MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

BORDERLINE PRODUCTS

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of a borderline medicine or a medical device or a combination of a medicine and medical device. It represents the Medicines Control Council's current thinking on the safety, quality and efficacy of medicines and the safety, quality and performance of medical devices. It is not intended as an exclusive approach. Council reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine and the safety, quality and performance of a medical device in keeping with the knowledge current at the time of application. Alternative approaches may be used but these should be scientifically and technically justified. The MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy and registered medical devices will be of the required safety, quality and performance. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

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1 INTRODUCTION

According to the World Health Organisation (WHO), “many products are used in the delivery of health care, yet not all fit comfortably within an existing definition for a medical product, more specifically the term “medical device”. Examples include medical gases, some laxatives, cosmetic articles, clinical laboratory reagents and articles of protective clothing worn by medical personnel during procedures. A lack of clarity in such cases may lead to overlap or conflicting regulatory requirements for a product, or (worse), to no effective regulation being applied. It is in the public interest to ensure the safety, quality and performance of all such “borderline” products through appropriate regulatory controls; either those for medical devices or for other regulated product sectors (e.g. medicines including advanced therapy medicinal products (ATMP), cosmetics, food supplements or personal protective equipment).”

With increasing awareness of the value of pro-active engagement of men, women and children in their physiological health, people may seek solutions in channels outside of allopathic health professionals and often engage individuals who engage in so-called “alternative” or traditional approaches to health care.

In South Africa the allopathic disciplines of professional healthcare are largely recognised under the umbrella of the Health Professionals Council of South Africa (HPCSA), Pharmacy Council and the Nursing Council and the so-called alternative disciplines are recognised under the Allied Health Professionals Council of South Africa (AHPCSA).

Furthermore products used for health related matters may be categorised into two major categories according to intent, i.e. those which aim to diagnose, to treat and to prevent disease and injury; and general health and wellness products.

Health products which aim to diagnose, to treat and to prevent disease and injury include all medicines (allopathic and complementary) and medical devices (including in vitro diagnostic devices, IVDs). The regulation of safety and efficacy of medicines is well established for allopathic medicines and recently initiated for complementary medicines.

The regulation of safety and performance of medical devices has recently been initiated in South Africa.

Access to medicines, apart from those deemed to be of low risk to consumers, in South Africa is managed and controlled through different healthcare professionals, where their respective scope of clinical practice is identified together with their professional council / authority to prescribe different categories (schedules) of medicines.

The grouping of chemical entities (scheduled substances) into so called “schedules” is dependent on the risk profile of the substance for the patient.

The second type of products associated with health referred to above includes healthy foods and “general health products” or “general health and wellness devices”.

General health and wellness products may be described as products or devices that meet the following two factors: intended for general health and wellness use, and present a very low risk to users’ safety.

General health and wellness products / devices may include exercise equipment, monitoring devices, audio recordings, video games, software programs and other products / devices that are commonly, though not exclusively, available from retail establishments (including online retailers and distributors that offer software to be directly downloaded), when consistent with the two factors above.

Recent use of technology has reduced the size and weight of many of these devices to make them easy to transport and “mobile”. Furthermore developers have designed them to be “wearable” devices.

The regulatory approach for wearable health and wealth devices is presented in Section 5.

It should be noted that while “cosmetic products” are not included in the above mentioned descriptions, items which are deemed medicines and or medical devices may also be used for cosmetic purposes. However not all cosmetics are medicines or medical devices.

Advances in technology and increasing demand by consumers for medical and cosmetic items are challenging the traditional concepts and divides of “cosmetic” versus “health products”. For all of the above mentioned reasons – the traditional boundaries between health and wellness products, medicines, medical devices and cosmetics is challenged.

In South Africa, — 'cosmetic' means any article, preparation or substance (except a medicine as defined in the Medicines and Related Substances Act, 1965 (Act 101 of 1965)) intended to be rubbed, poured, sprinkled or sprayed on or otherwise applied to the human body, including the epidermis, hair, teeth, mucous membranes of the oral cavity, lips and external genital organs, for purposes of cleansing, perfuming, correcting body odours, conditioning, beautifying, protecting, promoting attractiveness or improving or altering the appearance, and includes any part or ingredient of any such article or substance.” (Act No. 39 of 2007: Foodstuffs, Cosmetics and Disinfectants Amendment Act, 2007.)

The diagram below (Figure 1) visualises the overlapping domains of health technologies, where ‘”Health Technologies” refers to the application of organised knowledge and skills in the form of (medical) devices, medicines, vaccines, procedures and systems developed to solve a health problem and to improve quality of lives. (WHA 60.29.)

A product which falls in more than one domain, i.e. an overlapping “domain” is often referred to as a “borderline” product. While use and intended use may vary for these “products”, including software, it is the safety of use which is the key concern for policy makers and national regulators.

1 Introduction – continued

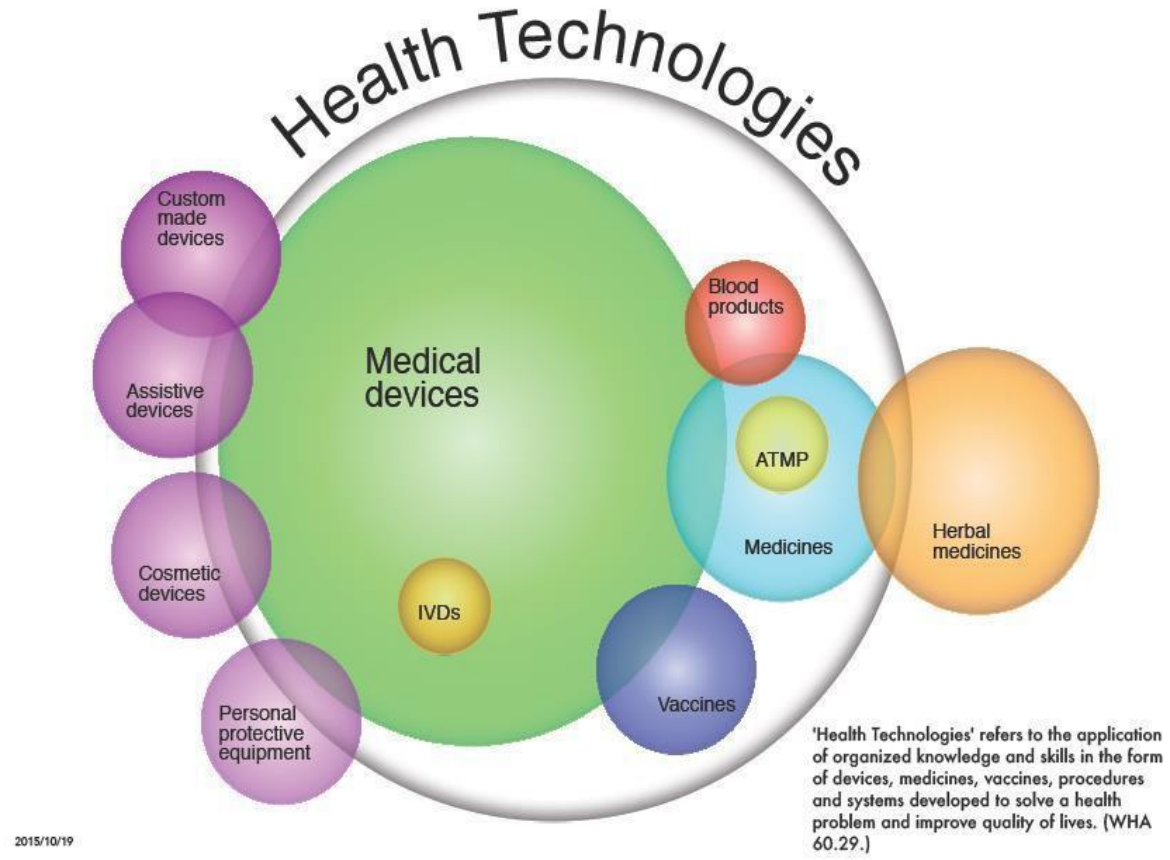

Figure 1. Inter-relation of (medical) products inside and outside healthcare.

According to the WHO, "Borderline products are generally medical products for which it is unclear which legislation applies. Although they may have some of the attributes of two or more categories of regulated products, they are not necessarily combination products. A combination product is a product comprised of two or more components which are regulated as medical products, i.e. medicine/medical device, or vaccine/medical device, that are physically, chemically or otherwise combined or mixed and produced as a single entity. (Modified from US FDA definition http://www.fda.gov/CombinationProducts/AboutCombinationProducts/ucm118332.htm)."

The WHO advises that "to be predictable and transparent, the regulator should develop criteria and mechanisms for determining the appropriate regulatory regime for such products through a guideline. It should describe considerations and the process whereby an applicant may obtain an advisory opinion from the regulatory authority. As necessary, that process should allow for consultation with subject matter experts as well as with regulatory authorities from other product sectors like medicines or food. It may also take into account determinations made by regulatory authorities of other jurisdictions. A decision by the regulatory authority on the regulatory status of a product should provide the option of appeal in case the applicant does not agree with the decision" (WHO QAS/16.664, May 2016).

A cosmetic may also be described as a personal care product or one which is not easily distinguished as a general wellness product, a medicine or a medical device.

There are a broad range of products at the cosmetic-medicine-medical device interface. It is recognized that at a minimum, these products are perceived to have cosmetic attributes such as cleansing, improving or altering the complexion, skin, hair or teeth. These products may also have claimed or inherent medical attributes. Examples of these types of products include anti-dandruff shampoos, skin whiteners, antiperspirants and sunburn protectants.

Depending on their representation for sale and composition, regulations under Act 101 may apply.

The foundation for the policy and this guideline on borderline products is developed on:

The strategic intent of Act 101 of 1965 as amended, which aims to ensure availability of safe and effective medical products to diagnose and treat South Africans within the overarching mission of protecting and promoting public health to improve, extend lives and minimise suffering of South Africans, is:

- to provide for the control of medicines and scheduled substances and medical devices;
- to effect certain technical corrections for the registration of medicines, medical devices, certain foodstuffs and cosmetics;
- to utilise a benefit-risk framework for premarket review of complex products including medical devices and implementing pre-market and post-market oversight;
- to bring timely access to devices without compromising standards of safety and performance;
- to keep pace with rapidly evolving new technologies, including mobile medical computer software applications ("Apps") and other health information technology (IT), companion diagnostics, and next generation sequencing tests and solutions;
- to utilise the principles of regulatory science that promote the lifecycle approach to regulation for both pre- market approvals and the post-market evaluation of the benefit-risk profile of medicines, medical devices, biologics and combinations thereof, during their entire time on the market; and
- to learn and benefit from work completed and outcomes observed elsewhere in the world.

2 SCOPE OF GUIDELINE

The scope of this guideline is noted below, with the understanding that borderline products encompass "combination" products; i.e. combination products are a specific type of borderline product.

- How the Regulatory Authority will decide and designate which "department" of the national Regulatory Authority (i.e. within MCC or SAPHRA) will have primary jurisdiction for review of borderline (single entity and combination products) products, when the jurisdiction is unclear or in dispute.
- "Borderline products" are comprised of any combination of a medicine and a medical device; a medical device and a biological; a biological and a medicine or a medicine, a medical device and a biological or a medical device used for cosmetic purposes.
- The procedure to enable timely and effective premarket review of borderline products for purposes of designation to a specific regulatory pathway.
- How to facilitate designation of medical products currently registered as medicines to the register of medical devices.
- Recognition of "health and wellness" products and the regulatory framework.

2.1 Examples of Borderline Products

Examples of borderline and combination products where the components are physically, chemically or otherwise combined (this list is not exhaustive and merely an indicator);

- Device coated or impregnated with a drug or biologic
- Drug-eluting stent; pacing lead with steroid-coated tip; catheter with antimicrobial coating; condom with spermicide
- Skin substitutes with cellular components; orthopaedic implant with growth factors

- Prefilled syringes, insulin injector pens, metered dose inhalers, transdermal patches;
- Head lice products;
- Monoclonal antibody combined with a therapeutic drug;
- Viscoelastic gels for joint lubrication;
- Irrigation solutions.

This guideline relates to management and organization within the Regulatory Authority and the action required by a person who imports or manufactures a borderline product.

Nothing in this guideline prevents the Regulatory Authority from using any resources it deems necessary to ensure adequate review of the safety and efficacy and safety and performance of any product, or the substantial equivalence of any device to a predicate medicine or medical device.

The scope of this policy does not include:

- A combination of products where the components are packaged together; for example:
  - Drug or biological product packaged with a delivery device (for example a cough syrup with a measuring spoon);
  - Surgical tray with surgical instruments, drapes, and lidocaine or alcohol swabs OR
- A combination of products where the components are separately provided but labelled for use together;
- Photosensitizing drug and activating laser/light source;
- Iontophoretic drug delivery patch and controller.

3 BORDERLINE MEDICAL PRODUCTS

Innovation and advances in technology have brought health products to market which are difficult to distinguish as a medicine, medical device, cosmetic, food supplement or biocidal product. These products are called “borderline” products until the classification status thereof is decided by the Regulatory Authority and the product is designated to a particular regulatory pathway. Some borderline products, although not all, include combinations of medicines, medical devices, and biologicals which may be used for medical or general wellness or cosmetic purposes.

This guideline aims is to provide direction and manage these “borderline” products (including combination products) with clarity and efficiency, as many of these technologies are innovative and potentially of significant value to the health of South Africans which means they are of significant public interest.

The entireties of both medicine and medical device definitions are taken into account to determine which one is the most applicable to the product and how it works. For example, a liquid for use as a body cavity filler can be classified as a medicine when considering only parts of the two definitions. However, its purpose is clearly best characterized as to modify the anatomy and act as a support structure once it has filled the limited volume of a cavity. Therefore it is more reasonably classified as a medical device.

The definition of a medical device and a medicine (as amended by Act 14 of 2015) are noted below for reference.

“medical device” means any instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, software, material or other similar or related article including Group III and IV Hazardous Substances contemplated in the Hazardous Substances Act, 1973 (Act No. 15 of 1973) —

(a) intended by the manufacturer to be used, alone or in combination, for humans or animals for one or more of the following:

(i) diagnosis, prevention, monitoring, treatment or alleviation of disease;
(ii) diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
(iii) investigation, replacement, modification, or support of the anatomy or of a physiological process;
(iv) supporting or sustaining life;
(v) control of conception;
(vi) disinfection of medical devices; or
(vii) providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body; and

(b) which does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human or animal body, but which may be assisted in its intended function by such means.

"medicine"

(a) means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in —
(i) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in humans; or
(ii) restoring, correcting or modifying any somatic or psychic or organic function in humans, and

(b) includes any veterinary medicine.

3.1 Designation of Borderline Medical Products

This section of the guideline addresses the key issues with regard to the designation of the medical product to a specific regulatory pathway.

The Regulatory Authority (MCC or SAHPRA) will appoint a committee, consisting of experts from the relevant multi-disciplines (medicines, medical devices, IVDs, human tissues and cells, biologicals, biocides, general wellness and cosmetics), to assess and assign all products including so-called borderline products (including combination products) to a primary regulatory pathway which will assess evidence presented in support of safety, quality and efficacy (for medicines) or safety, quality and performance (for medical devices).

This will ensure that like products will be similarly assigned and regulated, and will allow for designation of new medical products, for which the most important therapeutic action cannot be determined, to be assigned to the most appropriate department of the Regulatory Authority based on the most significant safety and efficacy and safety and performance issues they present.

In addition, by providing a defined framework for the assignment process, prompt assignment of borderline products, including combination products, may be achieved.

Nothing in this guideline prevents the Regulatory Authority from using any resources it deems necessary to ensure adequate review of the safety and efficacy or safety and performance of any product, or the substantial equivalence of any device to a predicate device.

The decisions of this body will be published on the Regulatory Authority's website. Publication will help to build a common understanding of the Regulatory Authority's practical implementation of the agreed policy.

The process for borderline products (including combination and non-combination/single entity products) is initiated by a person licensed to manufacture medicines or medical devices or a person licensed to import medical devices through the "Request for Designation" (RFD) process. When jurisdiction of a borderline or combination or non-combination product is unclear or in dispute, a completed RFD must be submitted to the office of the Registrar of the MCC or the CEO of SAHPRA.

Manufacturers and importers are encouraged to submit an RFD as soon as the relevant and sufficient information for the Regulatory Authority to make a decision regarding designation of a product is available. Refer to “REQUEST FOR DESIGNATION in section 7.

The designation of a borderline product (which may be a combination product) to either the Medicines or Medical Device department with primary jurisdiction within the Regulatory Authority (i.e. as the lead department) for pre-market review will be based on a determination of the “primary mode of action” (PMOA) of the product.

The primary mode of action (PMOA) means “the single mode of action of a borderline product that provides the most important therapeutic action of the borderline product.”

The most important therapeutic action is the mode of action expected to make the greatest contribution to the overall intended therapeutic effect(s) of the borderline product.

The claimed effect or purpose must be achieved by the most important therapeutic action.

Where the primary intended mode of action is achieved by pharmacological, immunological or metabolic means, in or on the human or animal body, the borderline product is designated to be a medicine; where

- Immunological - is understood as an action in or on the body by stimulation and/or mobilisation of cells and/or products involved in a specific immune reaction;
- Metabolic - is understood as an action which involves an alteration of the normal chemical processes participating in, and available for, normal body function. The fact that a product is itself metabolized does not imply that it achieves its principal intended action by metabolic means; and
- Pharmacological - is understood as an interaction between the molecules of the substance in question and a cellular constituent, usually referred to as a receptor, which either results in a direct response, or which blocks the response to another agent and, for the purposes of this policy, includes anti-infective activity.

Where the primary intended mode of action is achieved by pharmacological, immunological or metabolic means, and the action occurs *in vitro*, without reintroducing a modified cellular substance to the patient, the product will be designated to be a medical device.

Where the primary intended mode of action by which the claimed effect or purpose is not achieved by pharmacological, immunological, or metabolic means, but may be assisted in that effect or purpose by pharmacological, immunological, or metabolic means, the borderline product (including a combination product) will be designated to be a medical device.

A borderline product may be classified as a medicine or a medical device, even when no explicit therapeutic claim is made. A therapeutic claim may also be implicit. Both types of claims are considered when a product is classified. Explicit claims are stated with no ambiguity with regard to their meaning or intent. In contrast, implicit claims made in the representation of a product indirectly suggest a therapeutic benefit. Product representation includes the appearance, labelling, and advertising of a product.

In the absence of either an explicit or implicit claim, a product may be classified (e.g. as a medicine or a medical device) if the intrinsic properties of the product are such that there is no other possible use. For example, acetaminophen (paracetamol) has no other use but as a medicine, so the absence of a claim will not change its classification as a medicine.

Conversely, the presence of a health claim may not be sufficient to classify a product as being subject to the Act. For example, health claims associated with a consumer product or textile may be inappropriate, false or misleading. This can lead to compliance action in accordance with the provisions of the Consumer Protection Act, rather than classification of the product as a health product subject to the Medicines and Related Substances Act.

In addition to the primary mode of action – the composition and form of the product and the therapeutic effect of the product may be considered to assist in the designation of the product.

The composition and form of a product may help to distinguish a medicine from a medical device. A medical device exhibits structure in its final therapeutic form, that is, the structure of the product when it is achieving its effect. With a medical device, its structure contributes directly to its effect. In contrast, the physical structure of a medicine (that is, in its dosage form, such as a tablet or an ointment, not its chemical structure) does not usually contribute directly to its therapeutic effect.

As an example, solid substances formed by polymeric reactions, such as dental cements, or through evaporative mechanisms such as with liquid bandages, are initially applied to the patient in semi-solid or liquid states. In each case, however, the final therapeutic form exhibits a definable structure and the product is more appropriately classified as a device, rather than a medicine.

Consideration is also given to the therapeutic effect of a product and how this effect is achieved. In Act 101, as amended, the definition of a medicine and medical device differ respectively in whether a product is used to restore, correct or modify any somatic or psychic or organic function (as with a medicine) OR treat or alleviate a disease; treat, alleviate or compensate for an injury, or modify or support of the anatomy or of a physiological process (as with a medical device).

Under the medicine definition, an “organic function” is generally interpreted as including the various “functions of life” that occur without conscious assistance, such as digestion, metabolism, growth, secretion, excretion, circulation, and respiration. Effects that modify an organic function may be either local or systemic in nature.

Under the medical device definition, “anatomy” and ”physiological process” refer to physical components such as bodily cells, tissues, and organs, such as bones, muscles, and tendons. A ”physiological process” refers to the physical movement of the body structure. Effects that modify the anatomy or physiological process are strictly local.

When considering the claim made for a product, it is important to note whether more than one property can contribute to the overall effect of the product when used for this indication. For example, if a therapeutic substance is shown to modify an organic function as well as a physiological process (body function) or anatomy, then both medicine and medical device definitions can be satisfied. To make the necessary distinction, a comparative risk assessment should be made. Specifically, if it is determined that the greater risk is associated with the modification of an organic function, then the safety, quality and efficacy of the product would be more appropriately assessed under the medicine framework. The reverse will also apply.

Under the medical device definition, a product that is considered to be a “related article” is itself classified as a medical device. Before such a decision is made, however, it must be confirmed that the product does not meet the definition of a medicine under the recommended conditions of use. A product considered to be an “accessory to a medical device” does not possess therapeutic properties of its own related to the purposes of the device: its use is solely to assist in the therapeutic function of the primary medical device.

A combination product may also have two independent modes of action, neither of which is subordinate to the other. In cases where neither the Regulatory Authority nor an authorised person of the Manufacturer or Distributor can determine the most important therapeutic action at the time a request is submitted, an algorithm will be used to determine the primary regulatory pathway assignment. The algorithm directs an assignment based on consistency with other combination products raising similar types of safety and efficacy (for a medicine) or safety and performance (for a medical device) questions, or to the centre with the most expertise to evaluate the most significant safety and efficacy or performance questions raised by the combination product. (Refer to Section 7 Request for Designation Procedure).

3.2 Influence of Subordinate Regulations

Once a product has been classified as a medicine and not a medical device at the level of the Act, further classification is required to determine to which category of medicine the product belongs. (The scope of this guideline does not include such determination).

3.3 Comparative Standards of Evidence

The respective requirements for filing an application for registration of a medicine or medical device are not considered when classification decisions are made. Data requirements may differ when demonstrating quality, safety and efficacy (for a medicine) and safety and performance (for a medical device). However, some flexibility at both the regulation and policy levels is required to assure that evidence sufficiently demonstrates that the benefits of the therapeutic product outweigh its risks.

3.4 Decisions by Other Regulatory Authorities

Differences exist in the definitions adopted by South Africa and other jurisdictions. In addition, the respective interpretations of these definitions may further affect whether a product is classified as a medicine or medical device or cosmetic in different jurisdictions.

MCC or SAHPRA may consider the classification decisions of other Regulatory Authorities as a tool to assist in its interpretation and application of the definitions in the South African legislation.

4 BORDERLINE COSMETIC PRODUCTS

The following principles apply for designation of borderline cosmetic products:

The primary consideration will be to maintain the protection of public health and safety, consistent with the objectives of Act 101 and the applicable regulatory framework.

The definitions of “cosmetic‘ in the Foodstuffs, Disinfectants and Cosmetics Act (FD&C Act) and “medicine‘ and “medical device” in the Medicines and Related Substances Act must be respected.

Risk alone does not qualify a substance as either a cosmetic or a medicine or a medical device.

The distinction between medical products and cosmetics is based on two main factors:

- *The composition of the product:* Although the composition of a product alone does not necessarily determine its designation, the presence of an ingredient, or its concentration, may make the product unsuitable for designation as a cosmetic or as a medicine or medical device.
- *Representations made about the product:* The key consideration for the designation of a product is its proposed claim(s). A claim can be a word, a sentence, a picture, a symbol, a paragraph or an implication on product labels, package inserts or advertisements. Together, these claims are used to create a net impression of what the product is and does.

While both factors are important, ultimately the intended purpose of the product takes precedence in the classification decision.

4.1 Criteria

Respecting the definitions of “cosmetic‘ and “medicine” and “medical device” in the FD&C Act and Act 101, the following criteria and considerations stipulate the main factors in order to clarify the analysis and decision-making process.

The criteria below may not be given equal weight in support of a decision, as some factors may be more important to consider in one circumstance versus another. Not all criteria need be applied if a decision can be reached after the examination of one or a few criteria. In the event that the standard criteria do not lead to a clear decision, supplementary considerations may be taken into account. The final decision is dependent on the overall consideration.

4.1.1 Composition

Where the product’s composition suggests it is an agent for treating, diagnosing, preventing, monitoring, alleviating disease or injury; or restoring, correcting or modifying organic functions in human beings it is a medical device or a medicine.

A medicine exhibits therapeutic or pharmacological activity, such as interacting with a receptor site to achieve a biological response. Modification of an organic function can range from minor to major, which falls within the definition of a medicine as per the Act. This is determined by the mode of action, which is defined as the means by which a product achieves its intended effect.

Some ingredients are inherently medicines. For example, corticosteroids are internationally recognized as medicines. On the other hand, an ingredient may have a cosmetic function until it reaches a certain threshold, at which point it has a therapeutic or pharmacological effect.

In a case where a product makes a therapeutic representation, there is inherently one or more ingredients in the composition that contribute to this effect. As such, any substance supporting a therapeutic claim for a product is likely to be considered an active ingredient.

4.1.2 Representation

Where the product is represented in a manner suggesting it is used for treating, diagnosing, preventing, monitoring, alleviating disease or injury; or restoring, correcting or modifying somatic, psychic or organic functions in human beings it is a medical device or a medicine.

“Representation” includes indications of use, claims presented as a word, a sentence, a picture, a symbol, a paragraph or an implication on product labels, package inserts or advertisements.

Further, representations may be explicit or implied.

A designation decision is made on the definition and the representation for sale of a given product. False or misleading claims for cosmetics, medicine and medical devices are offences. Products for which therapeutic claims are made are evaluated as medicines or medical devices.

Another main distinguishing feature of representation is the aspect of specific dose instructions or instructions for use (IFU) to ensure efficacy or performance which is generally associated with medical products. Proof of efficacy is essential for medicines to ensure that the benefits of use outweigh the risks. There should be no risk from the lack of efficacy of a cosmetic, which is applied on an as-desired basis. This should not be confused with directions for safe use.

Where the product is likely to be understood by consumers to have characteristics of a medicine or medical device it is a medicine or medical device.

Perception includes the purpose for which the general public uses the product and whether it is likely to be understood by consumers to have characteristics of a cosmetic or medical product. Perception is further influenced by the extent or level of action promised by a product, in addition to the consumer's expectations for the level of regulatory control applied. For example, products claiming benefits comparable to the effects of cosmetic surgical procedures or medicines are considered therapeutic. While perception will not be considered the sole basis for a decision, in certain cases, it may have an influence on how a product is used by consumers.

4.1.3 Level of Action

In order to be a cosmetic, the product must exhibit a lack of percutaneous absorption and should not have to be absorbed systemically to achieve the effect.

Products that are administered through ingestion, inhalation, or by injection (intramuscular, subcutaneous, intravenous, etc.), with the sole exception of tattoo ink, are not considered to be cosmetics. However, it is generally understood that cosmetics may exert a negligible organic effect which is local and transient. An example of the latter would be a moisturizer which hydrates by adding water to the epidermis.

4.1.4 Other Considerations

The following may also be taken into consideration:

- *Inherent risk-benefit balance related to product efficacy*

  Risk of a product is generally mitigated under its applicable regulation. If a medical product is not efficacious, it can potentially incur a risk (e.g. ineffective anti-caries toothpaste creates the risk of developing cavities). On the other hand, if a cosmetic does not demonstrate efficacy, it should not incur an added risk.

- *Cases of precedence or past decisions*

  While these are to be kept in mind, they should be open to reconsideration in the event of new policies and knowledge.

- *Classification schemes of other regulatory authorities*

  MCC or SAHPRA may consider how other Regulatory Authorities classify certain products. This consideration must be tempered by differences in product category definitions, legal systems, and policies, as well as the current regulatory framework under which MCC or SAHPRA operates.

5 WEARABLE HEALTH AND WELLNESS DEVICES

This section of the guideline aims to:

- identify and define so-called "wearable health and wellness devices",
- identify the difference between a "general wellness device" and a "medical device";
- identify when a wearable health and wellness device is classified as a medical device;
- identify when an "App" is a medical device;
- recognise fitness "Apps" and wearable health / wellness devices; and
- identify the implications of a wearable device being a medical device.

5.1 A Risk Based Framework

The classification of a so-called "wearable health and wellness device" and consequent regulation thereof as a medical device is dependent on the developer and manufacturer's intended use of the device.

Regulatory control of medical devices follows a risk based framework.

Registration of medical devices by MCC or SAPHRA will depend on the risk classification of the medical device and ability of the manufacturer to provide evidence that the necessary safety and performance criteria have been met. Assessment, according to the Essential Principles of Safety & Performance, is done within the Conformity assessment framework. (Refer to Guideline on Conformity Assessment for Medical Devices)

"General health products" or "General health and wellness devices" may be defined as products or devices that are intended for only general health and wellness use, and present a very low risk to users' safety.

General health and wellness products / devices may include exercise equipment, monitoring devices, audio recordings, video games, software programs and other products / devices that are commonly, though not exclusively, available from retail establishments (including online retailers and distributors that offer software to be directly downloaded), when consistent with the two factors above.

Recent use of technology has reduced the size and weight of many of these devices to make them easy to transport and "mobile". Furthermore developers have designed them to be "wearable" devices.

The use of technologies such as smart phones, social networks and internet applications provides innovative ways for individuals to monitor health and well-being and give greater access to information. Together these advancements are leading to a convergence of people, information, technology and connectivity to improve health care and health outcomes.

Mobile phones are increasingly equipped with a range of devices capable of being used as sensors, including gyroscopes, accelerometers, microphones and cameras, and have sufficient processing power to analyse the data which those sensors produce.

Similarly, advancement in the battery efficiency of Bluetooth and other short-range radio technology means that ever-smaller devices can be created, capturing and logging data and triggering actions.

Many of these devices are used within the so-called area of "digital health" which includes categories such as mobile health (mHealth), health information technology (HIT), wearable devices, telehealth and telemedicine, and personalized medicine.

Consumers and patients may use digital health to better manage and track their health and wellness related activities. As well as use in fitness and exercise contexts, these computer software applications ("Apps") and wearables can be used to provide mobile health ("mHealth" services), potentially crossing the line from recreational to medical and healthcare applications.

The intended purpose of a device is the use to which it is intended according to data supplied by the manufacturer in the technical documentation, on the labelling, instructions for use, and promotional materials. How the manufacturer or "App" developer advertises and describes the product is therefore very important.

5.2 When a Wearable Health and Wellness Device is a "Medical Device"

A device for data gathering — for example, something which measures heart rate or motion — does not constitute a medical device in itself. However, where the device performs a medical assessment function, or is used as an accessory to a medical device (such as a wearable intended by the manufacturer to be used with a medical device app), and is used specifically to diagnose or monitor a disease, such device is a medical device and must comply with the requirements of Act 101 and the medical device regulatory framework.

For example, a thermometer to record human body temperature is not in itself a medical device. However a wearable device which detects and records body temperature is a medical device if the intended purpose of the device is to detect elevated body temperature associated with a medical condition. Furthermore a "smart thermometer" which detects and records body temperature and attempts to indicate whether the user has a medical condition is also a medical device.

Similarly a "wearable" device to measure and monitor blood glucose levels is a medical device. Inaccurate readings may have significant and serious impact on the health of the wearer / patient.

It should be noted that all devices, wearable or non-wearable, which perform a measuring function, even if not for medical purposes, are required to comply with the Legal Metrology Act (Act 9 of 2014).

5.3 When an "App" is a "Medical Device"

An "App" is specific software developed to perform a specific function, often, but not only, for a mobile device.

Therefore, if the developer / manufacturer of the "App" intends for it to be used, alone or in combination, for

- diagnosis, prevention, monitoring, treatment or alleviation of disease; or
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury; or
- investigation, replacement, modification or support of the anatomy or of a physiological process; or
- supporting or sustaining life; or
- for providing information for medical or diagnostic purposes by means of *in vitro* examination of specimens derived from the human body;

  then the "App" is a medical device.

Software used in or with medical devices is considered to be within the medical device regulatory framework.

For example, an "App", which uses a phone's camera to take a photograph of an area of skin, assesses that photograph against a database of known skin conditions and attempts to diagnose from which clinical condition the user is suffering, is a medical device.

The provision of non-personalised medical advice, such as an "App" which integrates with a surgery's booking system to speed up booking a doctor's appointment, falls outside the definition of a medical device.

5.4 Fitness "Apps" and Wearables

Unless an "App" or wearable device is intended by its manufacturer to be used for any of the regulated medical purposes set out above, it is not a medical device. As such, an "App" or wearable, or a combination of the two, may be used in a fitness context — for example, tracking a user's physical activity — without it necessarily falling within the medical device regulatory framework.

The focus on intended use means that one dataset or source of information can be used in two separate ways, one regulated and one not. For example, logging a user's pulse can be a data source for a medical device, monitoring the wearer's circulatory system and flagging when the user is suffering some form of cardiac irregularity, is regulated. However as part of a broader, non-medical, fitness tracking "App", showing a user the extent to which s/he is exerting her/ himself during exercise, is not regulated within the medical device regulatory framework.

Where a fitness "App" purports to provide a medical function, such as diagnosis of an injury, it moves into the regulated sector. As the manufacturer's intended use is a core test as to whether something is a medical device, a company which distributes a non-medical fitness "App" or wearable must not make claims which indicate that the device has a medical function. Aside from general advertising and liability issues, unfounded claims of this nature will give rise to criminal sanctions for non-compliance with the medical device regulatory framework.

5.5 Implications of being a Medical Device

Where an "App" or wearable is a medical device, or an accessory to such a device, it must comply with the regulatory framework if it is to be sold or distributed lawfully in South Africa. Failing to comply with the obligations of the framework is a criminal offence.

The regulatory framework for medical devices is a risk based framework.

The obligations to which a manufacturer must adhere depend on the classification of the medical device.

There are four classes of medical devices:

- Class A - Low Risk
- Class B - Low-moderate Risk
- Class C - Moderate-high Risk
- Class D - High Risk

where risk relates to the patient or user or to public health.

The higher the risk of the medical device for the recipient and user, the more highly it will be classified, with greater obligations imposed on devices of higher classifications.

A stand-alone "App" may be a Class A device, on the basis that it is inherently non-invasive and of low risk to the user and patient. A wearable (medical) device may also be Class A medical device, however depending on the manufacturer's intended use, it may be classified within a higher class.

In accordance with the Regulations for Medical Devices and IVDs a Class C and a Class D medical device (excluding condoms) may not be advertised to the Public or a lay-person.

6 MEDICAL DEVICES CURRENTLY REGISTERED AS MEDICINES

6.1 A person who currently holds a certificate of registration for a medicine which may be classified as a medical device may use the REQUEST FOR DESIGNATION procedure in Section 7 to motivate for the transfer of the product currently registered as a medicine to the medical device register.

6.2 The REQUEST FOR DESIGNATION as noted in 6.1 must also be accompanied by the following documents:

Class D medical device:

- South African Declaration of Conformity to the Essential Principles of Safety and Performance as per the Conformity Assessment Guideline;
- Full technical dossier, including design file
- Quality Assurance Certification as per ISO13485
- Product Quality Assurance Certificate(s).

Class C medical device:

- South African Declaration of Conformity to the Essential Principles of Safety and Performance as per the Conformity Assessment Guideline;
- Technical dossier
- Quality Assurance Certification as per ISO13485
- Product Quality Assurance Certificate(s).

Class B (non-sterile) medical device and Class A measuring medical device:

- South African Declaration of Conformity to the Essential Principles of Safety and Performance as per the Conformity Assessment Guideline;
- Quality Assurance Certification as per ISO13485
- Product Quality Assurance Certificate(s).

Class B sterile and Class A sterile medical device:

- South African Declaration of Conformity to the Essential Principles of Safety and Performance as per the Conformity Assessment Guideline;
- Quality Assurance Certification as per ISO13485
- Production Quality Assurance Certificate.

Class A medical device

- South African Self Declaration of Conformity to the Essential Principles of Safety and Performance, as per the Conformity Assessment Guideline.

7 REQUEST FOR DESIGNATION PROCEDURE

7.1 The owner / authorised representative of a health, cosmetic or medical product where the relevant governing legislation and governing agency with primary jurisdiction is unclear or in dispute, should submit a request for designation of the borderline product to a primary regulatory pathway by preparation of a REQUEST FOR DESIGNATION as noted below.

7.2 Ten printed (paper) copies of the REQUEST FOR DESIGNATION must be submitted to the Authority, together with the document saved onto a CD ROM (see 7.5 below).

7.3 Presentation

The submission must include a cover letter and table of contents,

The pages must be paginated sequentially and divided from the other documents by a labelled, tabbed divider

Font sizes should be of a style and size that are large enough to be easily legible, even after photocopying, Arial 12 point font is preferred for narrative text, but printing in a font size with a legibility equivalent to at least Arial 10 point black on white maybe used. The copies, including figures, tables, photo's should be clearly legible. Shading and/or coloured filling/background and/or print, e.g. in tables and headers, or across pages, is unacceptable and should be avoided.

The left-hand margin should be sufficiently large that information is not obscured through binding

The submission should be properly bound on the left side as this allows for easy update/addition of pages. The left margin of documents should be wide enough to allow for legibility after copying and binding.

Binding is left to the discretion of the applicant; however, the use of lever-arch files and ring binders is not accepted and the use of metal fasteners should be avoided regardless of the thickness of the document, as they injure and damage. The binding should enable the easy handling and evaluation of documents without it coming apart.

7.4 The REQUEST FOR DESIGNATION with supporting motivation, must not exceed 30 A4 size pages, including attachments, and must set forth the following information in the sequence as noted below:

- The identity of the owner and Authorised Representative or Responsible Pharmacist, including company name and physical address, establishment licence number (Act 101), company contact person, designation of the contact person, email address and telephone number;
- A description of the borderline product, including:

  Common, generic, or usual name of the borderline product and all component products or ingredients;
- Classification or schedule of the borderline product and all component products or ingredients, if applicable;
- Proprietary name of the borderline product;
- Identification of any component or ingredient of the borderline product that already has received premarket approval or is registered with any Regulatory Authority, is marketed as not being subject to premarket approval, or has received any type of exemption.
- The chemical, physical, or biological composition;
- Status and brief reports of the results of developmental work, including animal/ other testing;
- Description of the manufacturing processes, including the sources of all components or ingredients;
- Proposed intended use or indications;
- Description of all known modes of action, the owner's(s) and Authorised Representative's or Responsible Pharmacist's identification of the single mode of action that provides the most important therapeutic action of the product (i.e. the primary mode of action), and the basis for that determination;
- Schedule of the active ingredient(s) and concentration per standard dose / application / use (where applicable) and duration of use;
- Dose and route of administration of a medicine or biologic;
- Instructions For Use for a medical device;
- Risk assessment and risk management plan for the borderline product (refer ISO14971);
- Description of related products, including the regulatory status of those related products;
- Proposed claim(s);
- Any other relevant information and
- Summary checklist for Designation (see Attachment 1).

The owner(s) and Authorised Representative's or Responsible Pharmacist's recommendation as to which department within MCC or SAHPRA should have primary jurisdiction based on the mode of action that provides the most important therapeutic action of the combination product i.e. the Primary Mode of Action.

If the owner(s) and Authorised Representative or Responsible Pharmacist cannot present with reasonable certainty which mode of action provides the most important therapeutic action of the combination product, the owner(s) and Authorised Representative's or Responsible Pharmacist's recommendation must be based on the Regulatory Authority's component that regulates other combination products that present similar questions of safety and efficacy or safety and performance with regard to the borderline product as a whole; and

an assessment of the assignment of other borderline products (including combination products) the owner(s) and Authorised Representative or Responsible Pharmacist wishes MCC or SAHPRA to consider during the assignment of its borderline product.

When there are no other borderline products that present similar questions of safety and efficacy or safety and performance with regard to the borderline product under review (including combination products) as a whole, the Regulatory Authority will assign the borderline product to the department within the Authority with the most expertise related to the most significant safety and efficacy and safety and performance questions presented by the borderline product.

All communications relating to a request for designation must be addressed to the attention of the Registrar of the MCC or the CEO of SAHPRA. Such a request, in its mailing cover should be clearly marked "REQUEST FOR DESIGNATION".

7.5 For the RFD submitted on a CD-ROM, the following statement should be included in the letter of request, after having confirmed that the submission is virus-free:

"We confirm that the CD burning session is closed and the submission is checked with an up-to-date and state-of- the art virus check: [*name of the antivirus software and version of the virus checker*] and is virus-free."

Only a CD (CD-ROM) conforming to ISO9660 or ISO 13346 is accepted. The use of re-writable disks is not encouraged. When using a re-writable disk, all open sessions must be closed before sending the CD.

The CD must be packed adequately to prevent damage to the media.

Each CD must include the following label information, clearly presented and printed on the media:

- REQUEST for DESIGNATION
- The name of the person making application for the Request for Designation
- The submission date (DD-MM-YYYY)

The data on the CD must not be packed into a zip-file, rar-file or any other compressed file format.

A one-time security setting or password protection is not acceptable during delivery to the MCC or SAHPRA.

8 UPDATE HISTORY

Date	Reason for Update	Version & publication
February 2017	First publication for comment	v1 March 2017
31 May 2017	Due date for comment	

ATTACHMENT 1:
Summary Checklist for Designation of a Borderline Product

Product Name:		**Company Name:**		
Criteria to be considered (tick the relevant box for YES or NO)	**YES**	**Implications of "YES"**	**NO**	**Implications of "NO"**
Primary Mode of Action				
pharmacological		medicine		medical device or cosmetic or food
immunological		medicine		medical device or cosmetic or food
metabolic		medicine		medical device or cosmetic or food
Primary Therapeutic Effect				
Treat or alleviate or prevent a disease		medicine or medical device		cosmetic or food
Treat, alleviate or compensate for injury		medicine or medical device		cosmetic or food
Restore, correct or modify any somatic or psychic or organic function		medicine		medical device or cosmetic or food
Modifies or supports the anatomy		medical device		medicine or cosmetic or food
Modifies or supports a physiological process (body function)		medical device		medicine or cosmetic or food
Place of action				
In vivo		medicine or medical device or food or cosmetic		medical device (IVD)
In vitro		medical device		medicine or medical device or food or cosmetic
Claim				
Therapeutic health claim (explicit)		medicine or medical device		cosmetic or food
Implicit health claim		medicine or medical device		cosmetic or food
Composition				
One or more chemical ingredient(s) is a scheduled substance		medicine or medical device		medical device, cosmetic or food
Concentration of the active chemical ingredient qualifies this as a scheduled medicine		medicine or medical device		medical device, cosmetic or food

Criteria to be considered (tick the relevant box for YES or NO)	YES	Implications of "YES"	NO	Implications of "NO"
Property in final therapeutic form				
Tablet or capsule for ingestion		usually medicine		
Capsule		usually medicine or medical device or cosmetic		
Liquid syrup/solution		medicine or medical device or cosmetic		
Cream or ointment		medicine or medical device or cosmetic		
Dermal patch		medical device		
Plaster		medical device		
Bandage		medical device		
Medical & surgical equipment		medical device		
Surgical instrument		medical device		
Single use, sterile disposable item		usually medical device		
Cement		medical device		
Glue / adhesive		medical device or cosmetic		
Implant		medical device		
Mobility aid		medical device		
Washer / disinfectant of medical equipment		medical device		
Accessory to a medical device (cannot be used alone)		medical device		
Diagnostic test		medical device (IVD)		
Antiseptic		medicine or disinfectant		
Instructions				
Dose instructions		usually medicine		
Instructions for use (IFU) - training required		usually medical device		

Criteria to be considered (tick the relevant box for YES or NO)	YES	Implications of "YES"	NO	Implications of "NO"
Administration				
Ingestion		usually medicine		
Inhalation		usually medicine		
Injection (intramuscular, subcutaneous, intravenous, etc.)		medicine or medical device		
Infusion		usually medicine		
Surgical implant		medical device		
Inherent risk-benefit balance related to product efficacy				
Cases of precedence or past decisions				
Classification of other regulatory authorities				
For Regulatory Authority Use Only				
DESIGNATION: [circle chosen designation] **MEDICINE** **MEDICAL DEVICE** **COSMETIC** **FOOD**				
Notes / Comments				
Completed by: [PRINT NAME]		Signature:		
Date of assessment:				