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Impact of regulation on advertising and promotion of traditional herbal medicines and food supplements

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Abstract

Purpose – The purpose of this paper is to show that advertising as part of product promotion is in strict correlation with the specific regulation of each product category, food supplements and herbal/over-the-counter medicines. Main contributions of the paper are two-fold. First, it demonstrates that there are products when certain botanical is registered according to legislation as herbal medicine, but at the same time it can be found in sales as food supplement. This can happen within the same country, but it is more frequent within different countries. Second, the possibility for regulation harmonization is discussed.

Design/methodology/approach – In this paper, a comparative analysis of regulation for concerned products in European Union and countries of interest is made. In two case studies, a comparative analysis of marketing of the products in Macedonia and Serbia is made.

Findings – Food supplements are subject to more liberal regulation in comparison with herbal/over-the-counter medicines, but should not be attributed indications and properties that they do not possess. Regulation is stricter and more complex for over-the-counter medicines as a separate class of medicines, these must be correlated with registered properties and indications and are subject to approval by regulatory bodies (print media: advertisement in newspaper/magazine, poster, brochure, flyer, banner and billboard and electronic media: TV spot, radio advertising and internet advertisement).

Research limitations/implications – Countries of interest: EU, Macedonia, Serbia, Montenegro, Albania, Kosovo, Bosnia and Herzegovina.

Practical implications – The paper will contribute toward the creation of promotional and marketing steps in placement of these products on the market in countries of interest, based on regulation of the product category.

Social implications – The discussed opportunities for harmonization are applicable and realistic and can positively contribute for better flow and placement of food supplements and herbal/over-the-counter medicines in different countries. The results of the case studies can also be used for regulatory activities and preparation of marketing materials for other products on other markets of interest with same or similar regulation.

Originality/value – For the first time, a comparative analysis of regulation is made for concerned products in countries of interest. Possibility for regulation harmonization is discussed.

Keywords Advertising, Regulation, Promotion, Food supplements, Traditional herbal medicines

Paper type Research paper

Introduction

Food supplements are concentrated sources of nutrients or other substances with a nutritional or physiological effect, whose purpose is to supplement the normal diet.

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Food supplements are marketed "in dose" form, for example, as pills, tablets, capsules or liquids in measured doses. Supplements may be used to correct nutritional deficiencies or maintain an adequate intake of certain nutrients (Official Journal L 183, 2002).

Herbs and their preparations obtained from plants, algae, fungi or lichens are widespread in the EU in the form of food supplements. They can be purchased at pharmacies, supermarkets and specialty stores or online. Although most of these products have a long history of use in Europe, there are some concerns in terms of safety and quality. Contamination (chemical and microbiological) is a problem, associated, for example, with herbal products from Asia. Cases of death in Europe and the USA by consuming products contaminated with heavy metals, synthetic drugs and other undesirable substances are reported (Ernst, 2002).

Herbal medicinal product is 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. Traditional herbal medicinal products fulfil all of the following criteria:

- 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.
- They are exclusively for administration, in accordance with a specified strength and posology.
- They are an oral, external and/or inhalation preparation.
- The period of traditional use throughout a period of at least 30 years preceding the date of the application, including at least 15 years within the Community.
- The data on the traditional use of the medicinal product are 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 (Directive 2004/24/EC, 2004).

Potential problems associated with botanicals and their preparations are also observed worldwide; in terms of not only safety but also the declared quantity and stability of active substances (Sahoo *et al.*, 2010; Cordell, 2010; Calahan *et al.*, 2016; Parveen *et al.*, 2016; Masada, 2016; Pawar *et al.*, 2017; Heinrich and Anagnostou, 2017; Sgamma *et al.*, 2017; Vaclavik and Mastovska, 2017).

Materials and methods

Analytical, normative, inductive, deductive and synthesis methods are used, comparative methodology has a special place, as required by the subject of the research. The methods of induction and deduction are combined with the analytical approach, drawing general conclusions based on individually derived research results, from general conclusions the analysis comes down to individual examples, drawing conclusions.

In the studies regulation, advertising as part of promotion have been analyzed of food supplements and traditional herbal medicines/OTC (over-the-counter).

Results and discussion

Regulation of food supplements in countries of interest

European union. They are governed by the Joint FAO/WHO Food Standards Programme Codex Alimentarius, 2004 which is harmonized and EU Directive 2002/46/EC relating to food supplements containing vitamins and minerals, so that from July 12, 2002, food supplements are harmonized under EU food law (178/2002/EC). Macedonia follows EU legislation for food supplements and are regulated by the special requirements for safety of food supplements (Official Gazette of RM, no. 12/2012) and the Regulation amending the Regulation on special requirements for food supplements (Official Gazette of RM, no. 80/2013 and 17/2015), and in compliance with the Croatian Rule Amending the Regulation on food supplements in terms of their classification (Official Gazette of RC, no. 41/13). The European Commission has established harmonized rules to help ensure that food supplements are safe and properly labelled. The Directive sets out labelling requirements, and its Annex II contains a list of permitted vitamin or mineral substances that may be added for specific nutritional purposes in food supplements. Annex II has been amended by Regulation 1170/2009, 1161/2011 and 119/2014. European Food Safety Agency NDA Panel (Panel on Dietetic Products, Nutrition and Allergies) where possible, has established tolerable upper intake levels (ULs) of individual micronutrients 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 the NDA Panel and by the former Scientific Committee on Food are used as a reference by the ANS Panel (Panel on Food Additives and Nutrient Sources Added to Food) in its evaluations of the safety of nutrient substances added to food supplements. Companies wishing to market a substance not included in the permitted list need to apply to the European Commission ("Food supplements"). Use of substances with a nutritional or physiological effect other than vitamins and minerals in food supplements is permitted, for which is required establishment of specific rules for further harmonization, as ULs, and which belong to one of the following categories: amino acids, enzymes, pre- and probiotics, essential fatty acids, botanicals and botanical extracts and miscellaneous substances (European Advisory Services, 2007).

Herbal food supplements. A general framework for safety assessment is proposed by the EFSAs Scientific Committee, in which botanicals or botanical preparations for which an adequate body of knowledge exists could benefit from a "presumption of safety" without any need for further testing, based on long history of use without reported adverse effects and without significant larger exposition. Botanicals and botanical preparations for which a presumption of safety is not possible based on available knowledge would be subject to a more extensive safety assessment, requiring additional data to be provided. For botanicals and botanical preparations with a potential to contain toxic, addictive, psychotropic or other substances that may be of concern (given in the Compendium), presumption of safety can be applied only if there is convincing evidence that these undesirable substances in the specific plant parts or preparations are either absent in the source material, or significantly reduced if not excluded, or inactivated during processing (EFSA Journal, 2009).

In April 2009, EFSA published a Compendium of botanicals reported to contain naturally occurring substances of possible concern for human health, when used in food or food supplements. In 2012, a second version is published with two annexes, considering botanicals that appear on a negative list or subject to restricted use (e.g. max level or certain parts allowed only) in at least one European Member State. Annex

A lists botanicals for which not enough information on possible substances of concern could be found, or for which the information present could not be verified. Annex B lists botanicals for which, although some data were available, the Scientific Committee could not identify substances of concern, or other reasons for the inclusion in the compendium – for which species is needed systematic literature review. It lists in alphabetical order botanicals without any judgment on whether they are suitable for food applications in Europe; it has no legal or regulatory force pertaining to the legal classification of products or substances (EFSA Journal, 2012). It must be emphasized that absolute safety does not exist. Information about traditional use is an important element in assessing the safety of traditionally used botanicals. History of use should, as a minimum, cover use during one generation – 25 years (Anton *et al.*, 2012).

Besides with food law (Regulation (EC) No 178, 2002), there are also interactions with other legislations, as regulation concerning novel foods and novel food ingredients (Regulation [EC] No 258, 1997; Regulation [EU] 2015/22, 2015), genetically modified food and feed (Regulation (EC) No 1829, 2003), directive relating to the labeling, presentation and advertising of foodstuffs (Directive 2000/13/EC, 2000), nutrition and health claims (Corrigendum to Regulation [EC] No 1924, 2006), addition of vitamins and minerals and of certain other substances to foods (Regulation [EC] No 1925, 2006), permitted extraction solvents (Council Directive 2009/32/EC,2009), residues and contaminants (Official Journal L 37, 1993), hygiene (Corrigendum to Regulation [EC] No 852, 2004).

Nutrition and health claims are governed with Regulation No. 1924/2006; 107/2008;109/2008; 116/2010; 432/2012; 1047/2012; 907/2013; and 1066/2013. In Macedonia, they are regulated with Food Safety Law (Official Gazzette of RM no. 157/10 and 39/16) and the Rulebook for nutrition and health claims which are used in commercial communications relating to the labelling, presentation and advertising (Official Gazzette of RM no. 65/13).

Mutual recognition principle. When certain product is legally manufactured or sold in one of EU Member States, according to the principle of mutual recognition, the same can be sold in all Member States, according to Article 28 of the Treaty (Official Journal C 326, 2012), where a Member State may not quantitatively prohibit the sales among the Member States, and concerns the not yet harmonized aspects of food supplements. The only exceptions to that principle are restrictions which are justified on the grounds set out in Article 30 of the Treaty, concerning the protection of health and life of humans. Regulation no. 764/2008 of mutual recognition is valid from May 13, 2009 (Official Journal L 218, 2008).

Borderline products. One extremely important element for food supplements is the borderline with medicines. It exists in context of different national traditions and practices concerning the interpretation, market, regulations, control and implementation. In part 7 of the Directive relating to medicinal products for human use is said: Where a product comes clearly under the definition of other product categories, in particular food, food supplements, medical devices, biocides or cosmetics, this Directive should not apply (Official Journal L 136, 2004a). In part 12 of the Directive for traditional herbal medicinal products it is clearly stated that this Directive allows non-medicinal herbal products, fulfilling the criteria of food legislation, to be regulated under food legislation in the Community (Official Journal L 136, 2004b)

If the intended use of the product is medicinal, i.e. involving therapeutic action, effects on diseases and changes in physiological processes, then medicinal legislation will apply to verify safety and efficacy in relation to the intended use. If the intended

use is health promoting, i.e. involving function-enhancing properties, effects on health and the proper functioning of normal physiological processes, illustrated through the making of a health claim, then the food legal framework will apply (Coppens *et al.*, 2006).

There are products, for example, in Germany when certain botanical is registered according to legislation as herbal medicine, but at the same time it can be found in sales as food supplement (Ginkgo).

Republic of Macedonia. Macedonia is the only country from the countries of interest, which is not member of the EU, which has implemented, as of January 01, 2014, the regulation on nutrition and health claims and novel food regulation, as well as law on using symbols on packaging and packaging waste from January 01, 2012.

Republic of Serbia. Serbia also follows EU legislation, but has not implemented the regulation on nutrition and health claims, novel food regulation and the law on using symbols on packaging and packaging waste.

Republic of Montenegro and Kosovo. In these countries, there is no need for notification of food supplements. Import license obtained from the Ministry of Health is enough. In Montenegro, health food analysis is also needed.

Republic of Albania. Albania follows EU legislation partly, but has not implemented the before mentioned 3 regulations. All food supplements containing herbs, herbal substances or herbal preparations are treated as herbal medicines. They should be present on the market for minimum two years in the country of origin. Import license can be obtained without registration, in that case import costs are higher.

Republic of Bosnia And Herzegovina. Food supplements until end of 2013 could be imported with import license from the Ministry of Health and analysis of food supplements safety. From 2014, registration is obligatory according to Law on health safety of food and items of general use (Official Gazette of RBiH no. 2/92 and 13/94) and the Rulebook on health safety of food which can be released on the market (Official Gazette of RBiH no. 7/04; 45/04 and 2/13).

Harmonization. Harmonized legal framework covering food supplements in EU is quite extensive and deals with more relevant aspects of consumer protection. It covers the responsibilities of food business operators, the modalities of the processing, consumer information and procedures for dealing with safety concerns. It already represents a substantial basis for commerce within the EU Community. In all member states, a notification by sending a copy of the text on the packaging/labeling is sufficient if it is a food supplement that is composed of only vitamins and minerals, except in Belgium, Denmark, Slovenia and the UK where no notification is required.

Least harmonization of regulation in the EU exists in food supplements compared to the other studied group of THM, especially for the supplements that contain herbal substances. The current situation of approval of health claims for herbal food supplements in the EU is on hold or in most cases results with rejections, therefore these products are regulated differently nationwide. According to current regulations for herbal food supplements, more stringent clinical trials are required for approval of health claims as opposed to THM, which are not required proof of effectiveness. Some manufacturers use the unsettled situation using health claims put on hold because they have not been rejected; it actually represents a legal gray zone. European countries continue to use the national legislation based on tradition, which is a much divided picture for non-EU countries which want to sell their products in the EU (Gruenwald, 2014, 2015, 2017a). Another positive signal is the new Regulation EU 2017/745 on medical devices, because with the previous regulation, European food business

operators were using a loophole marketing the botanicals as medical devices, which would not be so easy anymore with the new Regulation (Gruenwald, 2017b). The same applies to Macedonia following EU legislation. Because some products in some countries are registered as herbal medicines, while in other countries belong to the food supplements, they will be elaborated through two case studies of selected products of Bionika Pharmaceuticals.

Because of this situation, Belgium, France and Italy have developed a joint approach to the evaluation of plants which resulted in BELFRIT list of herbs that can be used in food supplements, taking into account the safety of consumers. The data used for traditional uses are published in the monographs of European Pharmacopoeia, WHO, ESCOP (European Scientific Cooperative on Phytotherapy), European Medicines Agency (EMA), the German Commission and so on (Cousyn *et al.*, 2013). On March 27, 2014, the Italian Ministry of Health with Decree adopted the positive list of herbs that can be used in food supplements (Klaus and Gherardini, 2014); in France, 60 per cent of the plants on the list were accepted (Starling, 2014) and Belgium had notified the list to the European Commission (Dunn and Rose, 2015). This is the first step in harmonization, which can result in further harmonization in Europe if other countries accept and join, and implement it in the national laws.

Regulation of herbal medicines in countries of interest

European Union. The European Commission has taken measures to harmonize the legislation on herbal products in the EU and to ensure the free movement in the European internal market. Directive 2004/24/EC on traditional herbal medicinal products allows their registration in the group of medicines in all Member States, and its transition period ended on 30.04.2011. Herbal medicine (HM) should be classified as a drug based on its presentation (indications concerning the treatment or prevention of disease) or its function (pharmacological, immunological or metabolic activity). They are categorized into three groups: new (herbal) medicines, herbal medicines with well-established use from minimum 10 years (WEU - bibliographic application) and THM used throughout a period of at least 30 years preceding the date of the application, including at least 15 years within the Community. For all groups, there are requirements to prove safety and efficacy, depending on the history of usage, the proposed indication and the available amount of data. Like all medicines, for HM registration with complete documentation with preclinical and clinical data is required to demonstrate their safety and efficacy. Many HM have a long history of use and could have (pre) clinical data. For WEU HM and THM scientific data can be used from accepted scientific databases, historical books and monographs of the European Union, WHO (World Health Organization, 1997, 1999, 2002, 2007, 2009), ESCOP (European Scientific cooperative on Phytotherapy, 2003) (Hooyenga *et al.*, 2009; Witkamp and Groen, 2009; Vlietinck *et al.*, 2009). WEU HM is regulated also with the Directive1999/83/EC. Medicines are regulated with the Directive 2001/83/EC.

Republic of Macedonia. Macedonia fully follows the regulations for medicines in the EU. HM are regulated by the Law on Medicines and Medical Devices (Official Gazette of RM no. 106/2007; 88/10 and 88/15) and the Regulation on the registration of traditional herbal medicinal products (Official Gazette of RM no. 143/2008). In case the medicine is registered in EU with the process of mutual recognition, decentralized or centralized procedure for obtaining marketing authorization, application may be according to recognition procedure for marketing approval, which is shorter and simplified. Marketing authorization is issued with validity for 5 years.

Advertising of medicinal products is regulated by the Law on Medicinal Products and Medical Devices (Official Gazette of RM no. 106/2007 and 88/15) and the Guideline on advertising of medicinal products and medical devices (Official Gazette of RM no. 66/2008). Under Article 91 of the Law:

> [. . .] advertising of medicinal products means any form of informing in written, visual, audio, oral, electronic, digital or any other form aimed at a general or professional public to promote the prescription of medicines, to stimulate dispensing, supply of medicines, as well as their sales and use.

The same provisions that apply to advertising of THM in EU, are applied in Macedonia.

Republic of Serbia, Montenegro, Bosnia And Herzegovina and Kosovo. Serbia, Montenegro, Bosnia and Herzegovina and Kosovo also follow the EU legislation. The same comments for Macedonia are also valid in these countries.

Republic of Albania. Albania also follows EU legislation; any medicine whose active substance contains one or more herbal substances in combination with one or more herbal preparations is HM. In case the medicine is registered in EU, the application shall be decided with simplified and accelerated procedure of authorization. Simplified regulation except for THM, is also applied to traditional non-herbal substances used in products that have a medical use, such as fish oil, royal jelly or other products of insects, bacterial products such as acidophilus/acidobifidus/Lactobacillus and other bacterial products, and other substances, which is also the proposal of the Committee on Herbal Medicinal Products (HMPC) for extension of regulation in traditional products with a long tradition of use in the EU (COM/2008/0584 final, 29.9.2008). Marketing authorization is issued for a period of 5 years. The provisions applicable to advertising of THM in EU are also applied in Albania.

Harmonization. To promote harmonization, Member States should recognize the registration of THM granted by another Member State on the basis of the monographs of the European Union for herbal medicines and THM or consisting of substances, preparations or combinations thereof contained in the list of European Union for safe use, it is their responsibility for the application of this Directive (procedure of mutual recognition or decentralized procedure). With the introduction of Directive 2004/24/EC of 2004 more than 1,700 THM are registered and more than 800 HM are with a well-established use in the EU (European Medicines Agency, 2017). These medicines are accompanied by harmonized patient leaflets in EU, enabling citizens to make informed choices when using HM for self-medication and health professionals to base their prescription on the basis of comprehensive information on medicines. HMPC has published more than 20 scientific guidelines that are common standards for registration of HM in EU and on harmonization. According to HMPC chairman Werner Knöss "The establishment of common standards for registration of herbal medicines in Europe is essential to protect human health and allow citizens to trust the products they choose to use" (European Medicines Agency, 2014).

Focus of HMPC, which was formed in 2004, expands from medicines with one active substance to medicines containing a combination of herbal substances, as well as the non-European THM. In 2012 the first Chinese THM Diao Xin Xue Kang (Dioscorea nipponica) is registered for the treatment of myocardial ischemia in Netherlands. The Committee has completed the assessment of the most important individual herbal substances that are commonly used in the EU – 152 (up to July 2016). The European Pharmacopoeia has adopted selected herbal monographs from the Chinese Pharmacopoeia. If the herbal substance is currently under assessment, Priority List

(EMA/HMPC/278067/2006) shows the current status of each monograph during the evaluation process [Committee on Herbal Medicinal Products (HMPC), EMA/HMPC/278067/2006, 2016]. Census of herbal substances assessment (EMA/HMPC/494079/2007, 2017) provides a complete overview of all herbal substances, including those proposed for herbal monograph by the interested party (European Medicines Agency, 2017). These lists are updated regularly and can be found on the website of EMA (www.ema.europa.eu/ema). There is a proposal to create a more favorable regulatory environment for the pharmaceutical registration of new and innovative HM (Minghetti *et al.*, 2016). The Committee cooperates with the European Directorate for the Quality of Medicines and Healthcare (EDQM), and with other European organizations and international regulatory bodies, to enable a harmonized approach to the assessment of herbal substances and to delivering consistent, reliable and clear information to users of HM worldwide and harmonized scientific opinions on the use of herbal preparations in cosmetic products, medical devices and food supplements.

Case studies

Case study 1: Imunix (food supplement). Imunix is a natural food supplement in the form of soft gelatin capsules containing 100 mg of spirulina powder (Spirulina spp.) and 10 mg of yeast enriched with organic selenium (equivalent to a content of 10-20 μg selenium). It belongs to the group of supplements to boost immunity, a category that is very broad and diverse.

In all countries it is registered as a food supplement (Macedonia, Serbia, Croatia and Bosnia and Herzegovina). It is also present in Kosovo and Albania. In Macedonia and Croatia, the health claim that "selenium helps to boost immunity" is approved. Only in Croatia it is necessary to state that people who take drugs should consult a doctor before taking the supplement and it is not recommended for the supplement to be taken by people with phenylketonuria and kidney damage. In RBiH, because of economic reasons, a Croatian package and leaflet is used as one of the official languages used in this country, although it is not an applicable approval of health claims. In Serbia there is greater freedom of expression in the leaflet and the effects of spirulina and brewer's yeast can be stated, so the leaflet states:

> Using Imunix helps boost immunity. The most important feature of brewer's yeast is its high content of vitamins B group (B1, B2, B6, biotin, niacin), which helps in the regeneration of the nervous system. Beer yeast helps in cases of physical and mental fatigue, improves digestion, and removes nausea and weight in the stomach. Beer yeast reduces tension and anxiety. Spirulina is a blue - greenalgae that contains about 60% protein, essential amino acids and high amounts of gamma linolenic acid (GLA), which helps with proper functioning of the heart and circulation.

The dosage is the same for all countries: children 7-14 years 1 capsule, adults 1-3 capsules daily.

Advertising campaigns. In all countries, the same packaging is used with red and stylized cubist display of heart/cardiovascular system/immunity and minimalist look; text box differs according to national regulation.

Television advertising in Macedonia with a strong and distinctive message combined with the promoting activities of the company helped to achieve significant market share of the product in this segment (Dzeparoski and Trajkovic-Jolevska, 2016b).

TV commercials

Imunix – food supplement (Macedonia)

Analysis. The message that should remain in the subconscious of the viewer is that when Imunix is used, it will beat colds, sneezing and disease and any activities can be smoothly

continued to be performed. Apart from promoting the product in advertising, at the same time the new pharmaceutical company is promoted. For this advertisement Regulation to health claims applies, and since the health claim is approved, it can be used for commercial purposes.
Imunix – food supplement (Serbia)

Analysis. The message that should remain in the subconscious of the viewer is that it is a natural product for healthy people, which if used will help reduce certain symptoms. Besides promoting preparations with advertising, the new pharmaceutical company is also promoted.

This advertisement does not need approval for advertising in Serbia because it is based on generally accepted scientific data and is understandable for the average consumer.

Case study 2: Sentis (THM and food supplement). The results of this case study were published as short communication under the title "Comparative analysis of advertising and promotion of traditional herbal medicine and food supplement at different markets – case study" (Dzeparoski and Trajkovic-Jolevska,2016a). The choice of countries is based upon different product categorization in which Sentis is classified.

Promotional materials are with similar text content and same design in both countries, except the statement that it is THM or food supplement. The other difference for the THM is also that "the patient leaflet should be read, for more information you should consult your pharmacist or doctor". The last is true for all forms of advertisement.

Except product promotion, with both advertisements the new pharmaceutical company is also promoted. TV advertising in Macedonia with a strong and distinctive message, along with the promotion activities, helped the company to achieve significant market share in this segment.

Conclusion

Regulation is stricter and more complex for over-the-counter medicines as a separate class of medicines. The least harmonization is achieved for herbal food supplements. There are products when certain botanical is registered according to legislation as herbal medicine, but at the same time can be found in sales as a food supplement. This can happen within the same country, but is more frequent within different countries.

Marketing of products by companies should be in accordance with the current country's regulation for the specific product category.

There are major differences in the marketing of THM/OTC and food supplements.

All promotional materials for THM to the general public are subject to approval by regulatory bodies, based on the approved summary of product characteristics and patient leaflet.

The marketing of food supplements is more liberal in advertising and in Serbia and other non-EU countries of interest is not subject to approval, if based on generally accepted scientific data. Macedonia follows the EU Regulation on nutrition and health claims for food supplements.

The results of the case studies can also be used for regulatory activities and preparation of marketing materials for other products for other markets of interest with same or similar regulation.

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