



**IRISH MEDICINES BOARD
GUIDE TO THE DEFINITION OF A HUMAN MEDICINE**

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This guide does not purport to be an interpretation of the law and/or regulations relating to the authorisation and is for guidance purposes only.

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1. SCOPE

The guidance in this document applies to the classification of medicinal products for human use.

2. INTRODUCTION

The IMB is the competent authority in Ireland for medicinal products for human and veterinary use and for medical devices, pursuant to the provisions of the Irish Medicines Board Acts 1995 and 2006.

The IMB regulates the licensing and sale of medicinal products for human use in Ireland according to the requirements of the Medicinal Products (Control of Placing on the Market) Regulations (S.I. No. 540 of 2007) and relevant EC Directives, in particular Council Directive 2001/83/EC as amended by Directive 2004/27/EC and Directive 2004/24/EC. (Directive 2001/83/EC replaced the earlier European legislation laid down in Council Directive 65/65/EEC as amended.)

These regulations require that a medicinal product shall not be marketed without a marketing authorisation or a certificate of registration. The granting of such an authorisation/certificate ensures that a product complies with the required standards of quality, safety and efficacy. It is the responsibility of those marketing medicinal products to comply with the relevant legislation and to ensure that such products are only marketed in accordance with this legislation.

In most cases the classification of a product as a medicine is clear in that the nature of the substance, its effects on the body, the indications for use/contraindications, its presentation and the manner of marketing are consistent with the definition of the European Directives regarding medicinal products.

The definition of a medicinal product in Article 1 of Directive 2001/83/EC was amended by Directive 2004/27/EC. The new definition states that a medicinal product is:

- (i) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or
- (ii) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

A new provision has been added to Article 2. Article 2(2) of Directive 2001/83/EC as amended now states that:

“In cases of doubt, where taking into account all its characteristics, a product may fall within the definition of a medicinal product and within a definition covered by other Community legislation, the provisions of this Directive shall apply”.

Recital 7 to Directive 2004/27/EC explains that the definition was amended to take account of the growing number of borderline products between the medicinal products sector and other sectors, such as foodstuffs and cosmetics. This recital goes on to explain

“...Where a given product comes clearly under the definition of other product categories, in particular food, food supplements, medical devices, biocides or cosmetics then this directive [i.e. medicinal products] should not apply”.

Taken together, these provisions are intended to ensure that where doubt exists over the classification of a product the stricter medicinal products regulatory regime should apply. This will ensure that products that are on the borderline area e.g. medicinal product/medical device, medicinal product/food supplement, medicinal product/cosmetic etc. are brought under the appropriate regulatory control and ultimately protect the user of the product.

However, if a product can be clearly regulated appropriately under another category then the regulatory control for that category should take precedence. Consequently, the IMB works together with the other regulatory authorities in its classification activities in order to ensure that each product is regulated, according to the principles of risk management, in order to best protect the public.

While the impact of the change in legislation described above on conventional medicinal products and medical devices is not intended to cause confusion (where it is clear that a product falls within the scope of the medicinal products or medical devices legislation) these changes are intended to help clarify the procedure when the appropriate regulatory framework is not clear. There may, consequently, be some products on the borderline between medicinal products and medical devices, which will need to be re-categorised following the implementation of the revised legislation.

The new legislation also brought in specific provisions to regulate herbal medicinal products (Directive 2004/24/EC) and updates the special provisions for homeopathic medicinal products. Thus homeopathic medicinal products may be registered by a simplified registration procedure in accordance with Article 14 of Directive 2001/83/EC as amended by Directive 2004/27/EC. However, in cases where products do not meet the requirements for the simplified registration procedure, then a marketing authorisation must be obtained, in order to place the product on the market in Ireland.

In the case of herbal medicinal products, Directive 2004/24/EC makes special provisions to regulate traditional herbal medicinal products which meet the criteria specified in Article 16a of the amended Directive. Such products, provided that they have indications appropriate to traditional herbal usage and are intended and designed to be suitable for self medication, can be marketed under a certificate of traditional-use registration.

It should be noted however that both traditional herbal and homeopathic products are still medicinal products. Consequently, those traditional herbal or homeopathic medicinal products which do not meet the criteria appropriate for registration for traditional herbal usage or for the simplified homeopathic registration procedure, respectively, require a marketing authorisation before being placed on the market as for any other medicinal product.

These changes are made effective by the Medicinal Products (Control of Placing on the Market) Regulations, 2007, from July 23 2007. This IMB guideline, *Guide to the definition of a human medicine* has consequently been revised to reflect these and other changes arising from updates to the legislation.

3. REQUIREMENTS IN RELATION TO MEDICINAL PRODUCTS

Before a medicinal product can be placed on the market in Ireland, an application must be made for a marketing authorisation or certificate of registration to the IMB, (or in the case of centrally authorised products to the European Medicines Agency). Such applications should contain the data necessary to support the quality, safety and – for conventional and traditional herbal medicinal products – efficacy or traditional use respectively. These data are reviewed by the IMB and a conclusion reached based upon the likely balance of the benefits versus risks associated with the product. As indicated above, the marketing authorisation must be granted prior to the product being placed on the market. The IMB requires that the interests of consumers of medicines should be protected, notably in the following areas:

- A medicinal product should be of adequate quality such that its contents and its pharmaceutical performance should conform to acceptable standards.
- The risk of using a medicinal product should be acceptable and reasonable, taking into account that the use of any medicine carries a risk, which should be considered in the light of the likely benefit. The IMB must be kept informed of any new safety data which emerge, and which might affect the risk-benefit balance.
- There should be a demonstrable therapeutic benefit for medicinal products with the exception that for certain product categories the demonstration of efficacy may

not be required (e.g. homeopathic products – see below). If a medicinal claim is made, the consumer is entitled to expect a benefit and the review process should protect the consumer, so far as possible, from products which do not offer a potential for such benefit.

4. DEFINITION OF A MEDICINAL PRODUCT

The definition of a medicinal product is given in Article 1 of Directive 2001/83/EC, as amended by 2004/27/EC as described above. The definition is set out in two paragraphs, covering the presentation of the product and the purpose for which it is administered respectively.

4.1 Presentation

The first paragraph refers to the ‘presentation’ of the product and for convenience is repeated below:

‘Any substance or combination of substances presented as having properties for treating or preventing disease in human beings.’

In reviewing a product in this context the IMB examines the ‘totality’ of the product as discussed in the following sections.

4.1.1 Products for which (explicitly or implicitly) claims to cure, alleviate or prevent disease are made are considered as medicinal products. Any particular words or phrases which imply such a claim will be taken into account.

Where the principle intended action of the product is pharmacological, metabolic or immunological then the product is regulated as a medicinal product, whereas where the principle intended action is physical or mechanical then the product is regulated as a medical device.

While not intending to be exhaustive, the following list contains examples of such words or phrases: ...cures, heals, treats, restores, prevents, clears, stops, protects, helps with, traditionally used for, strengthens the immune system, calms, helps maintain normal water balance....

In addition the IMB has regard to judgements of the European Court of Justice (ECJ) in determining such claims. The ECJ has held that: *‘A product which is recommended or described as having preventative or curative properties is a medicinal product within the meaning of the provisions of Article 1. of Council Directive 65/65/EEC...even if it is generally considered as a foodstuff and even if it has no known therapeutic effect in the present state of scientific knowledge’.*

4.1.2 Products which are presented in a way that the labelling, the packaging, the pharmaceutical form, the promotional material or the intended audience (for example specific promotion to a group of people with a specific medical condition), implies a medicinal usage may be considered as medicinal products.

4.1.3 Once a given product has been classified by the IMB as a medicinal product it logically follows that closely related products will be similarly classified. Such a relationship could relate to the content, labelling intended use or presentation of the product.

4.2 The purpose for which a product is administered

The second paragraph of Article 1 (2) of Directive 2001/83/EC as amended by 2004/27/EC provides:

‘Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or by making a medical diagnosis’.

Thus any product containing a substance with a known pharmacological effect or in the case of traditional herbal medicinal products a pharmacological effect that is plausible based on long-standing use and experience, will usually be classified as a medicinal product by the IMB irrespective of the presence or absence of claims in the product packaging or literature.

It should be further noted that any product containing a substance which is confined to supply on a medical prescription by virtue of the Medicinal Products (Prescription and Control of Supply) Regulations, the Poisons Regulations or the Misuse of Drugs Regulations is automatically deemed to be a medicinal product requiring an authorisation.

4.3 IMB policy and practice

ECJ judgements, the evolution of professional opinion, changes in marketing practices, and other changing circumstances have required corresponding changes to the way the IMB assesses products. In particular, it takes full account of the ECJ view that competent authorities of Member States should consider all the characteristics of the individual products, and are obliged to consider what impression of the product ‘an averagely-well-informed consumer’ would be likely to gain.

In practice, the IMB considers each individual product on its merits and any information which may have a bearing on the product’s status, such as:

- (a) The claims made for the product, implicit as well as explicit, (including any claims made on linked ‘help-lines’” websites or publications, or in the product’s actual name).
- (b) The pharmacological, metabolic or immunological properties of the ingredient(s) and any significant effect(s) they have on human beings.
- (c) The labelling, and the packaging literature, including any pictorial descriptions.
- (d) The promotional literature (including testimonials and any literature issued by a third party on behalf of the manufacturer or producer) and advertisements.
- (e) The product form, (e.g. tablet, capsule, ointment etc.) and the way in which it is intended to be used. Any form intended for usage of a generally medicinal nature, including certain topical preparations, renders the product a medicinal product or in some circumstances a medical device.
- (f) To whom the product or information about the product is directed, perhaps sections of the population with, or vulnerable to, a specific condition.
- (g) Similar authorised medicinal products on the market, fulfilling similar functions.

5. CLASSIFICATION OF MEDICINAL PRODUCTS

As stated above Article 2.2 of Directive 2001/83/EC as amended by Directive 2004/27/EC, makes it clear that for products at the borderline between medicinal and other categories such as foods or cosmetics, then the classification of the product becomes very important since the users need to be aware of the legal restrictions on marketing of medicinal products and the fact that the more stringent legislation takes precedence.

Any company or individual who attempts to market a product in a given category may discover that the product is controlled under medicines legislation for which prior authorisation or registration is required as appropriate. It is for this reason that the IMB has set up a classification procedure whereby applicants can request an opinion on the categorisation of a given product intended for administration to humans prior to placing it on the market. In this way applicants can obtain an authoritative opinion and avoid the risk of inadvertently breaking the law by placing a medicinal product on the market without the necessary authorisation.

The classification service is operated by a clearly defined procedure following application to the IMB using the standard form which can be downloaded from the IMB website www.imb.ie. Details of the fees applicable can be found on the website and applications should be made to the Classification Administrator at the IMB.

To assist in this process the IMB has set up an internal multidisciplinary committee which meets approximately once a month to consider such applications and to provide a written opinion to the enquirer within a reasonably short timeframe. Parallel

processes exist for medical device and veterinary medicinal product classification queries, using similar approaches and principles.

In arriving at any decision in regard to classification the IMB must always be provided with sufficient information about the product and its intended usage including all promotional material. Should an applicant disagree with a decision of the Classification Committee, they are free to appeal the decision to the IMB Management Committee, which may request the advice of the Advisory Committee on Human Medicines (ACHM) set up under the Irish Medicines Board Act, 1995. The request for the appeal should be directed to the Classification Administrator together with all supporting information. The data package forming the basis of the appeal will then be scheduled for consideration at the next available meeting of the Management Committee which meets approximately every two weeks. The decision of the Management Committee is final.

6. EXAMPLES OF PRODUCT CATEGORIES

The following examples of different product categories are provided to illustrate and explain the IMB thinking in regard to categorisation of products as medicinal or otherwise. This list is by no means exhaustive and will be subject to regular update as new decisions are made, new product categories emerge, or other external factors (such as legislation or case law) change.

6.1 Herbal medicines (products containing plant-based medicinal ingredients)

Herbal medicinal products are medicinal products containing as active ingredients one or more herbal substances, one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations.

Herbal substances are defined as mainly whole, fragmented or cut, plants, parts of plants, algae, fungi, lichen in an unprocessed state, usually in 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 binominal system (genus, species, variety and author). Herbal preparations are obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These substances include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

In 2004, a new European proposal for the registration of 'traditional herbal medicinal products' was established by European Council Directive 2004/24/EC. This recognises that while all such products remain medicinal products, they have specific characteristics that can make them eligible for a simplified registration procedure on

the grounds of traditional usage for appropriate indications suitable for self-medication, where the requirement for demonstration of therapeutic efficacy is reduced. The IMB has a new procedure for the registration of such products and further information is available on the IMB website.

Herbal products which are not eligible for the simplified registration scheme by virtue of, for example, their composition, route of administration or indications which are not compatible with the requirements of Directive 2004/24/EC must still be authorised as for any other medicinal product, prior to being placed on the market.

6.2 Homeopathic medicinal products

Homeopathic medicines represent special types of medicinal product for which particular rules may be applied by Member States recognising their tradition of homeopathic practice, in accordance with the requirements of Directive 2004/27/EC. This Directive is given effect in Irish legislation by the Medicinal Products (Control of Placing on the Market) Regulations (S.I. No. 540 of 2007) made under the Irish Medicines Board Acts, 1995 and 2006. Under this legislation it is recognised that the requirements for authorisation apply to any homeopathic medicinal product being placed on the market with therapeutic indications or in a form which may present risks which must be balanced against the desired therapeutic benefit. However, a simplified registration procedure in accordance with Article 14 of Directive 2001/83/EC as amended by Directive 2004/27/EC, may be applicable to those homeopathic products marketed without medicinal claims as provided for in Regulation 6 of these regulations (S.I. No. 540 of 2007). In order to obtain the certificate of registration referred to above, an application should be made to the IMB setting out the documents specified in Regulation 9 of these regulations

6.3 Slimming products

Many products intended for assistance in weight loss programmes are properly marketed as foods particularly where such products are intended as food replacements. Such products are regulated by the Food Safety Authority of Ireland and must meet appropriate food standards and comply with food labelling regulations.

Some slimming products however contain agents with clear pharmacological or metabolic activity and/or make medicinal claims. Such products are clearly medicinal products as outlined in Section 3 above and require authorisation prior to marketing. Examples of such products would be appetite suppressants, starch blockers, and certain bulk forming agents containing for example methylcellulose which have other medicinal uses. Oral anti-cellulite products have also been regarded as medicinal products as well as products which claim to increase blood supply or have 'thermogenic' activity (so called fat burners).

6.4 Hair loss products

Products claiming to treat or prevent baldness, (male or female pattern) alopecia or to stop, slow down or reverse hair loss are all categorised as medicinal products. Products presented for promoting or strengthening existing hair growth and thereby reducing hair loss or to nourish thinning hair would not be considered to be making medicinal claims and therefore would not be regarded as medicinal products provided they did not contain ingredients with specific medicinal (pharmacological) activity. The latter group of products would therefore not be subject to authorisation as medicinal products but would be more properly regulated as foods or cosmetics depending upon whether they were taken by mouth or administered topically.

6.5 Head lice products

Products intended for treatment or prevention of head lice infestation are always categorised as medicinal products requiring authorisation, irrespective of their composition. The only exception to this rule are products which act by a purely physical or mechanical means e.g. solutions which are used with a medical device to facilitate the physical removal of lice or their eggs from the scalp. Such products are usually oils or shampoos acting as lubricants to assist in the removal of the lice by a medical device such as a comb. Such products are considered to be medical devices and are regulated by the European Communities (Medical Devices) Regulations 1994, S.I. No. 252 of 1994 as amended and are required to carry the CE mark.

6.6 Products for use in the eye

The IMB considers that any product intended for administration to the eye must be regulated as either a medicinal product or medical device depending upon whether the mode of action is by pharmacological, metabolic or immunological means in the former case or by physical or mechanical means in the latter.

Thus, in keeping with European guidelines on classification of medical devices, products intended for use as irrigation solutions for washing the eye are medical devices. Similarly, products intended for use with contact lenses such as disinfecting, cleaning and rinsing agents and solutions which aid insertion or wearing of contact lenses, even without a therapeutic claim, are considered to be medical devices. All other products intended to be placed in the eye are medicinal products requiring authorisation.

6.7 Medicated swabs

Medicated swabs have traditionally been considered as medicinal products within Ireland requiring authorisation before being placed on the market. These products typically contain antiseptics such as chlorhexidine or iodine used either as pre-injection swabs or wound cleansers. These products are categorised as medicinal products because they exert an antimicrobial activity.

In contrast, medicated swabs containing alcohol intended as pre-injection swabs and used entirely for the sanitisation of unbroken skin prior to injection are often regulated as medical devices and require the CE mark before being marketed in the EU. Bearing in mind that there are some differences in the way different Member States classify these products, the IMB is prepared to accept a certain crossover of these two categories but insists that all such products bear either the CE mark or a product authorisation in order to be legitimately on the market in Ireland

6.8 Vitamin and mineral supplements

These products are considered to be medicinal products when their labelling or accompanying or associated literature make preventative, curative or remedial claim. In the past the IMB has classified as medicinal products any product containing vitamins and/or mineral ingredients where the recommended intake calculated with respect to any of the added vitamin or mineral constituents exceeds the maximum recommended daily dietary allowance for such constituents as published by the Minister for Health. However, with the implementation of the European Communities (Food Supplements) Regulations of 2003, S.I. No. 539 of 2003, a legislative framework for control of such products has been provided. This legislation has since been superseded by the European Communities (Food Supplements) Regulations 2007, S.I. No. 506 of 2007.

The schedules to the regulations set out those vitamin and minerals which may be used in the manufacture of food supplements in the form in which they can be added to food supplements. Under this legislation, the Food Safety Authority of Ireland is named as the official authority responsible for the supervision of this legislation. It is intended in the future to introduce maximum safe upper limits of the vitamin and mineral supplements listed in the schedules to the regulations. Once this has been achieved, then products containing vitamin and mineral supplements at levels up to these upper safe limits will be legitimately marketed under food legislation. Products that exceed the upper safe limit will not be permitted as food supplements and where such products fall under the definition of medicinal products, as above, then they will of course require to be authorised in accordance with the medicinal products legislation.

It should be also noted that in some cases there are levels of vitamins stated in the Medicinal Products (Prescription and Control of Supply) Regulations, 2003 which must not be exceeded by products otherwise presented as food supplements since any products which are restricted under this legislation can only be supplied on foot of a medical prescription from a registered pharmacy and are of course medicinal products requiring authorisation.

Consequently, vitamin and mineral supplements which meet the provisions of the Food Supplements Regulations may be marketed as food supplements and must

comply with food safety law including labelling restrictions. Products which make a medicinal claim or which contain levels of vitamin or minerals which exceed those restricted in the Medicinal Products (Prescription and Control of Supply) Regulations 2003 require a marketing authorisation issued by the IMB before being placed on the market in Ireland.

7. CONCLUSION

The codification of legislation and the revision of the definition of a medicinal product provided by EC Directive 2004/27/EC is a welcome development. Taken in conjunction with developments in the regulation of other categories such as medical devices, food supplements and cosmetics, the status of borderline products and the mechanism of their regulation should become clearer for the benefit of public health. The IMB classification process can aid in the clarification of the medicinal status and enquiries can be made to IMB as described above, when it is intended to provide an informed response, promptly and efficiently. The IMB collaborates with its regulatory partners in safeguarding public health for the population of Ireland, in accordance with the terms of its mission statement.

APPENDIX REFERENCES TO LEGISLATION

European

1. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Official Journal L 311, 28/11/2001 p. 67 – 128).

As amended by Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use (Official Journal L 136, 30/4/2004, p. 85 – 90).

And by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (Official Journal L136, 30/4/2004 p. 34 – 57).

2. Directive 2002/46/EC 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 (Official Journal L 193, 2002, p.51).
3. EC Directive 76/768/EEC5 of the European Council of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (OJ No. L262, 27/9/76, p169) (as amended)
4. EC Directive 93/42/EEC of the Council of the European Communities of 12th July 1993 concerning medical devices (OJ L.169, 12/7/2003, p1-43).

National

1. Medicinal Products (Control of Placing on the Market) Regulations, 2007, S.I. No.540 of 2007
2. Medicinal Products (Prescription and Control of Supply) Regulations 2003, S.I. No. 540 of 2003, as amended.
3. European Communities (Food Supplements) Regulations, 2007, S.I. No. 506 of 2007
4. European Communities (Cosmetic Products) Regulations, 2004, S.I. No. 870 of 2004 (as amended).
5. European Communities (Medical Devices) Regulations, 1994, S.I. No 252 of 1994
6. European Communities (Active Implantable Medical Devices) Regulations of 1994, S.I. No. 253 of 1994.