en	Provides details and links to regulation of foods and food supplements.
United Kingdom	**Traditional herbal medicines** Medicines and Healthcare products Regulatory Agency – https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency	Details on regulations of traditional herbal medicines.
	Food supplements Food Standards Agency – https://www.food.gov.uk/	Responsible for food safety and food hygiene in England, Wales and Northern Ireland.
Canada	Health Canada – https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription.html	Details on the existing NHP regulations, policies and guidelines.
US	Food and Drug Administration – https://www.fda.gov/food/dietary-supplements	Details on regulations, policies and guidelines dealing with dietary supplements.
China	National Medical Products Administration – http://english.nmpa.gov.cn/	Regulates the registration, and undertakes standards management of all drugs in China, including TCMs.
	National Administration of Traditional Chinese Medicine – http://www.natcm.gov.cn/ (in Chinese)	Responsible for the regulation and development of TCMs.

Jurisdiction	Government body	Notes
	State Administration for Market Regulation (SAMR) – https://www.samr.gov.cn/ (in Chinese)	Responsible for overall Chinese market supervision and management, including standards for raw material requirements and health function claims.
Germany (homeopathy only)	Federal Institute for Drugs and Medical Devices – https://www.bfarm.de/EN/Home/_node.html	Responsible for the authorisation of homeopathic products.
India (Ayurveda only)	The Food Safety and Standards Authority of India – https://www.fssai.gov.in/	Government direction, standards and regulation of health supplements and nutraceuticals.
	Ministry of Ayurveda, Yoga, Unani, Siddha and Homeopathy (AYUSH) – https://ayush.gov.in/	Policies, guidelines and regulations dealing with Indian traditional medicines.

2. Australia

2.1 Legislative definitions

Therapeutic Good – The Therapeutic Goods Regulations 1990 defines complementary medicine as "a therapeutic good consisting wholly or principally of one or more designated active ingredients, each of which has a clearly established identity and a traditional use."

Traditional use, for a designated active ingredient, is defined as the use of the designated active ingredient that:

> (a) is well documented, or otherwise established, according to the accumulated experience of many traditional health care practitioners over an extended period of time; and
>
> (b) accords with well-established procedures of preparation, application and dosage.

Designated active ingredient – for a complementary medicine, is defined as an active ingredient, or a kind of active ingredient, mentioned in Schedule 14 of the Therapeutic Goods Regulations 1990 and includes:

1. an amino acid
2. charcoal
3. a choline salt
4. an essential oil
5. plant or herbal material (or a synthetically produced substitute for material of that kind), including plant fibres, enzymes, algae, fungi, cellulose and derivatives of cellulose and chlorophyll
6. a homoeopathic preparation
7. a microorganism, whole or extracted, except a vaccine
8. a mineral including a mineral salt and a naturally occurring mineral
9. a mucopolysaccharide
10. non-human animal material (or a synthetically produced substitute for material of that kind) including dried material, bone and cartilage, fats and oils and other extracts or concentrates
11. a lipid, including an essential fatty acid or phospholipid
12. a substance produced by or obtained from bees, including royal jelly, bee pollen and propolis
13. a sugar, polysaccharide or carbohydrate
14. a vitamin or provitamin.

2.2 Definitional interface

2.2.1 Complementary medicines

The Therapeutic Goods Administration has developed regulatory guidelines for complementary medicines. Medicinal products containing ingredients such as herbs, vitamins and minerals, nutritional supplements, homeopathic medicines, and aromatherapy products are typically considered complementary medicines. Page 20 of the document outlines the different types of complementary medicines.

1. Herbal medicines

These are herbal substances or products that comprise primarily of herbal substances for therapeutic use. Herbal substances are typically defined as plants under the International Code of Botanical Nomenclature.

2. Traditional medicines

These are medicines that derive from traditional health practices, and includes TCMs, Ayurveda, Aboriginal and Torres Strait Islander medicines and Western herbal medicines. Traditional medicines are formally defined in Part 1(2) of the Therapeutic Goods Regulations 1990. The traditional practice must be well-documented over an extended period of time, and traditional medicines must be prepared in accordance with the well-established processes, ingredients and application. Around three generations or 75 years is considered to be an acceptable period of time to be well-documented.

3. Homeopathic medicines

Australian regulation considers homeopathic medicines to be low-risk. In some instances, homeopathic medicines may be exempt from having to be entered on the Australian Register of Therapeutic Goods (ARTG). Part 1(2) of the Therapeutic Goods Regulation 1990 formally defines homeopathic preparation in the context of producing medicines as:

(a) formulated for use on the principle that it is capable of producing in a healthy person symptoms similar to those which it is administered to alleviate; and
(b) prepared according to the practices of homoeopathic pharmacy using the methods of:
    a. serial dilution and succussion of a mother tincture in water, ethanol, aqueous ethanol or glycerol; or
    b. serial trituration in lactose.

Homeopathic dilutions can be measured in a number of ways which are expressed in the regulatory guidelines. The potency measure depends on the manufacturing standards described in homeopathic pharmacopoeias.

4. Essential oils

See section 2.10.2 for information on aromatherapy products.

5. Vitamins and minerals

Some vitamins and minerals may be subject to legal restrictions as scheduled medicines depending on factors such as dosage (for example, see Moses, 2021 and TGA). Some vitamins and minerals are also scheduled in the Poisons Standard and may be prohibited or may face restrictions on aspects such as pack size or container dimensions.

6. Nutritional substances

Some nutritional substances are regulated as foods, but others such as fish oil, shark cartilage and krill oil are regulated as complementary medicines. Sports supplements making a claim and in medicinal dosage form (such as tablets or pills) are also regulated as complementary medicines (for example, see TGA). Refer to section 2.2.2 of this report to distinguish between products at the food-therapeutic good interface.

2.2.2 Food

There is the potential for products to be at the food-therapeutic good interface. The TGA has released an interactive guidance tool to help classify products at the interface, as well as this diagram. Generally speaking, the following factors would indicate that the product is likely to be a food:

- It is orally ingested.
- It is not declared a therapeutic good under section 7 of the Therapeutic Goods Act (the latest declared Therapeutic Goods order can be found here).
- It is included in a section 7AA declaration of the Therapeutic Goods Act.
- If there is a standard related to the product in the Food Standards Code.
- If the primary purpose of the product is not traditionally a therapeutic use.

Note that this only applies to goods that could reasonably be at the food-therapeutic good interface, and does not extend to products that could reasonably be cosmetic in nature. We recommend looking at the diagram of products at the interface in its entirety to understand what conditions must exactly be met to classify a product as a therapeutic good or food.

Food/dietary supplements

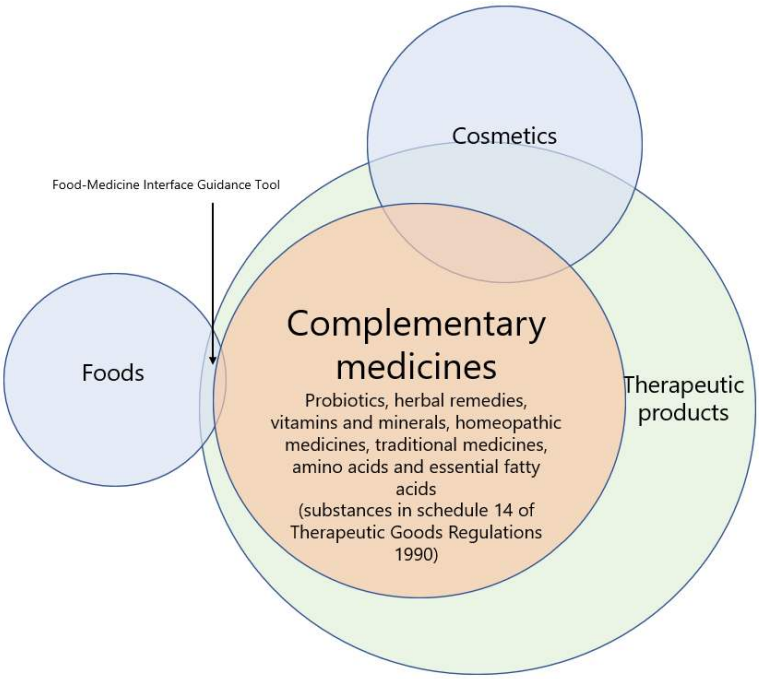
'Dietary supplements' and 'food-type supplements' are not concepts in Australian legislation. Dietary supplements are a type of complementary medicine (e.g. vitamin C) while food supplements are not permitted under the Food Standards Code (e.g. foods with higher levels of certain vitamins and minerals than in the Food Standards Code, and/or containing ingredients not permitted in the Food Standards Code).

Cosmetics

Cosmetics are not regulated by the TGA, but there may be instances of cosmetics being at the therapeutic good interface. Classification depends on ingredients, route of administration and whether indicative claims are made either on the label or in advertising. For instance, Part 2 of Schedule 1 of the Declared Therapeutic Goods Order 2019 indicates that goods that are labelled for cosmetic purposes but administered orally are therapeutic goods.

Figure 1 below shows our interpretation of products at the complementary medicine interface.

Figure 1: Products at the complementary medicine interface in Australia



2.3 Getting a product on the market

Therapeutic goods where health indications are made must be entered (either 'listed' or 'registered') on the Australian Register of Therapeutic Goods (ARTG) before they can be marketed, manufactured, imported or exported (TGA). For a therapeutic good to be supplied in the Australian market, applicants must pay an application fee and an annual charge to maintain their product on the ARTG according to the schedule of fees and charges. There is a risk-based approach to regulation. Complementary medicines fall into one of three types:

1. Listed medicines

Most complementary medicines are listed, along with some over-the-counter medicines. Listing complementary medicines is a relatively basic administrative process compared to registered medicines, where the pre-market approval process is to help ensure that submitted documentation is in accordance with relevant standards and rules. Any post-market evaluation is done through a review (either random or targeted) by the TGA (see TGA – listed complementary medicines). This is because complementary medicines are considered to be 'low-risk' medicines. Complementary medicines that are listed on the ARTG must adhere to the following requirements:

- They should only contain low-risk ingredients, such as active, excipient and homeopathic preparation ingredients. These are specified in the Permissible Ingredients Determination.
- They should only use indications permitted for use in listed medicines (see Permissible Indications Determination). The TGA has produced a guidance document for permitted indications for listed medicines.
- They must not be a prohibited import under Division 1 of the Customs Act 1901.

- They must not be required to be sterile.
- They must comply with all legislative requirements related to quality, safety and efficacy under the Therapeutic Goods Act 1989 and the Therapeutic Goods Regulations 1990.

Complementary medicines can be listed on the ARTG if they follow the requirements of Section 26A(2)(a)-(k) of the Therapeutic Goods Act 1989. This generally ensures the product is safe, contains only permissible ingredients, and the presentation of the medicine is acceptable (i.e. name, indications, directions, warnings and disclaimers, packaging dosage, logos and symbols and pictures on the label).

Unacceptable presentation is outlined in Section 3(5) of the Therapeutic Goods Act and Section 3(A) of the Therapeutic Goods Regulations.

Additional requirements for complementary medicines to be listed on the ARTG include:

- following applicable standards for therapeutic goods
- following GMP in the manufacturing process
- following advertising codes
- possessing evidence to substantiate indications. Evidence guidelines can be found here
- keeping adequate records (see page 53 of the regulatory guidelines for complementary medicines)
- proper quality control is undertaken, including for testing and manufacturing (see page 55 of Regulatory Guidelines for Complementary Medicines); a certificate of analysis for the finished product is obtained.

The application process of listing a complementary medicine on the ARTG is online. The necessary tools for lodging, modifying or maintaining an application can be found on the TGA Business Services Site. Once the applicant gains access to the application portal, they can enter medicine details. If the application passes validation in the TGA Business Services application portal, a statutory declaration can be signed by the applicant and the application can be submitted. The applicant then pays the necessary fees outlined in the schedule of fees and charges and the application is processed by the TGA. If approved, the application is recorded on the ARTG and the medicine is assigned an AUST L number. A 'certificate of medicine listing' and conditions for listing are then generated for the medicine. The applicant can then market the product subject to the conditions for listing.

2. Assessed listed medicines

Assessed listed medicines are similar to listed medicines but are able to make intermediate indications and can include a 'TGA assessed claim' on labels and advertising. They therefore require pre-market evaluation by the TGA (see TGA).

3. Registered complementary medicines

These are assessed by the TGA for quality, safety, and efficacy. Some complementary medicines may be registered, along with most prescription medicines and over-the-counter medicines (see TGA). Registered complementary medicines are fully evaluated and can include a TGA assessed claim. An application and submission user guide can be found here. Registered medicines are considered higher risk than listed medicines. Complementary medicines should be registered on the ARTG if:

- they do not solely comprise ingredients permitted for use in listed medicines, specified in the Permissible Ingredients Determination
- they contain an ingredient or component that is subject to the conditions of a Schedule (except Schedules 4, 8 and 9) or Appendix to the Poisons Standard
- they are required to be sterile
- they have indications not included on the indications permitted for use in listed medicines (see this Guidance Document).

The application process for registering a complementary medicine to the ARTG is slightly more rigorous than that of listed medicines. The process is outlined from page 101 of the regulatory guidelines for complementary medicines:

- Verification of a complementary medicine and securing access to TGA Business services.
- Verifying ingredients and evaluation of the medicine either through the over-the-counter pathway or prescription pathway. A guideline for pathways to evaluate medicine can be found here. A proprietary ID number for each ingredient will have to be included to complete an application for registration. Proprietary ID numbers can be found here. If the proprietary ingredients are new, a notification of a proprietary ingredient form must be submitted to obtain an ID number.
- Ensuring valid GMP evidence through either a GMP licence (if in Australia) or GMP clearance (if outside Australia) issued by the TGA (see page 105 of the regulatory guidelines for complementary medicines).
- Determining application category of risk. There are five categories where the applicant can register, with category 1 being the lowest risk, and 5 being the highest. Factors to consider when determining an application category include presentation, history of use, likeness to other products and indications (detailed specifications of fulfilling conditions of the following categories can be found from page 150 of the regulatory guidelines for complementary medicines).
    - Category 1 medicines typically have a close resemblance to an 'originator' medicine, and thus have reduced requirements for supporting data.
    - Category 2 medicines comply with a TGA complementary medicine monograph.
    - Category 3 medicines are where previous evaluations by either the TGA or relevant authority have been able to substantiate safety and efficacy.
    - Category 4 medicines are where quality, safety and efficacy have been established.
    - Category 5 is for new complementary medicines registered on the ARTG that have had no prior evaluations for quality, safety, and efficacy.
- Submitting relevant documentation in accordance with requirements, including:
    - Common Technical Document (CTD) module 1
    - General Dossier Requirements
    - Cover letter (see page 155 of the regulatory guidelines)
    - CTDs for the relevant application category:
        - Module 2 for quality, safety and efficacy
        - Module 3 is quality data for Categories 3, 4 and 5
        - Module 4 is safety for Categories 4 (if not previously demonstrated) and 5
        - Module 5 is efficacy for Categories 4 (if not previously demonstrated) and 5

    - New registration or Changes to existing ARTG data requirements matrix.
- If applicable, requesting an exemption for a restricted representation on the label.
- The TGA recommends a pre-submission meeting to ensure a high-quality submission of a new registered complementary medicine.
- Submitting the application and paying relevant fees. The application is then screened and evaluated and the TGA may request additional information. If accepted, the medicine will be registered on the ARTG and a certificate will be issued. An AUST R number is provided for the medicine.

2.3.1 Format of evidence that can be submitted

Potential market authorisation holders can provide two types of evidence to substantiate the efficacy of listed medicines (as per the listed medicines evidence guidelines):

1. Evidence of traditional use

Sources of evidence of traditional use can include, but are not limited to:

- materia medica
- official pharmacopoeias
- monographs
- publications from various international regulatory authorities
- texts that are relevant to the traditional paradigm
- well-recognised evidence-based reference texts.

2. Scientific evidence

Sources of scientific evidence can include, but are not limited to:

- a systematic review
- a randomised controlled trial (RCT)
- a pseudo-randomised controlled trial (alternate allocation or some other method)
- a comparative study with concurrent controls
- a comparative study without concurrent controls
- case series with either post-test or pre-test/post-test outcomes
- a review article.

Applicants can also generate their own scientific evidence by, for example, conducting their own clinical trial.

2.4 Permissible ingredients

All listed medicines must only contain ingredients included in the Therapeutic Goods (Permissible Ingredients) Determination (no. 4) 2023. This Determination specifies those ingredients that may be contained in a medicine listed in the Australian Register of Therapeutic Goods, and is made under subsection 26BB(1) of the Therapeutic Goods Act 1989.

Schedule 1 of the Determination lists the specified permissible ingredients and specific requirements that apply to the ingredients when contained in a medicine (e.g. maximum concentrations, restricted uses, requirements for warning statements on labels). The ingredients have specified purposes in Schedule 1 that they can be used for, namely as an active ingredient, an excipient, or a homeopathic preparation ingredient.

If the substance is not included in the Determination, or someone wants to vary the restrictions for an existing substance, they must make an application to have that substance evaluated under section 26BD of the Therapeutic Goods Act 1989.

The Therapeutic Goods (Permissible Ingredients – Information that Must Accompany Application for Variation) Determination 2023 specifies how applications for substances to vary the Permissible Ingredients Determination must be made. This requires applicants to follow the mandatory requirements for an application to vary the Permissible Ingredients Determination, which includes information on the safety and quality of the proposed substance.

Registered complementary medicines may not comprise solely of ingredients in the Therapeutic Goods (Permissible Ingredients) Determination (no. 4) 2023, but can also be subject to the conditions of ingredients or components of ingredients in the Schedules or Appendices of the Poisons Standard except for Schedules 4, 8 and 9.

2.5 Health benefit claims

2.5.1 Listed complementary medicines

The TGA has released a guidance document for permitted indications for listed medicines. These requirements apply to all medicines under section 26A of the Therapeutic Goods Act 1989 except for those that are listed for export only and medicine kits. The Permissible Indications Determination for Therapeutic Goods outlines what indications can be made by medicines in Australia. This is a list of indications and the evidential/other requirements that must be met in order to make health claims. The exact wording of the claim can be altered, but must not change the underlying meaning behind the permissible indication.

According to TGA, medicines can only make low risk indications related to:

- health maintenance
- health enhancement
- prevention of a non-serious vitamin or mineral dietary deficiency. 'Serious' is defined in Section 28 of the Therapeutic Goods Advertising Code 2015
- certain non-serious, self-limiting diseases, ailments, defects, or injuries.

2.5.2 Registered complementary medicines

Registered complementary medicines can include a TGA assessed claim. These can be indications about more serious conditions (see TGA – Registered complementary medicines). 'Serious' is defined in Section 28 of the Therapeutic Goods Advertising Code 2021:

For the purposes of section 42DD of the Act, a form of a disease, condition, ailment or defect is a serious form if:

a) it is medically accepted that the form requires diagnosis or treatment or supervision by a health practitioner who is suitably qualified, except where the form has been medically diagnosed and medically accepted as being suitable for self-treatment and management; or
b) there is a diagnostic (including screening), preventative, monitoring, susceptibility or pre-disposition test available for the form (including a self-administered test), which requires medical interpretation or follow-up

but does not include:

c) pregnancy, other than pregnancy with a medical, obstetric, or surgical complication.

2.5.3 Foods and food supplements

All food in Australia (and New Zealand) must comply with Foods Standards Code – Standard 1.2.7 in relation to health claims. Claims cannot be therapeutic in nature, i.e. refer to the prevention, cure, or alleviation of a condition, nor can food products compare themselves to products that are therapeutic in nature.

Part 3 Division 2 of Standard 1.2.7 outlines the requirements for food products to make health claims. Generally, foods cannot make health claims unless they meet the Nutrient Profiling Scoring Calculator (NPSC), and the health claim is a high level or general level health claim. The conditions for making high level and general level health claims are outlined in Schedules 2 and 3 of the Standard 1.2.7 respectively.

Nutrition content claims or health claims cannot be made for kava, alcoholic foods (>1.15 per cent alcohol by volume),[2] or an infant formula product (see Part 2(3) of Standard 1.2.7).

2.5.4 Advertising

All therapeutic goods must follow the Advertising Code, including general requirements on accuracy, safe and proper use, consistency with current public health campaigns, clinical representations and prohibition on advertising to children. Depending on the nature of the product and the advertisement, the advertisements of the therapeutic good must also adhere to mandatory statements outlined in Division 2 and 3 of the Advertising Code, such as "ASK YOUR PHARMACIST ABOUT THIS PRODUCT" if the therapeutic good is only available from a pharmacist.

[2] For alcoholic foods, nutrition content claims can be made about the presence or absence of energy content, carbohydrate content or gluten content. If not a beverage, claims may also be made for salt or sodium content.

2.6 Manufacturing requirements

Part 3-3 of the Therapeutic Goods Act 1989 sets out the manufacturing requirements for therapeutic goods, including the manufacturing principles that must be followed. Under s36 of the Act, 'good manufacturing principles' may be set by the Minister as legislative instruments. The current instrument is the Therapeutic Goods (Manufacturing Principles) Determination 2020.

This Determination currently states that the manufacture of therapeutic goods must comply with applicable procedures and requirements in the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to GMP. This Guide covers both the manufacture of medicinal products and the manufacture of active substances as starting materials. The PIC/S Guide to GMP has legal force in Australia, except for Annexes 4, 5 and 14 which are not adopted by Australia and relate to veterinary products and products derived from human blood or plasma.[3] The aspects of manufacturing that are covered by PIC/S Guide to GMP include:

- pharmaceutical quality system
- personnel
- premises and equipment
- documentation
- production
- quality control
- outsourced activities
- complaints and product recall
- self-inspection.

Where the PIC/S Guide provides a procedure or requirement that 'should' be followed, the manufacturer must follow that procedure or requirement unless they demonstrate to a relevant officer that failure to adopt that procedure or requirement will not increase the risk of harm/injury or the risk of compliance failure for applicable standards/conditions. The same approach applies if a manufacturer adopts an alternative to the procedure or requirement (Schedule 1, Part 1 of the Determination).

Appropriate records should be kept for at least 12 months after the expiry date of the goods for which they relate to, or if expiry dates are not used, at least six years after the goods have been manufactured (TGA).

2.6.1 Applying for a licence to manufacture

All therapeutic products with health indications must be registered or listed on the ARTG to be able to be legally manufactured in Australia. Australian manufacturers of therapeutic foods must also apply for a manufacturing licence for a particular site. The TGA has produced a step-by-step guide for site licensing and overseas GMP certification.

After satisfying the requirements of being entered on the ARTG discussed in section 2.3, the applicant must become a TGA client through TGA Business Services and compile relevant documents, including: contact information; details of personnel in charge of quality control, production and supply; and

[3] Annex 4: Manufacture of veterinary medicinal products other than immunologicals; Annex 5: Manufacture of immunological veterinary medical products; Annex 14: Manufacture of products derived from human blood or human plasma.

information on the therapeutic products being manufactured such as manufacturing type, sterility, dosage, product code, and manufacturing steps. If there is a secondary site involved in the supply or production process, the same information for this site must be provided.

New manufacturing licences must also make a statutory declaration on a certificate for paragraph 38(1)(g) of the Therapeutic Goods Act 1989. This is generally to verify that no one involved in the manufacturing process has had specific convictions or faced financial penalties in recent history.

An application can then be submitted with the relevant documentation, and will be subject to an inspection by the TGA. If necessary, deficiencies will be outlined in a post-inspection letter for the potential manufacturer to address and respond to. A subsequent inspection will be undertaken and a licence will be issued if all requirements have been fulfilled and fees have been paid.

Inspections

Licenced manufacturers are subject to regular inspections for compliance with GMP. The frequency of inspection is determined by a risk-based approach by the TGA. This is highlighted by the inspection frequency matrices.

2.7 Exporting requirements

The TGA have produced a guidance document on the export of medicines which covers prescription medicines, over-the-counter medicines and complementary medicines. As discussed in section 2.3, the therapeutic product must be entered on the ARTG defined in Chapter 2 of the Therapeutic Products Act 1989 before it can be exported for commercial use.

Australian manufacturers are also able to produce export-only medicines which cannot be sold in Australia, including in Australian duty-free outlets (see page 7 of the export guidance document). The Therapeutic Goods Order No. 70C sets out the standards for export-only medicine, which generally ensure that it follows the regulatory requirements of the importing country, regardless of whether or not it is regulated as a medicine.

Medicines for export must follow the market authorisation and manufacturing requirements outlined in sections 2.3 and 2.6 respectively. There are a few exemptions for export-only medicines:

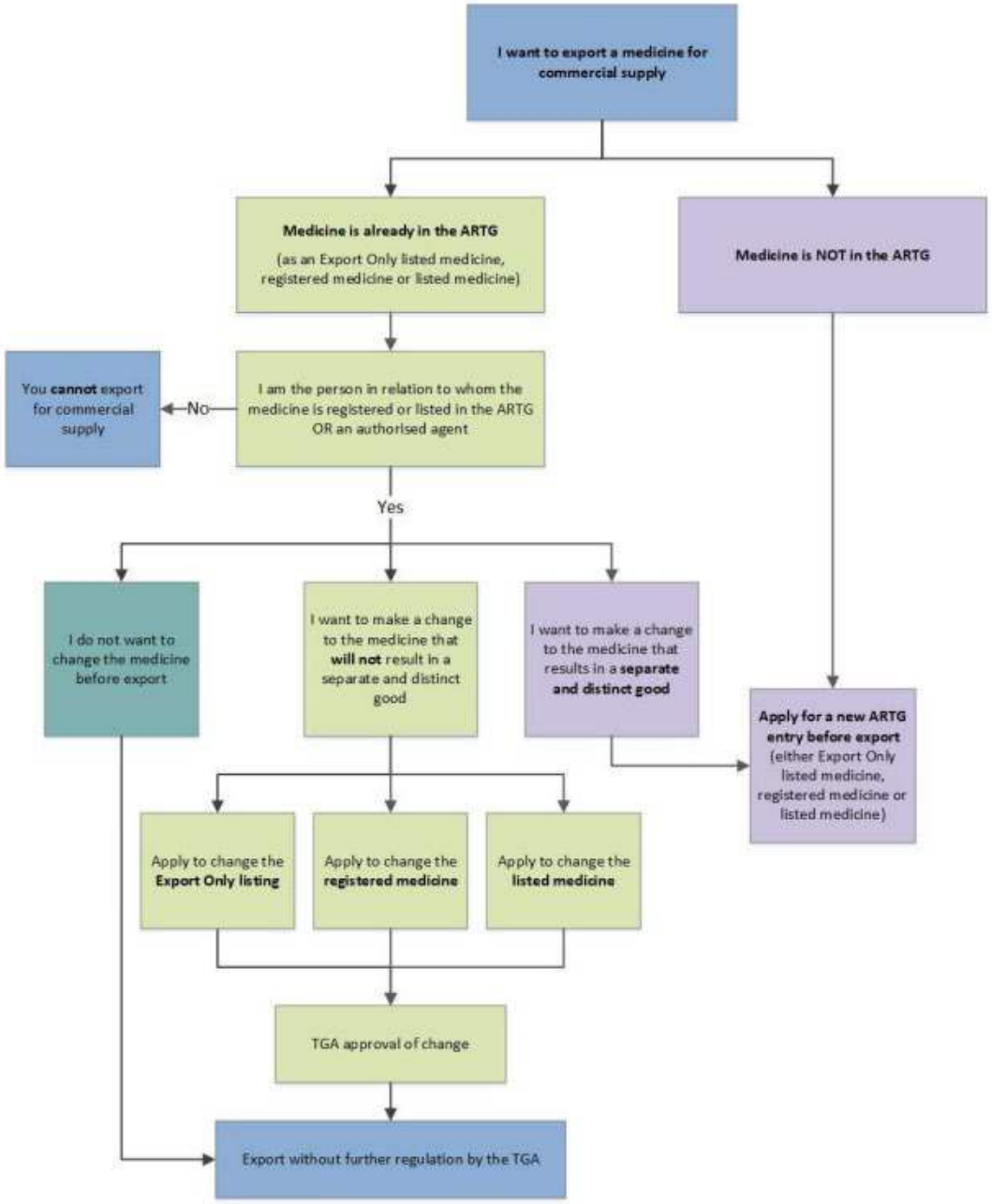
- Export-only medicines do not need to include the AUST L or AUST R number on their label.
- Export-only medicines do not need to comply with labelling standards for medicines in Australia outlined in Therapeutic Goods Orders No. 91 and 92.

However, export-only medicines that are novel in an importing country may require confirmation from the importing country of its willingness to import goods, which may also mean additional evidence may be required from the importing country's relevant authority in order to list the product on the ARTG.

Export licences are not required, but certification may be required from importing countries, such as export certificates or GMP certificates. The Australian Government has guidance in place for relevant certificates to meet the requirements of importing countries.

Figure 2 below outlines the process for exporting medicines from Australia.

Figure 2: Overview of exporting medicines for commercial supply



Source: TGA, retrieved from tga.gov.au

2.8 Importing requirements

If the manufacturing site of therapeutic products is overseas, the site must receive GMP clearance, which can be obtained by a sponsor based in Australia. The TGA has produced a GMP Clearance Guidance document. GMP clearance serves as a mechanism to verify that overseas manufacturers of therapeutic products comply with the principles of GMP products that are in supply within the Australian market, i.e. to support safety, quality, efficacy and timely supply of therapeutic goods. A GMP clearance can be obtained through one of three pathways.

1. A Mutual Recognition Agreement (MRA) desktop assessment

This allows manufacturers to receive GMP clearance if the overseas manufacturer's country has an MRA with Australia and it has been inspected by the relevant regulatory authority in their country. Australia has MRAs with the EU, UK, Canada, Singapore, and New Zealand.

2. A Compliance Verification (CV) desktop assessment

This pathway can be used if the manufacturer has been inspected by their regulatory authority and has an agreement with the TGA other than an MRA. For instance, the TGA has a cooperative agreement with the United States Food and Drugs Administration that covers sunscreens (see cooperative agreements and other arrangements here, noting that sunscreens are classified as a complementary medicine in Australia).

3. An inspection by the TGA

If neither MRA nor CV desktop assessments are viable, the sponsor can request a TGA inspection and pay relevant fees – the sponsor or market authorisation holder will receive GMP clearance if successful.

The table below has been recreated from TGA's GMP Clearance Guidance and, for each pathway, shows whether fees are relevant or not.

Table 2: Overview of fees for GMP Clearance applications (Note: LoA – Letter of Access)

Application type	Evidence provided	Application processing fee	Obtaining evidence fee	Compliance verification fee
MRA	MRA documentation	Yes	When requested or required	Not applicable
	LoA to Evidence			
	LoA to Clearance			
CV Sterile/Non-Sterile API	CV documentation	Yes	When requested or required	Yes
	LoA to Evidence			
	LoA to Clearance	Yes	Not applicable	Not applicable
CV Sterile/Non-Sterile finished product	CV documentation	Yes	When requested or required	Yes
	LoA to Evidence			
	LoA to Clearance	Yes	Not applicable	Yes
CV Contract testing laboratory or steriliser	CV documentation	Yes	When requested or required	Yes
	LoA to Evidence			
	LoA to Clearance	Yes	Not applicable	Yes
TGA Certificate	CV documentation	Yes	Not applicable	Not applicable

Application type	Evidence provided	Application processing fee	Obtaining evidence fee	Compliance verification fee
	LoA to Evidence			
	LoA to Clearance			

2.9 Exemption requirements

Schedules 5 and 5a of the Therapeutic Goods Regulations 1990 sets out therapeutic products which are exempt from Parts 3-2 and 3-2A of the Therapeutic Goods Act, i.e. registration or listing, and biologicals. Schedule 5a is a list of therapeutic goods that are exempt subject to conditions. For example:

- Item 8 of Schedule 5 of the Therapeutic Goods Regulations 1990 sets out homoeopathic preparations exempt from having to be placed on the ARTG. This generally includes homeopathic preparations more dilute than a 1,000-fold dilution of a mother tincture and that are not required to be sterile, and do not also include ingredients of human or animal origin generally derived from cattle, sheep, goats, or mule deer.

Schedule 7 of the Therapeutic Goods Regulations 1990 contains a list of goods exempt from the operation of Part 3-3 of the Therapeutic Goods Act 1989 (manufacturing requirements – licensing) unless they are supplied as "pharmaceutical benefits". This schedule contains substances such as:

- ingredients, except water, used in the manufacture of therapeutic goods where the ingredients:

  (a) do not have a therapeutic action; or
  (b) are herbs, bulk hamamelis water or oils extracted from herbs, the sole therapeutic use of which is as starting materials for use by a licensed manufacturer

- homeopathic preparations more dilute than a one-thousand-fold dilution of a mother tincture and that are not required to be sterile.

2.10 Specific groups of products

2.10.1 Homeopathic products

As discussed in section 2.2.1, homeopathic medicines are considered low-risk, and are not required to hold a GMP licence if they are not required to be sterile, and their preparations are more dilute than a 1,000-fold dilution of the mother tincture (4X or above).

2.10.2 Aromatherapy

Essential oils are regulated by the TGA only if a therapeutic claim is made. If the product makes a cosmetic claim, then it is regulated by the National Industrial Chemicals Notification and Assessment Scheme (NICNAS).

If marketing aromatherapy products as therapeutic goods, applicants must follow all marketing authorisation and manufacturing requirements outlined in this chapter.

3. European Union

3.1 Legislative definitions

Food supplements, according to article 2 of the Directive 2002/46/EC – means:

> foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities.

Herbal Medicines, according to Directive 2004/24 – means:

> Herbal medicinal product: Any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations.
>
> Herbal substances: All mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety, and author).
>
> Herbal preparations: Preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

3.1.1 A note on EU law

There are two types of legal instruments mentioned in this section (Petkova-Gueorguieva et al., 2019):

- Regulations, which establish binding, general application in all Member States.
- Directives, which do not generally have a binding effect, i.e. it regulates the result, but leaves to the national authorities to choose the form and methods for its achievement. This results in exporters finding, for example, that their product has been classified as a food supplement in one EU Member State but as a regular food in a second Member State, or even as a medicinal product in a third one (USDA Foreign Agricultural Service).

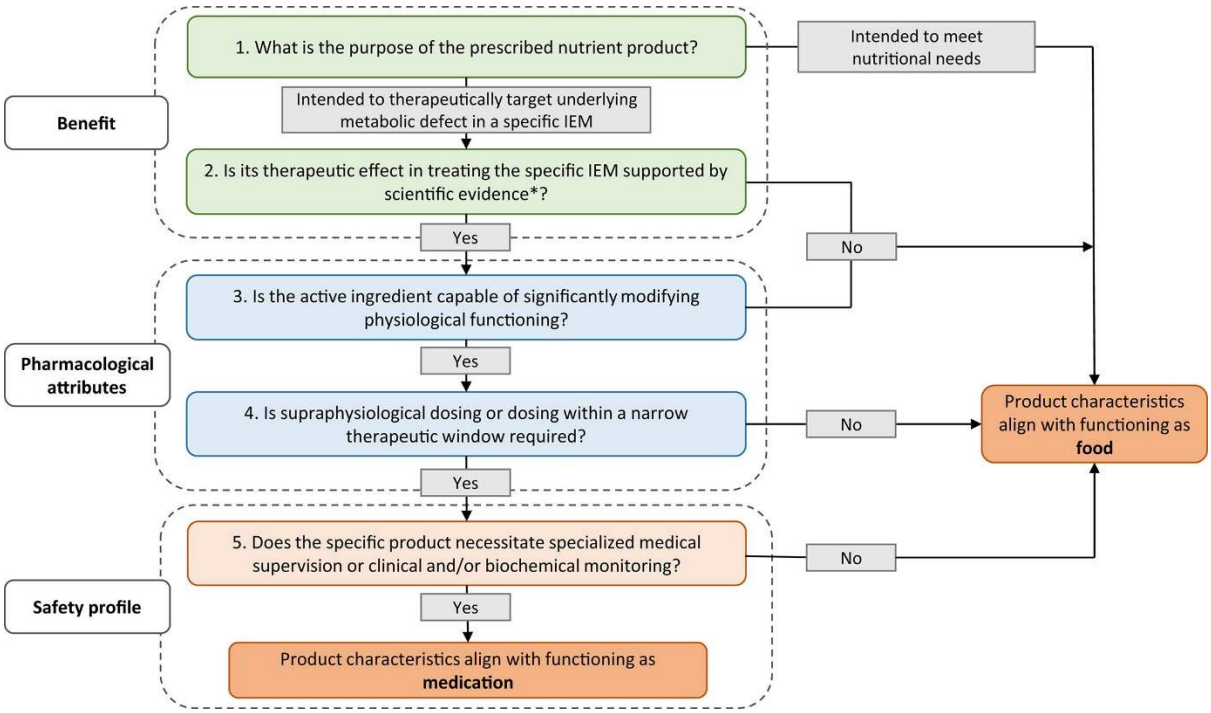
3.2 Definitional interface

Depending on the product, it is most likely to be classified as either a food or a medicine. The legal frameworks of food and pharmaceuticals are mutually exclusive. The split is based on the function the product has, or how it is presented to a consumer (Lenssen et al., 2019).

When a product contains a dose that will give rise to a pharmacological effect, it is considered a pharmaceutical (i.e. medicine by function). When a product is claimed to have a pharmacological effect on the label (compared with a physiological effect), it is also considered a pharmaceutical (i.e. medicine by presentation) (Lenssen et al., 2019).

Stolwijk et al., (2023) sets out a proposed flowchart for determining whether a product is a food or medicine:

Figure 3: Flowchart to determine if a product is a food or medicine



Source: Stolwijk et al., 2023

The EU published guidance in 2020 on borderline cosmetic products, and guidance in 2015 on the interface between cosmetics and medicines. The definition of cosmetic is based on the target site of application and the intended function, as set out in Regulation 1223/2009. Like the food/medicine interface described above, if a cosmetic claims to treat or prevent disease (medicine by presentation) or exerts a pharmacological effect (medicine by function), then it will be classified as a medicine. The interface guidance notes that decisions are made on a case-by-case basis:

> The Court has repeatedly held that "the national authorities, acting under the supervision of the courts, must proceed on a case-by-case basis, taking account of all the characteristics of the product, in particular its composition, its pharmacological properties, to the extent to which they can be established in the present state of scientific knowledge, the manner in which it is used, the extent of its distribution, its familiarity to consumers and the risks which its use may entail."

3.3 Getting a product on the market

The applicable legislation varies according to the type of product being put on the market. Supplements are generally considered food in the EU for regulatory purposes. The below table is reproduced from Vettorazzi et al., (2020) and sets out the applicable EU Regulations.

Table 3: Applicable EU Regulations relating to food-related products

Title	Topic	Comments
Regulation 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety.	General	Lays down the general framework of food law and safety; and establishes the European Food Safety Authority (EFSA).
Directive 2002/46 of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements.	Food supplements	Focused on vitamins and minerals (only vitamins and minerals listed in Annex I, in the forms listed in Annex II, may be used for the manufacture of food supplements). Bioactive compounds are marketed in a pre-packaged form (pills, capsules, etc). This regulation explicitly excludes any bioactive compound aimed to be used as a medicinal product.
Regulation 2015/2283 of the European Parliament and the council of 25 November 2015 on novel foods, amending Regulation 1169/2011 of the European Parliament and of the Council and repealing Regulation 258/97 of the European Parliament and of the Council and Commission Regulation 1852/2001.	Novel foods	Food not used for human consumption to a significant degree at EU level before 15 May 1997. This regulation does not affect food enzymes, additives and flavourings, GMO, intended to be used in the production of foodstuffs or food ingredients.
Commission Implementing Regulation 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation 2015/2283 of the European Parliament and of the Council on novel foods.	Novel foods	Novel foods authorised to be placed on the market within the Union as referred in Regulation 2015/2283. Contains Table 1, with the conditions of use (including maximum levels), labelling and other requirements and Table 2 containing the specifications of the authorised novel foods.

3.3.1 Food supplements

Directive 2002/46 regulates food supplements and establishes harmonised lists of vitamins and minerals that can be used in the manufacture of food supplements, and sets out labelling requirements. The use of substances other than vitamins and minerals in the manufacture of food supplements may be governed by other EU legislation or national rules. The addition of nutrients or other substances to fortify a food does not fall within the definition of food supplement and is addressed by Regulation 1925/2006 (Martini et al., 2019).

Some EU Member States require notification for food supplements before being placed on the market, for monitoring purposes (McDaid et al., 2020). Suppliers provide notification to the Member State competent authority, in accordance with Article 10 of Directive 2002/46, when placing their product on the market (European Commission).

Novel foods

Products, including food supplements, that are not listed in the Directive above, need to go through a safety evaluation under Regulation 2015/2283 – Novel foods. According to the European Food Safety Authority (EFSA), any food that was not consumed "significantly" prior to May 1997 is considered to be a novel food. The category covers new foods, food from new sources, new substances used in food as well as new ways and technologies for producing food. For example, oil rich in omega-3 fatty acids from krill as a new source of food, edible insects, or plant sterols as a new substance or nanotechnology as a new way of producing food (European Food Safety Authority, EFSA).

This document sets out the application procedure. EFSA assesses applications by performing risk assessments on the safety of the substance. Dossiers need to contain data on the compositional, nutritional, toxicological and allergenic properties of the novel food as well as information on respective production processes, and the proposed uses and use levels (EFSA). EFSA has provided guidance in 2016 for applicants on how to prepare and present an application for authorisation of a novel food. Requirements include:

- the description of the novel food
- production process
- compositional data
- specification
- proposed uses and use levels
- anticipated intake
- the history of use of the novel food and/or its source
- absorption
- distribution
- metabolism
- excretion
- nutritional information
- toxicological information
- allergenicity.

If a manufacturer/importer can show that their product is not a novel food, as defined under Regulation 2015/2283, they do not have to undergo a safety evaluation. For example, producers of mussel oil could argue that (MuMiPro Presentation):

- the fat and proteins of mussels have been widely consumed prior to 1997, and
- the product is not produced using new technologies and production processes (post-1997), and
- comparable products (fish oil) have already been placed on the market.

3.3.2 Traditional foods (outside the EU)

If the product is a 'traditional food' from outside the EU (and is not currently listed in Directive 2002/46), there is a special procedure for safety assessment under Regulation 2015/2283, which is based on a history of safe food use for a period of at least 25 years in at least one country outside the EU and applies only to products deriving from primary production (EFSA).

The authorisation process is centralised, and is a faster and more simplified process than standard novel foods (Martini et al., 2019, p. 18):

1. Applicants need to provide data related to product composition, country of origin, specific conditions of use, and labelling.
2. The European Commission assesses the validity and completeness of the application and then forwards the notification to Member States and the EFSA. This is called the 'notification' step.
3. If no duly reasoned safety objections are provided, the Commission submits a draft implementing Act to the Standing Committee on Plants, Animals, Food and Feed, authorising the placing of the product on the market.
4. If one or more Member States or EFSA highlight safety objections, the product cannot be authorised and the applicant must apply to the Commission following the requirements of Article 16, as set out in section 3.3.1 of this report.

This document sets out the notification-application procedure for a traditional food.

3.3.3 Traditional herbal medicinal products

Under Directive 2001/83, relating to medicinal products for human use, herbal medicinal products (HMPs) can be classified into three categories, and therefore three regulatory pathways for registration/authorisation:

1. New HMPs without any human-use experience.
2. Well-established use HMPs with recognised efficacy based on extensive (10 years) clinical evidence.
3. Traditional use HMPs with documented medicinal use for at least 30 years including more than 15 years within the EU.

The below table sets out the high-level requirements for the different categories (Qu et al., 2022).

Table 4: Authorisation requirements for different categories of herbal medicinal products

Categories	Market authorization for new HMPs (2001/83/EC)	Market authorization for WEU HMPs (2001/83/EC)	Simplified registration for TU HMPs (2004/24 /EC)
Indications	No specific limitations	No specific limitations	Limited to self-medication
Medicinal usage	No specific limitations	At least 10 years medicinal use for demonstration recognized efficacy	30 years medicinal use including at least 15 years in EU for demonstration plausible efficacy
Dosage form	No specific limitations	No specific limitations	Limit to oral, external use and inhalation
Safety and efficacy	Nonclinical tests and clinical trials	Bibliographic data and pharmacovigilance Additional tests	Bibliographic documents and pharmacovigilance Additional safety tests if needed
Quality control	GACP, GMP and CMC	GACP, GMP and CMC	GACP, GMP and CMC

Abbreviations: CMC, Chemical Manufacturing and Control ; EU, European Union; GACP, good agricultural and collection practices; GMP, good manufacturing; practices; HMP, herbal medicinal product; TU, traditional use; WEU, well-established use.

Source: Qu et al., 2022

Directive 2004/24 amending Directive 2001/83 sets out the requirements for traditional herbal medicinal products. Section 16(a)(1) of the Directive sets out the requirements for a product to be classified as a traditional herbal medicinal product, and therefore qualify for a simplified registration procedure.

A simplified registration procedure (hereinafter 'traditional-use registration') is established for herbal medicinal products which fulfil all of the following criteria:

a) They have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment.
b) They are exclusively for administration in accordance with a specified strength and posology.
c) They are an oral, external and/or inhalation preparation.
d) The period of traditional use as laid down in Article 16c(1)(c)[4] has elapsed.
e) The data on the traditional use of the medicinal product is sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience.

Not all herbal medicines are traditional herbal medicinal products. If the herbal medicine does not meet one of the conditions listed above in Article 16a(1) (e.g. the product is intended to treat

[4] Bibliographical or expert evidence to the effect that the medicinal product in question, or a corresponding product has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years within the community.

something more than a minor condition without medical supervision), then the product will be subject to the usual registration and assessment process for medicines (McDaid et al., 2020). Likewise, if Article 16(a)(1) conditions are not met, and the product does not fall under a 'well-established use' under Directive 2001/83.

The European Pharmacopoeia is the single reference point for the quality control of medicines. It consists of a collection of monographs, describing both the individual and general quality standards for ingredients, dosage forms, and methods of analysis for medicines. All producers of medicines and/or substances for pharmaceutical use must apply these quality standards in order to market their products in the signatory states of the Convention. Directive 2001/83 on medicines for human use maintains the mandatory use of European Pharmacopoeia monographs when requesting marketing authorisation (Council of Europe).

Simplified registration procedure for traditional use herbal medicinal products

Assessment of traditional use submissions is undertaken by the Member States Competent Authority (compared with applications for standard applications and well-established use applications, which can also be evaluated by the EMA).

There is guidance issued by the EMA in 2016 on how to present the application for registration in a 'Common Technical Document' – the internationally agreed structure and format for an application dossier and format currently used for marketing authorisation applications.

The simplified procedure does not require evidence of clinical efficacy (unlike standard applications). This requirement is replaced by evidence that the efficacy of a product is plausible on the basis of long-standing use and experience. Applicants must provide sufficient evidence of the medicinal use of a product for a period of at least 30 years, including at least 15 years in the EU. A full review of published safety data and an expert report must be provided (Health Products Regulatory Authority). This Q and A document from the EMA provides further useful information.

EU herbal monographs and list entries

EU herbal monographs are published by the Committee for Herbal Medicinal Products (HMPC), part of the European Medicines Agency. Monographs aim to set a standard for the safety and efficacy evaluation of herbal medicinal products. To create a monograph, the HMPC evaluates all the available information, including non-clinical and clinical data, but also documented long-standing use and experience within the EU. They contain all information necessary for the use of a medicinal product containing a specific herbal substance or preparation. There are currently 169 herbal monographs, including herbs such as ginseng, dandelion root and cinnamon.

EU herbal monographs are divided into two sections: well-established use (marketing authorisation) and traditional use (simplified registration). A final EU monograph can be used in application reference material by a marketing authorisation applicant (well-established use part) and by a traditional-use registration applicant (traditional-use part) (European Medicines Agency). Member States are not obliged to follow the monographs in their assessment of the application.

The HMPC is also developing the European Union list (formerly known as Community list) through 'list entries'. Unlike monographs, EU list entries are legally binding on applicants and national competent authorities in the Member States. Draft list entries are developed by the HMPC, but the final list

entries (which includes, for example, echinacea and calendula) are adopted and published by the European Commission. The final list also includes the indications, specified strengths and posology, route of administration and any other information necessary for the safe use. There are currently 14 draft EU list monographs listed.

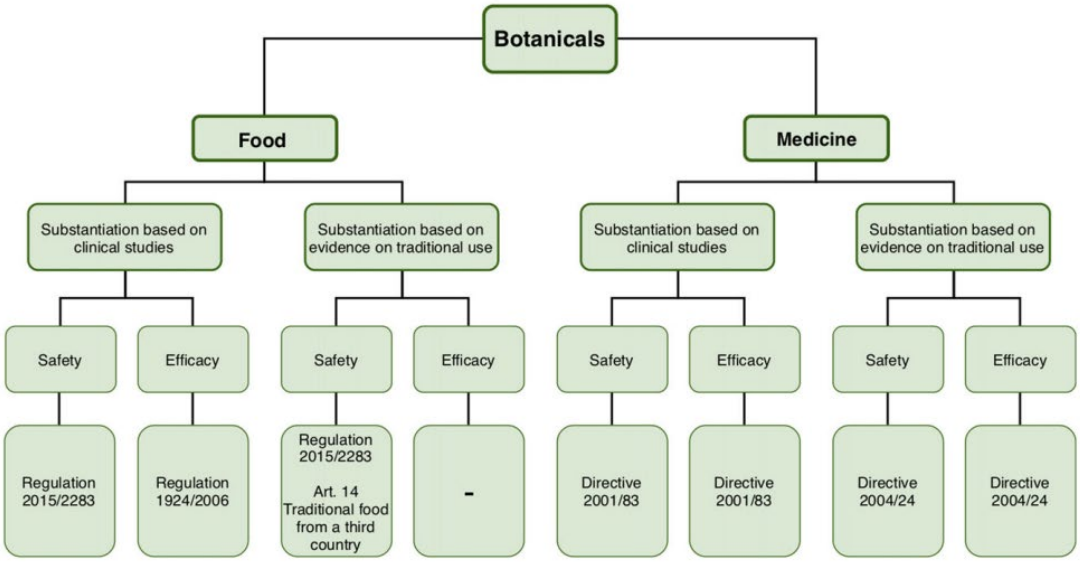
If applicants for traditional use registration can demonstrate that their product and claims comply with the information contained in the EU list, they do not need to provide evidence of its safe and traditional use. National competent authorities cannot require additional data to assess the safety and the traditional use of the product.

3.3.4 Botanicals

Botanicals can be used in both food supplements and herbal medicines. The classification responsibility is at the national level in EU Member States. Therefore, the same botanical can be classified as a food in one Member State and a medicine in another (McDaid et al., 2020).

Depending on the use and effect of the product, botanicals may be considered as traditional herbal medicinal products (see below) (Lenssen et al., 2019).

Figure 4: Botanical classification and regulation



Source: Lenssen et al., 2019

The EU does not currently have a centralised authorisation procedure for the use of botanicals and derived preparations in food supplements, but the use of such substances is still required to comply with general requirements of EU food law (e.g. regulations for general food law and for novel foods) (Low et al., 2017).

3.4 Permissible ingredients

3.4.1 Food supplements

Directive 2002/46 establishes harmonised lists of vitamins and minerals that can be used in the manufacture of food supplements in Annex I. Annex II contains a list of substances that are authorised as sources of the vitamins and minerals listed in Annex I.

There is a lack of harmonisation in EU law for ingredients in food supplements, other than vitamins and minerals, such as botanicals (see next section), enzymes, amino acids, and probiotics. Therefore, the incorporation of substances other than vitamins and minerals listed in Direction 2002/246 are regulated by Member State national rules (Domínguez Díaz et al., 2020). As a result, some Member States adopt a list-based approach to attempt to provide more stringency and harmonisation (McDaid et al., 2020).

The lack of harmonisation has also led to inconsistencies between Member States regarding acceptable limits of certain substances. Different limits, from zero tolerance to maximum acceptable limits, are set by individual Member States. Some limits are based on daily intakes whereas others are based on the concentration of substances found in the final product. These approaches reflect the outcomes of risk management actions taken by individual Member States (Low et al., 2017).

Although no maximums or minimums for permitted vitamins and minerals are set by the EU, EFSA has established, where possible, tolerable upper intake levels (ULs) for different population groups. ULs represent the highest level of chronic daily intake of a nutrient that is not likely to pose a risk of adverse health effects to humans. The ULs defined by EFSA and by the former Scientific Committee on Food (SCF) are used as a reference in EFSA's evaluations of the safety of nutrient sources added to food supplements. Throughout this work EFSA provides support to the European Commission in establishing maximum limits for vitamins and minerals in food supplements and fortified foods.

There is also a list of substances that are prohibited, restricted, or under community scrutiny. Article 8 of Regulation 1925/2006 provides the procedure to be followed where a substance other than vitamins or minerals, or an ingredient containing a substance other than vitamins or minerals, is added to foods or used in the manufacture of foods under conditions that would result in the ingestion of amounts of this substance greatly exceeding those reasonably expected to be ingested under normal conditions of consumption of a balanced and varied diet and/or would otherwise represent a potential risk to consumers. Such substances are then listed in Annex III – substances whose use in food is prohibited, restricted or under community scrutiny. For example, ephedra herb and its preparations are listed in Annex III, Part A – prohibited substances.

3.4.2 Botanicals

For botanical ingredients used in food, while they are still required to comply with general food law, there is no centralised legal authorisation procedure or permissible list. The European Food Safety Authority has created a compendium of botanicals reported to contain substances of possible concern for human health that might be used in food, but this is not exhaustive and has no legal force

(Vettorazzi et al., 2020). Some Member States have published their own positive lists for acceptable ingredients (Shao, 2017).

3.5 Health benefit claims

3.5.1 The regulations for food supplements

In the EU, health claims on food are considered as voluntary food labelling information and can only refer to nutritional physiological effects, not pharmacological effects (Kušar & Pravst, 2022). Regulation 1924/2006 sets out the nutrition and health claims that can be made on food, including food supplements. Claims are based on, and substantiated by, generally accepted scientific data (Article 6(1)). Under Article 3, the use of nutrition and health claims shall not:

(a) be false, ambiguous or misleading
(b) give rise to doubt about the safety and/or the nutritional adequacy of other foods
(c) encourage or condone excess consumption of a food
(d) state, suggest or imply that a balanced and varied diet cannot provide appropriate quantities of nutrients in general. Derogations in the case of nutrients for which sufficient quantities cannot be provided by a balanced and varied diet, including the conditions for their application, and designed to amend non-essential elements of this Regulation by supplementing it may be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 25(3), taking into account the special conditions present in Member States
(e) refer to changes in bodily functions which could give rise to or exploit fear in the consumer, either textually or through pictorial, graphic or symbolic representations.

The Annex of Regulation 1924/2006 contains the list of permissible nutrition claims and the conditions that apply to such claims. Amendments to this annex are made under article 25(3) – Committee procedure, where Regulation 182/2011 shall apply.

For health claims, Regulation 432/2012 sets out the list of permitted health claims able to be made on food, alongside the conditions on the use of the claim and any requirements for additional statements/warnings. There is also a public EU Register of Health Claims. This register lists all authorised and non-authorised health claims. Claims cannot suggest a product is intended to prevent or treat a disease, as this may render the product as a 'medicine,' which has different regulatory requirements. Where a business wants to make a health claim that is not authorised in the register of health claims, they must apply for authorisation under Article 15 of 1924/2006. The full register is also available for download in Excel format.

3.5.2 The assessment process for health claims on food supplements

The European Food Safety Authority is the assessment body for health claims. The authorisation of health claims for foods does not include an assessment of safety. While there is a safety assessment of novel foods under Regulation 2015/2283, this is a separate authorisation procedure and cannot be joined with the authorisation of a new health claim (Kušar & Pravst, 2022).

Authorisation of health claims on food under Article 15 of Regulation 1924/2006 are assessed under Regulation 353/2008. There is also associated scientific and technical guidance for the preparation and presentation of a health claim application. The guidance states the following:

- For claims based on the essentiality of nutrients, data on the essential mechanistic role in a metabolic function and/or the specific clinical signs/symptoms of deficiency is required.
- For all other claims, study data in humans that addresses the relationship between the consumption and the claimed effect are required. A comprehensive review of published human studies addressing the specific relationship between the food/constituent and the claimed effect is required. The review needs to be performed in a systematic and transparent manner. The guidance also suggests that applicants consider the EFSA guidance on the application of systematic review methodology to food and feed safety assessments.

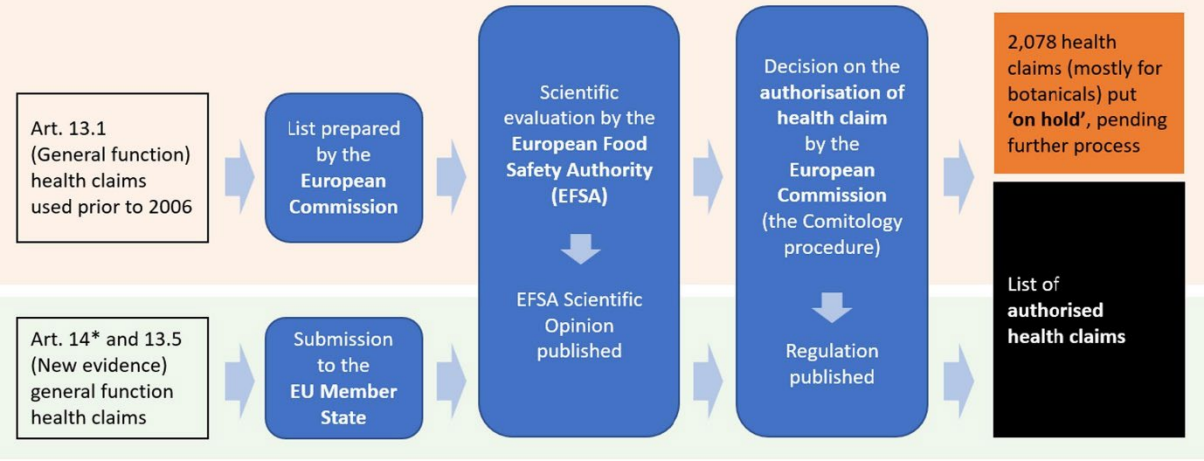
Currently, health claims can only be substantiated with scientific data from human clinical intervention studies and there is no possibility to make use of evidence on traditional use to substantiate health effects (Lenssen et al., 2019). Data from studies in animals or other model systems alone cannot substitute for human data, but may be included only as supporting evidence, for example to provide evidence on the biological plausibility of the specific claim.

When Regulation 1924/2006 was accepted, it created a situation where many ingredients (e.g. probiotics, most botanicals) did not meet the standard of substantiation of health claims. Over 2,000 health claims for botanicals were sent to EFSA for scientific evaluation at the same time as EFSA started publishing negative scientific opinions (Kušar & Pravst, 2022). The EC decided to put health claims for botanicals on hold. As such, the requirements for use of these 'on hold' health claims are different among EU Member States, with some allowing their usage without any notification procedure (Kušar & Pravst, 2022).

The decision to put the botanical health claims assessment on hold was due to the debate on whether to allow the use of traditional evidence to substantiate claims – similar to the evidence requirements for the safety and efficacy of traditional herbal medicinal products (Lenssen et al., 2019).

Kušar & Pravst (2022) set out the high-level process for authorisation of health claims in the diagram below.

Figure 5: Process for assessing health claims in the EU



Source: Kušar & Pravst (2022)

3.5.3 Health claims on traditional herbal medicines

For products classified as traditional herbal medicines under Directive 2004/24, which amended Directive 2001/83, the simplified registration procedure includes substantiation of claims. Compared to authorising health claims on food supplements, described above, the criteria are less stringent (e.g. evidence from human clinical trials is not required). The below table provides further comparisons by Lapenna et al., (2015).

Table 5: Differences in the requirements for traditional herbal medicines and foods bearing health claims under the relevant legislation (reproduced from Lapenna et al (2015))

Traditional Herbal Medicine Directive 2004/24	Regulation on Nutrition & Health claims on foods 1924/006
• Covers medicinal products for treating or preventing disease in human beings or having a pharmacological, immunological or metabolic action. • Lack of harmful effects under the specified conditions of use. • Review of safety data. • Track record of prior authorisations or rejections by national food safety authorities. • No clinical trials required – "plausible" pharmacologic effects or efficiency on the basis of longstanding use and experience is accepted. • Evidence of medicinal use for 30yrs, of which 15 are in an EU country.	• Covers foods which are not intended for treatment but for improving physiological body functions or reducing a disease risk in healthy people. • Safe and sufficiently characterised food. • Claimed effect relevant for human health. • Cause and effect relationship between the consumption of food and the claimed effect proved by relevant clinical trials. • Necessary quantity of food needed to obtain the claimed effect. • Claimed effect studied in a population representative of the target population for which the claim is intended.

3.6 Manufacturing requirements

EU regulations require food supplement manufacturers to comply with strict quality control standards, including good manufacturing practice (GMP) and Hazard Analysis Critical Control Point (HACCP) procedures (Djaoudene et al., 2023).

The requirement to adhere to GMP is not specifically required for the manufacture of the supplement itself (Stolwijk et al., 2023). However, GMP is required for materials that come into contact with supplements (e.g. packaging and printing inks on packaging). Regulation 1935/2004 sets out the requirements for materials and articles intended to come into contact with food, including the requirement for GMP. Regulation 2023/2006 sets out the requirements for GMP for materials and articles intended to come into contact with food. Regulation 2023/2006 applies to all sectors and to all stages of manufacture, processing and distribution of materials and articles, excluding the production of starting substances.

Regulation 852/2004 sets out the general requirements for food hygiene, particularly the HACCP principles that must be followed.

If the product is classified as a medicine (which includes products classified as traditional herbal medicinal products), Directive 2017/1572 requires GMP to be followed. This Directive also applies to medicinal products intended only for export. For medicinal products imported from outside the EU, the Directive states that the Member States should ensure the products have been manufactured in accordance with standards that are at least equivalent to GMP standards.

Volume 4 of "The rules governing medicinal products in the European Union" contains guidance for the interpretation of the principles and guidelines of GMP for medicinal products for human use. The basic requirements for medicinal products include:

- Chapter 1 - Pharmaceutical Quality System
- Chapter 2 - Personnel
- Chapter 3 - Premise and Equipment
    - See transitional arrangement for toxicological evaluation on page 1 of Chapter 3
    - Previous version
- Chapter 4 - Documentation
- Chapter 5 - Production
    - See transitional arrangement for toxicological evaluation on pages 1-2 of Chapter 5
    - Previous version
- Chapter 6 - Quality Control
- Chapter 7 - Outsourced activities
- Chapter 8 - Complaints and Product Recall
- Chapter 9 - Self Inspection

3.6.1 Applying for a licence to manufacture

3.6.1.1 Manufacture of food supplements

Regulation 852/2004 requires that establishments preparing foodstuffs be registered in each Member State: "…every food business operator shall notify the appropriate competent authority, in the manner

that the latter requires, of each establishment under its control that carries out any of the stages of production, processing and distribution of food, with a view to the registration of each such establishment." Registration requirements vary according to Member State law and will depend on the risk of the foodstuff. However, Article 6(3) states that food business operators must ensure that establishments are approved by the competent authority, including at least one on-site visit, where required under Member State Law or under Regulation 853/2004 (see below).

Regulation 853/2004 requires that establishments that handle products of animal origin be registered and approved by the competent authority of each Member State. Approval processes vary by Member State. For products that contain both plant and animal origin products (also known as Composite Products), there is no requirement for these to be manufactured in an approved establishment (Article 1(2)). Member States are required to maintain and keep up to date the lists of food business establishments that were approved in accordance with Article 6(3) of Regulation 852/2004 – this list is found here.

3.6.1.2 Manufacture of herbal medicinal products

All herbal medicinal products in the EU are required to be manufactured by authorised manufacturers only (Kroes, 2014). Becoming an authorised manufacturer requires assessment and approval by their Member State. Article 40(1) of Directive 2001/83 states that "Member States shall take all appropriate measures to ensure that the manufacture of the medicinal products within their territory is subject to the holding of an authorisation. This manufacturing authorisation shall be required notwithstanding that the medicinal products manufactured are intended for export."

These authorisations are issued by the competent authority of each Member State, and assessment processes will vary between each Member State. However, Article 41 sets out the minimum requirements to obtain a manufacturing authorisation – namely to:

a) specify the medicinal products and pharmaceutical forms which are to be manufactured or imported and also the place where they are to be manufactured and/or controlled
b) have at their disposal, for the manufacture or import of the above, suitable and sufficient premises, technical equipment and control facilities complying with the legal requirements which the Member State concerned lays down as regards both manufacture and control and the storage of medicinal products, in accordance with Article 20
c) have at their disposal the services of at least one qualified person within the meaning of Article 48.

3.7 Exporting requirements

Businesses that import or export goods into or out of the EU require an Economic Operators Registration and Identification (EORI) number. Businesses request the assignment of an EORI number to the customs authorities of the EU country in which they are established (European Commission).

Other export requirements depend on the type of product. For example, exporting natural ingredients for health products requires a business to follow the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). CITES provides a list of plant and wild animal species that cannot be imported or exported, or are restricted (CBI Ministry of Foreign Affairs). If the product is

listed in Regulation 2019/2117, an export permit is required under Regulation 338/97 from the country's CITES authority, along with an import permit from the country receiving the product.

For products classified as medicines, businesses engaged in the activity of wholesale distribution must hold a wholesale distribution authorisation issued by the national competent authority of the Member State where they carry out these activities. Those who hold a manufacturing authorisation (see 3.6.1.2) do not require a separate authorisation to distribute products that are already subject to a manufacturing authorisation (European Medicines Agency). Directive 2001/83 requires distributors to follow good distribution practice (GDP), and publishes guidelines, which include the following:

- The maintenance of a quality system that sets out responsibilities, processes and risk management principles in relation to their activities. The quality system should ensure that:
    - medicinal products are procured, held, supplied or exported in a way that is compliant with the requirements of GDP
    - management responsibilities are clearly specified
    - products are delivered to the right recipients within a satisfactory time period
    - records are made contemporaneously
    - deviations from established procedures are documented and investigated
    - appropriate corrective and preventive actions (commonly known as 'CAPA') are taken to correct deviations and prevent them in line with the principles of quality risk management.
- Designation of a Responsible Person who meets the qualifications and all conditions provided for by the legislation of the Member State concerned. A degree in pharmacy is desirable. The responsible person should have appropriate competence and experience as well as knowledge of and training in GDP.
- Wholesale distributors must have suitable and adequate premises, installations and equipment.
- Documentation requirements, including approvals, retention, required information, form and access.
- Operations requirements, including qualifications of suppliers and customers, receipt of medicinal products, storage, destruction, supply and exporting.
- Procedures relating to complaints, returns, suspected falsified medicinal products and medicinal product recalls.
- Requirements relating to outsourced activities.
- Self-inspections.
- Transport requirements, including labelling and packaging.
- Specific requirements for brokers.

3.8 Importing requirements

3.8.1 Food supplements

In addition to ensuring the product complies with all applicable legislation (both EU and specific Member State laws) discussed in section 3.3.1 of this report (e.g. labelling, claims and permitted

ingredients), there are also specific requirements with regards to importing products from outside the EU.

For food supplements containing solely products of animal origin, Regulation 2017/625 sets out the rules governing official controls along the agri-food chain, including the importing of products. These products can only be imported into the EU if they do the following:

- Comply with the general rules on hygiene of foodstuffs and other specification for food of animal origin (e.g. Regulation 852/2004 and 853/2004).
- Come from an approved establishment of a country outside the EU that is included in a positive list of eligible countries for the relevant product. Lists are published in Regulation 2021/405, and more information can be found here. A country must apply for listing to the Commission, which will evaluate the application.
- Have official certificates signed by the competent authority in the exporting country outside the EU certifying the products are suitable to be exported to the EU. There are different types of certificates required according to the category of product.
- Pass the mandatory control at the border. Regulation 2019/2130 sets out the detailed rules on the operations to be carried out during and after documentary checks, identity checks and physical checks on animals and goods subject to official controls at border control posts. The list of products that is subject to official controls is set out in Regulation 2021/632 and includes substances such as royal jelly, propolis, and empty shells to use as raw material for glucosamine and fish oils. However, see section 3.9 of this report for exemptions to this requirement.

For products containing plants, the following protective measures are in place:

- Import bans – some products are banned under Regulation 2019/2072 or provisionally prohibited pending a risk assessment under Regulation 2018/2019.
- Phytosanitary certificate – imports of plants and plant products listed in Annex XI and Annex XII to Regulation 2019/2072 must be accompanied by an official phytosanitary certificate. The exporting country's national plant protection authorities issue the certificate. Once in the EU, a plant passport may replace the phytosanitary certificate for imported plants, plant products and other objects.
- Inspection and plant health checks – this includes documentary, identity and physical checks at point of entry. Regulation 2022/2389 sets out the frequency of checks required.
- Importers register – importers, whether or not producers, of plants, plant products or other objects must be included in an official register of a Member State under an official registration number.
- Emergency measures set out here (product dependent).

For food, the following protective measures are in place:

- Compliance with food law – imported food must comply with the relevant requirements of food law and conditions recognised by the EU to be at least equivalent. The competent authority of the exporting country must offer guarantees as to compliance or equivalence with EU requirements.

- Traceability across all stages of production, processing and distribution – this document sets out the relevant regulations for products. Operators also have traceability requirements (one step back-one step forward principle). Operators are required to have systems and procedures in place to allow for the information to be made available to the Competent Authorities.
- Responsibilities at all stages of production, processing and distribution – operators need to ensure foods satisfy legal requirements.

See this page for more detailed information on the importing requirements.

3.8.2 Traditional herbal medicinal products

The importation of medicinal products is subject to the following requirements:

- Importing authorisation – the competent Authority of the importing Member State needs to grant an authorisation. The applicant must:
    - specify the products to be imported as well as the place where they are to be manufactured/controlled
    - have suitable and sufficient premises, technical equipment and facilities for control and storage
    - have the services of at least one suitably qualified person in one of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology or biology.
- Marketing authorisation and register of the product – the competent Authority of a Member State, or the European Medicines Agency needs to issue the authorisation. Only applicants established in the EU may be granted a marketing authorisation. The authorisation holder is the person responsible for placing the product on the market. See section 3.3.3 of this report for the marketing authorisation procedure for traditional herbal medicinal products.
- Labelling and packaging provisions – there are multiple requirements with regards to the labelling of the outer and immediate packaging, the package leaflet, and safety measures set out in Regulation 2016/161 relating to unique identifiers and anti-tampering devices for certain products.
- Control of each batch – each production batch imported from outside the EU has to undergo full qualitative analysis, a quantitative analysis of at least the active substances, and any other tests necessary to ensure the quality, in accordance with the marketing authorisation.
- Pharmacovigilance system – marketing authorisation holders must implement a pharmacovigilance system equivalent to the system put in place by Member States as required by Regulation 726/2004 relating to procedures for the authorisation and supervision of medicinal products for human use.

3.9 Exemption requirements

The following exemptions to regulatory requirements have been identified.

Regulation 853/2004 (hygiene rules for animal origin products) specifies certain exemptions for products of animal origin under Article 1(3), meaning the following are not required to follow the rules on food hygiene as set out in Regulation 853/2004, i.e. there is no requirement for establishments that

handle animal products to be registered and approved in the following cases (which may apply to food supplements of purely animal origin):

a) primary production for private domestic use
b) the domestic preparation, handling or storage of food for private domestic consumption
c) the direct supply, by the producer, of small quantities of primary products to the final consumer or to local retail establishments directly supplying the final consumer.

Regulation 2021/630 sets out certain categories of goods exempt from official controls at border control posts (see importing requirements). Included are food supplements packaged for the final consumer containing processed animal products (including glucosamine, chondroitin or chitosan) that meet the requirements of Article 3(1)(a) – i.e. a shelf-stable composite product that does not contain colostrum-based products or processed meat other than gelatine, collagen or highly refined products.

3.10 Specific groups of products

3.10.1 Essential oils for aromatherapy

Depending on how essential oils for aromatherapy are marketed, the product could be classified as a medicine or a cosmetic, which have differing legal requirements (CBI Ministry of Foreign Affairs):

- Cosmetics Regulation 1223/2009: The Cosmetics Regulation is the central regulatory framework for cosmetic products for the European market, covering the safety and effectiveness of cosmetic products.
- Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH): Essential oils used in aromatherapy also need to comply with the REACH regulation. The aim of REACH is to improve the protection of human health and the environment from the risks that can be posed by chemicals.
- If the final product is marketed as a medicinal product, an essential oil needs to comply with pharmaceutical requirements, i.e. Directive 2004/24 on traditional herbal medicinal products, which amends Directive 2001/83 relating to medicinal products for human use.

3.10.2 Homeopathy

The manufacture, sale, and export of homeopathic medicinal products in the EU are subject to specific rules and regulations. The Homeopathic Medicinal Products Working Group (part of the Heads of Medicines Agencies (HMA)) sets out multiple guidance documents for getting a homeopathic product on the market:

- Directive 2001/83: This directive classifies homeopathic preparations as medicinal products and requires national governments to establish a simplified registration procedure outside the otherwise prescribed rules for marketing authorisation for medicines.
- Market Access: Directive 2001/83 on medicinal products for human use outlines two procedures for market access of homeopathic and homeopathically produced medicinal products: Special Simplified Registration Procedure (Article 14) and Marketing Authorisation

(Article 16). This document from the HMA in 2020 contains useful information regarding the regulatory process of homeopathic products.

4. United Kingdom

The EU Food Supplements Directive 2002/46 mentioned in the previous section of this report took effect on August 1, 2005, and was enforced in the UK through the Food Supplements (England) Regulations 2003, with similar regulations in Scotland, Wales, and Northern Ireland.

On 1 January 2021, the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020 transferred responsibilities from EU organisations involved in the risk assessment and risk management processes covered by nutrition legislation to bodies in Great Britain, and fixed inoperabilities of retained Directive 2002/46 that would otherwise have arisen. Excepting those transfers, EU Regulations and tertiary legislation relating to nutrition have been retained under the powers contained within the European Union (Withdrawal) Act 2018 as UK law (see Department of Health and Social Care).

Northern Ireland, despite leaving the EU, remains aligned with EU single market rules for goods and maintains access to this market – therefore, it can take a different approach to Great Britain (i.e. England, Wales and Scotland). Thus, this chapter will refer to either the UK or Great Britain, depending on what the regulations cover.

In essence, a significant portion of EU law remains applicable for the time being. It is important to remember that, even with the presence of EU law, some specific laws among Member States may vary, e.g. different positive lists for acceptable ingredients in relation to botanicals. Therefore, this section sets out any specific UK laws identified as part of this project. However, as the state of the law is likely in flux after the EU Exit, this information may undergo rapid change.

4.1 Legislative definitions

Medicinal product, according to The Human Medicines Regulations 2012 – means:

(a) any substance or combination of substances presented as having properties of preventing or treating disease in human beings; or

(b) any substance or combination of substances that may be used by or administered to human beings with a view to:

> (i) restoring, correcting or modifying a physiological function by exerting a pharmacological, immunological or metabolic action, or
>
> (ii) making a medical diagnosis.

Food supplement, according to the Food Supplements (England) Regulations 2003 (and equivalent Scotland and Wales regulations) – means:

Any food, the purpose of which is to supplement the normal diet and which:

(a) is a concentrated source of a vitamin or mineral or other substance with a nutritional or physiological effect, alone or in combination; and

(b) is sold in dose form.

This may include vitamins, minerals, amino acids, essential fatty acids, fibre, and various plants and herbal extracts. Their use is not intended to treat or prevent diseases in humans or to modify physiological functions (Food Standards Agency).

Herbal medicinal product, as defined in section 8 of the Human Medicines Regulations 2012, means:

A medicinal product whose only active ingredients are herbal substances or herbal preparations.

For a herbal medicinal product to be registered as a *Traditional Herbal Medicine*, as defined in section 125, Part 7 of the Human Medicines Regulations 2012, the following conditions must be met:

- Condition A is met if by virtue of its composition and indications the product is appropriate for use without the need for a medical practitioner to:

  (a) diagnose the condition to be treated by the product
  (b) prescribe the product
  (c) monitor the product's use.

- Condition B is met if the product is intended to be administered at a particular strength and in accordance with a particular posology.
- Condition C is met if the product is intended to be administered externally, orally or by inhalation.
- Condition D is met if:

  (a) the product has been in medicinal use for a continuous period of at least 30 years; and
  (b) in relation to:

  (i) a Traditional Herbal Registration (THR) (Northern Ireland) or THR (UK), the product has been in medicinal use in the European Union for a continuous period of at least 15 years

  (ii) a THR (Great Britain), the product has been in medicinal use in the United Kingdom or a country included in the list published under regulation 125A(1) for a continuous period of at least 15 years.

  It is immaterial for the purposes of condition D whether or not during a period mentioned in that condition:

  (a) the sale or supply of the product has been based on a specific authorisation
  (b) the number or quantity of the ingredients (or any of them) has been reduced.

- Condition E is met if there is sufficient information about the use of the product as mentioned in condition D (referred to in this Part as its "traditional use"), so that (in particular):

  (a) it has been established that the traditional use of the product is not harmful; and
  (b) the pharmacological effects or efficacy of the product are plausible on the basis of long-standing use and experience.

4.2 Definitional interface

The Medicines and Healthcare products Regulatory Agency (MHRA), on behalf of the UK licensing authority, determines whether a product is a medicinal product. If a product is medicinal, it will be subject to The Human Medicines Regulations 2012. The MHRA only classifies finished products, not individual substances and ingredients. The MHRA published a guide in 2020 on what a medicinal product is.

Part 9 of the Human Medicines Regulations provides for the statutory process of assessing borderline products. The borderline section of the MHRA makes determinations on a case-by-case basis, looking at:

- the definitions of a medicinal product
- following an assessment of all the available evidence
- relevant Court precedents.

The MHRA has also published a guide in 2023 on borderlines between medical devices and other products.

4.3 Getting a product on the market

4.3.1 Food supplements

UK food law regulates the content, labelling and promotion of food supplements. There is no requirement for food supplements to be licensed or registered with the UK government (Department of Health and Social Care). To sell food supplements in the UK, a business must register as a Food Business Operator with their local authority (Food Standards Agency). The supplements must be labelled as a 'food supplement', not a 'dietary supplement'. Labelling requirements are set out in the Food Supplements (England) Regulations 2003 (and equivalent regulations in Scotland and Wales).

4.3.2 Traditional herbal medicines

To sell a product as a traditional herbal medicine, a person must apply for a registration under the Human Medicines Regulations 2012. A Traditional Herbal Registration (THR) is only granted if the medicine is used for minor health conditions that do not require medical supervision (e.g. colds). If a person wants to market a traditional herbal medicine that claims to treat major health conditions, they need to apply for marketing authorisation first (i.e. the standard application process for new medicines). Not all herbal products are medicines. Some may be classified as food supplements or cosmetics (see applying for a traditional herbal registration).

To sell or supply medicines to anyone other than the patient using the medicine, a wholesaler licence is needed. This is also known as a wholesale dealer licence or a wholesale distribution authorisation. To qualify, applicants need to comply with good distribution practice (GDP) (see applying for manufacture or wholesale of medicines licences). The wholesale dealer licence allows the holder to:

- sell, supply, offer for sale or supply traditional herbal medicines wholesale

- import unlicensed medicinal products from countries inside the European Economic Area (EEA)
- export medicinal products to countries outside the EEA.

The MHRA has published a guidance note for applicants and holders of the licence. To apply for a licence, applicants must undergo a full review of their proposed wholesale operation, including:

- a written document that describes the company's proposed business model, detailing both product and fiscal flows
- details of the premises and equipment involved in the wholesale operation (including details of ambient and cold chain storage facilities, transport arrangements, computerised systems and any business contingency plans)
- details of any outsourced activities and copies of any associated quality/technical agreements held for such arrangements
- having an approved quality management system in place (including the quality manual, policies, standard operating procedures and relevant forms), including any index
- a detailed list of the risk assessments that have been carried out
- having detailed training records and job descriptions for all persons involved in the proposed wholesale operation, especially that of the Responsible Person
- being able to demonstrate that a temperature mapping exercise has been conducted of the proposed wholesale area with a clear methodology
- having a list of qualified prospective suppliers and customers
- being able to demonstrate a clear schedule and methodology for self-inspections
- having records of management review meetings
- being able to provide evidence of transport validation.

4.4 Permissible ingredients

The food supplement regulations in England, Scotland, Wales and Northern Ireland cross reference the annex of retained Directive 2002/46 setting out the permitted vitamins and minerals, and their permitted forms (discussed in section 3.4 of this report). These lists have been inserted into the Nutrition (Amendment etc) (EU Exit) Regulations 2019 as schedules to ensure that they continue to have effect (Department of Health and Social Care).

The UK does not have any national legislation setting maximum levels for vitamins and minerals and vitamin and mineral substances which may be used in the manufacture of food supplements. However, it does have voluntary guideline safe upper levels which are based upon a report issued in 2003 by the Expert Group on Vitamins and Minerals (EVM), Safe upper levels for vitamins and minerals.

There are also specific bans or restrictions, including kava-kava, tryptophan and Senecio (ragwort).

4.5 Health benefit claims

From 31 December 2020, voluntary nutrition or health claims must comply with the requirements of retained EU Regulation 1924/2006 on nutrition and health claims made on foods, discussed in section

3.5.1 of this report. All nutrition and health claims that were listed in the EU Register on 31 December 2020 were adopted and included in the Great Britain nutrition and health claims register. Northern Ireland continues to use the EU Register.

For new claims, an application must be submitted to the appropriate authorities for assessment for the claim to be authorised for use in the Great Britain market. Where a scientific opinion regarding the efficacy of a claim is available from the European Food Safety Authority or other scientific advisory body, this should be included with an application.

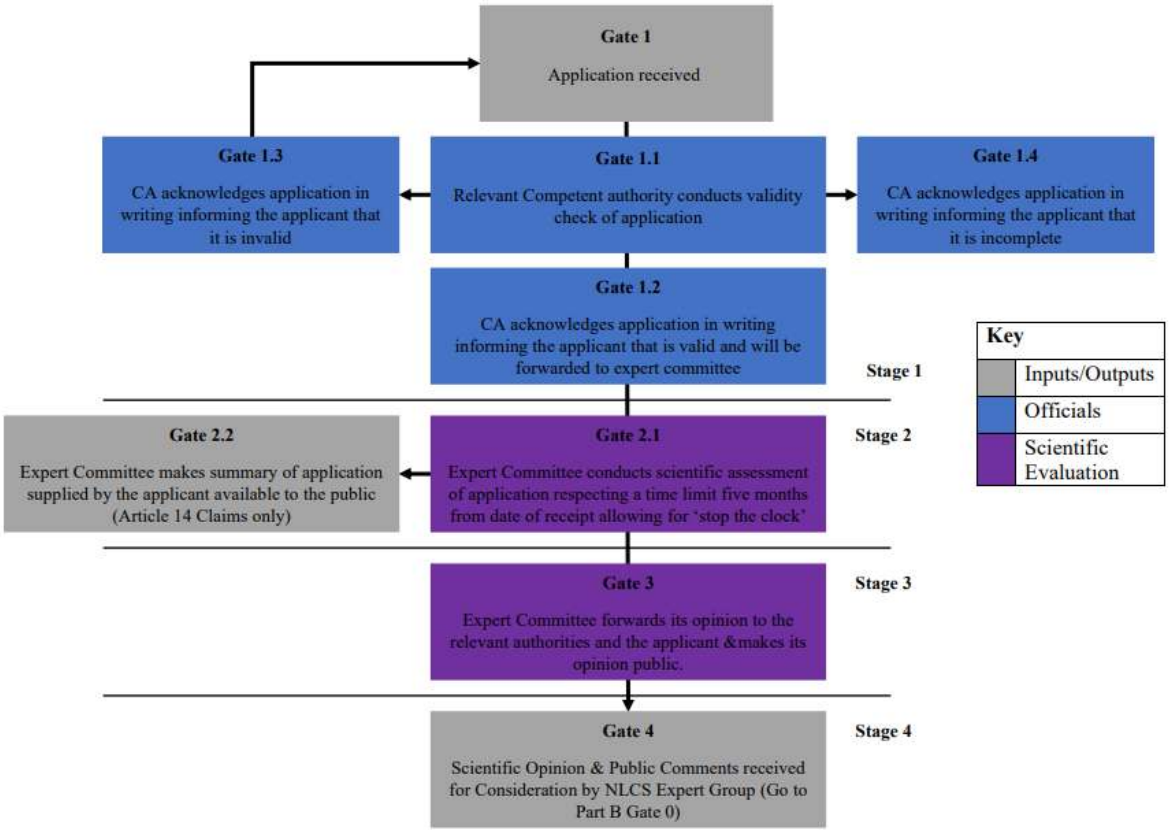
The application form requires:

- administrative and technical data
- characterisation of the food/constituent
- characterisation of the claimed effect
- identification of pertinent scientific data, e.g. the requirement for a comprehensive review of published human studies
- overall summary of pertinent scientific data.

The assessment process is set out by the Nutrition Related Labelling, Composition and Standards Provisional Common Framework (a "command paper responding to direct EU nutrition-related legislation that will form part of domestic law under the Withdrawal Agreement")[5] (see below figure).

[5] https://www.gov.uk/government/publications/nutrition-labelling-composition-and-standards-provisional-common-framework-command-paper

Figure 6: UK application process for new Nutrition and Health Claims



Source: Department of Health and Social Care (2020)

4.6 Manufacturing requirements

For supplements classified as food, while the UK has left the EU, some EU regulations relating to food law were retained. The Food Standards Agency has published a draft guide, following the UK's exit from the EU, which sets out all the requirements under the food law, including manufacturing, registration of food establishments, approval of establishments and Hazard Analysis and Critical Control Point (HACCP) requirements. This guidance is aimed at Competent Authorities, rather than manufacturers, and is aimed at assisting Competent Authorities with the discharge of their statutory duty to enforce food law and supporting the quality, consistency, effectiveness and appropriateness of official food controls and other official activities.

Retained regulations relating to HACCP mean that all food businesses in the UK are still required to have a HACCP-based food safety management system in place. Businesses must comply with HACCP procedures or a HACCP-based food safety management system such as the Safer Food Better Business Guide.

For supplements classified as medicines, under Chapter 1A, B17, the Human Medicines Regulations 2012 state that "the Ministers may by regulations set out principles and guidelines of good manufacturing practice in respect of medicinal products and investigational medicinal products." However, they also note that "subject to any provision made in regulations under paragraph (1), the principles and guidelines set out in the Good Manufacturing Practice Directive [i.e. Directive 2001/83]

have effect in Great Britain on and after IP completion day[6] as they had effect immediately before IP completion day."

This review could not identify any new regulations relating to GMP, therefore it is assumed from the wording of the regulations that the requirement of compliance with GMP under Directive 2001/83 is still in effect. See section 3.5.3 of this report for more detail on what is required under GMP in the EU.

4.6.1 Applying for a licence to manufacture

4.6.1.1 Manufacture of food supplements

Other than registering as a Food Business Operator, as set out in section 4.3.1 of this report, if a manufacturer is handling meat, fish, egg or dairy products, they must apply for a food premises approval licence (similar to the requirements of EU businesses under Regulation 853/2004). This must be applied for through the local council, which will inspect the premises. Products include gelatine and collagen. Responsibility rests with Local Authorities for the approval and enforcement of establishments (Food Law Practice Guidance).

Before reaching a decision on an application for approval, the Competent Authority must ensure that an on-site visit is made in the form of an inspection of the establishment to verify that, where necessary, all systems, procedures and documentation meet the relevant requirements of Regulation 852/2004 and Regulation 853/2004.

The same exemptions to approval apply that are set out in the EU legislation, namely the retail exemption set out in section 3.9 of this report and exemptions for food containing both products of plant origin and processed products of animal origin (composite products), set out in section 3.6.1.1 of this report.

4.6.1.2 Manufacture of herbal medicinal products

The manufacture of a traditional herbal medicine requires a licence, issued by the MHRA. This is called a manufacturer/importer licence and may be granted for the manufacture and assembly of products, or just the assembly. Holders of the licence do not need to apply for an additional wholesaler's licence set out in section 4.3.2 of this report.

Companies applying for a marketing authorisation need to have a manufacturer licence first. The manufacturer licence must be granted first, providing the product is in the process of being approved (see applying for manufacture or wholesale of medicine licences).

[6] Implementation Period completion day (31 December 2020).

There are different types of manufacturers' licences available:

Table 6: Types of manufacturers' licences

Type of licence	Purpose
Manufacturer/importer licence	Manufacture and/or assemble licensed medicinal products, including export to a country outside the EEA. Import licensed medicinal products from countries outside the EEA.
Manufacturer 'specials' licence	Manufacture unlicensed medicines 'specials'. Import unlicensed medicinal products from outside the EEA.
Manufacturer licence for investigational medicinal products	Manufacture investigational medicinal products for use in clinical trials.
Manufacturer licence exempt advanced therapy products (hospital exemption licence)	Manufacture exempt 'advanced therapy medicinal products' on a non-routine basis for use in UK hospitals.
Manufacturer licence for non-orthodox practitioners	Mix and assemble licensed general sales list (GSL) medicinal products.

To qualify for the licence, the applicant needs to show they comply with GMP and pass regular GMP inspections. The MHRA has issued guidance for applicants and holders of such a licence. To comply with GMP, licence holders must:

- establish and implement an effective pharmaceutical quality assurance system
- have competent and appropriately qualified personnel, sufficient in number to achieve the pharmaceutical quality objective(s)
- define the duties of managerial and supervisory staff responsible for implementing and operating GMP in their job descriptions
- give personnel sufficient authority and training to meet the pharmaceutical quality objective(s)
- institute and maintain hygiene programmes relating to health, hygiene and clothing
- provide and maintain premises and equipment appropriate to the intended operations
- have system(s) of documentation covering all the processes and specifications covering the various operations. Batch documentation must be retained at least one year after the expiry date of the batch to which it relates or five years post QP certification, whichever is the longer (refer to EU GMP Chapter 4)
- provide and maintain an independent quality control department, under the authority of the person nominated as responsible for overall quality control
- retain records and samples of starting materials and finished products for the required periods
- ensure that any work contracted out is the subject of a written contract
- maintain an effective system whereby complaints are reviewed and products may be recalled
- carry out a programme of regular self-inspection.

4.7 Exporting requirements

4.7.1 Food supplements

For exporting composite products (i.e. a mix of plant and animal origin ingredients) to the EU and Northern Ireland, an exporter may need (export of food products):

- a composite export health certificate (for non-shelf-stable products). Certificate 8350 is the certificate relating to composite food products intended for human consumption containing any quantity of meat products (except gelatine, collagen and highly refined products)
- a private attestation (if the product is shelf-stable)
- a catch certificate (if the product contains 20% or more marine-caught fish or fishery products caught in Great Britain.

For exporting products of animal origin to the EU and Northern Ireland, an exporter may need:

- an export health certificate. For example, Certificate 8399 relates to highly refined chondroitin sulphate, hyaluronic acid, other hydrolysed cartilage products, chitosan, glucosamine, rennet, isinglass and amino acids intended for human consumption to the European Union and Northern Ireland.

Products that do not contain products of animal origin do not generally require an export health certificate (export of food products).

Products being exported to any other country may also require a Certificate of Free Sale, depending on the receiving country's food authority requirements.

Food supplements packaged for the final consumer, containing processed animal products (including glucosamine, chondroitin or chitosan) are exempt from border controls if they are shelf-stable, can be identified as a product intended for human consumption, are securely packaged and sealed and meet EU production or processing requirements (export of food products).

4.7.2 Traditional herbal medicines

See section 4.6.1 of this report for details on the manufacturer/importer licence, which allows for manufacture and/or assembly of licensed medicines, including export to a country outside the EEA.

Export certificates are also required, of which there are five types (which ones are needed depends on the requirements of the importing country):

1. **Certificate of a pharmaceutical product (licensed)**. The certificate shows details including:
   (a) the marketing authorisation holder
   (b) the active ingredients and excipients
   (c) the manufacturing, packaging and batch release sites
   (d) whether or not the product is on the market in the UK.
2. **Certificate of a pharmaceutical product (unlicensed).** The drug must have been manufactured in the UK and the exporter must have a manufacturer licence for the drug.

3. **Certificate of manufacturing status.** The certificate confirms the named sites on a specified manufacturer licence meet GMP requirements. All or any of the sites named on the manufacturer licence can be listed on the certificate.
4. **Certificate of licensing status.** The certificate of licensing status is for importing agents who must screen bids made by an international tender for licensed or unlicensed products (excluding specials).
   (a) The certificate has a limit of 10 products and one country for each certificate. The product name, dosage form, active ingredients and amounts should be the same as the medicine's product licence (if it's licensed).
5. **Certificate for the importation of a pharmaceutical constituent.** The specific active ingredient or excipient must be in either a current licensed human medicine or a national or international pharmacopoeia. The manufacturing site must hold a valid certificate of inspection from Medicines and Healthcare products Regulatory Agency. The certificate is country and ingredient specific. A certificate can only be for one site function, for example manufacture, packaging or batch release. Exporters can apply for a certificate for each function.

These certificates can all be applied for online through the MHRA, and the data requirements for each type differ.

4.8 Importing requirements

4.8.1 Food supplements

Currently, importers and import agents must use the Import of Products, Animals, Food and Feed system (IPAFFS) to notify authorities in Great Britain before goods such as composite food products, plant products and products of animal origin arrive from EU and non-EU countries.

Great Britain is introducing a Border Target Operating Model as a new approach to importing goods into Great Britain, to be progressively introduced from the end of January 2024. This document sets out the new approach to safety and security controls (applying to all imports), and sanitary and phytosanitary controls (applying to imports of live animals, germinal products, animal products, plants and plant products) at the border. It sets out how controls will be delivered through simplification, digitisation and the UK's new Single Trade Window. Sanitary and phytosanitary controls will take a risk-based approach with simplified and digitised health certificates, using trust through the use of pilot schemes.

4.8.2 Traditional herbal medicines

See section 4.6.1 of this report for details on the manufacturer/importer licence, which allows for imports of licensed medicinal products from countries outside the EEA.

See section 4.3.2 of this report for details on the wholesaler licence, which allows for the import of unlicensed medicinal products from countries inside the EEA. There is a guidance document for importing a human medicine. People can import an unlicensed medicine if:

- they import it from a country other than an approved country for import to export it back to a country other than an approved country for import (called an introduced product)[7]
- they are in Northern Ireland and they import it from a non-EEA country to export it back to a country outside the EEA (called an introduced product)
- licensed medicines do not work for the special clinical needs of a patient (called a special product)
- there are no licensed medicines available for the clinical needs of a patient (also called a special product).

4.9 Exemption requirements

According to the MHRA, herbal practitioners do not need a licence to supply herbal medicinal products that are created on their own premises and supplied to patients following one-on-one consultations.

A Food Premises licence (for handling meat, fish, egg or dairy products – which may include food supplements) is not required if the applicant sells direct to the public or retailers, as long as:

- food is less than 25 per cent of the business trade
- they do not handle any wild game meat products
- they do not sell food outside the county the business is registered in.

4.10 Specific groups of products

4.10.1 Essential oils for aromatherapy

Depending on the product composition, presentation and intended use, it may be classified as medicines, medical devices, cosmetics, foods, food additives or flavourings. Aromatherapy products that do not meet any of those definitions will be regulated by the General Product Safety Regulation 2005 (see a guide to medicinal products).

If they are classified as cosmetics, the Product Safety and Metrology etc. (Amendment etc.) (EU Exit) Regulations 2019 will apply, specifically schedule 34, which sets out the amendment of the EU Cosmetics Regulation 1223/2009. Under Regulation 1223/2009, a 'cosmetic product' means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours.

[7] An introduced medicinal product will not have Marketing Authorisation for the UK or a country on an approved country for import list.

4.10.2 Homeopathy

There are two regulatory schemes for homeopathic medicinal products (see registering a homeopathic medicine):

- the Simplified Registration Scheme
- the National Rules Scheme.

Under the Simplified Registration Scheme, indications (description of diseases or conditions for which the product is used for) are not allowed. An applicant must:

- submit data on the quality of the product and show that it is dilute enough to guarantee safety; and
- the first dilution to be registered must be at least a 1 in 10,000 dilution of the starting material.

Under the National Rules Scheme:

- there is no restriction on the first dilution to be authorised or the pharmaceutical form
- applicants can claim that the product is used within the UK homeopathic tradition for the relief or treatment of minor symptoms and conditions which do not require the supervision of a doctor
- applicants must submit data that demonstrates quality, safety and use within the UK homeopathic tradition
- applicants must include details of labelling and product literature with the application.

There is a national system for submitting applications to the MHRA. The MHRA takes around 210 days to evaluate completed applications.

5. Canada

5.1 Legislative definitions

Foods, cosmetics, drugs, and devices are regulated by the Food and Drugs Act.

Drug (Section 2 of the Food and Drugs Act) – any substance or mixture of substances manufactured, sold or represented for use in:

(a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals,
(b) restoring, correcting or modifying organic functions in human beings or animals, or
(c) disinfection in premises in which food is manufactured, prepared or kept.

Cosmetic (Section 2 of the Food and Drugs Act) – any substance or mixture of substances manufactured, sold or represented for use in cleaning, improving or altering the complexion, skin, hair or teeth, and includes deodorants and perfumes.

Food (Section 2 of the Food and Drugs Act) – any article manufactured, sold or represented for use as food or drink for human beings, chewing gum, and any ingredient that may be mixed with food for any purpose whatever.

Natural Health Product (Section 1 of the Natural Health Products Regulations) – a subset of drugs pertaining to medicinal ingredients of natural origin, defined in the Natural Health Products Regulations as:

> a substance set out in Schedule 1 or a combination of substances in which all the medicinal ingredients are substances set out in Schedule 1, a homeopathic medicine or a traditional medicine, that is manufactured, sold or represented for use in:
>
> a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans
>
> b) restoring or correcting organic functions in humans
>
> c) modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health.
>
> However, a natural health product does not include a substance set out in Schedule 2, any combination of substances that includes a substance set out in Schedule 2 or a homeopathic medicine or a traditional medicine that is or includes a substance set out in Schedule 2.

Non-medicinal ingredient – any substance that is added to a product to confer suitable consistency or form to the medicinal ingredients (suitable as per dosage form and route of administration). Non-medicinal ingredients:

- should not exhibit pharmacological effects
- should not have any effect contradictory to the product's recommended purpose
- should not exceed the minimum concentration required for the formulation

- should not adversely affect the bioavailability, pharmacological activity, or safety of the medicinal ingredients
- should be safe.

5.2 Definitional interface

5.2.1 Natural health products (NHPs)

Simply put, the Natural Health Products Regulations (NHPR) of Canada define NHPs as:

- probiotics
- herbal remedies
- vitamins and minerals
- homeopathic medicines
- traditional medicines, including traditional Chinese medicines and Ayurveda
- amino acids and essential fatty acids.

Under section (s)2 of the NHPR, a product is not an NHP if it is required to be sold with a valid prescription. NHPs must therefore be able to be sold without a prescription. NHPs can include everyday consumer products such as toothpastes, antiperspirants, shampoos, facial products and mouthwashes.

As outlined in section 5.1 of this report, NHPs cannot include a substance in Schedule 2 of the NHPR which includes substances that are injected. Therefore, NHPs including homeopathic medicines marketed for injectable use are not covered under the NHPR and are regulated under the Food and Drug Regulations.

Medicinal ingredients

Medicinal ingredients are defined as substances set out in Schedule 1 of the NHPR. They have an effect on living matter, and are included in the make-up of an NHP.

5.2.2 Foods

There are interface issues where, for instance, beverages with vitamins, minerals or amino acids can be classified as an NHP. The Canadian Government has released a Guidance Document on classifying products at the food-natural health product interface. Decisions on classification are made on a case-by-case basis that considers the following factors:

- Product composition – all ingredients and their purposes are considered. The presence of medicinal ingredients is not sufficient to meet the requirements of an NHP.
- Product representation – indication of use and claims are considered. For example, the label mentioning flavour may support the classification of a food. Where the product is intended to be sold is also considered.
- Product format – the presentation of the product, such as its packaging, is considered. NHPs are sold in a format that they can be consumed in measured or controlled amounts.
- Public perception and history of use.

Appendix 1 of the Guidance Document contains general rules on the classification of categories of products into either foods or NHPs. A high-level summary of these classification rules suggests that products with a format and perception that is consistent with food products will likely be classified as a food.

5.2.3 Cosmetics

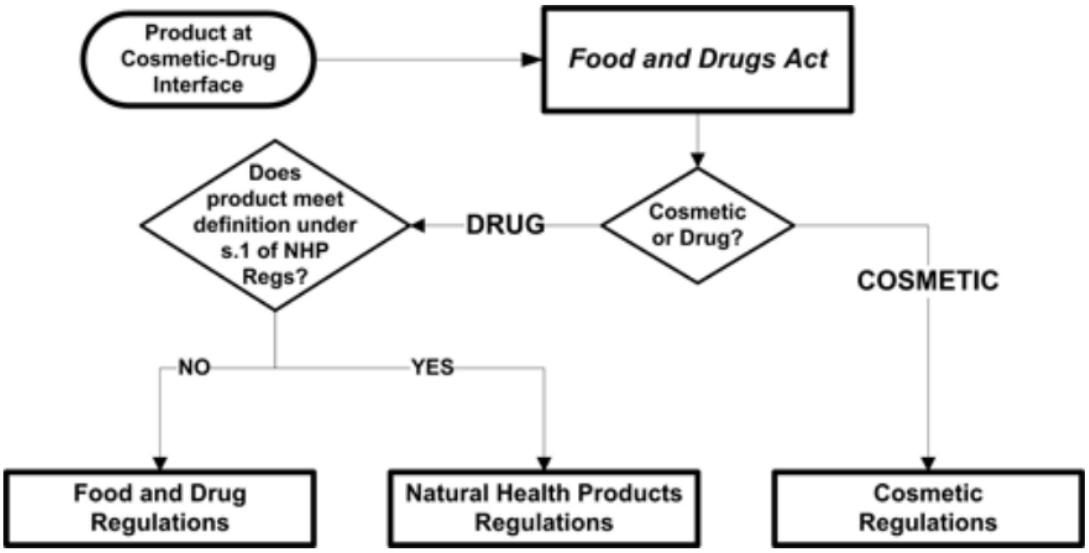
The Canadian Government has released a Guidance Document on the classification of products that share characteristics of a cosmetic and a drug. Cosmetics at the cosmetic-drug interface are perceived to, at the minimum, have characteristics such as cleansing, altering complexion, skin, hair, or teeth, and may also have drug attributes. The following factors are considered when making a decision on classification:

- Representation – indication of use and claims made are considered. The general perception of whether the product would typically be characterised as a drug is also considered.
- Product composition – ingredients and their purposes are considered.
- Level of action – cosmetic products must have a solely superficial effect to generally be considered a cosmetic.
- Other considerations such as the risk of inefficacy, precedence and classification schemes of other jurisdictions are considered.

Cosmetics can further be classified as NHPs if they contain a substance in Schedule 1 of the NHPR.

The figure below shows the regulatory regimes for classifying a product at the cosmetic-drug interface.

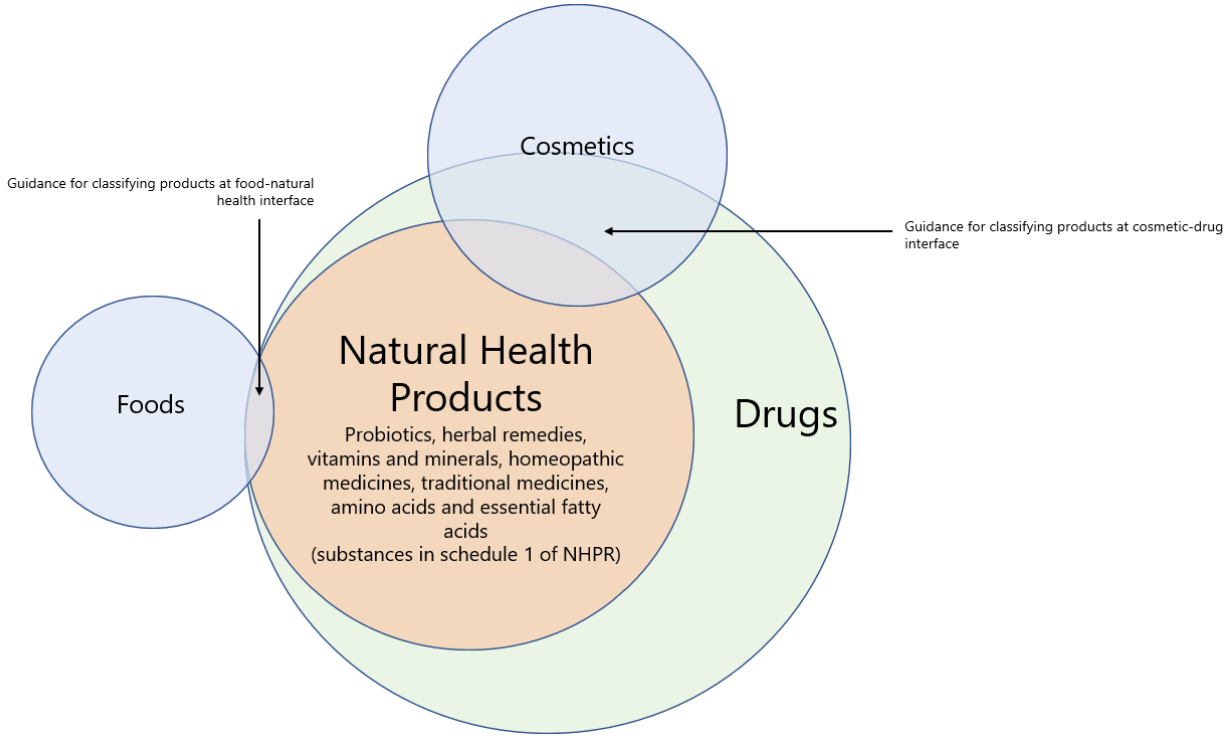
Figure 7: Regulatory regimes of classifying cosmetic-drug interface products



Source: Health Canada, retrieved from www.canada.ca

The figure below highlights our perception of products at the Canadian NHP interface. The overlaps represent where there might be potential grey areas in terms of understanding the classification of a product.

Figure 8: Products at the NHP interface in Canada



5.3 Getting a product on the market

5.3.1 Licensing

A product licence must be obtained for the sale of a NHP (NHPR ss4). NHPR ss5 outlines the requirements for a licence application. A summary of the application form can be found here. Licence application requires:

- contact information
- medicinal ingredients used in the product:
  - their proper names and common names
  - quantity per dosage
  - if applicable, its potency
  - description of its source material
  - indication of whether it is synthetically manufactured
- non-medicinal ingredient used in the product and its purpose
- each brand name under which the product will be sold
- the recommended conditions for use of the product
- information on the safety and efficacy of its use
- the text of labels that will be used with the product
- an attestation that the product will follow the requirements of GMP in Part 3 of the NHPR. These requirements are recommendations of safety, competence, and sanitation aspects of the manufacturing of NHPs.

There is a 60-day disposition clause, which allows for fast-tracking of product licensing decisions if the NHP has only one medicinal ingredient contained in the Compendium of single-ingredient monographs, or if the combination of medicinal ingredients is included in the Natural and Non-prescription Health Products Directorate (NNHPD) Compendium of Monographs. This is essentially pre-cleared information that has been reviewed by the NNHPD and is acceptable. The monographs also contain information on acceptable directions for use, dosage, and other acceptable wording for labels based on the ingredients of the product.

There are three general classes of applications (see Natural Health Products Management of Applications Policy):

1. Class II

   These applications must comply with all parameters of an individual monograph. Modifications to any of the parameters of a monograph are not permitted.

2. Class II

   Applications supported by a combination of two or more monographs. There may be slight deviations to monograph statement so long as they maintain the intent.

3. Class III

   Essentially for any other application that does not follow monographs, i.e., is not captured in Class I or II above. This application can be used for the following scenarios:

   - Products with a novel preparation and/or dosage delivery system presenting unique safety and/or efficacy profiles.
   - Applications referencing a Master File to support safety, efficacy and/or quality (see section 4.5 for information on Master Files, including a definition).
   - Products with ingredient combination issues (including those covered by a monograph) that may require safety assessment. These combinations include but are not exclusive to particular lower certainty combinations and combination risk factors (e.g. stimulant laxatives combined with diuretics, weight management ingredients/claims in combination with diuretics, combination hormonal effect products, combination sedative ingredients). These combinations are reviewed on a case-by-case basis.
   - Applications partially referencing monograph information but going beyond the parameters established in the relevant monograph(s). For example, a dosage form or route of administration not indicated on the monograph(s) that requires further assessment.
   - Homeopathic applications with specific claims.

The application is approved by fulfilling the requirements of the application and meeting the requirements of evidence to substantiate health claims highlighted in section 5.5 of this report. If requested, the applicant must also submit additional information and/or samples. According to Smith et al. (2014), acceptable evidence can come from a range of sources, such as clinical studies, pharmacopoeias, textbooks, peer-reviewed published articles, regulatory authority reports and traditional references (see homeopathic labels in section 5.10.1 of this report). Upon approval, the NHP receives a product number.

If there is a change in the NHP listed under the NHPR ss11, the product licence must be amended by submitting an application that cites the product number, a statement identifying the changes made, revised text of the label (if applicable) and/or a copy of revised specifications (if applicable). To broadly summarise, the changes made that would constitute an amendment are:

- a change in recommended dosage or use
- a change in ingredients or their potency
- changes affecting safety or efficacy that does not arise from changes in ingredients, quantity of ingredients, dosage, or how the product is administered
- changes in specifications such as the removal or modification of a test method.

NHPs that have been affected by changes but not yet licensed cannot be sold.

In contrast to the regulatory requirements in the USA that are highlighted in section 6.3 of this report, many Canadian firms comply with regulatory requirements, which could be a testament to the effectiveness of a pre-market authorisation process (Laeeque et al., 2006). However, this study also cites the concern that it is easier for large firms to comply with regulations, while smaller businesses may struggle and lack assistance to adhere to rigorous rules and requirements.

There are also challenges arising from being able to monitor licensed products. The Canadian Office of the Auditor General (COAG) found that because there were no fees associated with applying for a product licence, many companies apply for hypothetical products that do not become developed. This leads to a large number of site licences that Health Canada is not able to keep track of and monitor (see COAG).

5.4 Permissible ingredients

Generally, a drug is considered an NHP if it contains a substance in Schedule 1 of the NHPR, but not if it contains a substance in Schedule 2 of the NHPR.

As highlighted in section 5.3.1 of this report, there is a fast-tracked process for licensing an NHP if the NHP has a single ingredient which is contained in the Compendium of single-ingredient monographs, or a combination of ingredients not exceeding the dosage specified in the Compendium of Monographs.

5.5 Health benefit claims

5.5.1 Advertising and sale of NHPs

NHPs must make a health claim and can generally make the same health claims as non-prescription drugs. An NHP cannot be sold as a medicine if it does not have supporting proof of efficacy and safety.

There are restrictions on the types of claims an NHP can make. The NHPR ss103.2 allows NHPs to be advertised and sold representing themselves as preventatives to diseases, disorders or abnormalities listed in Schedule A.1 of the Act, but not as treatments or cures. The diseases, disorders and abnormalities in Schedule A.1 are generally serious diseases that are difficult to treat or cure, ranging

from asthma to psychosis, and include conditions such as obesity and alcoholism. Applicants can reference a monograph to substantiate the safety and efficacy of a product (Smith et al., 2014).

Risk-based assessment

Health Canada conducts a risk-based assessment approach based on the seriousness of the health claim. The assessment approach is highlighted in Figure 9. The higher the level of risk, the more evidence is required to substantiate the health claim. Page 15 and 16 of the Pathway for Licensing document guidance on the efficacy evidence required to substantiate health claims at each risk level.

For context, the low-risk category of NHPs generally includes most vitamins, minerals, and essential nutrients. The general types of health claims that have low therapeutic impact include:

- claims to support the maintenance of health, e.g. source of vitamin C to support good health, promotes liver health, etc.
- claims to relieve minimal conditions, e.g. relieves dry eyes, helps to relieve runny nose, etc.
- claims for minor conditions, e.g. helps to reduce the recurrence of cold sores
- claims that, if they are ineffective, cause little to no harm, e.g. claims of anti-flatulence.

More serious health claims may indicate preventions, treatments or cures to diseases, disorders and abnormalities in, but are not limited to, Schedule A.1 of the Food and Drug Regulation Act. Evidence must be provided for all medicinal ingredients in the NHP, and all evidence must be relevant and critically reviewed by the Regulator. The full evidence criteria can be found in Appendix F of the Pathway for Licensing document. Low-risk products have pre-cleared information for which claims relating to their safety, efficacy and quality are readily available. Pre-cleared information includes pharmacopoeias, monographs, labelling standards, opinion reports, international standards, and information from other regulatory bodies including their market authorisation decisions (Mine & Young, 2009).

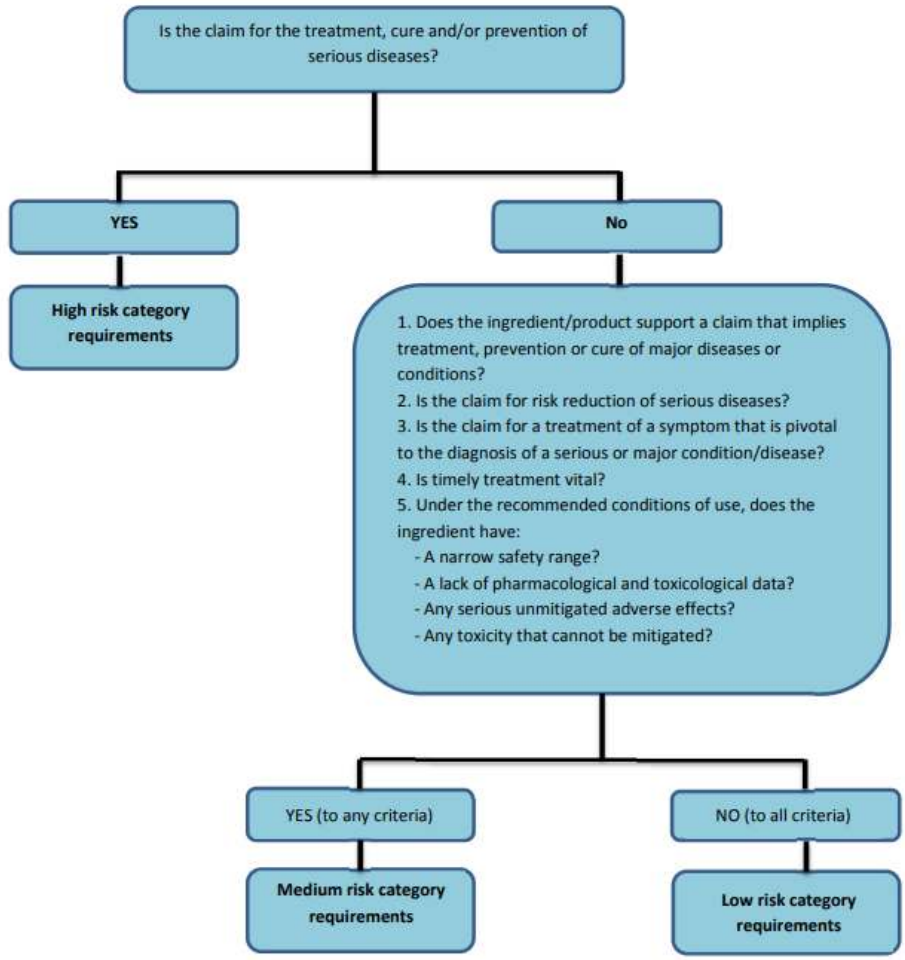
The following table is recreated from Mine & Young (2009) and highlights the traditional and non-traditional evidence required to substantiate a health claim.

Table 7: Description and evidence required for traditional and non-traditional claims

Claim category	Description	Evidence of efficacy
Traditional	Refers to the practices, based on the experience of indigenous or different cultures, used in the maintenance of health or the prevention, diagnosis or treatment of physical and/or mental illness for at least 50 consecutive years.	At least two independent references.
Non-traditional	Any use that does not conform to the description of "traditional" above.	Supported by a variety of scientific evidence ranging from highest to lowest strength: • randomised control clinical trials • non-randomised and non-control clinical trials • descriptive and observational studies

		• expert opinion reports, peer-reviewed published articles, conclusions of other agencies • references to traditional uses.

Figure 9: Risk-based approach for determining safety and efficacy evidence for NHPs making modern health claims



Source: Health Canada, retrieved from www.canada.ca

Criticism

Despite having robust regulations surrounding health claims, in 2021, the OACG claimed that Health Canada did not sufficiently monitor whether the product labels and advertising complied with its product licence. The OACG found that from a sample of 75 NHPs, 88 per cent of products were advertised with misleading information, while 56 per cent were labelled with misleading information, including (see OACG):

- unauthorised health claims

- erroneous statement claiming product was recommended for children aged three and over when it was only authorised for adolescents and adults
- an incomplete list of risks and authorised ingredients
- incorrect dosage of medicinal ingredients
- ineligible label information, such as safety warnings.

5.5.2 Food health claims

Although the distinction between food and NHPs can sometimes be ambiguous, regulations around health claims for food in Canada are markedly different from NHPs. The marketing of food must neither be false nor misleading. Health claims are optional for foods, and are also subject to Section 3 of the Food and Drugs Act in that they cannot represent themselves to be a treatment, preventative, or cure for diseases, disorders or abnormalities in Schedule A.1 of the Act.

5.5.3 Cosmetic products

Health Canada has released Guidelines for Cosmetic Advertising and Labelling Claims. This document highlights acceptable and unacceptable claims that cosmetic products can make by category. Acceptable claims can generally describe the product's effect on a person's appearance, and the performance of a product without attributing a therapeutic effect, for example, "makes hair soft and healthy looking." Unacceptable claims attribute a therapeutic effect, for example, "makes your hair grow."

5.6 Manufacturing requirements

Subject to Part 2 of the NHPR, companies must hold a site licence to manufacture, package, label or import NHPs that they intend to sell. The application requirements to manufacture an NHP are highlighted below.

Part 3 of the NHPR highlights manufacturing processes that NHP manufacturers must comply with to be able to sell an NHP. This generally includes processes and procedures to ensure clean, safe and functional premises and equipment, as well as trained and competent personnel.

It is also a requirement that someone with training, experience and technical knowledge in quality assurance is responsible for assuring the quality of the NHP. This person must also approve the manufacturing, packaging, labelling and storage processes.

The manufacturer/importer of NHPs must also determine the period of time where after being packaged for sale, the NHP maintains purity and physical characteristics and its medicinal ingredients maintain their quantity per dosage and potency when it is either stored in ideal conditions, or if not applicable, when it is stored at room temperature (s52 of the NHPR).

Under s53 of the NHPR, manufacturers are required to maintain an extensive list of records at the site where the NHP is manufactured for one year following the expiry date of the NHP, including records of all steps of the manufacturing process. Section 55 of the NHPR outlines the record-keeping requirements for labellers of NHPs. Records generally relate to ensuring that labellers follow the requirements of the NHPR, recalling all products made available for sale, listing all NHPs being

labelled at the site, and a copy of the sanitation programme in use. This must again be kept for a year following the expiration date of the NHP.

Sterile NHPs

Sterile NHPs must be manufactured and packaged in a separate, enclosed area under the supervision of a trained microbiologist. Sterile NHP manufacturers must also use a scientifically proven sterilisation method (see s59 of the NHPR). Examples of NHPs that are required to be sterile include those for ophthalmic use (see below), including homeopathic products for ophthalmic use.

NHPs for ophthalmic use

These are subject to regulation under sC.01.064 and sC.01.065 of the Food and Drug Regulations. These sections state that ophthalmic drugs must contain a minimal amount of a preservative ingredient necessary to preserve the drug, while not interfering with the therapeutic properties of the drug. It also requires the drug to be sterile and tested to ensure that the drug is accurately representing its proper name.

Criticism

During its 2021 audit of NHPs, the OACG found that Health Canada did not have a programme to conduct routine on-site inspections of manufacturing sites. Other jurisdictions like Australia developed a cycle for conducting routine inspections of manufacturers (see OACG).

In addition, Health Canada only inspected a limited number of high-risk licensed manufacturers and those that manufactured sterile products. It did not inspect licensed manufacturing sites for products:

- for vulnerable populations such as children and pregnant or breastfeeding women
- making claims for specific health conditions like diabetes
- with a compliance history of having substituted ingredients.

5.6.1 Site licence application

Manufacturers must submit to the NNHPD (see the Site Licensing Guidance Document):

- a site licence application form
- evidence of GMP compliance such as:
    - Drug Establishment Licence (DEL) – lists buildings and activities that are authorised for drug products under the Food and Drug Act
    - Foreign Site Reference Number (FSRM) Authorisation – demonstrates that a foreign site is compliant with GMP
    - GMP Certificate – a certificate granted by a qualified authority upon an inspection of a manufacturer's processes.
- Designated Party Authorisation Form (if applicable) – only if the licensee has designated a third party to file a submission to NNHPD.

5.6.2 Record keeping

Manufacturers, packagers, labellers, importers, and distributors must maintain the relevant NHP records for one year following the expiry date of the NHP, outlined in GMP, sections 53 to 58 of the NHPR. The specific records that must be maintained vary depending on the activity that is carried out. For instance, manufacturers must maintain extensive records compared to distributors.

5.6.3 Applying for a licence to manufacture

Application for a site licence requires the following information:

(a) Contact information.
(b) A statement that specifies their activity or activities, e.g. manufacturing, packaging, labelling or importing.
(c) If manufacturing, packaging, or labelling, the address of the location where these activities will take place. If importing, the address where the products will be stored.
(d) Whether the product that the activity is pertaining to is in sterile dosage form.
(e) Equipment, practices, and procedures used to conduct the activity in (b) above.
(f) A report from a quality assurance person that the site licence applicant complies with the requirements of good manufacturing practices (Part 3 of the NHPR).

5.7 Exporting requirements

NHPs are subject to the regulations around exporting drugs highlighted in sA.01.045 to sA.01.048 of the Food and Drug Regulations. This generally means that NHPs must be licensed through the requirements outlined in section 5.3.1 of this report, although unlicensed NHPs can also be exported provided:

- they are manufactured or prepared in Canada
- they are manufactured for the purpose of export only, and not made for consumption in Canada
- an export certificate is obtained that states the product does not contravene any known laws of the importing country.

Classification allows the unlicensed NHP solely for export to be exempt from s8, ss9(1) and s11 of the Food and Drugs Act, so long as the importing country does not have regulations which could potentially reverse the exemption.

Exporters of NHPs are required to sign and issue an export certificate as outlined in Section A.01.045 of the Food and Drugs Act. In 2013, Health Canada transferred the responsibility of International Trade Certificates (ITCs) to third parties; for instance, Food, Health & Consumer Products of Canada and Cosmetics Alliance Canada. It should be noted that ITCs are not required under NHPR. However, ITCs may be a requirement from importing countries. This can be a potential problem for exporting to countries such as China, who require authorisation from relevant government agencies to import NHPs (see section 7.8 of this report).

5.8 Importing requirements

Importers must generally adhere to the manufacturing requirements outlined in section 5.6 of this report except for maintaining the records required by a manufacturer outlined in s53 of the NHPR. In lieu of these records, s56 of the NHPR specifies that importers must maintain the following records for one year following the expiry date of the NHP:

(a) The master production document for the NHP.
(b) A list of all ingredients contained in each lot or batch of the NHP.
(c) Records of any testing conducted by or for the importer in respect of a lot or batch of the NHP.
(d) A copy of the specifications for the NHP.
(e) A record of each determination made by the importer in accordance with section 52 and the information that supports that determination.
(f) Records containing sufficient information to enable the recall of every lot or batch of the NHP that has been made available for sale.
(g) A copy of the sanitation program in use by the importer.

Section 100 of the NHPR states that sections A.01.040 to A.01.044 of the Food and Drug Regulations apply to imported NHPs. This allows inspectors to take samples of and examine an NHP that is being imported. If the NHP is found to breach the NHPR or the Food and Drugs Act, the importer must then detail the purpose of importation, and relabel or modify the NHP so that it can be sold in accordance with its regulations.

5.9 Exemption requirements

Importing for personal use

Residents and visitors are allowed to bring up to a 90-day supply or a single course of treatment of an NHP for personal use without the requirements in section 5.8 of this report.

Exemptions to practices (see 1.4 of Site Licensing Guidance Document)

Practitioners that compound NHPs for the sale solely to an individual who requests it, such as pharmacists, aboriginal healers, TCM practitioners and general health care practitioners, do not require a licence. See the NHP Compounding Policy for what Health Canada defines as compounding.

Other exemptions (see 1.4 of Site Licence Guidance Document)

The following are exempt from having to obtain a site licence:

- Manufacturers that produce NHPs for the sole purpose of exporting by invoking Section 37 of the Food and Drugs Act.
- Distributors that do not import NHPs. A distributor is one who sells NHPs for the purpose of reselling.
- Manufacturing, packaging, labelling, or importing NHPs for a clinical trial.
- Testing labs.

5.10 Specific groups of products

5.10.1 Homeopathy

Homeopathic products are regulated as an NHP in Canada (see section 5.2.1 of this report). Homeopathic products include a "DIN-HM" number, which is used as an indication that it is a homeopathic product (see Information on Homeopathic Products). Recently new labelling requirements were introduced for homeopathic products in Canada. They must now include the statement "This/These claim(s) is/are based on traditional homeopathic references and not modern scientific evidence" (Information on Homeopathic Products).

Homeopathic products with certain ingredients may only be authorised for sale if they meet a minimum homeopathic potency established by the NNHPD (see Evidence for homeopathic medicines). Products in Appendix 2 of this page are also not eligible for a DIN-HM number.

5.10.2 Aromatherapy

There is a monograph for Aromatherapy when it is regulated as an NHP.

5.10.3 Kava

Kava is traditionally consumed in ceremonial or social settings. In 2002, Health Canada issued a stop sale order for kava or products containing kava, but now classifies it as an NHP under Schedule 1 of the NHPR (being derived from a plant). However, there are still safety concerns around kava due to hepatotoxicity risks. Consequently, the amount of kavalactones present in the product must be declared during the application process. Furthermore, as highlighted in 5.5.1, NHPs such as kava or products containing kava must make a health claim, include directions for use and list ingredients.

6. United States

6.1 Legislative definitions

Dietary supplement – is intended for ingestion and contains at least one dietary ingredient (vitamins and minerals, herbs and other botanicals, amino acids, and probiotics).

New dietary ingredient (see FDA) – a dietary ingredient that was not marketed in the US in a dietary supplement before 15 October 1994.

6.2 Definitional interface

6.2.1 Dietary supplement

Dietary supplements

With the exception of homeopathic products, products captured as dietary supplements are equivalent to NHPs in Canada (Nichini, 2022). They are also similar to complementary medicines in Australia with the exception of a few products, including but not limited to homeopathic products, essential oils, toothpastes and sunscreens. Dietary supplements are not presented as conventional food as a "sole item of a meal or diet," but can take the form of a conventional food such as teas or bars (FDA). Dietary supplements must be appropriately labelled as dietary supplements or something similar, e.g. "iron supplement." Dietary supplements are ingested in the form of tablets, capsules, powders, softgel, gelcaps, teas, bars, or liquid form (specified under s411(c)(1)(B)(i) of the Federal Food, Drug, and Cosmetic Act).

Traditional medicines

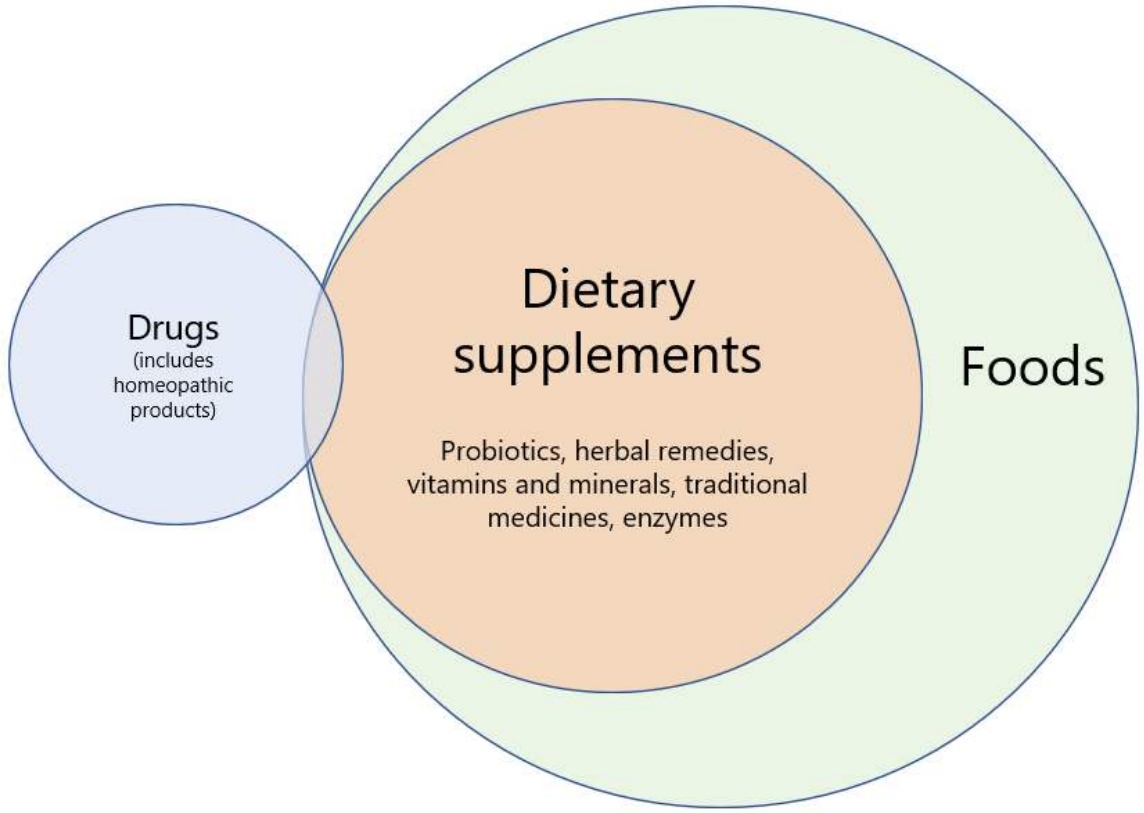
Traditional medicines such as TCMs are generally captured under dietary supplements if they include herbal and botanical ingredients and follow the criteria of the definition of a dietary supplement (Gilbert, 2011). If they are ingested, they are classified as a dietary supplement. If traditional medicines are applied externally, they are captured under the definition of a cosmetic (see FDA).

6.2.2 Homeopathic products

Homeopathic products are subject to the same regulations as other drug products, although there are currently no homeopathic products that have been approved by the Food and Drug Administration (FDA). However, if a homeopathic product contains at least one dietary ingredient, it is not considered a homeopathic product, but a dietary supplement.

Figure 10 below shows our interpretation of products at the dietary supplement interface in the US.

Figure 10: Products at the dietary supplement interface in the US



6.3 Getting a product on the market

6.3.1 Dietary supplements

Dietary supplements and conventional food do not require pre-market authorisation from the FDA. Dietary products are subject to regulatory action if they do not meet the regulatory requirements, such as adulterated products, unapproved or misrepresented claims, non-compliance with GMP, or if ingredients are unapproved "new drugs." New drugs refer to drugs that are not recognised by experts to use under the prescriptions prescribed or recommended in the labelling. The lack of a pre-market authorisation process has come under scrutiny, in that despite having regulatory requirements, the absent authorisation process creates disincentives from following regulatory requirements. Examples of this, notably by Starr (2015), are highlighted throughout this chapter.

The Dietary Supplements Listing Act of 2022 was introduced as a Bill into Congress. The aim of this Bill was to provide greater regulation surrounding the transparency of dietary supplements by requiring manufacturers to provide the FDA with product information, including their names, ingredients, warnings, labels, allergens and a list of health claims or structure/function claims. The legislation did not pass (Talkington, 2023).

However, a pre-market notification to the FDA must be made at least 75 days prior to entering the market if the dietary supplement contains a new dietary ingredient. See FDA for the new dietary

ingredient process. New dietary ingredients are considered adulterated under section 402(f) of the FD&C Act except if:

- the dietary ingredients have been used in conventional foods where the foods have not been chemically altered
- there is a history of use or other evidence that establishes the safety of the dietary ingredient.

If the dietary ingredients do not meet the above requirements, evidence that establishes the safety of the ingredient can be included alongside the pre-market authorisation. Despite pre-market notification of dietary ingredients being a regulatory requirement, it has been documented that this is only done for a very small proportion of new dietary ingredients (Starr, 2015). This has been highlighted to be one of many issues that arise from the lack of a pre-market authorisation framework.

6.4 Permissible ingredients

Dietary supplements must contain at least one dietary supplement which include vitamins, minerals, herbs, amino acids and enzymes. A full directory of dietary ingredients can be found here.

6.5 Health benefit claims

Health claims are optional for dietary supplements. The health claims that can be made by dietary supplements in the US are heavily restricted. Unlike in Canada, dietary supplements are considered to be food, and therefore are not allowed to make claims that they are able to prevent, treat or cure diseases or other conditions (Nichini, 2022). Claims are typically restricted to the following:

1. Claims affecting the structure and function of the human body and may further characterise how a dietary ingredient maintains structure and function in the human body, e.g. "calcium builds strong bones."
2. General wellbeing claims from the consumption of a nutrient or supplementary ingredient.
3. Nutrient deficiency disease claims, which must state the relationship between a nutrient and deficiency diseases and must also be reasonably substantiated (e.g. vitamin C and scurvy).

The FDA does not pre-approve claims before the dietary supplement is on the market, but the manufacturer must submit a notification with the text of the claim to the FDA within 30 days of marketing a dietary supplement with a claim (see FDA).

The manufacturer must also include a disclaimer that the FDA has not evaluated the claim, and that the dietary supplement is not intended to diagnose, treat, cure, or prevent any disease (FDA).

6.6 Manufacturing requirements

6.6.1 Dietary supplements

The FDA has published a compliance guide for small entities for current good processes of manufacturing, packaging, labelling and storage of dietary supplements. This outlines rules for personnel, sanitation, equipment, quality control, components for packaging, and manufacturing

operations including laboratory, production, packaging, labelling, storage and distribution. Compliance is mandatory to ensure a dietary supplement can stay on the market and is not subject to regulatory action:

- personnel (Subpart B of 21 CFR 111)
- facility (Subpart C of 21 CFR 111)
- equipment (Subpart D of 21 CFR 111)
- production and process control system (Subpart E of 21 CFR 111)
- quality control (Subpart F of 21 CFR 111)
- records and record-keeping (Subpart P of 21 CFR 111 / Subpart F of 21 CFR 111)
- packaging and labelling – subparts G (products received) and L (products manufactured)
- lab operations – Subpart J
- manufacturing operations – Subpart K
- storage – Subpart M
- returned products – Subpart N
- complaints – Subpart O.

Records outlined in subpart P and F of 21 CFR 111 must be kept for either:

- one year past the shelf-life date of dietary supplements (if shelf life used), or
- two years after the distribution of the batch of dietary supplements.

However, Starr (2015) highlights issues with the regulatory framework, despite GMP being a regulatory requirement. A 2010 US Government Accountability Office report on the analysis of 40 dietary supplements found traces of contaminants in 93 per cent of the products.

6.7 Exporting requirements

A "Certificate of Free Sale" is available for the export of dietary supplements. Compared to conventional foods which require a "Certificate of Exportability," there is no fee associated with the free sale certificate (see Online Applications for Export Certificates for Food). The free sale certificate is generally a requirement from certain importing countries that certifies that goods intended for export are sold freely and lawfully in the origin country.

6.8 Importing requirements

As in 6.3.1, of this report the FDA does not authorise dietary supplements prior to entering the market, so imports can be made without a licence (USA Customs and Clearance). However, if any of the ingredients in the dietary supplements are of animal origin, a permit that ensures animal products are permitted from the Animal and Plant Health Inspection Service (APHIS) is required (see APHIS website). APHIS has created an assistant tool that helps determine whether a permit is needed to import a product based on ingredients of animal origin and to assist with processing a permit. There is also a detailed guide for animal products that do not require a permit.

Importing dietary supplements requires the importer to follow the same rules as if they were importing food products. These rules are to generally ensure that the manufacturing process of the product undergoes a similar process as it would have if manufactured in the US. USA Customs and

Clearance recommends considering Prior Notice, good processes of manufacturing, packaging, labelling and storage of dietary supplements outlined in section 6.6.1 of this report, and the foreign supplier verification program (FSVP).

Prior Notice must be filed with the FDA for all dietary supplements before the shipment arrives in the US. It generally includes information on the origin of the product and the origin of the shipment. The FSVP ensures that dietary supplements and other foods are produced in a manner that ensures the same level of public health as it would if it were produced in the US.

6.9 Exemption requirements

This section does not apply to regulations in the US because licensing is not required for manufacturing, marketing, or the supply of dietary supplements.

6.10 Specific groups of products

6.10.1 Homeopathy

Homeopathic products are not classified as dietary supplements in the US and are regulated as drugs. The FDA has released information on the regulation of homeopathic products. Homeopathic products in the US must include the word "homeopathic" on the label and ingredients used in terms of dilution. There are currently no homeopathic products that have been approved by the FDA, i.e. the FDA has not verified any claims that homeopathic products have made on treating, curing or preventing conditions. It therefore warns that homeopathic products potentially pose a higher risk to public health (see the FDA's guidance document). However, the FDA does have a framework for enforcing laws surrounding illegal marketing of homeopathic products which can be found under its FDA staff and industry guidance document.

6.10.2 Aromatherapy

The FDA has a page that defines aromatherapy on the drug-cosmetic interface. Depending on the purpose of the product, aromatherapy can be marketed as a drug, cosmetic or both. If the product is intended for superficial effects, such as cleansing or smell, it is defined as a cosmetic. If the product has claims of preventing, treating or mitigating conditions, it is defined as a drug. Products that make both cosmetic and drug claims can be defined as both, and as such must meet the requirements for both cosmetics and drugs. No claim, ingredient, direction for use, or aspect of labelling, whether cosmetic or other, must be misleading.

7. China

7.1 Legislative definitions

Drug – substance used to prevent, treat, or diagnose human diseases and is intended to regulate human physiological functions, for which usage and dosage are specified for indication/primary treatment. Under the Drug Administration Law (DAL), drugs are categorised into three types:

- Traditional Chinese medicines (TCMs).

  TCMs are defined in Article 2 of the Traditional Chinese Medicine and Drug Law (henceforth the TCM Law, in Chinese) as "the collective name for the medicines of all ethnic groups in [China], including the medicines of the Han and ethnic minorities. It reflects the Chinese nation's understanding of life, health and disease and has a long historical tradition and unique theories and technical methods."

- Chemical drugs.
- Biological products.

Foods for special medical purposes (FSMP) – specifically processed and prepared foods for special needs of the population groups with eating restrictions, disorders of digestion and absorption, metabolic disorders, or special diseases with respect to nutrients or diets.

Health foods – which are foods with specific health functions or for the purpose of supplementing vitamins and minerals, which are suitable for special population groups to eat, have functions of regulating the body, are not aimed at curing diseases, and will not cause any acute, sub-acute or chronic harm to the human body. The nature, use, purpose, and formulation of vitamins and minerals determines whether they are registered as health foods or drugs.

7.2 Definitional interface

7.2.1 Traditional Chinese medicines

TCMs are classified as drugs (see section 7.1 of this report). Ji et al., (2022) describes TCMs as "The traditional medicine that originated in China and is characterised by holism and treatment based on pattern identification/syndrome differentiation." An expert states that there is a well-defined theoretical framework amongst the many ethnic groups in China for TCMs. There is therefore an evidence-based mechanism for the standardisation of TCMs.

There are two laws that regulate TCMs:

1. Drug Administration Law (DAL) – The DAL regulates all drugs, including chemical drugs, biological products and TCMs. Article 1 of the DAL states that the purpose of the law is to "to strengthen drug administration, ensure drug quality, protect drug safety and legitimate rights and interests of the public, and protect and promote public health." This is administered by the National Medical Products Association (NMPA).

2. TCM Law (in Chinese) – an expert verified that this is largely to protect the cultural aspects and support the development of TCMs. We understand that in addition to its protective mechanism, it also manages the use of chemicals in the cultivation of Chinese medicinal materials. The TCM Law is administered by the National Administration of Traditional Chinese Medicine (NATCM).

Chinese medicinal materials and crude drugs

Drugs or ingredients from plants, animals and microbial origin that have not undergone extensive processing (beyond cutting or drying) do not require NMPA approval to be marketed, except for where they are listed as subject to approval designated by NMPA and NATCM.

7.2.2 Special foods

Special foods could be classified into health foods or FSMPs. Health foods or FSMPs are regulated differently from regular food products. They include products such as vitamins, minerals, probiotics, etc.

Health foods are food products (e.g. supplements) which may have health function claims on a scientific evidence basis. **FSMPs** are food products made using a special processing formula to meet special dietary needs, e.g. limited feeding, digestion absorption disorders, metabolism disorders or conditions arising from diseases (Chemical Inspection and Regulation Service).

Health foods and FSMPs are also not regulated by the Traditional Medicine and Drug Law, and thus are considered separately from TCMs. However, there are several Chinese medicinal materials that could be considered a TCM or a food, and these can be used to make health foods or FSMPs. For instance, deer velvet and ginseng are considered a TCM if grown for a certain length of time (New Zealand Ministry for Primary Industries, 2022). Health foods/FSMPs must not be used as drugs or promoted as having drug efficacy (see s section 7.5.2 of this report).

Article 50 of the Food Safety Law ensures that food products cannot contain medicinal materials.

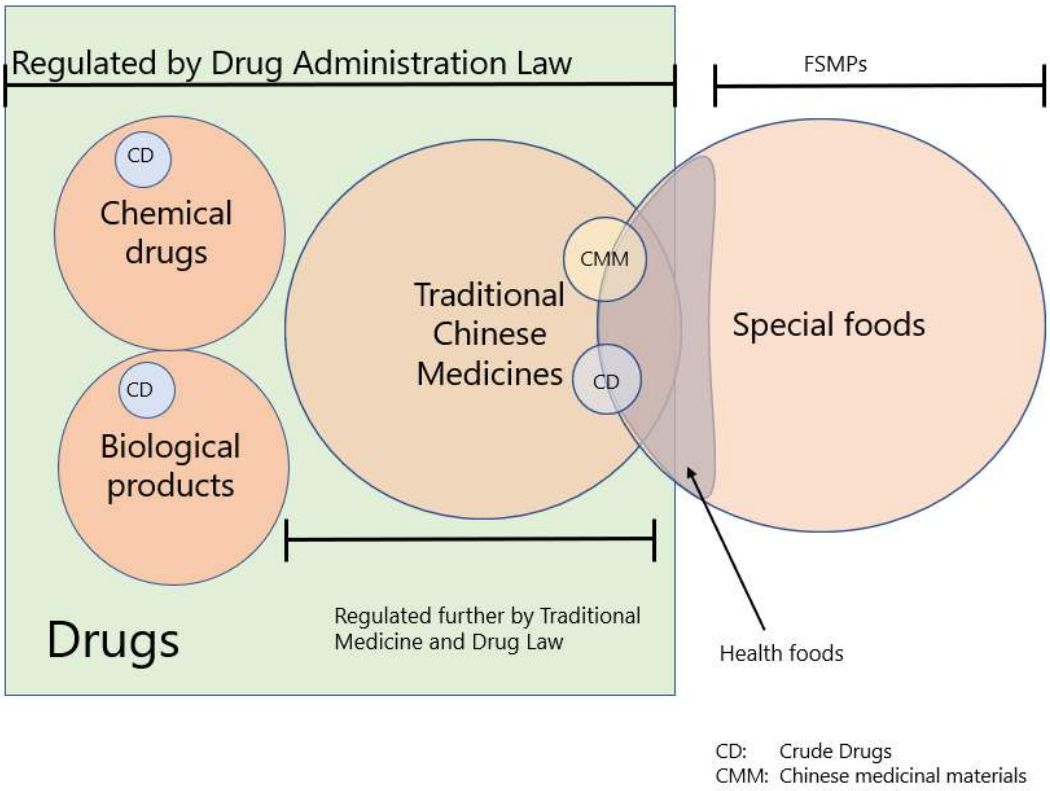
The following table has been recreated from the Chemical Inspection and Regulation Service to illustrate the differences in regulation between health foods and FSMPs.

Table 8: Health foods and FSMPs

	Health food	FSMP
Can claim a health function	Yes	No
Claims to prevent or treat diseases	No	No
Provides energy and nutrition	No	Yes
Can be administered alternatively to oral use	No	Tube use
Daily intake limits	Yes	Yes
Used under supervision of doctor or clinical dietitian	No	Yes
Can contain substances used in both foods and drugs	Yes	No
Allowed to have side effects on humans	No	No

The figure below shows our interpretation of products at the food/drug interface.

Figure 11: Products at the food/drug interface



7.3 Getting a product on the market

7.3.1 Traditional Chinese medicines

NMPA regulates the registration of products, and undertakes standards management of all drugs in China, including TCMs. The National Administration of Traditional Chinese Medicine (NATCM) is responsible for the regulation and development of TCMs. The NATCM also monitors all tertiary courses of TCMs (Chan, 2005).

Article 24 of the DAL states that drugs (generally including TCMs) are subject to licence approval by the NMPA (DAL and Thomson Reuters).[8] However, there is an exception to Chinese medicinal materials and crude drugs (raw natural materials used in TCM formulation), which do not require review and approval except for those subject to review.

The process for authorising TCMs to sell on the market is generally the same as with other drugs, i.e. chemical drugs and biological products, in that the TCM must receive market authorisation by applying to the NMPA – the application must follow the International Council for Harmonisation of

[8] May require institutional access or a free trial to access this webpage.

Technical Requirements for Pharmaceuticals for Human Use (M4) to prove the drug's safety, efficacy, and quality. It should also include data from any clinical trials. There are three different types of authorisation applications:

- **Initial registration**: for new products on the market. The application is submitted to the NMPA's Centre for Drug Evaluation, which performs a check on the active ingredients of the drug. If authorised, the applicant receives a drug registration certificate and becomes a market authorisation holder (MAH) for the drug. To avoid doubt, an MAH is issued specifically to a drug product, and will specify the active ingredients, dosage form, and strength.
- **Re-registration:** to renew the five-year term of the initial certification.
- **Supplemental registration:** made when there are changes to drugs that already have certification, such as changes related to drug safety and efficacy claims, or a change of MAH.

However, the market authorisation process can be waived if the drug is imported in small amounts by a medical institution for urgent clinical needs, or a small number of drugs is imported for personal use.

The requirements for the registration dossier for a new TCM in China (for each new potential MAH) are (Liang et al. 2021):

- the production information of crude drugs used in the TCM
- the resource evaluation of crude drugs used in the TCM
- quality standards study data of crude drugs used in the TCM
- test report on crude drugs used in the TCM
- quality data on corresponding objects of substance benchmark
- data on the manufacturing method at each step
- manufacturing verification or recorded data
- description of manufacturing method
- data for containers and packaging
- single-dose toxicity report
- repeated-dose toxicity report
- carcinogenicity report (on a case basis)
- reproductive toxicity report (on a case basis)
- reference documentation on product efficacy.

We were not able to identify the exact requirements of each item in the registration dossier, but the documentation required should give an informed indication of what is considered before market approval is provided. It should be noted that according to Liang et al. (2021), there is a simplified process for becoming an MAH for TCMs that have a long-standing history of use, assuming there is a credible historical safety and efficacy. However, we have not been able to identify legislative records that confirm this.

The stages of the application process are:

1. A formal review by NMPA's Administrative Services Centre.
2. Sample testing by the drug control institute (fees are paid for sample testing).
3. Technical review by the Center for Drug Evaluation (a risk-assessment will determine whether on-site inspections should occur).

4. Administrative review by the NMPA (an official registration fee is paid).

If all requirements are met, including the Good Supply Practice for Drugs (which generally ensures quality control, audits, review, and responsibility), the MAH can distribute the approved product through wholesales or contracts with qualified distributors to sell the approved product, without obtaining additional administrative approvals.

7.3.2 Health foods/Foods for special medical purposes

Article 12 of the Health Food Registration and Filing Management Measures outlines the requirements for the market approval of health foods. This includes:

- an application form
- product research and development report
- ingredients of the product
- evidence of health and safety claims
- sample of product labels and instructions for use
- identity of packaging materials that are in direct contact with food.

If the applicant is importing health foods, the following must also be submitted:

- government registration of the product from the country of origin
- health food certification issued by the relevant government agency
- the technical regulations of health food production in country of origin
- samples of packaging, labels and instructions of the NHP from the country of origin.

7.4 Permissible ingredients

According to an expert, there are two editions of the Chinese Pharmacopeia. The first edition sets out approved TCMs (and other drugs) for use. The 2020 edition of the TCM Pharmacopoeia outlines 2711 approved TCMs and is generally updated every five years. The Pharmacopoeia details monographs for TCMs which generally include standards for ingredients, tests, dosage and strength of drugs. The Chinese Pharmacopoeia Commission is responsible for the formulation of the Chinese Pharmacopoeia, which generally includes research, evaluation of standards, regional coordination of drug standards and performing other tasks that are assigned by the NMPA.

7.5 Health benefit claims

7.5.1 Traditional Chinese medicines

Since TCMs are classified as drugs, TCMs are allowed to claim health indications as long as the drug's safety, efficacy and quality have been proven in the market authorisation process.

7.5.2 Health foods and FSMPs

Under Article 51 of the Food Safety Law, health foods and FSMPs may not make claims that they can be used to treat, prevent or cure diseases. Health foods and FSMPs can make nutritional content

claims under GB 28050-2011 and GB 14880-2012 (Baker McKenzie and NZ Ministry for Primary Industries, 2022). In addition, health foods can make health function claims, such as "supplies vitamin C."

All food products must also indicate whether the following potential allergens are ingredients of the product (Baker McKenzie):

- wheat and gluten
- fish and shellfish
- eggs
- peanuts or other nuts
- soy beans
- dairy products.

From January 2022, labels must also include appropriate warnings and disclaimers, and state "health foods are not medicines and cannot replace medicine to treat diseases" (Article 55 of the Administrative Measures on the Registration and Record Filing of Health Foods).

7.6 Manufacturing requirements

7.6.1 Traditional Chinese medicines

Manufacturers of TCMs are required to follow GMP. GMP for TCMs has requirements surrounding (He et al., 2015):

- personnel
- premises and equipment
- documentation
- self-inspection.

The Good Manufacturing Processes for TCMs (TCM GMP) outlines the requirements for manufacturing TCMs. One area that TCM GMP differs from GMP in other jurisdictions is that there are specific requirements for the harvest and cultivation of Chinese medicinal materials, such as by Article 24. Essentially, the sanitation and maintenance requirements extend to farm tools, while there are specific safety requirements surrounding fertilisers and pesticides, including the dosage and frequency at which they are used, and the prohibition of highly toxic fertilisers and pesticides (such as in Article 50 of TCM GMP).

As such, any breeding procedures, transportation and distribution of seeds and seedlings must also be established, as outlined in Articles 38 and 39 of the TCM GMP.

7.6.2 Applying for a licence to manufacture

After filing for registration of the product on the market, the applicant applies for a food manufacturing licence. The applicant submits the following documentation to their provincial Administration for Market Regulation (AMR) (see Thomson Reuters):[8]

- application form

- manufacturing equipment layout
- flowchart of the health food or food for special medical purpose (FSMP) production
- safety-related standard operating procedure (SOP)
- quality management SOP
- other documents required by the provincial AMR.

The provincial AMR reviews documentation and may also conduct on-site checks before granting a manufacturing licence.

7.7 Exporting requirements

There is a lack of online information in English on exporting TCMs and special foods from China. To our knowledge, there are no special administrative requirements to export health foods and FSMPs outside of China (Thomson Reuters).[8]

However, there may also be restrictions on TCMs being exported from China (Thomson Reuters).[8]

7.8 Importing requirements

7.8.1 Traditional Chinese medicines

Importing TCMs is allowed. They must follow the same MAH approval process outlined in section 7.3.1 of this report (Wang and Lin, 2023). TCMs can only be imported through designated ports of entry.

Stricter requirements apply to first-time imports of TCMs, Chinese medicinal materials and other medicinal materials. A first-time import refers to every new TCM import per exporter, and where an ingredient is not present on the catalogue of non-first-time imported medicinal materials. A first time import will require (see GACC):

- an application form
- a copy of drug production licence or drug business licence
- a copy of government registration of the exporter
- a copy of the purchase contract and notarised documents
- information on harvesting and cultivation processes from the country of origin
- standards and sources of medicinal materials
- official certification of medicinal materials including its identity, samples, appraiser, official seal, etc.

Overseas manufacturers of TCMs of animal origin must register with China's General Administration of Customs (GACC). Registration is granted under the following conditions (see GACC):

- The foreign country's food safety management system is passed.
- The foreign regulator is deemed effective.
- The manufacturer has established GMP for their equivalence of health foods and complies with Chinese laws.
- The product conforms to inspection and quarantine requirements in China.

When the overseas manufacturer first registers a product to the GACC, the ingredients must be included in a list of permitted ingredients that can be found here.

7.8.2 Chinese medicinal materials

Chinese medicinal materials without market authorisation can be imported after obtaining an import permit from the provincial MPA at the port of entry.

7.8.3 Health foods and FSMPs

Generally, health foods and FSMPs must be filed and registered in China. They first undergo the registration process highlighted in section 7.3 of this report, and then subsequently submit the following documentation:

- qualification certificate from the overseas manufacturer
- proof of more than one year's sales, or a safety report
- the relevant laws, standards and regulations that are enforced in the country of origin
- the package, label and instructions of the product that is marketed in the country of origin
- any other documentation required by the State Administration for Market Regulation (SAMR).

Importers must also register as a foreign trade operator with the local commerce bureau and with China's General Administration of Customs (see NZTE requirements and guidance), allow customs to review the imported food and documents, and pay required customs tariffs.

Exceptions to 7.8.3

Health foods approved in another jurisdiction may be able to be distributed without the requirements above if they are sold to consumers in China through cross-border e-commerce (CBEC) and they follow customs and tax requirements associated with CBEC imports (refer to Q25 of Thomson Reuters.)[8] For clarity:

- Online purchase bonded imports mode: imported goods are temporarily stored in a bonded/customs-controlled warehouse in China. Customers' clearance and delivery is made after a consumer places an order. Large levels of stock are required (see Deloitte).
- Direct purchase import mode: overseas suppliers ship the goods to China and the goods clear customs after a consumer has placed an order.

To our understanding, exemptions are issued on a product basis, which are included on the 2019 Positive List (in Chinese) with 2022 adjustments. The list also contains the requirements under which a product can be imported with an exemption to SAMR approval. For instance, some products may only be able to be imported through bonded mode.

7.9 Exemption requirements

Market authorisation for importing TCMs

The market authorisation process for TCMs can be waived if the drug is being imported in small amounts by a medical institution for urgent clinical needs, or a small number of drugs is imported for personal use (see Thomson Reuters).[8]

7.10 Specific groups of products

No information was found.

8. Regulation of homeopathy in Germany

8.1 Definition

Homeopathy is recognised under the German Medicinal Products Act *Arzneimittelgesetz* (AMG) as a 'particular therapeutic approach', along with phytotherapy and anthroposophic medicine (Federal Institute for Drugs and Medical Devices). Section 4 (26) of the AMG defines homeopathic medicine as any medicinal product with a homeopathic manufacturing procedure defined in the European Pharmacopoeia.

8.2 Registration

Section 38 and 39 of the AMG outline the requirements for the registration of homeopathic medicinal products. Homeopathic products can enter the market if they are on the Register for Homeopathic Medicinal Products. Our understanding of Section 38 in conjunction with Section 39(2) no. 8 is that homeopathic products do not require market authorisation, which is reserved for other medicinal products. However, the homeopathic medicine must have market authorisation if the party marketing the product wishes to make a health claim (see 8.4 and Keller, 1998).

According to Section 39 of the AMG, registration must be made with complete documents that verify the product's safety, ingredients, and potency. Section 39(2) outlines the conditions under which registration should be denied, which generally surround incomplete documents, insufficient evidence or misclassification. The federal authority in charge of registration can create certain conditions to grant registration subsequent to the application.

Section 39(2b) states that if there is a change in the composition of the homeopathic medicinal product or there is a change in the pharmaceutical form of the homeopathic medicine, a new registration process must begin.

Exemptions

Homeopathic medicines do not need to be registered if less than 1,000 units of the medicine are marketed per market holder, per year. However, this does not apply to products of animal origin, if they contain microorganisms or metabolic products, if they contain a relatively high proportion of non-homeopathic medicinal products that require a prescription (relative to homeopathic medicinal products), or if the product is deemed to be of low quality, could have harmful effects, requires a prescription, or if the homeopathic product is manufactured in a procedure not outlined in the homeopathic section of the European Pharmacopoeia (Section 38 of the AMG).

8.3 Market authorisation

Market authorisation is optional for homeopathic medicines. However, some homeopathic medicines must be authorised, including products making a health claim (see section 8.4 and Keller, 1998). The market authorisation, if provided, relates only to the medicinal product specified in the marketing authorisation notice and only applies to the level of dilution of the product published in accordance

with section 25(7) sentence 1 of the version of the AMG in force prior to 17 August 1994,[9] and as specified in the marketing notice.

Homeopathic medicinal products that are required to obtain marketing authorisation can do so by submitting an application to the Federal Institute for Drugs and Medical Devices. This requirement is dependent on several factors, including the health claims made and available data on the homeopathic medicine (Thomson Reuters).[8]

Section 22 of the AMG outlines the documents required for the market authorisation of a medicinal product (including homeopathic medicines), including:

- contact information of the applicant and the manufacturer
- the name of the medicinal product
- the ingredients, including its measurements, of the medicinal product
- the pharmaceutical form of the medicinal product (e.g. pill, powder, etc.)
- the effects of the medicinal product
- therapeutic indications of the medicinal product
- potential contra-indications (suggestions of when to NOT use the medicine)
- potential adverse reactions
- potential interactions with other products
- dosage
- the method of manufacture
- method of administration and duration of use
- package sizes
- ideal method of preservation, shelf-life, storage conditions
- results of stability tests
- methods of quality control.

Results of tests that determine the product's safety, such as clinical trials; physical, chemical, biological or microbiological examinations; and pharmacological and toxicological tests should also be submitted. However, Section 25(5b) of the AMG exempts products manufactured using homeopathic procedures from an assessment report on these test results.

Section 105 of the AMG states that notification indicating active substances and their quantity, and therapeutic indications of finished medicinal products, including market authorised homeopathic products, should be made within six months to the higher federal authority.

8.4 Labels

Under section 10(4) of the AMG, products on the homeopathic medicinal products register must include a 'Homöopathisches Arzneimittel' (homeopathic medicinal product) indication as well as:

[9] In this prior version of the AMG, homeopathic medicines were required to be authorised and the notice of authorisation included the dilution level. This requirement in the current AMG is to simply incorporate the content of any notices issued pursuant to the earlier Act, as well as the new requirements in the marketing authorisation under the current Act.

- ingredients and relevant symbols from the pharmacopoeia and the level of dilution
- the name and address of the pharmaceutical retailer
- directions for use
- expiration date
- measurements of content by volume
- disclaimers to keep out of reach of children, safe storage, warnings, and directions for safe use
- batch identification
- the registration number obtained from 8.2
- the phrase 'Registriertes homöopathisches Arzneimittel, daher ohne Angabe einer therapeutischen Indikation' (registered homeopathic medicinal product therefore no therapeutic indication stated)
- disclaimer to seek medical advice if symptoms persist while using the homeopathic medicinal product
- if the medicinal product is only approved to be dispensed to customers in pharmacies, the disclaimer 'Apothekenpflichtig' (pharmacy-only)
- if a sample, the indication 'unverkäufliches Muster' (sample – not for sale).

8.5 Import and export requirements

Importers of homeopathic medicines (manufactured using homeopathic procedures outlined by the European Pharmacopoeia) are exempt from having to obtain a permit from the higher federal authority (section 72 of the AMG), and likewise, do not require certificates of GMP and Quality Control of Medicinal Products (section 72a(1a) of the AMG).

Section 73a of the AMG allows for the export of all medicinal products so long as they are safe for consumption and are not misleading. The relevant authority from the importing country must also have authorised the importation and introduction of the medicinal product. The higher federal authority may then issue an export certificate in line with the WHO's certification scheme.

8.6 Health benefit claims

Homeopathic medicines that have not been market authorised cannot make a health claim, and must include the disclaimer 'Registriertes homöopathisches Arzneimittel, daher ohne Angabe einer therapeutischen Indikation' (registered homeopathic medicinal product therefore no therapeutic indication stated) on their label (section 10(4) of the AMG).

Market authorised medicinal products, which can include some homeopathic medicines, must be able to substantiate their health claim in the market authorisation process. This includes results from clinical trials and other test results to substantiate safety and efficacy (see section 8.3 of this report). The European Pharmacopoeia also includes monographs on homeopathic preparations.

9. Regulation of Ayurveda in India

The Food Safety and Standards Authority of India (FSSAI) has formulated Food Safety and Standards Regulations (FSSR) (in Hindi). These regulations provide standards for Ayurveda Aahara, which is defined as foods produced under Ayurvedic processes with ingredients contained in Schedule A of the Regulations (in Hindi).

9.1 Market authorisation and health claims

Ayurveda Aahara should be produced according to the regulations set out in Schedule B of the FSSR (in Hindi). Depending on the ingredients of the ayurvedic food product, there are different requirements for market authorisation and the ability to make "disease risk reduction" claims. Generally, Ayurveda Aahara ingredients listed solely in Schedule A do not require pre-market authorisation but do require evidence to substantiate disease risk reduction claims. Ayurveda Aahara that contain other ingredients such as other botanical excipients are required to provide evidence to substantiate any disease risk reduction claims that the marketer may make. Manufacturers are not permitted to produce Ayurveda Aahara intended for infants 24 months old or younger.

Ayurveda Aahara are not permitted to make claims of preventing, treating or curing diseases or conditions.

Safety requirements

Schedule D of the FSSR (in Hindi) outlines the testing and sampling requirements for Ayurveda Aahara products to receive market authorisation. A summarised version of Schedule D in English can be found here.

9.2 Permissible ingredients

Schedule A of the FSSR (in Hindi) includes a list of Ayurveda Aahara, while Schedule C of the FSSR (in Hindi) lists permitted additives and their quantities in Ayurveda Aahara. Vitamins, minerals and amino acids are not permitted in Ayurveda Aahara.

9.3 Labelling

The FSSR outlines requirements for the labelling and packaging of Ayurveda Aahara, including:

- the words "Ayurveda Aahara" printed right next to the name, or brand name of the product. There is also a logo in Schedule E of the FSSR which must be included on packaging
- the disclaimer "for dietary use only"
- a statement that Ayurveda Aahara should not be used as a substitute for a modified diet
- information on the timing and method of administration, other precautions to be taken, potential adverse side effects, potential contraindications, ideal storage conditions of the product, and a warning to be kept out of reach of children
- a disclaimer that the product is for oral use only, and not for parenteral use.

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Appendix A Search strategy

Search run date: 14 November 2023 and 27 November 2023 (for homeopathy and ayurveda)

PubMed

last 10 years

("natural health product*"[Title/Abstract] OR Nutraceutical*[Title/Abstract] OR "Dietary supplement*"[Title/Abstract] OR "Herbal medicine"[Title/Abstract] OR "traditional Chinese medicine"[Title/Abstract] OR "functional food*"[Title/Abstract])) AND (regulatory[Title] OR regulation*[Title])

((homeopath*[Title]) AND (Germany[Title/Abstract])) AND (regulatory[Title/Abstract] OR regulation*[Title/Abstract])

("Homeopathy/legislation and jurisprudence"[MeSH] AND (y_10[Filter])) AND (Germany[Title/Abstract]) Filters: in the last 10 years

(("Medicine, Ayurvedic"[MeSH] AND (y_10[Filter])) AND (regulation*[Title/Abstract] OR regulatory[Title/Abstract])) AND (India[Title/Abstract])

ScienceDirect

"natural health product*" OR Nutraceutical* OR "Dietary supplement*" OR "Herbal medicine" OR "traditional Chinese medicine" OR "functional food*"

("natural health product" OR Nutraceutical OR "Dietary supplement OR "Herbal medicine" OR "traditional Chinese medicine" OR "functional food") AND (regulatory or regulations)

AND UK

AND Australia

natural health product* OR Nutraceutical* OR "Dietary supplement*" OR "Herbal medicine" OR "traditional Chinese medicine" OR "functional food*" AND "importing requirements" OR "exemption requirements"

Gale – Power search

"natural health product*" OR Nutraceutical* OR "Dietary supplement*" OR "Herbal medicine" OR "traditional Chinese medicine" OR "functional food*"

regulatory OR regulations

"Ayurvedic medicine"ANDAbstract: IndiaANDAbstract: regulations OR regulatory

Abstract: homeopathy OR homeopathicANDAbstract: GermanyANDAbstract: regulations OR regulatory

ABI/Inform

"natural health product*" OR Nutraceutical* OR "Dietary supplement* OR "Herbal medicine" OR "traditional Chinese medicine" OR "functional food*"

regulatory OR regulations

abstract(ayurveda or ayurvedic) AND abstract(India) AND abstract(regulation* OR regulatory)

abstract(homeopathy OR homeopathic) AND abstract(Germany) AND abstract(regulation* OR regulatory)

Google Scholar

natural health product "regulatory requirements" australia

ScienceDirect

Title, abstract, keywords: (ayurveda OR ayurvedic) AND India AND (regulatory OR regulations)

Title, abstract, keywords: (homeopathic OR homeopathy) AND Germany AND (regulatory OR regulations)

Appendix B Detailed tables

Definitional interface

	Summary
Australia	The TGA has regulatory guidelines for complementary medicines which define complementary medicines as a therapeutic good consisting wholly or principally of one or more designated active ingredients, each of which has a clearly established identity and a traditional use. Designated active ingredients are those included in Schedule 14 of the Therapeutic Goods Regulations. Complementary medicines include herbal medicines, traditional medicines, homeopathic medicines, essential oils or aromatherapy, vitamins and minerals and nutritional substances. Products at the food-medicine interface are likely to be classified as a food if they do not fall under the definition of a therapeutic good. There is an interactive tool and a diagram to assist with classification at the interface. Cosmetics are not regulated by the TGA. Classification at the interface is determined by ingredients, route of administration and whether indicative claims are made on labelling or advertising. Products that are orally ingested, contain active ingredients or make indicative claims are more likely to be classified as a therapeutic product.
EU	A product that claims to treat or prevent disease (medicine by presentation) or exerts a pharmacological effect (medicine by function) is classified as a medicine. Medicines include traditional herbal medicinal products. Products are classified as food if they do not fall under the definition of a medicine. There is a guidance document on borderline cosmetic products, and guidance on the interface between cosmetics and medicines. The definition of cosmetic is based on the target site of application and the intended function, as set out in Regulation 1223/2009.
UK	The Medicines and Healthcare Products Regulatory Agency (MHRA) classifies finished products into medicinal products or other. There is a 2020 guide to determine a medicinal product, which are subject to the Human Medicines Regulations 2012. For borderline products, which are products at the medicine-food/cosmetics/general product interface, the MHRA classifies products on a case-by-case basis under Part 9 of the Human Medicines Regulations.

Canada	NHPs are regulated under the Food and Drugs Act by the NHPR. NHP ingredients are listed in Schedule 1 of NHPR. In summary, this includes probiotics, herbal remedies, vitamins and minerals, homeopathic medicines, traditional medicines (TCMs and Ayurveda), amino acids and essential fatty acids (see NHPs in Canada). It can include everyday hygiene products like toothpastes, antiperspirants, shampoos, facial products and mouthwashes. NHPs must be able to be sold without prescription (s2 of NHPR), and cannot be injected. They must have at least one health claim. Food, cosmetics and drugs are regulated by the Food and Drugs Act. There is a Guidance Document that aids in classifying products at the food-NHP interface. Interface decisions are made on a case-by-case basis that considers representation, composition, format and public perception and history of use. For cosmetics, there is a Guidance Document to help classify products at the cosmetic-drug interface and further at the NHP interface. Representation, composition, format, and public perception and history of use are again factors that must be considered.
USA	Dietary supplements are regulated by the FDA as food and are under the Food and Drugs Act. A dietary supplement must include at least one dietary ingredient, which include vitamins, minerals, herbs, amino acids and probiotics. Traditional medicines such as TCMs are mostly classified as dietary supplements, although this is dependent on the ingredients used. Homeopathic products are not considered dietary supplements, and are regulated as drugs under the FDDC.
China	The NMPA defines TCMs as "medicinal substances and preparations used under the guidance of traditional Chinese medicine theory." TCMs are regulated as a drug by the NMPA and NATCM (see Liang et al., 2021) Article 24 of the Drug Administration Law (DAL) states that drugs, including TCMs, need to have a licence. There is an exception for Chinese medicinal materials and crude drugs which are not subject to review. Special foods such as health foods or foods for special medical purposes (FSMPs) are not regulated by the Traditional Medicine and Drug Law. However, there are instances of products at the food-TCM interface (for instance, see Section 2 of NZ MPI)

Getting a product on the market

	Summary
Australia	*Listed medicine* Most complementary medicines are listed, along with some over-the-counter medicines. Listing complementary medicines is an administrative process where the pre-market approval process is to ensure that submitted documentation is in accordance with relevant standards and rules. They are considered to be 'low-risk,' but are subject to post-market reviews. These can either be random or targeted. *Registered medicine* Registered complementary medicines are fully evaluated and can include a TGA assessed claim. Complementary medicines should be registered if: • they do not solely comprise ingredients permitted for use in listed medicines, specified in the Permissible Ingredients Determination • they contain an ingredient or component that is subject to the conditions of a Schedule (except Schedules 4, 8 and 9) or Appendix to the Poisons Standard • they are required to be sterile • they have indications not included on the indications permitted for use in listed medicines. To be entered on the ARTG, information on ingredients, risk (health claims and ingredients), and documentation on safety and efficacy of product and manufacturing processes must be submitted. Evidence from traditional sources or scientific sources can be provided.
EU	*Food supplements* Notification only required by some Member States. Products not listed in Directive 2002/46 need to go through a safety evaluation under Regulation 2015/2283 – novel foods. This document sets out the application procedure.

	Traditional food If the product is a 'traditional food' from outside the EU (and not currently listed in Directive 2002/46), there is a special procedure for safety assessment under Regulation 2015/2283, based on a history of safe food use for a period of at least 25 years in at least one country outside the EU and applies only to products deriving from primary production. *Botanicals* The EU does not currently have a centralised authorisation procedure. Depending on the use and effect of the product, botanicals may be considered as traditional herbal medicinal products. *Traditional herbal medicines* Directive 2004/24 amending Directive 2001/83 sets out the requirements for traditional herbal medicinal products. Section 16(a)(1) of the Directive sets out the requirements for a product to be classified as a traditional herbal medicinal product, and therefore qualify for a simplified registration procedure.
UK	*Food supplements* There is no requirement for food supplements to be licensed or registered with the UK government (Department of Health and Social Care). *Traditional herbal medicines* To sell a product as a traditional herbal medicine, a person must apply for a registration under the Human Medicines Regulations 2012. A Traditional Herbal Registration (THR) is only granted if the medicine is used for minor health conditions that do not require medical supervision (e.g. colds).
Canada	The applicant must apply to the minister with information on product safety and efficacy, ingredients, brands, and labels. Full requirements are outlined in s5 of the NHPR. If the product's ingredients are contained in the Compendium of Monographs (one ingredient or more than one ingredient), there is an expedited disposition process (within 60 days) on the market authorisation of the NHP.

	If there is a change in the content, recommended use, or test process of the NHP – modified NHPs cannot be sold until an amendment has been made to the licence.
USA	Dietary supplements and conventional food do not require pre-market authorisation from the FDA. However, a pre-market notification to the FDA must be made at least 75 days prior to entering the market if the dietary supplement contains a "new dietary ingredient." See FDA for the new dietary ingredient process.
China	*TCMs* Article 24 of the Drug Administration Law (DAL) requires applicants to receive market authorisation by applying to the National Medical Products Association (NMPA), except for Chinese medicinal materials and crude drugs that are not subject to review. TCMs must follow the technical requirements for Pharmaceuticals for Human Use (M4) set out by the International Council for Harmonisation. The documents required to process market authorisation include information on ingredients, test reports, and safety and efficacy documentation (Liang et al., 2021). The NMPA and Centre for Drug Evaluation (CDE) then reviews the application and samples before approving the TCM for an applicant (Thomson Reuters).[8]

Permissible ingredients

	Summary
Australia	All listed medicines must only contain ingredients included in the Therapeutic Goods (Permissible Ingredients) Determination (no. 4) 2023. The Therapeutic Goods (Permissible Ingredients–Information that Must Accompany Application for Variation) Determination 2023 specifies how applications for substances to vary the Permissible Ingredients Determination must be made.
EU	*Food supplements* Directive 2002/46/EC establishes harmonised lists of vitamins and minerals that can be used in the manufacture of food supplements and their permitted forms. There is a lack of harmonisation in EU law for ingredients in food supplements, other than vitamins and minerals, such as botanicals, enzymes, amino acids, probiotics. The incorporation of substances other than vitamins and minerals listed in Direction 2002/246 are regulated by Member State national rules, and some Member States have published their own positive lists for acceptable ingredients. There is no centralised permissible list for botanicals. The European Food Safety Authority has created a compendium of botanicals reported to contain substances of possible concern for human health that might be used in food, but this is not exhaustive and has no legal force.
UK	The food supplement regulations cross reference the Annex of retained Directive 2002/46 with regard to vitamins and minerals. These lists have been inserted into the Nutrition (Amendment etc) (EU Exit) Regulations 2019 as Schedules to ensure they continue to have effect (Department of Health and Social Care). There are also specific bans or restrictions. In contrast to some EU Member States adopting a list-based approach to permissible ingredients, the UK assesses products on a case-by-case basis, in line with case law.
Canada	NHPs must include ingredients from Schedule 1 of the NHPR and cannot include substances in Schedule 2 of the NHPR. A comprehensive NHP ingredients database can be found here.
USA	Dietary supplements must contain at least one dietary ingredient. A directory of dietary ingredients can be found here.

China	The Chinese Pharmacopoeia sets out approved TCMs (and other drugs) for use. This includes ingredients, tests, dosage and potency. Approved ingredients for health foods and FSMPs are set out in the Health Food Raw Materials Directory (NZ MPI).

Health benefit claims

	Summary
Australia	*Listed complementary medicines* The TGA have released a guidance document for permitted indications for listed medicines. The Permissible Indications Determination for Therapeutic Goods outlines what indications can be made by medicines in Australia. *Registered complementary medicines* Registered complementary medicines can include a TGA assessed claim. These can be indications about more serious conditions (see TGA – Registered complementary medicines).
EU	The Annex of Regulation 1924/2006 contains the list of permissible nutrition claims and the conditions that apply to such claims. For health claims, Regulation 432/2012 sets out the list of permitted health claims able to be made on food, alongside the conditions on the use of the claim and any requirements for additional statements/warnings. There is also a public EU Register of Health Claims. Claims cannot suggest a product is intended to prevent or treat a disease, as this may render the product as a 'medicine.' Where a business wants to make a health claim that is not authorised in the register of health claims, they must apply for authorisation under Article 15 of 1924/2006. The European Food Safety Authority is the assessment body for health claims. The authorisation of health claims for foods does not include an assessment of safety. Currently, health claims can only be substantiated with scientific data from human clinical intervention studies and there is no possibility to make use of evidence on traditional use to substantiate health effects. For products classified as traditional herbal medicines under Directive 2004/24 amending Directive 2001/83 the simplified registration procedure includes substantiation of claims. Evidence from human clinical trials is not required – "plausible" pharmacologic effects or efficiency on the basis of long-standing use and experience are accepted.

UK	From 31 December 2020, voluntary nutrition or health claims must comply with the requirements of retained EU Regulation 1924/2006. All nutrition and health claims that were listed in the EU Register on 31 December 2020 were adopted and included in the Great Britain nutrition and health claims register. For new claims, an application must be submitted to the appropriate authorities for assessment for the claim to be authorised for use in the Great Britain market. The assessment process is set out by the Nutrition Related Labelling, Composition and Standards Provisional Common Framework.
Canada	S103.2 of the NHPR allows NHPs to represent themselves as preventatives to conditions of Schedule A.1 of the Food and Drugs Act, but not as treatments or cures. The conditions outlined in Schedule A.1 are generally more serious or incurable conditions. Health Canada has a risk-based approach to the permission of a health claim of an NHP. Page 15 and 16 of Pathway for Licensing highlights efficacy evidence required for health claims at each risk level. Generally, higher level health claims require more evidence to substantiate the health claim (e.g. systematic review).
USA	Health claims are optional for dietary supplements. Claims of prevention, treatment or cures for conditions are not permitted for dietary supplements (Nichini, 2022). The FDA does not pre-approve health claims, but must be notified of a health claim made by a product within 30 days of entering the market. A disclaimer must also be made on the product stating that the FDA has not evaluated the claim (FDA).
China	Health foods and FSMPs may only make nutritional content claims permitted under GB 28050-2011 and GB 14880-2012. Health foods must also include a disclaimer stating, "health foods are not medicines and cannot replace medicines to treat diseases" (NZ MPI). Since TCMs are classified as a drug, TCMs are allowed to claim health indications so long as the drug's safety, efficacy and quality have been substantiated in the market authorisation process.

Manufacturing requirements

	Summary
Australia	Part 3-3 of the Therapeutic Goods Act 1989 sets out the manufacturing requirements. Under s36 of the Act, 'good manufacturing principles' may be set by the Minister as legislative instruments (currently Therapeutic Goods (Manufacturing Principles) Determination 2020). This Determination states that the manufacture of therapeutic goods must comply with the PIC/S Guide to GMP. *Licensing* Australian manufacturers of therapeutic goods must also apply for a manufacturing licence for a particular site. The TGA have produced a step-by-step guide for site licensing and overseas GMP certification.
EU	Regulation 2023/2006 sets out the requirements for good manufacturing practice (GMP) for materials and articles intended to come into contact with food (rather than the food itself). Regulation 852/2004 sets out the requirements for food hygiene, particularly the HACCP principles that must be followed. If the product is classified as a medicine, Directive 2017/1572 requires GMP to be followed. This also applies to medicinal products intended only for export. Volume 4 of "The rules governing medicinal products in the European Union" contains guidance for the interpretation of the principles and guidelines of GMP for medicinal products for human use. *Licensing* Regulation 852/2004 requires that establishments preparing foodstuffs be registered. In other words, no licence is required. Regulation 853/2004 requires that establishments that handle products of animal origin to be registered and approved by the competent authority of each Member State. Directive 2001/83 states that "Member States shall take all appropriate measures to ensure that the manufacture of the medicinal products within their territory is subject to the holding of an authorisation. This manufacturing authorisation shall be required notwithstanding that the medicinal products manufactured are intended for export." These authorisations are issued by the competent authority of each Member State

	and assessment processes will vary between each Member State. However, Article 41 sets out the minimum requirements to obtain a manufacturing authorisation.
UK	For supplements classified as food, while the UK has left the EU, some EU regulations relating to food law have been retained. Retained regulations relating to Hazard Analysis and Critical Control Point (HACCP) means that all food businesses in the UK are still required to have a HACCP-based food safety management system in place. For supplements classified as medicines the requirement of compliance with GMP under Directive 2001/83 is still in effect. *Licensing* Other than registering as a Food Business Operator, as set out in section 4.3.1 of this report, if a manufacturer is handling meat, fish, egg or dairy products, they must apply for a Food Premises approval licence (similar to the requirements of EU businesses under Regulation 853/2004). This must be applied for through the local council. The manufacture of a traditional herbal medicine requires a licence, issued by the MHRA. This is called a manufacturer/importer licence and may be granted for the manufacture and assembly of products, or just the assembly (see applying for manufacture or wholesale of medicine licences).
Canada	Subject to a site licence, manufacturers must also ensure they follow good manufacturing practices laid out in Part 3 of the NHPR. Manufacturers, packagers, labellers, distributors and importers are required to follow GMP requirements for processes (s45 to s52 of NHPR) and record keeping (s53 of NHPR) surrounding personnel, sanitation, plant design and maintenance, equipment design and maintenance, production processes and quality control. Records are required to be kept for up to one year after the expiry date for a particular batch as per GMP (section 53 to 58 of NHPR). *Licensing* A site licence is required for the manufacture, packaging, labelling, import of natural health products (Part 2 of NHPR).
USA	Manufacturers must follow current good processes of manufacturing, packaging, labelling and storage of dietary supplements, GMP requirements and documentation surrounding personnel, sanitation, plant design and maintenance, equipment design and maintenance, production processes and quality control in 21 CFR 111.

	The FDA has released a guidance document for small entities for simplicity. As per GMP, records must be kept for either: one year past the shelf-life date of dietary supplements (if shelf life used), or two years after the distribution of the batch of dietary supplements (see Subpart F and P of CFR 21). *Licensing* Do not need a licence to manufacture.
China	Manufacturers of TCMs must follow the GMP of TCMs (in Chinese) which covers personnel, production, storage, sanitation, record keeping and quality control. There are also additional requirements for the harvest and cultivation of Chinese medicinal materials under Articles 24, 50, and 38-39 of the TCM GMP (in Chinese). *Licensing* Applicants need to apply for a food manufacturing licence. The applicant submits documentation (application form and documentation on equipment, production flowcharts, safety, and quality control procedures) to their provincial Administration for Market Regulation.

Exporting requirements

	Summary
Australia	The TGA has published a guidance document on the export of medicines. The therapeutic good must be entered, i.e. either listed or registered on the ARTG before it can be exported for commercial use (Part 2 of the Therapeutic Goods Act 1989). All medicines must follow the market authorisation process for the therapeutic good. *Export only medicines* These can be produced whereby they can follow the standards Therapeutic Goods Order No. 70C. This generally ensures they follow the importing country's requirements. Export only medicines are exempt from some labelling standards. Export licences are not required, but still can be obtained if it is a requirement from the importing country. See guidance for export certificates here.
EU	All exporters require an EORI number. Exporters of NHP equivalents must comply with the Convention on International Trade in Endangered (CITES) which has a list of prohibited and restricted plant species for import or export (see requirements to export natural ingredients). Wholesale distributors require a wholesale distribution authorisation or a manufacturing authorisation to export medicines. This ensures that distributors follow good distribution practice and publishes guidelines for their distribution processes.
UK	*Food supplements* To export composite products (i.e. a mix of plant and animal origin ingredients) exporters may need a composite export health certificate (such as Certificate 8350 if the product is a non-shelf-stable product), a private attestation (if shelf-stable), and a catch certificate (only if the product contains more than 20 per cent of marine-caught fish or fishery products caught in Great Britain). Exporters of products of animal origin to the EU, the exporter may need an export health certificate, such as Certificate 8399. Certificates of Free Sale are available if required by the importing country.

	Food supplements packaged for the final consumer, containing processed animal products (including glucosamine, chondroitin or chitosan) are exempt from border controls if they are shelf-stable, can be identified as a product intended for human consumption, are securely packaged and sealed and meets EU production or processing requirements (export of food products). *Traditional herbal medicines* Manufacturers require a manufacturing licence to produce traditional herbal medicines for export. Export certificates are required; there are five types depending on the nature of the medicine (see section 4.7.2 of this report for more information).
Canada	Exporters must hold a product licence, although some unlicensed NHPs can be exported if they are manufactured in Canada for export only, and hold an export certificate. All exporters of NHPs must also sign an export certificate. While not a requirement, NHPs can also obtain an International Trade Certificate which is done by third parties. This could be a requirement or aid for the importing country.
USA	A "Certificate of Free Sale" is available for the export of dietary supplements. Compared to conventional foods which require a "Certificate of Exportability," there is no fee associated with the free sale certificate (see Online Applications for Export Certificates for Food). The free sale certificate is generally a requirement from certain importing countries that certifies that goods intended for export are sold freely and lawfully in the origin country.
China	There is a lack of information surrounding the exports of TCMs and special foods from China. To our knowledge, there are no special administrative requirements to export health foods and FSMPs outside of China (Thomson Reuters).[8] However, there may also be restrictions on TCMs being exported from China (Thomson Reuters).[8]

Importing requirements

	Summary
Australia	Overseas manufacturers of therapeutic products must receive GMP clearance to verify that the manufacturing process complies with that of goods that would typically be in the Australian market. This is done through one of three pathways, depending on Australia's relationship with the exporting country and their relevant laws and regulations: • a mutual recognition desktop assessment • a compliance verification desktop assessment • an inspection by the TGA. Depending on the pathway, more evidence may be required, and fees may vary.
EU	*Food supplements* Food supplements must comply with applicable EU legislation for market authorisation. For supplements of solely animal origin, Regulation 2017/625 sets out the rules governing official controls along the agri-food chain, including the importing of products. Products of plant origin are subject to potential import bans, phytosanitary certificates, inspections, importers register and potential emergency measures. Full details of protective measures for products of plant origin are discussed in section 3.8 of this report. Food products must also comply with food law and other manufacturing and distribution processes. More detailed information on importing requirements can be found here. *Traditional herbal medicines* The importation of medicinal products is subject to the following requirements: • import authorisation • marketing authorisation and registering the product • labelling and packaging requirements • control of each batch • pharmacovigilance system.

UK	There are safety and security controls for all imports, and sanitary and phytosanitary controls for products of animal or plant origin set out in this document on a new Border Target Operating Model. *Food supplements* Importers of composite food products, plant products and products of animal origin must notify authorities in Great Britain before importing such products. *Traditional herbal medicines* Importers can hold a manufacturer/importer licence, which allows for imports of licensed medicine products outside the EEA. Alternatively, importers can hold a wholesaler licence, which allows for the import of unlicensed medicinal products from countries inside the EEA (see the guidance document for importing a human medicine). Unlicensed medicines can be imported if they are for export again, or if there are no viable licensed medicine alternatives for the clinical needs of a patient.
Canada	Retailers, manufacturers, packagers, labellers or importers must apply for a site licence. They must also maintain adequate records surrounding the production, ingredients, tests, and sanitation as in s56 of the NHPR. Section 100 of the NHPR states that sections A.01.040 to A.01.044 of the Food and Drug Regulations apply to imported NHPs. This allows inspectors to take samples of and examine an NHP that is being imported.
USA	Importers do not need a specific licence to import. A permit from APHIS (Animal and Plant Health Inspection Service) may be needed if the product contains animal ingredients. See assistant tool and a detailed guide for ingredients that require/do not require a permit. Prior Notice must be filed by the importer prior to goods entering the country, to inform U.S Customs that food is entering the country. FSVP regulations also ensures that importers keep relevant documents to ensure that goods were manufactured in a similar manner as they would be under GMP in the US.

China	*Traditional Chinese medicines* Importers of TCMs must follow the same market authorisation process as with authorising TCMs for the Chinese market (see Thomson Reuters).[10] First time importers of TCM (every new TCM import per new exporter) have to undergo more rigorous importing process which involves obtaining and submitting various official documents from the exporting country (see GACC). Overseas manufacturers must also have official documentation of following safety processes and GMP, and must consent to inspection and quarantine in China. Chinese medicinal materials without market authorisation can be imported after obtaining an import permit from the provincial MPA at the port of entry. *Health Foods and FSMPs* Special foods for import must be filed and registered in China and include safety information, alongside other information about the product. Importers must also register as a foreign trade operator with the local commerce bureau and with China's General Administration of Customs (see NZTE requirements and guidance), allow customs to review the imported food and documents, and pay required customs tariffs. Special foods may be exempt from the above processes if they are imported through cross-border e-commerce, which generally can be done for products on the on the 2019 Positive List (in Chinese) with 2022 adjustments.

[10] May require institutional access or a free trial to access this webpage.

Exemption requirements

Please note: We have listed the exemptions identified in the course of our analysis. However, due to the incredibly complex regulatory environment, there will be other exemptions that may apply in certain situations.

	Summary
Australia	Schedules 5 and 5a of the Therapeutic Goods Regulations 1990 sets out therapeutic goods which are exempt from Parts 3-2 and 3-2A of the Therapeutic Goods Act, i.e. registration or listing. Schedule 7 of the Therapeutic Goods Regulations 1990 contains a list of goods exempt from the operation of Part 3-3 of the Therapeutic Goods Act 1989 (manufacturing requirements - licensing) unless they are supplied as pharmaceutical benefits.
EU	Regulation 853/2004 (hygiene rules for animal origin products) specifies certain exemptions for products of animal origin, i.e. there is no requirement for establishments that handle animal products to be registered and approved in the following cases (which may apply to food supplements of purely animal origin): a) primary production for private domestic use b) the domestic preparation, handling or storage of food for private domestic consumption c) the direct supply, by the producer, of small quantities of primary products to the final consumer or to local retail establishments directly supplying the final consumer. Regulation 2021/630 sets out certain categories of goods exempt from official controls at border control posts. Included are food supplements packaged for the final consumer containing processed animal products (including glucosamine, chondroitin or chitosan) that are a shelf-stable composite product that does not contain colostrum-based products or processed meat other than gelatine, collagen or highly refined products.

UK	Herbal practitioners do not need a licence to supply herbal medicinal products that are created on their own premises and supplied to patients following one-on-one consultations. A Food Premises licence (for handling meat, fish, egg or dairy products – which may include food supplements) is not required if the applicant sells direct to the public or retailers, as long as: • food is less than 25 per cent of the business trade • they do not handle any wild game meat products • they do not sell food outside the county the business is registered in.
Canada	**Importing for personal use:** Residents and visitors are allowed to bring up to a 90-day supply or a single course of treatment of an NHP for personal use without adhering to importing requirements. **Exemptions to practices** (see 1.4 of Site Licensing Guidance Document): Practitioners that compound NHPs for the sale solely to an individual who requests it, such as pharmacists, aboriginal healers, TCM practitioners and general health care practitioners do not require a site licence. **Other exemptions** (see 1.4 of Site Licence Guidance Document): The following are exempt from having to obtain a site licence: • manufacturers that produce NHPs for the sole purpose of exporting by invoking Section 37 of the Food and Drugs Act • distributors that do not import NHPs. A distributor is one who sells NHPs for the purpose of reselling • manufacturing, packaging, labelling, or importing NHPs for a clinical trial • testing labs.
USA	Not applicable as licensing is not required for manufacturing, marketing, or the supply of dietary supplements in the US.
China	The market authorisation process for TCMs can be waived if the drug is being imported in small amounts by a medical institution for urgent clinical needs, or a small number of drugs is imported for personal use (see Thomson Reuters).[8]

Specific groups of products

	Summary
Australia	**Homeopathy** Homeopathic medicines are classified as a complementary medicine. They are considered low-risk, and are not required to hold a GMP licence if they are not required to be sterile, and its preparations are more dilute than a 1,000 fold dilution of the mother tincture (4X or above). **Aromatherapy** Essential oils are regulated by the TGA only if a therapeutic claim is made. If the product makes a cosmetic claim, then it is regulated by the National Industrial Chemicals Notification and Assessment Scheme (NICNAS).
EU	**Homeopathy** The manufacture, sale, and export of homeopathic medicinal products in the EU are subject to specific rules and regulations. The Homeopathic Medicinal Products Working Group (part of the Heads of Medicines Agencies (HMA)) sets out multiple guidance documents for getting a homeopathic product on the market. Directive 2001/83 on medicinal products for human use outlines two procedures for market access of homeopathic and homeopathically produced medicinal products: Special Simplified Registration Procedure (Article 14) and Marketing Authorisation (Article 16). This document from the HMA in 2020 contains useful information regarding the regulatory process of homeopathic products. **Aromatherapy** Depending on how essential oils for aromatherapy are marketed, the product could be classified as a medicine or a cosmetic, which have differing legal requirements.

UK	**Homeopathy** There are two regulatory schemes for homeopathic medicinal products (see registering a homeopathic medicine): the Simplified Registration Scheme and the National Rules Scheme. There is a national system for submitting applications to the MHRA. The MHRA takes around 210 days to evaluate completed applications. **Aromatherapy** Depending on the product composition, presentation and intended use, it may be classified, may be classified as medicines, medical devices, cosmetics, foods, food additives or flavourings. Aromatherapy products that do not meet any of those definitions will be regulated by the General Product Safety Regulation 2005 (see a guide to medicinal products).
Canada	**Homeopathy** Homeopathic products are regulated as a Natural Health Product. Homeopathic products include a "DIN-HM" number, which is used as an indication that it is a homeopathic product (see Information on Homeopathic Products). There are also new labelling requirements e.g. products must include the statement "This/These claim(s) is/are based on traditional homeopathic references and not modern scientific evidence" (Information on Homeopathic Products). Homeopathic products with certain ingredients may only be authorised for sale if they meet a minimum homeopathic potency established by the NNHPD (see Evidence for homeopathic medicines) **Aromatherapy** Regulated as an NHP (monograph for Aromatherapy). **Kava** Kava is classified as an NHP under Schedule 1 of the NHPR (being derived from a plant). The amount of kavalactones present in the product must be declared during the application process. NHPs such as kava or products containing kava must make a health claim, include directions for use and list ingredients.

USA	**Homeopathy** Homeopathic products are not classified as dietary supplements and are regulated as drugs. The FDA has released information on the regulation of homeopathic products. Homeopathic products must include the word "homeopathic" on the label and ingredients used in terms of dilution. The FDA does not review homeopathic products for safety and effectiveness to treat, cure, prevent or mitigate conditions prior to entering the market. **Aromatherapy** The FDA has a page that defines aromatherapy on the drug-cosmetic interface. Depending on the purpose of the product, aromatherapy can be marketed as a drug, cosmetic or both. If the product is intended for superficial effects, such as cleansing or smell, it is defined as a cosmetic. If the product has claims of preventing, treating or mitigating conditions, it is defined as a drug.
China	No information found.

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For more information, please contact:

David Moore
Mobile: +64 21 518 002
Email: dmoore@thinkSapere.com

Wellington	Auckland	Sydney	Melbourne	Canberra	Perth
Level 9 1 Willeston Street PO Box 587 Wellington 6140	Level 8 203 Queen Street PO Box 2475 Shortland Street Auckland 1140	Level 18 135 King Street Sydney NSW 2000	Level 5 171 Collins Street Melbourne VIC 3000	GPO Box 252 Canberra City ACT 2601	PO Box 1210 Booragoon WA 6954
P +64 4 915 7590	P +64 9 909 5810	P +61 2 9234 0200	P +61 3 9005 1454	P +61 2 6100 6363	P+61 8 6186 1410

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