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Import Regulation and Market of Herbal Medicines in United States of America & Canada

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Abstract: Herbal medicine was used around the world for many centuries and it is still in use by society quite extensively. Herbal medicines have a very significant role in international trade. Herbal medicine recognition is widely growing around the world on the merit of their clinical, pharmaceutical and economic value. Herbal medicine classification varies from country to country such that in the USA it comes under Dietary supplement and Botanical drugs, Natural Health Product term is used in Canada. In the USA and Canada, Herbal products are mainly used by the younger generation. The present review deals with import regulation requirement of herbal medicine in the USA and Canada. In both countries, it is regulated by USFDA and Health Canada. Herbal medicine market of USA and Canada is growing at a healthy rate. Importers must follow the regulatory requirements of USFDA and Health Canada for fluid marketing approval for their product.

Key word: Herbal medicine, Dietary supplement, Natural health product, USFDA, Health Canada

Introduction

Herbal medicine is in use since centuries. It is used in all cultures throughout history and the oldest healthcare system is known by humankind. According to the World Health Organization, herbs, herbal product and finished herbal products are collectively known as herbal medicine(1). In the last era, medical science has made remarkable progress around the globe. The latest improvement in the area of technology has increased the potential of modern medicine, a lot of new life-saving drugs discovered which helps us fight against the various deadly infection and other diseases, the mortality rate decreased, the prospect of life increased.

World Health Organization (WHO) accentuate on primary healthcare in an international conference in 1978, commonly known as 'Declaration of Alma-Ata'. It expresses the need to accomplish the goal ‘Health for All’ step by step manner through stopping the poverty, illiteracy and poor sanitation. In 1998, WHO consolidates a new global health policy 'Health for All in the 21st Century' and set the goal to complete health security, health equity, increased healthy life expectancy and to ensure access to primary quality healthcare for all. After so many advancements in modern medicine, it is still not in the reach of every people and deals with the increasing problem of various diseases. In developing and under-developing nation a huge amount of the population is still, does not have the access to modern medicine, so they are using tried and tested herbal medicine, many of these systems are much older than allopathic medicine. In the current century, pollution,

unsanitary lifestyle, environmental toxins enhance the risk of diseases. One of the major concerns of allopathic drug is a side effect and misuse of drugs.
In 2013, WHO refined and lunched 'WHO Traditional Medicine Strategy 2014-2023' launched by WHO in 2013 to indicated to combine traditional and complementary medicine to promote universal healthcare and to ensure the quality, safety and effectiveness of such medicines[(2)].

United States Herbal Dietary Supplement Market

According to Nutrition Business Journal (NBJ), Total sales of herbal dietary supplements increased by an estimated 8.6% from 2018, continued to experience strong sales growth in the united states in 2019. In 2019 on herbal supplements consumes spent around $9.602 billion across all market channels, more than three-quarters of a billion dollar that was spent in 2018. In united states, herbal supplement sales have grown each year since 2004 and in 2018-2019, it records second-highest percentage since 1998.
In the first half of 2020 sales of herbal supplement continued to climb despite covid-19 pandemic because of the high demand for a herbal and nutritional supplement with potential immune-enhancing effects. SPINS, a market research firm based in Chicago, Illinois, and NBJ, a natural products industry magazine of Informa's New Hope Network based in Boulder, Colorado, provided the US retail sales figures for this report.
Total retail sales of herbal dietary supplements increased in each of NBJ's three market channels in 2019 — the 11th consecutive year of growth in all channels, in addition to 8.65 sales growth from 2018 to 2019. In 2019 the three market channel sales reached a total $4.955 billion in which direct sales of herbal supplement, which includes online sales, had the strongest sales growth. The mass-market channel shows higher growth than natural and health food channel since 2016 and the same happens in 2019 also. In 2019 total $1.704 billion mass market sales happened, a 9.4% increase from the previous year. In 2019, sales in the natural and health food channel were an estimated $2.904 billion, a 3.6% increase from 2018[(3)].
In USA supplement market Vitamins represent 30% of the total sale in 2018. Herbal and botanical product shared 19% of the total market thanks to the combination product. Specialty supplement or Probiotics are growing faster than others, represents 18% of total sales of supplement in 2018. Sports nutrition and Meal supplement represent combined 26% of the total share, one of the main reason is that plant-based protein sales are increasing[(4)]. (Refer figure no.1)

Canada Natural Health Product Market

In Canada more than 80% of people use natural health products, so it is a growing market for brands that are able to acquire product registration and other requirements by health Canada. According to Agriculture and Agri-Food Canada (AAFC), Many factors are helping to grow the functional food and natural health product (FFNHP) market substantially such as growing consumer interest, combined with a greater understanding of food-health relationship, ageing population and high health care costs. In 2011 FFNHP sector generated USD 11.3 billion in revenues according to a survey conducted by statistical Canada on behalf of AAFC.
In 2012 a report is presented by Ipsos Canadian Interactive Reid Report, according to this report more than 8 Canadians in 10 used natural health product. In this report around 56% Canadians said that in future they will be purchasing more NHPs. There are some most commonly used products in Canada are vitamins/ minerals(71%), Omega-3s/essential fatty acids (EFAs) (45%),Probiotics (34%), and Antioxidants (33%)[(5)].
Naturally healthy fruit/herbal tea and naturally healthy Ready to Drink (RTD) tea remain the two fastest-growing categories in 2017 at a CAGR of 40.8% and 23.4% respectively for naturally healthy beverages[(6)].
In 2014, the $5.6 billion in retail spending on consumer health products directly contributed $2.1 billion to Canada's gross domestic product (GDP). This represents $300 million in manufacturing and $1.8 billion in wholesale and retail trade value-added output[(7)].

Import Regulation of Herbal medicine in United States:

In united states Herbal drug comes under dietary supplement. The Federal Food, Drug, and Cosmetic Act defines "a dietary ingredient as a vitamin; mineral; herb or other botanical; amino acid; dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of the preceding substances".

Contrary to drugs, supplements are not indicated for treatment, diagnosis, prevention, or as a cure to predisposed ailments. This implies that supplements marketed should refrain from making claims such as to reduce pain or cure heart diseases. Dissertations like these should only be made for well-documented drugs and not supplements. Supplementation in diet can be in the form of vitamins, minerals, amino acids and enzymes. These supplements are prevalent as capsules, tablets, soft gels, gel caps and powders. The FDA has the authority to remove these products from the markets under its law that governs usage, dietary supplement health and education act passed by congress in 1994, prerequisite that the agency establishes the marketed drugs are adulterated or misbranded(7). Botanical drug products are different from the dietary supplement because they used for diagnosis, cure, mitigation, and treatment of disease in humans. The main substance of botanical drug product are vegetable material, algae, macroscopic fungi, or combinations thereof. It can be available in many forms such as solution (e.g. tea), tablet, powder, capsule, elixir, topical or injection. These drug products often have unique characteristics, for example, complex mixture, lack of definitive active ingredient, and tangible prior use[(8)](Refer table no. 2).

Current Good Manufacturing Practice (CGMP) In Manufacturing, Packaging, Labeling, Or Holding Operations for Dietary Supplements (72 FR 34752) is published in the federal register a final rule that authorized a regulation by FDA on June 25, 2007. It is necessary that a person who manufactures, packages or hold a dietary supplement follows "The Dietary Supplements (DS) CGMP rule in 21 CFR part 111" to practice and follow current good manufacturing practice. To ensure the quality of the dietary supplement and to guarantee that the dietary supplement is packaged and labelled as specified in the master manufacturing record manufacture needs to follow CGMP. 21 CFR part 111 has various subparts with each covers different aspect of current good manufacturing practices[(9)](Refer figure no. 2).

FDA requires registration of any foreign food facility that manufactures, process, pack or hold any kind of food and drugs. Form FDA 3537 is used by registrants to register their facility. It can also be used for renewal or update a registration. It can be filled in online mode or paper form. Registrants must use Form FDA 3537 to register, renew, or update a registration. This form is available online and in paper form. Various sections are required to fill in this form according to the registrants need. The importer needs to give prior notice to FDA about their incoming shipment and detailed information required by the FDA. After that FDA inspectors inspect the drugs at the port. they will take samples to analysis and check that product is safe, sanitary and labelled according to FDA requirements. If FDA satisfies with the product quality then they will order to release the product from the port and it will be ready for the market distribution (Refer table No. 3).

Import Regulation of Herbal Medicine in Canada

Natural health products (NHPs) can be vitamins, herbs or other plants, minerals, amino acids, homoeopathic medicine or other parts of these substances. They are naturally-occurring material that can be used to maintain or recover health. Natural health products are available in many forms such as capsule, tablet or liquid form. they can improve or add to the diet but should not be recognized as food. Manufacturers of natural health product cannot legally claim that they can cure, prevent or diagnose disease. They can say that it will help with health maintenance and well-being[(10)]. Canadian consumers, health care practitioners, academicians and industry stakeholder were consulted to design 'The Natural Health Product Regulation'. House of Commons

standing committee gave 53 recommendation on the regulation of natural health product and many Canadians were also concerned about safety and availability of NHP. The committee who designed the regulation addresses all recommendation and concerns.

If anyone wants to legally sell natural health products in Canada then they must have a product license, and the Canadian sites that manufacture, package, label and import these products must have site licenses. For a natural health product, specific labelling and packaging requirement must be fulfilled to get product and site license. Also, proper safety and efficacy evidence must be provided and good manufacturing practices must be followed.

Product licensing: Natural health products must have a product license before they can be sold in Canada. Health Canada issues a product license along with an eight-digit Natural Product Number (NPN), must appear on the label.

Evidence requirements for safety and efficacy: Must be supported by proper evidence. Evidence may include clinical trial data or references to published studies, journals, pharmacopoeias and traditional resources. The type and amount of supporting evidence required depends on the proposed health claim of the product and its overall risks.

Labelling: Information required on NHP labels includes:

- product name
- product license number
- quantity of product in the bottle
- complete list of medicinal and non-medicinal ingredients
- recommended use (including purpose or health claim, route of administration and dose)
- any cautionary statements, warnings, contra-indications and possible adverse reactions associated with the product
- any special storage conditions.

Site licensing: All Canadian manufacturers, packagers, labelers, and importers of natural health products must have site licenses(Refer figure no.3). Also demonstrate that they meet good manufacturing practice requirements. They need to submit foreign site reference number authorization form.

Good Manufacturing Practices: Good Manufacturing Practices for NHPs cover:

- product specifications
- premises
- equipment
- personnel
- sanitation program
- operations
- quality assurance
- stability
- records
- sterile products
- lot or batch samples
- recall reporting

Adverse Reaction Reporting: The Natural Health Products Regulations require product license holders to monitor all adverse reactions related to their product. License holders must report serious adverse reactions to Health Canada.

NHP imported for use in a clinical trial: A Notice of Authorization (NOA) authorizing the use of the product in a clinical trial is issued by the Natural Health Products Directorate (NHPD) of Health Canada. A copy of this authorization must be provided at the port of entry [(11)].

Conclusion

The USA and Canadian market of herbal medicine is growing and getting more attention from pharmaceutical companies. Import regulation and requirements of both countries are important to know by importer so public safety and quality of product will not compromise. It also helps to gain quicker market approval by the respective regulatory authority. The legal requirement for approval of herbal medicine varied from one country to another thus making it challenging for the free distribution of such products.

Table 1: Total US retail sales of herbal supplement

Year	Total Sales	% change
2019	$ 9.602 billion	8.6%
2018	$8.842 billion	9.4%
2017	$8.805 billion	8.5%
2016	$7.452 billion	7.7%
2015	$6.922 billion	7.5%
2014	$6.441 billion	6.8%
2013	$6.033 billion	7.9%
2012	$5.593 billion	5.5%
2011	$5.302 billion	4.5%
2010	$5.049 billion	3.3%
2009	$5.037 billion	5.0%
2008	$4.800 billion	1.0%
2007	$4.756 billion	4.4%
2006	$4.558 billion	4.1%
2005	$4.378 billion	2.1%

Figure 1: U.S. supplement market share 2018

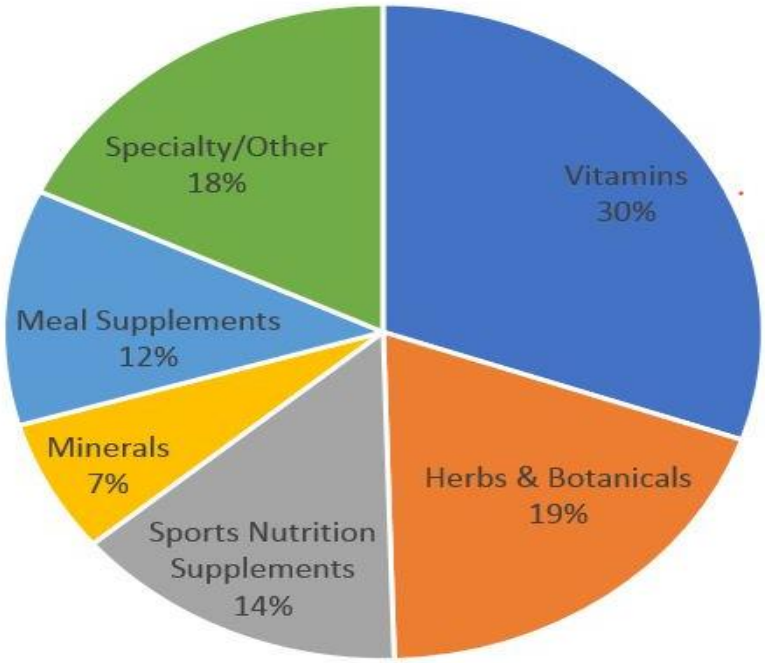

Table 2: Difference between dietary supplement and Botanical products

S. No.	Dietary Supplement	Botanical Product
1.	Supplements can include minerals, vitamins or other natural biological substances	A botanical drug product consists of vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof.
2.	Dietary supplements are not considered as drugs.	Botanical products are considered as drugs.
3.	Dietary supplement does not require to prove its safety and effectiveness.	Botanical drugs must be proven safe and effective.
4.	Dietary supplement can be bought without prescription.	Botanical drugs will require a prescription for purchasing.
5.	IND and NDA are not required for dietary supplement.	Submission of investigational new drug applications (INDs) in support of future NDA submissions for botanical drugs are required.
6.	For Dietary supplement no clinical trial required.	The FDA approval process requires that the drug be proven safe in a series of clinical trials.
7.	Current Good Manufacturing Practices (CGMPs) for Dietary Supplements rules apply (21 CFR Part 111 - Current good manufacturing practice in manufacturing, packaging, labeling, or holding operations for dietary supplements).	U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Botanical Drug Development Guidance for Industry used as supervision.

Figure 2: Subpart of DS CGMP rule in USA

21 CFR 111 Subpart	Descriptive summary
A	General Provision
B	Personnel
C	Physical Plant and Utensils
D	Equipment and Utensils
E	Production and Process Controls-Specification
F	Quality Control
G	Components, Packaging and Label Controls
H	Master Manufacturing Record
I	Batch Production Record
J	Laboratory Operation
K	Manufacturing Operations
L	Packaging and labeling Operation
M	Holding and Distribution Operations
N	Returned Products
O	Product Complaints
P	Recordkeeping

Table 3: Regulatory Process for the Clearance in USA

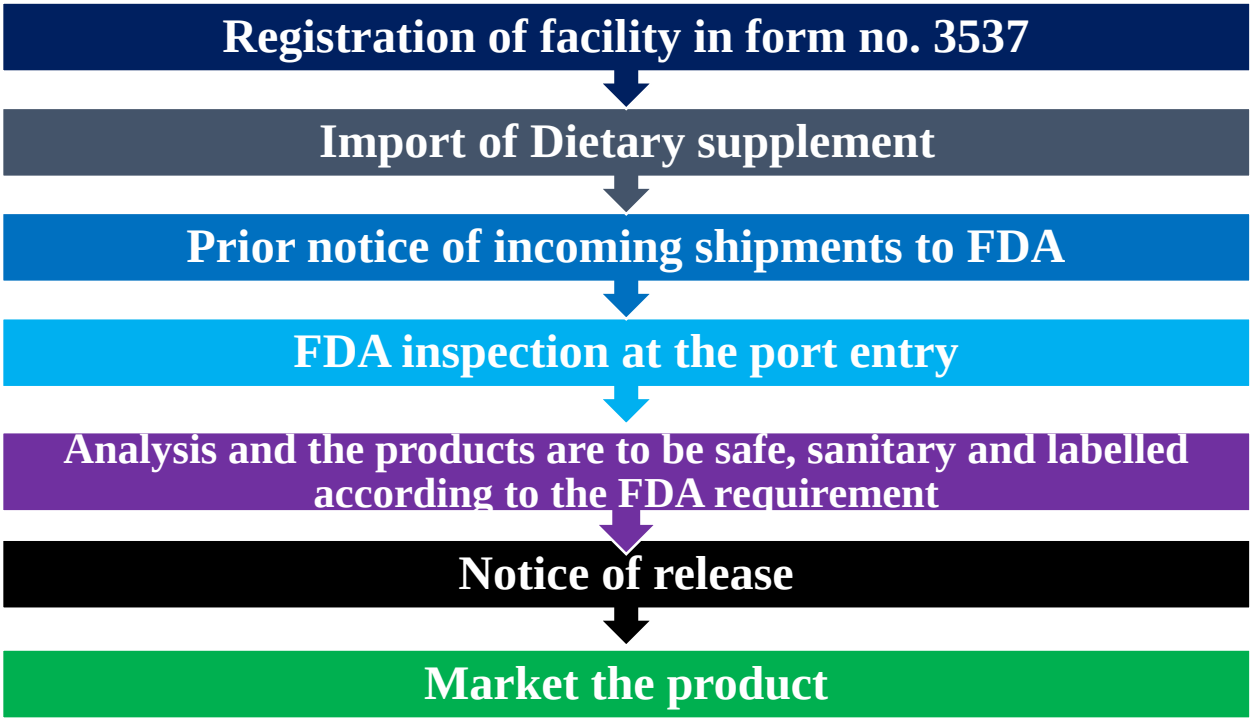

Table 4: Requirements based on application type In Health Canada

Requirements	Application Type						
				Homeopathic			
	Compendial (NHPD Monograph)	Traditional Claim	Non-traditional Claim	Specific Recommended use	Non-specific Recommended Use	TPD Category IV/ Labelling Standard	NHPD & Homeopathic Labelling Standards[1]
Product Licence Application form	X	X	X	X	X	X	X
NHPD Label text	X	X	X	X	X	X	X
References	X*	X	X	X	X	X	X*
Finished Product Specifications	Not applicable	X	X	X	X	X	X
Animal Tissue form (if applicable)	X	X	X	X	X	X	X
Safety, Evidence and/or Quality Summary Report	Not applicable	X**	X**	Not applicable	Not applicable	Not applicable	Not applicable
Cover Letter	Optional	Optional	Optional	Optional	Optional	Optional	Optional

*It is not required to include a copy of the Monograph or Labelling Standard.

**A summary report is optional and may be included to help explain information present to support the product licence application.

[1]If selecting one of these two application types, please indicate either Non-Traditional or Homeopathic on the Product Licence Application form.

Figure 3: Foreign site reference number authorization form (First Page)

Health Canada / Santé Canada

FOREIGN SITE REFERENCE NUMBER AUTHORIZATION FORM
Natural Health Products Directorate

Protected when completed

Refer to the instructions before proceeding

1. Foreign Site Reference Number:	2. Date GMP Evidence Last Updated: (to be completed by NHPD)

A. Foreign Site:

3. Company Name:

4. Building Name:

5. Address: Please follow the sequence- Street (name and number)/ Suite/ City- Town/ Province- State/ Postal Code/ Country

6 a. Activities conducted at the above site: (check only those that apply)	Non-Sterile	Sterile	Homeopathic
Manufacturing:	☐	☐	☐
Packaging:	☐	☐	☐
Labelling:	☐	☐	☐
Warehousing:	☐	☐	☐

6 b. Activities to be conducted for the Canadian Site indicated in part C: (check only those that apply)	Non-Sterile	Sterile	Homeopathic
Manufacturing:	☐	☐	☐
Packaging:	☐	☐	☐
Labelling:	☐	☐	☐
Warehousing:	☐	☐	☐

The foreign site is required in Part 2, Section 28 (f) of the *Natural Health Products Regulations* (NHPR) to provide to the Minister information and documents in respect to buildings, equipment, practices and procedures used to conduct each activity specified under paragraph (b) of the NHPR, including a report from a quality assurance person demonstrating that they comply with the requirements set out in Part 3 of the NHPR.

7a. Senior Official (Foreign Site):	7b. Phone Number:	7c. Email:
8a. Quality Assurance Person (Foreign Site):	8b. Phone Number:	8c. Email:

B. Authorization:

I hereby authorize Natural Health Products Directorate (NHPD) to access the GMP information on behalf of the authorized Importer listed below. NHPD may enlist the site information on the Site License of the aforementioned Canadian importer subject to validity of the foreign site information at the time of submission.

9. Name of the Senior Official (Foreign Site):
(Must be same as in Box 7a)

Signature of the Senior Official (Foreign Site):

Date Signed: mm/dd/yyyy

C. Site Licence Applicant/Holder (Importer):

Importer File Number (if Known):	Importer Company Code (if known):
10a. Site Licence Number (**if known**)	10b. Site Licence Expiry Date (**if known**)

11. Company Name:

12. Building Name:

13. Address: Please follow the sequence- Street (name and number)/ Suite/ City- Town/ Province- State/ Postal Code/ Country

14a. Senior Official (Importer):	14b. Phone Number:	14c. Email:	14d. Fax Number:
15a. Quality Assurance Person (Importer):	15b. Phone Number:	15c. Email:	15d. Fax Number:

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Reference

1. Kumar et al. - Regulations And Challenges Of Herbal Medicines In .pdf [Internet]. [cited 2020 Dec 22]. Available from: https://interscience.org.uk/images/article/v6-i1/15ijahm.pdf
2. Sen S, Chakraborty R. Revival, modernization and integration of Indian traditional herbal medicine in clinical practice: Importance, challenges and future. J Tradit Complement Med. 2016 Jun 28;7(2):234–44.
3. HerbalGram: US Sales of Herbal Supplements Increase by 8.6% in 2019 [Internet]. [cited 2020 Oct 26]. Available from: http://cms.herbalgram.org/herbalgram/issue127/hg127-mktrpt-2019.html?ts=1603694912&signature=8bbcca5ac1e14a3d1ddcc32242ba26cd
4. U.S. Supplements Industry :75% U.S. adults take dietary supplements [Internet]. Byclue. [cited 2020 Dec 9]. Available from: https://www.byclue.com/nutritional-supplement-overview/us-supplements-industry/
5. Selling natural health products in Canada [Internet]. Natural Products INSIDER. 2017 [cited 2020 Oct 28]. Available from: https://www.naturalproductsinsider.com/regulatory/selling-natural-health-products-canada
6. Canada A and A-F. Customized report service – Health and wellness trends in Canada [Internet]. 2019 [cited 2020 Oct 28]. Available from: https://www5.agr.gc.ca/eng/customized-report-service-health-and-wellness-trends-in-canada/?id=1554401656839
7. healthy_growth_final_report.pdf [Internet]. [cited 2020 Oct 28]. Available from: https://www.chpcanada.ca/sites/default/files/healthy_growth_final_report.pdf
8. Nutrition C for FS and A. Dietary Supplement Products & Ingredients [Internet]. FDA. FDA; 2020 [cited 2020 Nov 17]. Available from: https://www.fda.gov/food/dietary-supplements/dietary-supplement-products-ingredients
9. Research C for DE and. What is a Botanical Drug? FDA [Internet]. 2019 Oct 11 [cited 2020 Nov 17]; Available from: https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/what-botanical-drug
10. Nutrition C for FS and A. Small Entity Compliance Guide: Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements [Internet]. U.S. Food and Drug Administration. FDA; 2020 [cited 2020 Nov 18]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/small-entity-compliance-guide-current-good-manufacturing-practice-manufacturing-packaging-labeling
11. EUR-Lex - 32004L0024 - EN - EUR-Lex [Internet]. [cited 2020 Nov 27]. Available from: https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32004L0024