RESEARCH PAPER

REGULATORY MECHANISMS OF NATURAL PRODUCTS IN THE EUROPEAN UNION: PERSPECTIVES FOR INDIAN PRODUCTS FOR BETTER ACCEPTANCE

Ritu Dhankhar[1], Sonia Parashar[2], Munish Garg[1]*

[1]Department of Pharmaceutical Sciences, Maharshi Dayanand University Rohtak, Haryana 124001

[2]World College of Pharmaceutical Sciences, Girawar, Jhajjar

Email: rituritudhankhar@gmail.com

Corresponding author: email, munishgarg@mdurohtak.ac.in

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ABSTRACT

Background- This study examines the regulatory framework of the European Union for herbal medicinal products (HMPs) & food supplements and to explore how harmonization with EU regulations could improve accessibility of Indian herbal products in international market. Methodology- A systematic review of scientific literature and regulatory documents was undertaken to evaluate the regulatory framework for herbal medicinal products (HMPs) and food supplements in the European Union (EU), with comparative insights from India. Relevant data were retrieved using scientific search engines, including PubMed, Google Scholar, ScienceDirect, as well as official regulatory websites such as European Medicines Agency (EMA), CDSCO, Ministry of AYUSH and Food Safety and Standards Authority of India (FSSAI). Results-This study highlights substantial differences in the regulatory frameworks governing herbal products in India and the European Union. In India, Central Council for Research in Ayurvedic Sciences (CCRAS) has established general guidelines for standardization and quality assurance of herbal products. There are no specific guidelines for marker-based identification, quality control of multi-herb formulations, modern manufacturing technologies, non-pharmacopoeial reference standards, new analytical techniques for determination of contaminants etc. Therefore, adulteration and contamination in multi-herb formulations have emerged as a major challenge for Indian herbal industry. For preparation of non-clinical data, Central Council for Research in Ayurvedic Sciences (CCRAS) provides general guidelines for safety/toxicity evaluation of ayurvedic formulations whereas Committee on Herbal Medicinal Products (HMPC) has established specific guidelines for non-clinical documentation, genotoxicity assessment etc. Additionally, EMA provides comprehensive guidance for the design and conduct of clinical studies, while India lacks analogous specific regulatory guidelines in this domain. Pharmacovigilance system is still evolving in India whereas EU have robust pharmacovigilance system for reporting of adverse effects like EudraVigilance. Indian regulatory framework largely depends on traditional evidence than scientific substantiation while EU prefer scientific evidence. As a result, regulatory framework for herbal products in India is not drastic as EU's regulatory model for herbal products. Conclusion- EU Pharmacopeia and scientific guidelines for quality have provided high quality standards. Hence, Indian regulatory authorities should harmonize their herbal medicine monograph with EU monograph and incorporate scientific guidelines for marker based- standardization, fixed-combination products, new analytical techniques and artificial intelligence tools for supply chain transparency and quality assurance into their regulatory framework. Indian manufacturer should follow community herbal monograph, scientific guidelines for preclinical and clinical studies in EU for safety and efficacy of herbal formulations. Although India has developed an extensive regulatory and policy framework but its effective implementation requires systematic evaluation. The development of mutual recognition agreements between India and the EU could facilitate international trade under harmonized standards.

Keywords: Herbal Medicinal Products, FSSAI, European Medicine Agency, Scientific validation

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1. INTRODUCTION

Herbal products have emerged as a significant component of healthcare systems worldwide reflecting a growing preference for naturally derived therapeutic agents.[1] The rising global demand for herbal medicines highlights the necessity of maintaining the quality and purity of herbal raw materials as well as final products.[2] Ayurveda represents the principal traditional medical system in India and continues to play a significant role in healthcare delivery, particularly in rural communities. India's extensive ecological diversity, supported by its 15 agro-climatic zones, provides a vast repository of medicinal plant resources. Of the approximately 17,000–18,000 identified flowering plant species, more than 7,000 are recognized for their medicinal and aromatic properties.[3] Despite its substantial biodiversity, its participation in the global herbal products market remains limited.[4] A study by the Research and Information Systems for Developing Countries (RIS) highlighted that exports of herbal plants & extracts from India represents less than 40% of the sector's estimated export potential, indicating limited share in the global market.[5] This is due to various challenges faced by Indian manufacturers i.e, inadequate standardization, unsustainable raw

material supply, difficultly in identification and isolation of bioactive compounds due to their complex phytochemical composition, variations in international regulatory frameworks, limited scientific research. Moreover, the lack of robust scientific evidence supporting the safety and efficacy of medicinal and aromatic plants (MAP) products restricts their broader acceptance in international markets.[6] It has been reported that over half of the population in developed countries, including Europe and North America have used herbal medicines at least once in their lifetime. This trend presents a substantial opportunity for India to promote its traditional medicinal systems and herbal formulations in international markets.[7] After Asia, the European Union constitutes the largest market for herbal medicinal products.[8] EU has played a pioneering role in their regulation through the implementation of a comprehensive regulatory framework that includes directives, guidelines, herbal monographs and community list entries.[9] Historically, the EU has established rigorous quality standards for the evaluation & quality control of raw materials.[10] The European Union has emerged as a global benchmark in the development of herbal monographs that facilitates systematic evaluation of quality, safety and therapeutic efficacy of herbal medicinal products (HMPs). Its transparent and flexible regulatory framework provides a useful foundation for improving the international recognition, regulatory harmonization and wider acceptance of Indian herbal products.[9]

2. REGULATORY MECHANISMS OF NATURAL PRODUCTS IN THE EUROPEAN UNION

Plant-derived materials and their products are increasingly utilized in healthcare, driven by rising consumer demand for natural remedies and a growing holistic awareness of health and modern lifestyle-related concerns.[11] The regulatory framework for natural health products in the European Union is complex.[12] Within the European Union, natural products intended for health purposes are regulated under separate legal frameworks as either food supplements or herbal medicinal products, according to Directives 2002/46/EC and 2004/24/EC, respectively.[13]

2.1 Regulatory framework for Herbal Medicinal Products (HMPs)

As per EU legislation, HMP is defined as a medicinal product composed of one or more herbal substances and herbal preparations as active ingredients, either alone or in combination.[14] These products are further divided into three distinct categories: (i) Traditional use (TU) HMPs (ii) Well-established use (WEU) HMPs (iii) New HMPs.[15]

2.1.1 Traditional use (TU) HMPs

Traditional use (TU) HMPs are regulated through a simplified registration pathway under Article 16a(1) of Directive 2001/83/EC, without the requirement for clinical trials, as long as sufficient evidence of safety and plausible efficacy is available.[16] Community monographs & list entries are commonly used as reference standards for compiling the Summary of Product Characteristics (SPC).[17] TU-HMPs refer to herbal medicines for human use that meet the criteria laid down in Article 16a(1) of Directive 2001/83/EC, as revised by Directive 2004/24/EC of the European Union. They are designed for self-use without medical supervision and are restricted to oral, external, or inhalation administration at specified doses. Their registration requires evidence of at least 30 years of traditional medicinal use, including 15 years within the EU, along with sufficient evidence of safety and plausible therapeutic effects.[18]

Applications for traditional-use registration may be filed to the national competent authority (NCA) of a member state through decentralized, national or mutual recognition pathways. Under the national procedure, authorisation is granted by a single Member State and is valid only within that country. Under the mutual recognition procedure, a marketing authorization provided by the Reference Member State (RMS) is acknowledged by other EU Member States. In the decentralized procedure, applications are filed simultaneously in multiple Member States, with one designated as the RMS to lead the assessment.[19] Registration process for traditional HMPs as shown in Figure 1.

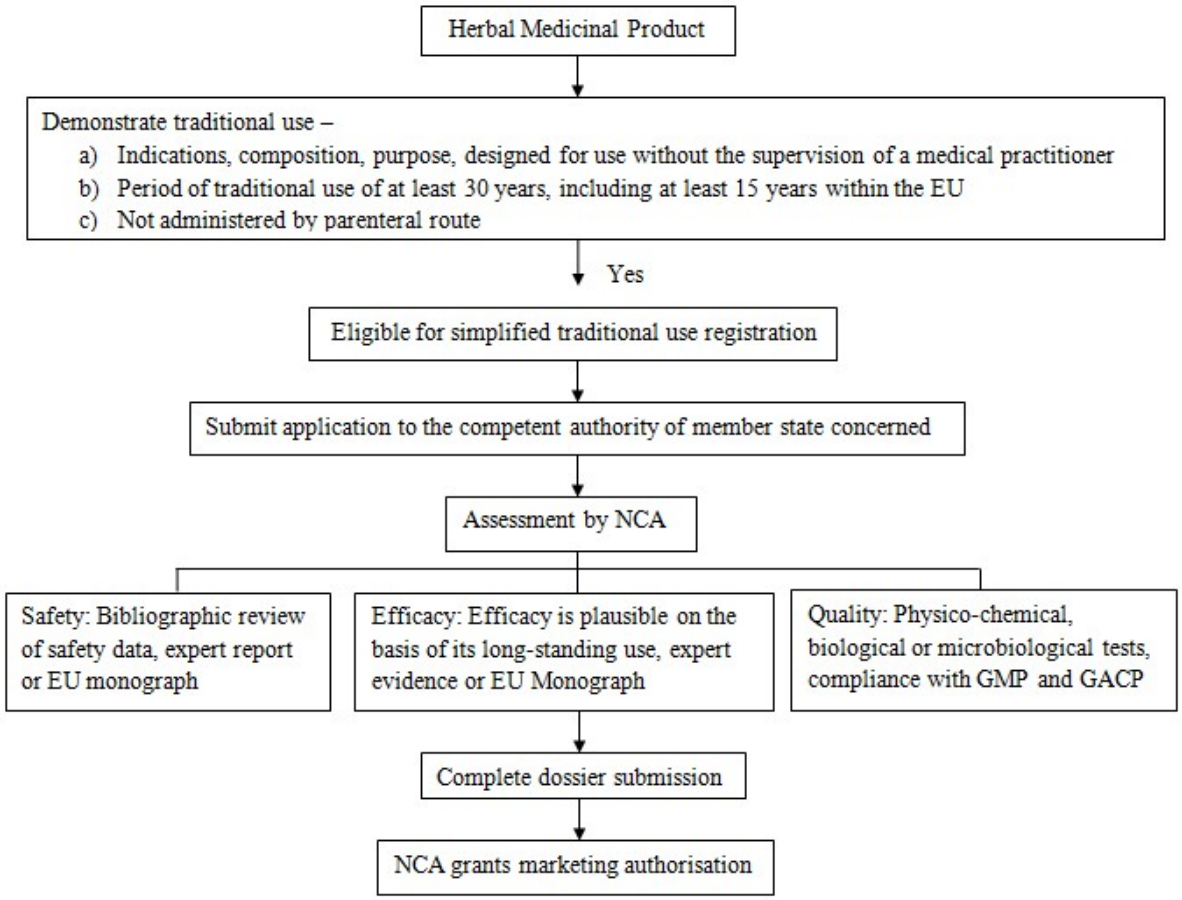

Figure 1: Registration process for traditional herbal medicinal products

2.1.2 Well-established use (WEU) HMPs

Well established use HMPs are authorized in accordance with the well-established use regulatory framework outlined in Article 10a of Directive 2001/83/EC. This pathway requires scientific literature demonstrating that the active substances have been in well-established medicinal use within the European Union for a minimum of 10 years, with acknowledged efficacy and an acceptable safety profile.[16] WEU-HMPs are supported by adequate clinical evidence, such as minimum of one controlled clinical study or adequately documented clinical evidence complemented by adequate pharmacological data, demonstrating its efficacy & an acceptable risk–benefit profile.[14] Well-established use marketing authorization can be obtained through national, mutual recognition, and decentralized procedures by NCA as well as centralized system administered by EMA.[19] Registration process for well established use HMPs as given in Figure 2.

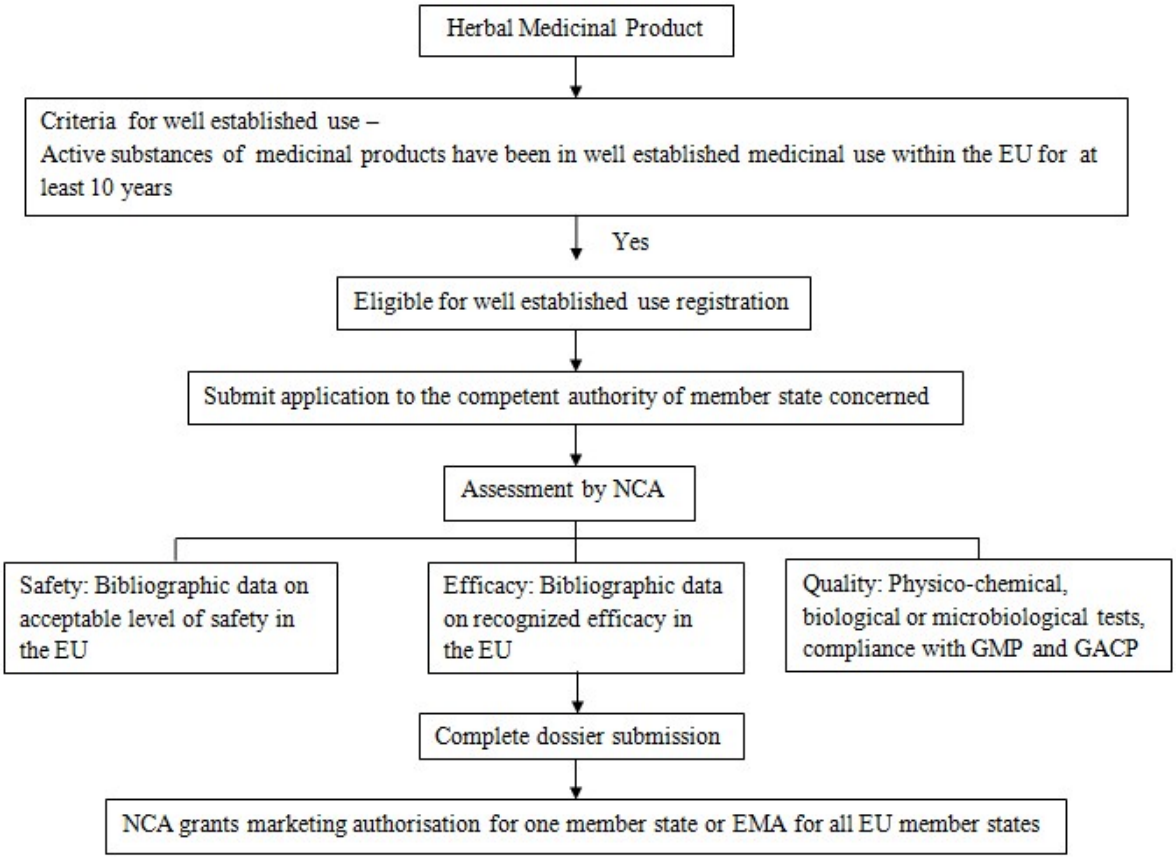

Figure 2: Registration process for well established use HMPs

2.1.3 New HMPs

New HMPs follow a mixed or stand-alone application pathway (Article 8(3) of Directive 2001/83/EC), with efficacy & safety demonstrated by the applicant's own research data or a combination of original studies and published literature.[16] This application requires a full clinical data dossier and is similar to the marketing authorization process for new conventional medicines. Stand-alone or mixed applications for marketing authorization may be submitted via national, mutual recognition, and decentralized procedures, as well as through the centralized procedure.[19] Consequently, if all requirements are fulfilled, marketing authorization is granted either by NCA or by EMA.[20] The centralized marketing authorization procedure is managed by EMA and involves a coordinated assessment by the Agency. If authorization is granted, the medicinal product may be marketed across all EU Member States.[21] Registration process for new HMPs as shown in Figure 3.

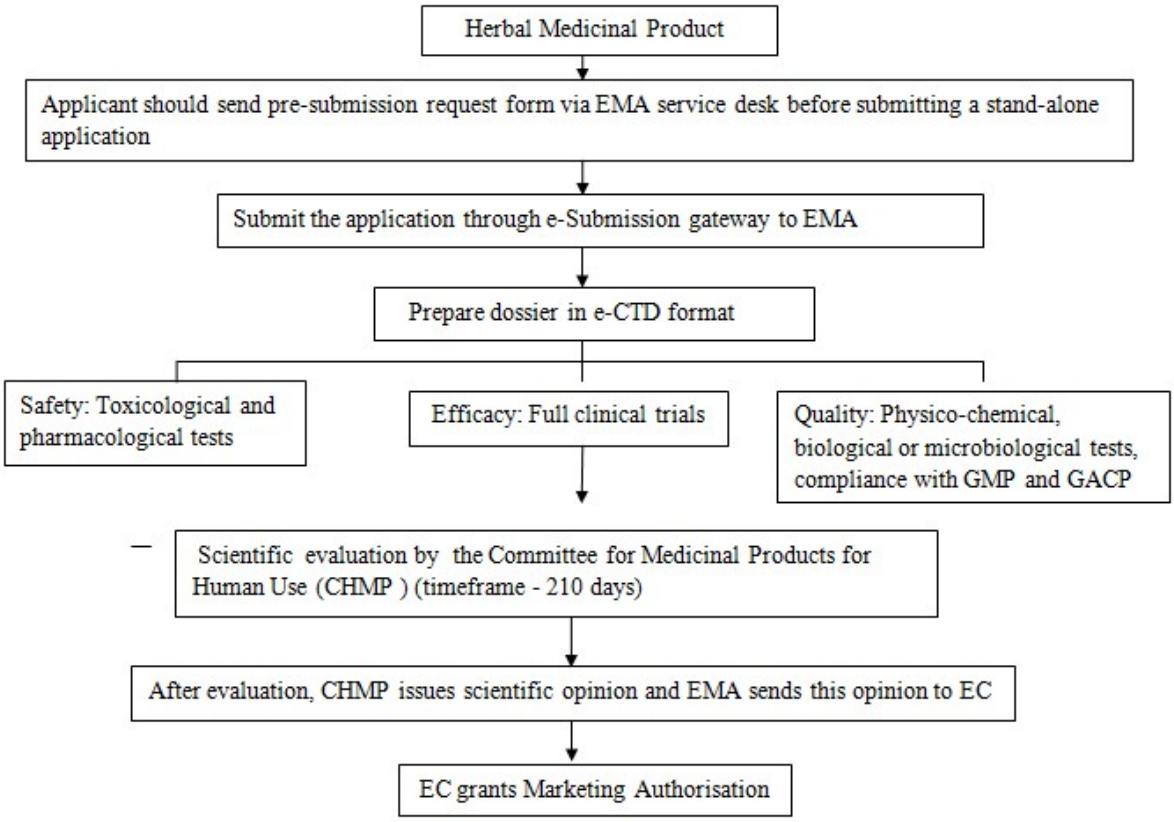

Figure 3: Registration process for new HMPs

2.1.1.1 Total number of applications and approvals for herbal medicinal products (HMPs)

The European Medicines Agency has maintained records of herbal medicinal products (HMPs) registration and authorization in European Union since the introduction of Directive 2004/24/EC until 31/12/2016. Analysis of these data shows that 1719 traditional use HMPs, 859 well-established use HMPs and 3 new HMPs have received marketing authorization in the EU, as shown in Figure 4. Table 1 further outlines the distribution of authorized HMPs across various EU Member States.[22]

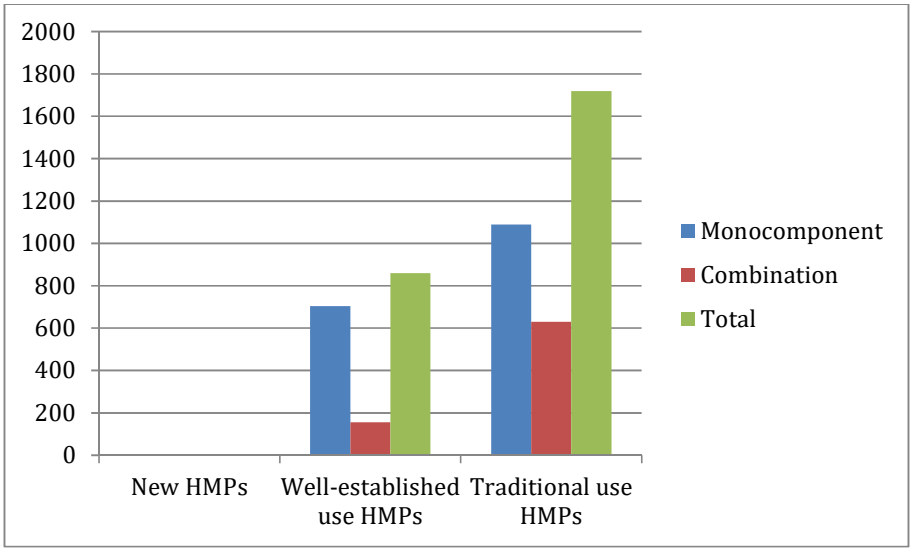

Figure 4 - Approved herbal medicinal products (HMPs) in the European Union

Table 2: Approved HMPs across EU Member States

Type	Member state	Applications	Granted	Refused	Withdrawn	Approval rate
TU	Germany	513	285	106	61	63.05%
	United Kingdom	450	348	18	26	88.77%
	Poland	315	215	19	19	84.98%
	Austria	224	209	0	1	99.52%
	France	171	33	0	11	75.00%
WEU	Germany	447	286	24	67	75.86%
	Austria	74	56	0	0	100%
	Czech Republic	73	36	6	15	63.16%
	Croatia	73	41	7	12	68.33%
	Romania	66	29	0	0	100%

2.2 Regulatory framework for Food Supplements (FSs)

Plant-derived materials are extensively utilized into diverse products designed to support human health and wellness, particularly in foods & food supplements.[11] Within the European Union, food supplements are recognized as concentrated preparations of nutrients, such as vitamins and minerals, along with other biologically active substances possessing nutritional or physiological functions, including amino acids, prebiotics, enzymes, essential fatty acids, probiotics, fibre, herbal extracts etc., intended to be administered in defined dosage forms to support and complement the regular diet.[23] Food supplements are regulated within the framework of general food legislation, with specific regulatory provisions established under Directive 2002/46/EC.[24] The provision of food information to consumers are laid down under Regulation (EU) No 1169/2011. As stipulated under Regulation (EU) No 1169/2011, food products must carry mandatory nutritional declarations, including the quantified content of energy, carbohydrates, fat, protein, saturated fat & salt.[25] For the determination of maximum permissible concentrations of vitamins and minerals in fortified foods and food supplements, the European Commission (EC) tasked the European Food Safety Authority (EFSA) to re-evaluate the earlier scientific opinions of the Scientific Committee on Food (SCF) by integrating recent scientific evidence and advancements.[26]

From a regulatory viewpoint, manufacturers hold the primary obligation for maintaining the safety, quality and regulatory compliance of food supplements. Although pre-market testing for quality, safety or efficacy is not mandatory, compliance with established standards such as GMP are anticipated to assure product safety, quality & consistency.[27] Regulation (EC) No. 1924/2006 establishes a pre-market approval process for health & nutrition claims applied to all types of foods products (including FSs).[28] The marketing of food supplements is governed by national legislation, which varies considerably across member states. In addition, a single botanical ingredient may be utilized either as medicinal product or food supplement, based on its intended application.[29] In several member states, including Germany, Italy, Belgium, Ireland, France, Spain & Romania, FSs must undergo pre-market notification process prior to commercialization. In contrast, Austria, Sweden, and the UK, applicant do not require registration or authorization prior to marketing.[11] Food supplements in the European Union are not subjected to centralized pre-market authorization system.[30] Registration process for food supplements as shown in Figure 5.

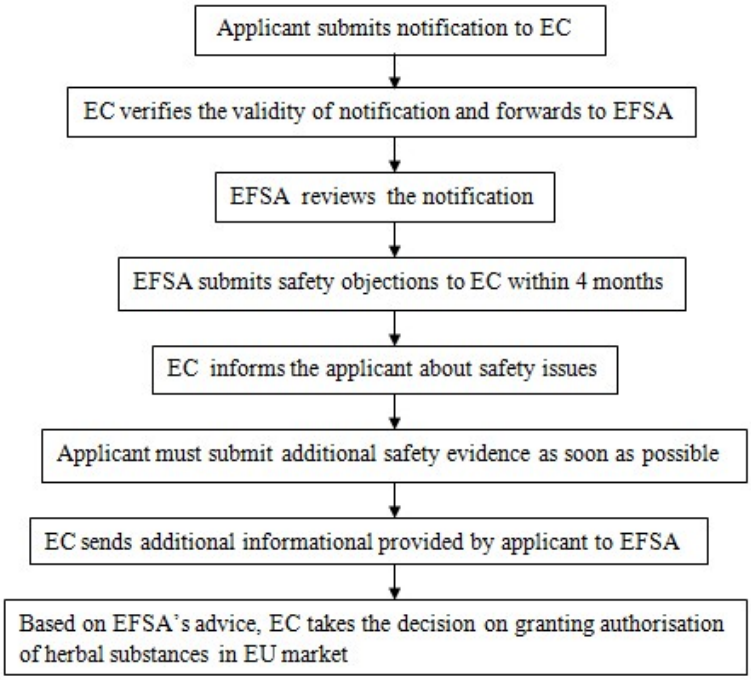

Figure 5: Registration process for food supplements

Ingredients intended for food supplements are considered as novel foods if they have no recognized history of safe use in the EU prior to 1997, manufactured using a novel production process, or contains nanomaterials.[13] Examples include foods produced using innovative processing techniques, including bread, yeast, UV-treated milk & mushrooms.[30] The novel food regulation, introduced in 1997 and revised in 2015, establishes the regulatory framework for assessing foods that have not substantial history of consumption within EU. All novel foods must undergo a safety assessment and obtain approval by Member States and the European Commission before being introduced to market.[31] For novel foods, the EU implements a uniform and centralized pre-market authorization system. A single Union list is maintained for all approved novel foods and their safety is centrally evaluated by EFSA.[32] To safeguard public health, novel food system was initially established under Regulation (EC) No. 258/97. With the growing introduction of new raw materials due to globalization and innovation, the EU subsequently revised the framework and adopted Regulation (EU) 2015/2283. Under new regulation (EU) 2015/2283, effective from January 2018, the novel food system in the EU is centrally regulated & strictly controlled at the Union level.[33] By December 2025, six traditional foods from non-European countries have been approved as new foods (Table 2). Registration process for novel food as given in Figure 6.

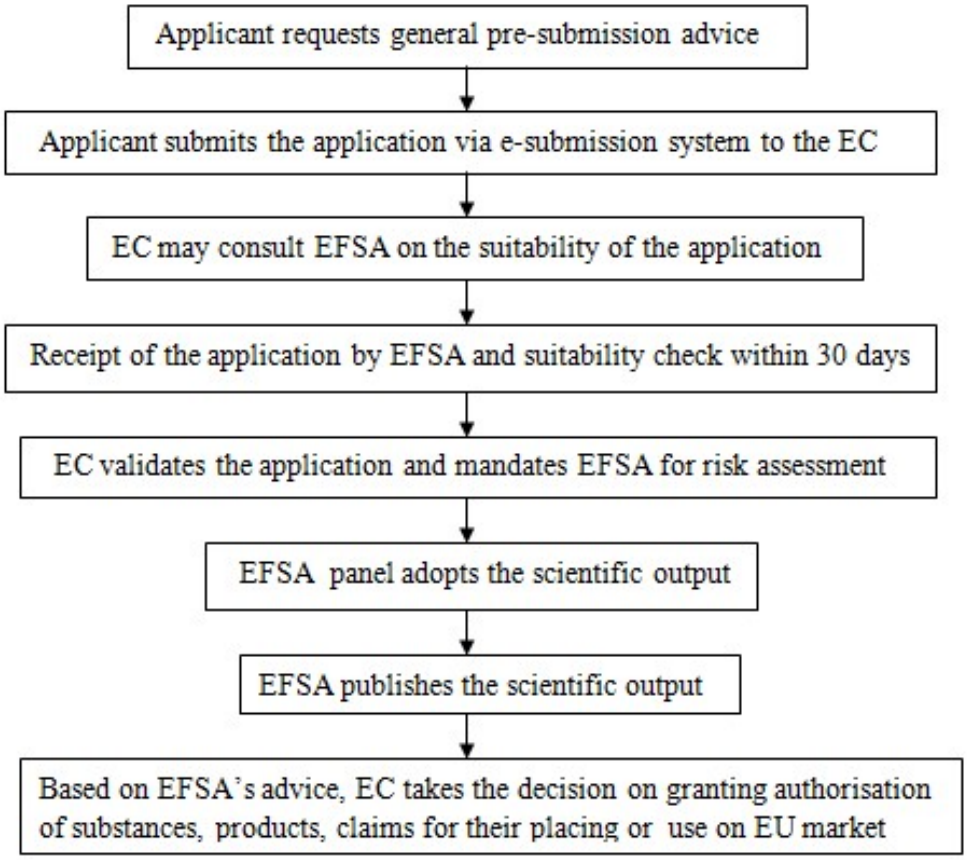

Figure 6: Registration process for novel food

Table :2 Novel foods recognized as traditional foods from non-EU countries

EU No	Title	Third country	References
2022/47	Coffea arabica L. and/or Coffea canephora Pierre ex A. Froehner dried cherry pulp and its infusion	Ethiopia	34
2023/267	Dried nuts of Canarium ovatum Engl.	Philippines	35
2023/652	Roasted and popped kernels from the seeds of Euryale ferox Salisb. (makhana)	India	36
2023/667	Canarium indicum L. dried nuts (also known as Canarium amboinense Hochr., or Kenari nuts)	Indonesia	37
2024/2047	Seeds and seed flour of Vigna subterranea (L.) Verdc.	Africa	38
2025/1263	Roasted seeds of Dipteryx alata Vogel (baru)	Brazil	39

3. REGULATORY MECHANISMS FOR NATURAL PRODUCTS IN THE INDIA

Natural products constitute a significant segment of India's healthcare system and commercial market.[40] In India, products fall into one of the two categories- Herbal medicines and

Supplements. Herbal medicines are categorized into two principal groups: traditional systems of medicine, including Ayurvedic, Siddha, and Unani (ASU) formulations (Classical and patent/proprietary medicines) and the emerging category of phytopharmaceuticals.[41] The regulatory oversight of traditional medicinal systems is administered by the Ministry of AYUSH, whereas phytopharmaceuticals products fall under the regulatory jurisdiction of the CDSCO. The legal requirements related to ASU formulations are laid down within section 33C to 33O of Chapter IV A of D & C Act.[42] Within the Indian regulatory framework, traditional medicinal systems such as ASU drugs are considered inherently safe based on their extensive historical and empirical use; therefore, classical ASU formulations are exempted from preclinical and clinical evaluation of safety and efficacy prior to market approval.[43]

As per CDSCO, a phytopharmaceutical drug refers to a purified and standardized extract or fraction of a medicinal plant containing a minimum of four qualitatively and quantitatively characterized phytochemical constituents, of which at least one should exhibit bioactivity. The formulation may contain either four bioactive constituents or a combination of one bioactive compound and three analytical marker compounds.[44] Appendix IB of Schedule Y under the Drugs and Cosmetics Rules outlines the data requirements for phytopharmaceuticals and requires that their clinical investigations must carried out in accordance with the regulatory standards applicable to new drugs.[45]

In the Indian regulatory context, the term nutraceuticals is used to denote dietary supplements. FSSAI acts as the central regulatory authority for food and nutrition, responsible for framing and enforcing guidelines to monitor the nutraceuticals industry.[46] Nutraceuticals are natural bioactive substances obtained through extraction, isolation or purification from food and non-food sources, which upon consumption confer physiological benefits and promote health maintenance.[47.] 'According to Food Safety and Standards (Nutraceuticals, Functional Foods, Health Supplements, Food for Special Medical Purposes, Food for Special Dietary Use & Novel Foods) Regulations, 2016'- Food Business Operators (FBOs) engaged in production of nutraceuticals must obtain an FSSAI license. These regulations are usually known as "Nutraceuticals Regulations".[48] Health-related claims associated with nutraceuticals are regulated by the FSSAI under the FSS (Advertising and Claims) Regulations, 2018.[49]

Table 3: Comparison of regulatory requirements for herbal medicines in India & EU

Parameter	India	EU
Term used for herbal Medicines	ASU drugs- Classical ASU drugs and Patent/ Proprietary medicines Phytopharmaceuticals	Herbal Medicinal Products (HMPs)
Legal framework	Drugs and Cosmetics Act, 1940 and Rules, 1945	Directive 2004/24/EC
Regulatory authority	Ministry of AYUSH for ASU drugs and CDSCO for Phytopharmaceuticals	European Medicine Agency (EMA) or National Competent Authorities (NCAs)
Quality Requirements	Comply with pharmacopoeial standards, GMP and CCRAS guidelines for standardization and quality assurance	Comply with European Pharmacopoeia (Ph. Eur.) and scientific guidelines for quality established by EMA
GMP	Schedule T	EudraLex Volume 4 Annex 7
Clinical trials	Clinical trials are not required for all ASU drugs but mandatory for phytopharmaceuticals	Mandatory for new HMPs. Scientific clinical evidence data based on bibliographic literatures is mandatory for traditional or well established use HMPs
Non-clinical guidelines	General guidelines for safety/toxicity evaluation of Ayurvedic formulations	Specific guidelines for non-clinical documentation, for assessment of genotoxicity of herbal substances, ICH guideline M3(R2) on non-clinical safety studies
Preclinical assessment	Mandatory for phytopharmaceutical drugs, not required for ASU drugs	Mandatory
Transparency in Supply chain	Limited	Strong supply chain audits
Pharmacovigilance	Pharmacovigilance in the development phase	Extensive pharmacovigilance system
Adverse event reporting system	Pharmacovigilance Programmes for ASU & H drugs, Ayush Suraksha digital portal	Eudravigilance: electronic reporting
Dossier submission	Not specified	eCTD format

Gaps in regulatory framework - India, despite its vast biodiversity and long-standing traditional herbal knowledge, continues to face a high prevalence of adulteration and contamination in herbal products. These issues include replacing expensive herbal ingredients with cheaper alternatives, as well as contamination with heavy metals and other harmful toxic substances. For identification of these contaminants, Department of AYUSH should integrate new analytical methods like biosensors, DNA sequencing etc. into their regulatory framework. India has not fully integrated modern analytical technologies such as DNA barcoding, DNA sequencing, biosensors, and other advanced fingerprinting techniques into routine regulatory quality control. In contrast, the EU systematically incorporates validated, state-of-the-art analytical methods for identity confirmation, quality assurance, and detection of adulteration. Unlike the EU, India lacks comprehensive regulatory guidelines for marker-based standardization of herbal medicines, non-pharmacopoeial reference standards and defined acceptance criteria for active constituents, leading to variability in product consistency and quality. Indian regulations do not sufficiently address modern manufacturing practices, level of extract purification and quality requirements for fixed-combination herbal products to ensure their safety, efficacy and batch to batch consistency. For preparation of non-clinical data, CCRAS has developed general safety and toxicity guidelines but India still lacks comprehensive regulatory frameworks for genotoxicity testing, selection of test materials for genotoxicity testing and structured non-clinical documentation as compared to EU. In India, clinical trials are not mandatory for marketing authorization of all ASU drugs, which are largely approved based on traditional use without clinical trial data. In contrast, the EU required scientific clinical data for registration of traditional use HMPs. The EU has a well-established pharmacovigilance system for continuous monitoring of herbal medicinal products, i.e. EudraVigilance. India's pharmacovigilance framework for ASU drugs is still evolving. To address these shortcomings, Ministry of AYUSH should integrate modern analytical methods, strict quality control standards, scientific preclinical & clinical studies guidelines, rigorous pharmacovigilance guidelines and digital tools for

reporting adverse effects associated with herbal medicines into their regulatory framework.

Note- Indian herbal products are predominantly marketed in the European Union as food supplements rather than herbal medicinal products (HMPs) due to regulatory differences. HMP registration under the traditional use framework requires ≥30 years of documented medicinal use, including ≥15 years within the EU. This requirement creates a significant barrier for many Indian traditional formulations, as their historical use is predominantly documented in the Indian medical systems such as Ayurveda, Siddha, and Unani, rather than within Europe. In contrast, food supplements are regulated under general food law. They generally do not require pre-market authorization; however, herbal products must undergo pre-market notification before being placed into EU market. Consequently, the food supplement category offers Indian manufacturers a more practical, cost-effective and faster route to enter the EU market.

Table 4: Comparison of regulatory requirements for dietary supplements in India and EU

Parameters	India	EU
Supplements	Nutraceuticals	Food Supplements
Legal framework	Food Safety and Standards Act, 2006	Directive 2002/46/EC
Regulatory body	FSSAI	EFSA
Approval process	No pre-market approval required, only registration required	Pre-market notification required
Pre-market safety assessment	Not required	Required for novel foods, not for food supplements
Health claim substantiation	Limited substantiation	Scientific evidence required
Health claims	Food Safety and Standards(Advertising and Claims) Regulations, 2018	Claims regulated under (EC) No. 1924/2006
Manufacturing and GMP enforcement	Developing GMP enforcement	Strict GMP compliance
Post-market surveillance	Reactive monitoring	Active monitoring system
Adverse event reporting system	Pharmacovigilance Programme of India (PvPI)	Emerging Risks Exchange Network (EREN), Rapid Alert System for Feed and Food and International nutrivigilance network

4. PERSPECTIVES FOR WIDER ACCEPTANCE OF INDIAN HERBAL PRODUCTS

The broader acceptance of Indian herbal products in developed markets is constrained by regulatory variations and non-uniform quality requirements. Key concerns regarding traditional herbal medicines include their quality, safety, and efficacy, which largely dependent on the authenticity, quality & standardization of the starting materials used in product manufacturing.[50] In contrast to conventional drugs that undergo rigorous preclinical and clinical assessment before approval, many herbal and traditional medicines have been used based on their long-standing empirical evidence. However, despite increasing scientific investigations, robust evidence regarding their safety remains inadequate.

Quality guidelines - To strengthen quality control in Ayurveda, Central Council for Research in Ayurvedic Sciences (CCRAS) has introduced guidelines for drug development, emphasizing standardization and quality assurance.[51] Additionally, Department of AYUSH and National Medicinal Plants Board (NMPB) have formulated India specific guidelines on GMP (Schedule T), Good Agricultural Practices (GAP) and Good Field Collection Practices (GFCP) guidelines to ensure the production of quality-assured herbal medicines.[52] Schedule T outlines the requirements regarding manufacturing facilities, hygienic practices, documentation, recommended machinery, equipment, production areas etc. to ensure product safety, quality and consistency. Stability studies for all ASU medicines shall be conducted as per the guidelines specified in the Ayurvedic Pharmacopoeia of India, Part-I, Volume-VIII and validated stability-indicating analytical methods should be employed for reliable evaluation of product stability and shelf life.[53] The AYUSH Good Manufacturing Practices (GMP) guidelines and Quality Standards promote product standardization through the use of pharmacopoeial monographs, DNA-based authentication techniques and chemical marker-based evaluation.[54] The Pharmacopoeia Commission for Indian Medicine & Homoeopathy develops formulary specifications and pharmacopoeial standards for Ayurveda, Siddha, Unani and Homoeopathy (ASU&H) drugs to ensure their quality, authenticity, purity, and strength. Adherence to these standards is compulsory for the manufacture of ASU&H medicines.[55] The Quality Certification Scheme, implemented by Quality Council of India awards quality certification to Ayurvedic, Siddha, and Unani products based on third-party evaluation of conformity with established domestic and international quality standards.[56] The herbal medicine sector continues to face challenges related to inadequate infrastructure, weak quality control mechanisms, limited toxicity monitoring. Furthermore, standardized protocols for dosage and administration have not yet been fully developed.[54]

As compared to Indian quality guidelines, various guidelines for quality of HMPs have been issued by EMA. Herbal Medicinal Products Committee (HMPC) has developed 'Guideline on declaration of herbal substances and herbal preparations in HMPs/traditional HMPs - Revision 2' which addresses the requirements for identifying and describing herbal ingredients used as active substances in HMPs.[57] EMA/HMPC guidance document on the 'Quality of Herbal Medicinal Products - Revision 3' which provides standardized requirements to ensure the quality and uniformity of HMPs. Additionally, 'Specifications, Test Procedures and Acceptance Criteria for Herbal Substances and Preparations -Revision 3' guidelines established by EMA outlines standardized requirements for herbal substance identification, analytical method validation and contaminant limits.[58] The EMA/HMPC guidance document on 'Good Agricultural and Collection Practice (GACP) for Starting Materials of Herbal Origin (Revision 1)' provides a framework for ensuring the traceability and quality of herbal raw materials. This guideline addresses quality aspects of cultivation, harvesting, collection & primary processing of medicinal plants, including those sourced from wild habitats and controlled cultivation environments.[59] The EMA/HMPC guidance document on 'Quality of combination HMPs/ traditional HMPs' outlines principles for the identification and quantitative assessment of herbal substances/herbal preparations used in multi-herb formulations.[60] HMPC has established 'reflection paper on markers used for quantitative and qualitative analysis of HMPs & traditional HMPs' provides guidance on the application of markers for analytical quality control. Compliance with Directives 2001/82/EC and Annex I of Directives 2001/83/EC, as well as relevant EU/ICH quality guidelines is essential to ensure product quality. Due to the specific and complex characteristics of HMPs, markers serve as an important tool for assessment of

product quality.[61] EMA/HMPC reflection paper on 'Microbiological aspects of HMPs & traditional HMPs', outlines key considerations for ensuring appropriate microbiological quality. It excludes guidance on sterilization processes or microbiological limits for herbal substances/preparations & products intended for sterile dosage forms.[62] EMA/HMPC reflection paper on 'Quality of essential oils as active substances in HMPs/traditional HMPs' which addresses quality considerations associated with inherent properties & specific manufacturing processes of essential oils.[63] Furthermore, EMA/HMPC reflection paper on 'Stability testing of herbal medicinal products and traditional herbal medicinal products' defines specific requirements for stability evaluation of HMPs.[64] 'Concept paper on the development of a Reflection Paper on modern manufacturing techniques used for herbal preparations' emphasizes the evaluation of advanced manufacturing technologies and their impact on critical quality attributes of herbal medicinal products. These include novel extraction techniques such as microwave-assisted, ultrasound-assisted, enzymatic-assisted, supercritical or subcritical fluid, deep eutectic extraction & pulsed electric field.[65] 'Concept paper on the development of a Reflection Paper on new analytical methods/technologies in the quality control of HMPs' developed by HMPC emphasizes the integration of new analytical techniques such as UV & IR spectroscopy with computational tools, DNA fingerprinting & sequencing, hyphenated methods, , multivariate and principal component analyses, biosensors, and NMR spectroscopy for both quantitative and qualitative evaluation of potential contaminants and bioactive constituents. The incorporation of these techniques into quality control systems enables the establishment of robust standards, ensures product consistency, verifies authenticity of herbal materials, detects adulteration and contaminants and strengthens the safety and reliability of HMPs.[66] EMA/HMPC concept paper on 'non-pharmacopoeial reference standards for herbal substances, herbal preparations and HMPs' defines the criteria to be considered when applying non-pharmacopoeial reference standards and outlines the documentation needed to confirm adequate characterization and suitability for intended use. The principles & guidelines for GMP in the EU are set out in Commission Directive (EU) 2017/1572, which complements Directive 2001/83/EC.[67] EudraLex Volume 4 Annex 7 provides information regarding the manufacture of HMPs.[68]

Overall, the EU's quality regulatory system for HMPs is more comprehensive, science-based and product-specific than the current Indian framework. India has established a quality regulatory framework for herbal medicines through AYUSH guidelines, pharmacopoeial standards, Schedule T, stability testing provisions and quality certification schemes while EU provides specific guidelines on quality of fixed-combination HMPs, declaration of herbal substances, marker-based qualitative and quantitative analysis, microbiological quality, stability testing, essential oils as active substances, non-pharmacopoeial reference standards, modern manufacturing technologies and the application of advanced analytical techniques. Furthermore, the EU framework promotes a risk-based and science-driven approach to ensure product consistency, authenticity, safety, and quality throughout the product lifecycle. Therefore, alignment of Indian quality regulations with HMPC guidelines would strengthen the scientific rigor, global acceptability, quality assurance and international market competitiveness of Indian herbal medicinal products.

Non-clinical guidelines - Preclinical studies are a critical step for evaluating the therapeutic potential of drugs or interventions prior to clinical evaluation. Guidelines for the safety/toxicity assessment of Ayurvedic formulations have established by CCRAS to support stakeholders. The main objective of nonclinical safety assessment includes identifying toxic effects in relation to target organs, dose–response relationships, exposure correlation and when applicable, reversibility.

For classical ASU medicines as well as for changes in the dosage forms of ASU products, non-clinical safety and efficacy data is generally waived. However, non-clinical efficacy data are necessary when classical ASU formulations are proposed for new indications. For Patent or Proprietary medicine containing Aqueous Extract(s) /crude drugs/ Hydro-Alcoholic Extracts) (with textual rationale or as per text), are generally exempt from the requirement of non-clinical safety and efficacy data. but for Patent or Proprietary Drugs containing other than Aqueous and Hydro-alcoholic extract(s) / any other solvent based extract(s) or any ingredients of Schedule E (1) of the D&C Act, 1940- acute toxicity, repeated-dose systemic toxicity studies, reproduction and developmental toxicity studies, carcinogenicity and genotoxicity should be carried out for safety evaluation of ASU drugs.[69]

In the EU, the safety of herbal substances/herbal preparations in traditional or well-established use HMPs can often be substantiated by long-standing documented medicinal use. However, when safety concerns arise, non-clinical studies may be required. EMA/HMPC guidance document on the 'assessment of genotoxicity of herbal substances/preparations' which provides a structured approach for evaluation, testing, and interpret the potential genotoxic effects of herbal substances and preparations.[70] 'Guideline on non-clinical documentation in applications for marketing authorisation/registration of traditional and well established HMPs' established by HMPC outlines the minimum non-clinical data requirements for bibliographical applications and specifies the safety aspects to be included in expert reports for simplified registration of traditional HMPs, along with any additional studies required to demonstrate safety. This guideline is also applicable for the development of EU herbal monographs and for inclusion in the list of traditional herbal substances.[71] EMA/HMPC guidance document on 'selection of test materials for genotoxicity testing for traditional HMPs' which outlines the standardized approach for identifying representative test materials to support genotoxicity testing of herbal substances/herbal preparations intended for inclusion in the community list.[72]

Overall, in India, non-clinical safety and toxicity evaluation of ASU drugs is primarily governed by regulatory provisions under the D & C Act, 1940 and Rules, 1945, along with supporting frameworks such as Schedule Y, OECD guidelines, CCRAS guidelines and GCP guidelines for ASU medicines**.** The approach is largely product based**.** In contrast, EU adopts a more standardized, monograph and guideline driven regulatory approach under the EMA/HMPC**.** The HMPC has issued several specialized guidelines, encompassing non-clinical documents required for traditional use registration, genotoxicity assessment and selection of representative test materials for genotoxicity testing**.** These guidelines provide structured methodologies for evaluating safety risks, defining minimum data requirements and ensuring consistency in herbal product assessment across the EU.

Clinical guidelines - In India, clinical trials is not a compulsory requirement for the approval of ASU drugs. At present, no dedicated regulatory framework exists for performing clinical studies on HMs. The current regulatory provisions, governed under the New Drugs and Clinical Trials Rules (NDCTR) 2019, which superseded Schedule Y of the Drugs and Cosmetics Act, are
primarily designed for conventional pharmaceuticals and may not be fully applicable to traditional herbal formulations. This creates distinct scientific and regulatory challenges in the design and implementation of clinical studies for traditional medicines.[73] Clinical studies on herbal formulations should be initiated only after adequate standardization and marker-based characterization to ensure uniformity of the investigational product. Inclusion of a qualified ASU physician as a co-investigator is crucial for scientifically and ethically appropriate evaluation within the traditional medicine context. Additionally, such studies must comply with Good Clinical Practice guidelines, ethical principles

of the Declaration of Helsinki, along with study participant protection guidelines as described in Third Schedule established by CDSCO and Indian Council of Medical Research.[74]

In the EU, there is specific guidelines for clinical study of HMPs. EMA/HMPC guidance document on the 'assessment of clinical safety and efficacy in the preparation of EU herbal monographs for traditional use and well established HMPs (Revision 1)' establishes principles for assessing the clinical safety & efficacy of traditional use and well-established use HMPs, supporting the development of EU list and community monographs of traditional herbal substances. It mandates a scientific assessment of clinical evidence within the assessment report. However, the unique characteristics of herbal medicinal products necessitate tailored clinical trial designs, making their evaluation complex, time - consuming and expensive.[75] For obtaining marketing authorization, safety & efficacy data should generated through minimum one controlled clinical trial or substantiated therapeutic experience, along with relevant pharmacological & toxicological data.[76] 'Guideline on the clinical assessment of fixed combinations of herbal substances/herbal preparations' was established in 2006. This guideline establishes recommendations for the systematic preparation of clinical data for herbal fixed-combination products and support the estimation of their clinical safety & therapeutic efficacy. It should be interpreted alongside other relevant EMEA guidance, particularly those related to preclinical and clinical evaluation.[77] Although HMPs are widely used but clinical research in pediatric and adolescent populations are insufficient. Hence, HMPC established 'Reflection paper on the necessity of initiatives to stimulate the conduct of clinical studies with HMPs in the paediatric population'. This document emphasizes the limited availability of clinical studies on HMPs in paediatric populations and highlights the urgent need for targeted initiative to support well-designed trials for establishing their safety, efficacy, and appropriate dosing.[78]

Overall, EU has specific guidelines for design and conduct of clinical studies of herbal preparations, clinical assessment of fixed combination herbal products whereas India lacks these specific guidelines in this field.

Pharmacovigilance guidelines - For the systematic collection, compilation and evaluation of adverse events related to AYUSH medicines, the Government of India initiated the National Pharmacovigilance Programme for ASU medicines (NPP-ASU) in 2007. Concurrently, drug safety surveillance is also supported by the nationwide Pharmacovigilance Programme of India (PvPI), coordinated by the Indian Pharmacopoeia Commission as the National Coordination Centre.[79] The Ministry of AYUSH, under central Ayush Oushadhi Gunvatta evam Uttpadan Samvardhan Yojana (AOGUSY) scheme, implements a pharmacovigilance programme for ASU&H medicines through a three-tier surveillance system consisting of ninety-seven Peripheral Pharmacovigilance Centres (PPvC), one National Pharmacovigilance Co-ordination Centre (NPvCC) & five Intermediary Pharmacovigilance Centres (IPvC) nationwide.[80] The existing PvPI & NPP-ASU&H continue to face limitations in accurate causality assessment and the persistent under-reporting of potential adverse events linked to ASU&H formulations.[79] To improve regulatory transparency and accountability in the AYUSH sector, the Department of AYUSH introduced an IT enabled 'Ayush Suraksha' portal on 30 May 2025.[80]

In the European Union, the pharmacovigilance framework was extensively reformed via Regulation (EC) No. 1235/2010 & Directive 2010/84/EC, which updated the earlier frameworks established under Regulation (EC) No. 726/2004 and Directive 2001/83/EC to improve the authorization, oversight and safety monitoring of human medicinal products.[81] CIR (EU) No 520/2012 is binding on all European Union member states and establishes the standardized structure and format of periodic safety update reports under the pharmacovigilance framework.[82] ICH E2C (R2) guideline provided the international standard for periodic benefit–risk evaluation reports, enabling a systematic and concise assessment of emerging safety data and therapeutic benefits to support evaluation of a medicinal product's overall benefit–risk profile in approved indications.[83] The European Medicines Agency has established a public-facing platform offering access to the EudraVigilance and its adverse drug reaction (ADR) reports. In addition, national regulatory authorities have developed safety portals that are interconnected with the EU platform to enable harmonized pharmacovigilance activities.[81] As compared to food products, pharmacovigilance activities is crucial for HMPs.[82]

Overall, EU have robust pharmacovigilance structure for addressing adverse events related to HMPs whereas pharmacovigilance system in India is still in the development stage.

5. CONCLUSION

India is progressively enhancing transparency and quality assurance systems for natural products, whereas the EU has formulated robust regulatory frameworks emphasizing strict manufacturing standards and scientific validation. The Indian regulatory framework is largely grounded in traditional evidence, while the EU adopts an evidence-based regulatory paradigm with standardized assessments for herbal medicines, enhancing product efficacy and consumer confidence. The EU framework also prioritizes documented human use experience through herbal monographs and list entries. Harmonization of regulatory standards, adoption of standardized clinical protocols and execution of precise quality controls are essential for improving evidence reliability, facilitating global acceptance and assuring safe incorporation of HMs into health service. The development of mutual recognition agreements between India and the EU could facilitate international trade under harmonized standards. Although India has developed an extensive regulatory and policy framework but its effective implementation requires systematic evaluation. Additionally, exporters of herbal and pharmaceutical products must obtain a Certificate of Pharmaceutical Product (CoPP), which enhances product credibility and supports global marketing.

REFERENCES

- He TT, Ung CO, Hu H, Wang YT. Good manufacturing practice (GMP) regulation of herbal medicine in comparative research: China GMP, cGMP, WHO-GMP, PIC/S and EU-GMP. European Journal of integrative Medicine. 2015 Feb 1;7(1):55-66. https://doi.org/10.1016/j.eujim.2014.11.007.
- Mukherjee PK. Quality evaluation of herbal medicines: challenges and opportunities. Quality Control and Evaluation of Herbal Drugs. 2019:53-77.DOI:10.1016/B978-0-12-813374-3.00003-X.
- Máthé Á, Khan IA. Medicinal and Aromatic Plants in India: A Bridge from Traditions to Modern Wellbeing. InMedicinal and Aromatic Plants of India Vol. 2 2023 Nov 1 (pp. 1-11). Cham: Springer International Publishing. DOI:10.1007/978-3-031-44914-7_1.
- Sengunthar S, Sarkar D, Jadhav P. Impact of tariff on Indian AYUSH products: Evidence from top importers of India. Journal of Ayurveda and Integrative Medicine. 2026 May 1;17(3):101329. https://doi.org/10.1016/j.jaim.2026.101329.
- Government of India. Global market share of Ayurvedic medicines. Ministry of AYUSH. 2025. Available from: https://sansad.in/getFile/annex/268/AS241_ly1K08.pdf?source=pqars.
- Zamani S, Fathi M, Ebadi MT, Máthé Á. Global trade of medicinal and aromatic plants. A review. Journal of Agriculture and Food Research. 2025 Jun 1;21:101910. https://doi.org/10.1016/j.jafr.2025.101910.
- Bhoi A, Dwivedi SD, Singh D, Singh MR, Keshavkant S. Worldwide health scenario from the perspective of herbal medicine research. In Phytopharmaceuticals and herbal drugs 2023 Jan 1 (pp. 13-32). Academic Press. DOI:10.1016/B978-0-323-99125-4.00014-7.

- Xu M, Nguyen DT, Purja S, Kim E. A global comparative analysis of guidelines for herbal medicines Pharmacopoeia and Good Manufacturing Practice, with a case study of Panax ginseng CA Meyer. European Journal of Integrative Medicine. 2024 Sep 1;70(1):102394. DOI:10.1016/j.eujim.2024.102394.
- Xiong R, Zhang H, Li Y, Zeng G, Liu Y, Xu Y. Enlightenment of EU Herbal Medicinal Products regulation on the registration of Traditional Chinese Medicines in the Guangdong-Hong Kong-Macao Greater Bay Area. Journal of Holistic Integrative Pharmacy. 2024 Dec 1;5(4):344-53. https://doi.org/10.1016/j.jhip.2024.11.005.
- Xiong Y, Li M, Sun P, Liang W, Hornbeck RG, Che X, Rao C, Zhao Y, Guo L, Huang Y, Yang H. Market access for Chinese herbal medicinal products in Europe—A ten-year review of relevant products, policies, and challenges. Phytomedicine. 2022 Aug:103:154237. DOI: 10.1016/j.phymed.2022.154237.
- Trovato M, Ballabio C. Botanical products: general aspects. In book: Food Supplements Containing Botanicals: Benefits, Side Effects and Regulatory Aspects. 2017 Oct 28 (pp. 3-26). Cham: Springer International Publishing. DOI:10.1007/978-3-319-62229-3_1.
- Lippert A, Renner B. Herb–drug interaction in inflammatory diseases: Review of phytomedicine and herbal supplements. Journal of clinical medicine. 2022 Mar 12;11(6):1567. DOI: 10.3390/jcm11061567.
- Qu L, Li X, Xiong Y, Wang Z, Zhou Y, Zou W, Tang J, Wang M. Opportunities and hurdles to European market access for multi-herbal traditional Chinese medicine products: an analysis of EU regulations for combination herbal medicinal products. Pharmacological research. 2022 Dec 1;186:106528. DOI: 10.1016/j.phrs.2022.106528.
- Chinou I, Knoess W, Calapai G. Regulation of herbal medicinal products in the EU: an up-to-date scientific review. Phytochemistry Reviews. 2014 Jun;13(2):539-45. DOI:10.1007/s11101-014-9354-4.
- Gatt AR, Vella Bonanno P, Zammit R. Ethical considerations in the regulation and use of herbal medicines in the European Union. Frontiers in Medical Technology. 2024 Jun 14;6:1358956. DOI: 10.3389/fmedt.2024.1358956.
- Bilia AR, do Céu Costa M. Medicinal plants and their preparations in the European market: Why has the harmonization failed? The cases of St. John's wort, valerian, ginkgo, ginseng, and green tea. Phytomedicine. 2021 Jan 1;81:153421. DOI: 10.1016/j.phymed.2020.153421.
- Quintus C, Schweim HG. European regulation of herbal medicinal products on the border area to the food sector. Phytomedicine. 2012 Feb 15;19(3-4):378-81. DOI: 10.1016/j.phymed.2011.10.002.
- EMA. Questions & Answers on the European Union framework for (traditional) herbal medicinal products, including those from a “non-European” tradition (EMA/HMPC/402684/2013 Rev. 1). 2023. Available from-https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/questions-answers-european-union-framework-traditional-herbal-medicinal-products-including-those-non-european-tradition_en.pdf.
- Wang M, Yao PF, Sun PY, Liang W, Chen XJ. Key quality factors for Chinese herbal medicines entering the EU market. Chinese medicine. 2022 Feb 22;17(1):29. DOI: 10.1186/s13020-022-00583-x.
- Verma N. Current regulatory challenges and approaches in the registration of herbal drugs in Europe. Clinical Research and Regulatory Affairs. 2016 Jan 2;33(1):9-24. DOI:10.3109/10601333.2016.1130717.
- Knoess W, Wiesner J. The globalization of traditional medicines: Perspectives related to the European Union regulatory environment. Engineering. 2019 Feb 1;5(1):22-31. https://doi.org/10.1016/j.eng.2018.11.012.
- EMA. Uptake of the traditional use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States(EMA/HMPC/322570/2011 Rev. 7). 2017. Available from-https://www.ema.europa.eu/en/documents/report/uptake-traditional-use-registration-scheme-and-implementation-provisions-directive-200424ec-european-union-member-states_en.pdf.
- Hribar M, Goljuf Š, Pravst I. Quality assessment of selected vitamins and minerals in effervescent food supplements. Journal of Food Composition and Analysis. 2025 Dec 16;149:108803. https://doi.org/10.1016/j.jfca.2025.108803.
- Slavcheva K, Staynova R, Kafalova D. Assessment of regulatory labeling compliance of red yeast rice supplements on the Bulgarian market. Pharmacia. 2026 May 8;73:e193045. https://doi.org/10.3897/pharmacia.73.e193045.
- Žmitek K, Hribar M, Hristov H, Vičič V, Pravst I. Hidden sodium in effervescent food supplements: labelling practices and product composition. Journal of Food Composition and Analysis. 2026 May 7;155:109224. https://doi.org/10.1016/j.jfca.2026.109224.
- EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA), Turck D, Bohn T, Cámara M, Castenmiller J, de Henauw S, Hirsch-Ernst KI, Jos A, Maciuk A, Mangelsdorf I, McNulty B. Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals. EFSA Journal. 2024 Nov 6;22(11):e9052. DOI: 10.2903/j.efsa.2024.9052.
- Lopes S, Cunha M, Fernandes AS, Oliveira NG, Ferreira-Pêgo C, Costa JG. Contamination and adulteration of food supplements: Risk perception and regulatory awareness in recreational athletes. Regulatory Toxicology and Pharmacology. 2026 Aug;169:106106. DOI: 10.1016/j.yrtph.2026.106106.
- Coppens P, Pettman S. The regulatory situation in Europe and other continents. In book: Food Supplements Containing Botanicals: Benefits, Side Effects and Regulatory Aspects: The Scientific Inheritance of the EU Project PlantLIBRA 2017 Oct 28 (pp. 27-59). (pp. 27-59). Cham: Springer International Publishing. DOI:10.1007/978-3-319-62229-3_2.
- Garcia-Alvarez A, Roman-Viñas B, Vargas-Murga L, Ribas-Barba L, Serra-Majem L. Assessment of food supplements containing botanicals in epidemiological research. InFood Supplements Containing Botanicals: Benefits, Side Effects and Regulatory Aspects: The Scientific Inheritance of the EU Project PlantLIBRA 2017 Oct 28 (pp. 61-115). Cham: Springer International Publishing. DOI:10.1007/978-3-319-62229-3_3.
- European Commission. Novel Food. Available from-https://food.ec.europa.eu/food-safety/novel-food_en.
- Nakadai M, Ramasamy PK, Jepsen PM. Regulatory landscape of microalgae-based novel foods in the European Union: Current status, trends, and challenges. Algal Research. 2026 May 22:104765.
- Thakkar S, Anklam E, Xu A, Ulberth F, Li J, Li B, Hugas M, Sarma N, Crerar S, Swift S, Hakamatsuka T. Regulatory landscape of dietary supplements and herbal medicines from a global perspective. Regulatory Toxicology and Pharmacology. 2020 Jul 1;114:104647. DOI: 10.1016/j.yrtph.2020.104647.
- Heo S, Lee G, Na HE, Park JH, Kim T, Oh SE, Jeong DW. Current status of the novel food ingredient safety evaluation system. Food Science and Biotechnology. 2023 Aug 9;33(1):1-11. DOI: 10.1007/s10068-023-01396-w.
- EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA), Turck D, Bohn T, Castenmiller J, De Henauw S, Hirsch-Ernst KI, Maciuk A, Mangelsdorf I, McArdle HJ,

Naska A, Pelaez C. Safety of dried coffee husk (cascara) from Coffea arabica L. as a Novel food pursuant to Regulation (EU) 2015/2283. EFSA Journal. 2022 Feb 25;20(2):e07085. https://doi.org/10.2903/j.efsa.2022.7085.

- European Food Safety Authority (EFSA). Technical Report on the notification of nuts of Canarium ovatum Engl. as a traditional food from a third country pursuant to Article 14 of Regulation (EU) 2015/2283. EFSA Supporting Publications. 2022 May 13. https://doi.org/10.2903/sp.efsa.2022.EN-7314.
- European Food Safety Authority (EFSA). Technical Report on the notification of roasted and popped kernels from the seeds of Euryale ferox Salisb. as a traditional food from a third country pursuant to Article 14 of Regulation (EU) 2015/2283. EFSA Supporting Publications. 2022 Sep 5. https://doi.org/10.2903/sp.efsa.2022.EN-7538.
- European Food Safety Authority (EFSA). Technical Report on the notification of dried nuts of Canarium amboinense Hochr. as a traditional food from a third country pursuant to Article 14 of Regulation (EU) 2015/2283. EFSA Supporting Publications. 2022 Nov 11. https://doi.org/10.2903/sp.efsa.2022.EN-7640.
- European Food Safety Authority (EFSA). Technical Report on the notification of dried seeds and flour thereof of Vigna subterranea (L.) Verdc. as a traditional food from a third country pursuant to Article 14 of Regulation (EU) 2015/2283. EFSA Supporting Publications. 2024 Jan 10. DOI: 10.2903/sp.efsa.2024.EN-8571.
- European Food safety Authority (EFSA), Engel KH, Kukuła-Koch W, Maciuk A, Pelaez C, Pilegaard K, van Loveren H, Beneventi E, Turla E, Laganaro M. Technical Report on the notification of roasted seeds of Dipteryx alata Vogel as a traditional food from a third country pursuant to Article 14 of Regulation (EU) 2015/2283. 2025 Feb 07. https://doi.org/10.2903/sp.efsa.2025.EN-9234.
- Sapoliya NK, Shah MB. Regulations on herbal products in India, United States and European union: a review. International Journal of Drug Regulatory Affairs. 2022 June;10(2):67-72. https://doi.org/10.22270/ijdra.v10i2.528.
- Mukherjee PK, Harwansh RK, Bahadur S, Banerjee S, Kar A. Evidence based validation of Indian traditional medicine–way forward. World Journal of Traditional Chinese Medicine. 2016 Jan 1;2(1):48-61. https://doi.org/10.15806/j.issn.2311-8571.2015.0018.
- Swathi J, Venkatesh DN. A review of herbal regulations in India and Worldwide. Research Journal of Pharmacy and Technology 2022 Mar 1;15(3):1348-52. https://doi.org/10.52711/0974-360X.2022.00225.
- Sahoo N, Manchikanti P. Herbal drug regulation and commercialization: an Indian industry perspective. Journal of Alternative and Complementary Medicine. 2013 Dec;19(12):957-63. DOI: 10.1089/acm.2012.0275.
- Central Drugs Standard Control Organization. Frequently Asked Questions (FAQs) on Approval of new Phytopharmaceutical Drugs [Internet]. New Delhi: CDSCO; [cited 2025 Jul 12]. Available from: https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/New-Drugs/FAQs/New_Drugs_FAQs.doc.
- Jadhav R, Das J, Rajyaguru S, Kyada S, Kale V, Teja PK, Bhutia DO, Chauthe SK. Regulations, current development, and future prospects of phytopharmaceuticals, a new class of herbal medicines in India. Discover Pharmaceutical Sciences. 2025 May 13;1(1):6. https://doi.org/10.1007/s44395-025-00006-4.
- Ray A, Joshi J, Gulati K. Regulatory aspects of nutraceuticals: An Indian perspective. In Nutraceuticals: Efficacy, Safety and Toxicity, Edited by Gupta RC. Hopkinsville, KY, USA. 2016: pp. 941-946. Academic Press. https://doi.org/10.1016/B978-0-12-802147-7.00066-8.
- Food Safety and Standards Authority of India(FSSAI). Guidance Note on Food for Special Medical Purpose (FSMP), 2020[Internet]. New Delhi: FSSAI; [cited 2025 Oct 04].Available from: https://fssai.gov.in/upload/uploadfiles/files/Guidance_Note_FSMP_28_08_2020.pdf.
- Food Safety and Standards Authority of India(FSSAI). Frequently Asked Questions (FAQs) on the Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016 (herein after referred as Nutraceutical Regulations) [Internet]. New Delhi: FSSAI; [updated 2021 Oct 06; cited 2025 Sept 17]. Available from: https://fssai.gov.in/upload/uploadfiles/files/FAQs_Nutraceutical_Regulations_06_10_2020.pdf.
- Bose A, Sharma S. Global regulatory trends and comparative insights: Nutraceuticals in the USA, India, and Europe. PharmaNutrition. 2025 Mar 1;31:100430. https://doi.org/10.1016/j.phanu.2025.100430.
- National Medicinal Plants Board (NMPB). Good Agricultural Practices Standard for Medicinal Plants-Requirements. Available from: https://nmpb.nic.in/sites/default/files/publications/Good_Agricultural_Practicies_GAPs_Standard_for_Medicinal_Plants.pdf.
- Kim M, Woo Y, Han CH. Current status of the spontaneous reporting and classification/coding system for herbal and traditional medicine in pharmacovigilance. Integrative Medicine Research. 2021 Mar 1;10(1):100467. https://doi.org/10.1016/j.imr.2020.100467.
- National Medicinal Plants Board (NMPB). Guidelines on Good Field Collection Practices for Indian Medicinal Plants. Available from: https://nmpb.nic.in/sites/default/files/publications/Good_Field_Collection_Practicies_GFCPs_Booklet-Part-I.pdf.
- Central Council for Research in Ayurvedic Sciences. General guidelines for drug development of ayurvedic formulations Volume-1. New Delhi: Ministry of AYUSH. 2018. Available from: https://ccras.nic.in/wp-content/uploads/2024/07/CCRAS_Guideline-of-Drug-Development.pdf.
- Sharma K. Herbal pharmacopeias: bridging ancient traditions, nanotechnological innovation, and global regulatory cohesion for equitable healthcare. Pharmacological Research-Natural Products. 2025 Sep 1;8:100301. https://doi.org/10.1016/j.prenap.2025.100301.
- Government of India. Standardization and quality control of AYUSH products. PIB Delhi. 2026. Available from: https://www.pib.gov.in/PressReleaseDetail.aspx?PRID=2241692&reg=3&lang=1.
- Government of India. Quality control of AYUSH drugs. Ministry of AYUSH. 2026. Available from: https://sansad.in/getFile/annex/270/AU2725_9mzVAN.pdf?source=pqars.
- EMA. Guideline on declaration of herbal substances and herbal preparations in herbal medicinal products /traditional herbal medicinal products (EMA/HMPC/CHMP/CVMP/287539/2005 Rev. 2). 2026. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-declaration-herbal-substancesherbal-preparations-herbal-medicinal-products-traditional-herbal-medicinal-products-revision-2_en.pdf.
- EMA. Guideline on specifications: test procedures and acceptance criteria for herbal substances , herbal preparations and herbal medicinal products/traditional herbal medicinal products(EMA/HMPC/162241/20051 3 Rev. 3). 2018. Available from: https://www.ema.europa.eu/en/documents/scientific-

guideline/draft-guideline-specifications-test-procedures-and-acceptance-criteria-herbal-substances-herbal-preparations-and-herbal-medicinal-products-traditional-herbal-medicinal-products-revision-3_en.pdf.

- EMA. Guideline on Good Agricultural and Collection Practice (GACP) for Starting Materials of Herbal Origin (EMA/HMPC/246816/2005 Rev. 1). 2025. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-agricultural-collection-practice-gacp-starting-materials-herbal-origin-revision-1_en.pdf.
- EMA. Guideline on quality of combination herbal medicinal products / traditional herbal medicinal products. 2008. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-quality-combination-herbal-medicinal-productstraditional-herbal-medicinal-products_en.pdf.
- EMA. Reflection paper on markers used for quantitative and qualitative analysis of herbal medicinal products and traditional herbal medicinal products. 2008. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-markers-used-quantitative-and-qualitative-analysis-herbal-medicinal-products-and-traditional-herbal-medicinal-products_en.pdf.
- EMA. Reflection paper on microbiological aspects of herbal medicinal products and traditional herbal medicinal products (EMA/HMPC/95714/2013). 2015. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-microbiological-aspects-herbal-medicinal-products-and-traditional-herbal-medicinal-products_en.pdf.
- EMA. Reflection paper on quality of essential oils as active substances in herbal medicinal products/traditional herbal medicinal products (EMA/HMPC/84789/2013). 2014. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-quality-essential-oils-active-substances-herbal-medicinal-productstraditional-herbal-medicinal-products_en.pdf.
- EMA. Reflection paper on stability testing of herbal medicinal products and traditional herbal medicinal products. 2009. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-reflection-paper-stability-testing-herbal-medicinal-products-and-traditional-herbal-medicinal-products_en.pdf.
- EMA. Concept paper on the development of a Reflection Paper on modern manufacturing techniques used for herbal preparations (EMA/HMPC/885124/2022). 2023. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/concept-paper-development-reflection-paper-modern-manufacturing-techniques-used-herbal-preparations_en.pdf.
- EMA. Concept paper on the development of a Reflection Paper on new analytical methods/technologies in the quality control of herbal medicinal products (EMA/HMPC/541422/2017 Corr.). 2017. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/concept-paper-development-reflection-paper-new-analytical-methods-technologies-quality-control-herbal-medicinal-products_en.pdf.
- EMA. Concept paper on non-pharmacopoeial reference standards for herbal substances, herbal preparations and herbal medicinal products / traditional herbal medicinal products(EMA/HMPC/312890/2012). 2012. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/concept-paper-non-pharmacopoeial-reference-standards-herbal-substances-herbal-preparations-and-herbal-medicinal-products-traditional-herbal-medicinal-products_en.pdf.
- European Commission. EudraLex -The Rules Governing Medicinal Products in the European Union. 2008. Available from: https://health.ec.europa.eu/document/download/fd318dd6-2404-4e67-82b0-2324825e4d90_en?filename=vol4_an7_2008_09_en.pdf.
- Central Council for Research in Ayurvedic Sciences. General guidelines for safety/toxicity evaluation of ayurvedic formulations Volume-II. Ministry of AYUSH. New Delhi. 2018. Available from: https://ccras.nic.in/wp-content/uploads/2024/07/CCRAS_Guideline-of-Safety_Toxicity.pdf.
- EMA. Guideline on the assessment of genotoxicity of herbal substances/preparations' (EMEA/HMPC/107079/2007). 2008. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-assessment-genotoxicity-herbal-substancespreparations_en.pdf.
- EMA. Guideline on non-clinical documentation in applications for marketing authorisation/registration of well established and traditional herbal medicinal products (EMEA/HMPC/32116/2005 Rev.1). 2018. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-non-clinical-documentation-applications-marketing-authorisationregistration-well-established-and-traditional-herbal-medicinal-products-revision-1_en.pdf
- EMA. Guideline on selection of test materials for genotoxicity testing for traditional herbal medicinal products/ herbal medicinal products". 2009. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-selection-test-materials-genotoxicity-testing-traditional-herbal-medicinal-productsherbal-medicinal-products_en.pdf
- Ahmad S, Gupta A, Katiyar CK. Clinical research on herbal/ASU/traditional drugs in India. In book: Evidence-Based Validation of Herbal Medicine. 2022 Jan 1 (pp. 739-753). Elsevier. https://doi.org/10.1016/B978-0-323-85542-6.00035-4.
- CDSCO. Guidelines on Good Clinical Practices. 2024. Available from: https://ethics.ncdirindia.org/asset/pdf/Indian_GCP_guideline.pdf.
- EMA. Guideline on the assessment of clinical safety and efficacy in the preparation of EU herbal monographs for well established and traditional herbal medicinal products (EMA/HMPC/104613/2005 – Rev. 1). 2017. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-assessment-clinical-safety-and-efficacy-preparation-eu-herbal-monographs-well-established-and-traditional-herbal-medicinal-products_en.pdf.
- Nguyen HA, Doerfler J, Buentzel J, Keinki C, Huebner J. Assessing indications for herbal medicinal products: a comparative analysis of EMA monographs and database records. BMC Complementary Medicine and Therapies. 2025 Apr 9;25(1):130. DOI: 10.1186/s12906-025-04852-8.
- EMA. Guideline on the clinical assessment of fixed combinations of herbal substances / herbal preparations (EMEA/HMPC/166326/2005). 2006. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-assessment-fixed-combinations-herbal-substances-herbal-preparations_en.pdf.
- EMA. Reflection paper on the necessity of initiatives to stimulate the conduct of clinical studies with herbal medicinal products in the paediatric population (EMA/HMPC/833398/2009). 2011. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-necessity-initiatives-stimulate-conduct-clinical-studies-herbal-medicinal-products-paediatric-population_en.pdf.
- Kalaiselvan V, Ruknuddin G. Pharmacovigilance for Indian traditional medicines. In book: Pharmacovigilance for Herbal and Traditional Medicines: Advances, Challenges and

International Perspectives. 2022 Aug 12 (pp. 347-356). Cham: Springer International Publishing.

- Government of India. Quality control of AYUSH drugs. 2026. Available from: https://sansad.in/getFile/annex/270/AU2725_9mzVAN.pdf?source=pqars.
- Borg JJ, Tanti A, Kouvelas D, Lungu C, Pirozynski M, Serracino-Inglott A, Aislaitner G. European Union pharmacovigilance capabilities: potential for the new legislation. Therapeutic advances in drug safety. 2015 Aug;6(4):120-40. https://doi.org/10.1177/2042098615591802.
- Choudhary A, Singh PA, Bajwa N, Dash S, Bisht P. Pharmacovigilance of herbal medicines: Concerns and future prospects. Journal of Ethnopharmacology. 2023 Jun 12;309:116383. DOI: 10.1016/j.jep.2023.116383.
- EMA. 'ICH guideline E2C (R2) on periodic benefit-risk evaluation report (PBRER)' (EMA/CHMP/ICH/544553/1998). 2013. Available from: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use-guideline-e2c-r2-periodic-benefit-risk-evaluation-report-step-5_en.pdf.