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PHARMACEUTICAL REGULATIONS IN EUROPEAN UNION

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ABSTRACT

This article provides the pharmaceutical regulatory guidelines in the European Union. This document provides the European Regulatory Authorities, European Union legislative tools, clinical trials guidelines, marketing authorization, the regulatory strategy of filing applications, mutual recognition procedure in the European Union, regulating instruments for early access to drugs, patents, data exclusivity, and data protection are all aspects of EMA pharmacovigilance and risk management.

Keywords: EU-European Union, European Drug Agency, Clinical Trials, Pharmacovigilance

INTRODUCTION

A political-economic union, the EU contains 27 member states, and it was placed in Europe the European Union covers an area of 4,233,255.3 and an estimated population of approximately 447 million and it was the 3rd following China and India in terms of population. France is the largest surface area in Europe and Malta is the smallest **[1]**.

The conclusion of discussions between international businesses and member states governs the EU. The European Central Bank, the European Court of Auditors, the European Council, the European Court of Justice, and the European Parliament are the key institutions of the EU. Every five years, EU citizens elect a new parliament. This document provides evidence of European

drug regulatory agencies, clinical trials, and the European Medical Agency, pharmacovigilance, and risk management within the European Union **[1]**.

DRUG REGULATIONS HISTORY IN THE EUROPEAN UNION

Following the Thalidomide catastrophe, regulatory rules for medicines were established in the EU. This may be because of the tragedy that prompted the EU to establish the first drug requirement, 65/65/EEC. The moderate anesthetic's teratogenicity shocked the general public and public health experts and made it abundantly clear that no medication should be remarketed without prior approval **[2, 3]**.

In 2000, the EU introduced a new law that provides a number of incentives for the treatment of orphans and other medical conditions for the development of rare disorders. By providing incentives to sponsors, The Orphan Act intends to promote medicinal product development for uncommon diseases **[2, 3]**.

In 2004, the EU established a legislative and regulatory framework for a biosimilar or related biomedical products, making it the first region in the world to do so. 2007 saw the launch of the Advanced Medicinal Products Control (ATMP) program. The Organization for Medication Safety's new EU Pharmacovigilance Rules, which were released in 2010, offer the best methods for preventing, recognizing, and evaluating adverse drug responses as well as the patient's direct reporting of adverse events.. In order to streamline procedures and promote cross-border collaboration in clinical trials abroad, the new Clinical Testing Regulation (CTR) was put into effect throughout the European Union in 2014 **[2, 3]**.

DRUG REGULATORY AUTHORITIES IN EUROPE:

European Medical Agency (EMA)

The European Medical Association, a decentralized organization within the EU, is liable for the technical assessment, oversight, and prosperity observation of pharmaceuticals created by medicinal corporations for treatment inside the EU **[4]**.

European Medical Agency Organisation

The Deputy Executive Director, seven divisions, advisory positions, and the Executive Director serve as its leaders **[5]**.

European Medical Agency Variance [5]

A. Support for Human Drug R&D Division, Division of Human Drug Assessment.
B. The detachments of reviews, human medicine pharmacovigilance, and boards Veterinary Drug Partition.
C. Detachment of Company and Organizational Supervision.
D. Detachment of Info Administration.
E. Detachment of Shareholders and Statement.

Scientific Committees of the European Drug Agency [4]

Seven scientific committees make up the European Drug Agency (EMA), which uses them to conduct its assessments.

a) Group of Drug Products for Humanoid Use (CHMP).

b) Committee for Pharmacovigilance Risk Assessment (PRAC)

c) Committee of the Veterinary Medical Products (CVMP)

d) Committee for Orphan Pharmaceuticals (COMP)

European Medicinal Regulatory Authorities [4]

a) Committee on Herbal Medicines (HMPC);
b) Advanced Therapies Committee (CAT);
c) Child Welfare Committee (PDCO).

European Medical Agency Tasks [4]

European Medical Association is answerable for:

a) In accordance with a standardized procedure, applications for EU marketing authorizations for medications used in humans and animals are examined scientifically.

b) Transfer processes.

c) Checking the health of drug users.

d) Reviews.

e) Fleet Management System**.**

f) Inspiring novelty.

g) Technical instruction and other support.

h) Issuing rules.

Heads of Medical Organizations [6]

The directors of the National Competent Authorities (NCA) make up the Heads of Medicines Agencies (HMA) network. It is a distinct form of collaboration and workload distribution on both mandatory and optional regulatory tasks that the heads of drug organizations work with the European Drug Association and the European Commission to manage the European drugs supervisory web. These organizations are in charge of overseeing the guideline of drugs for human and veterinary consumption in the European Financial Region.

Main Activities [6]

The main activities of the Head of Medicines Agencies are:

1) Explains significant network strategic issues such as information sharing, developments in information technology, and the sharing of best practices.

2) Focuses on enhancing, integrating, and sustaining the pharmaceutical regulatory system in Europe.

3) Incorporates decentralized processes and mutual recognition (DCP).

European Directorate for the Quality of Drugs

This top organization for the protection of public health promotes, supports, and keeps an eye on the use of

safe drugs and quality requirements for their safe use. Its criteria are globally acknowledged as a norm in science**.** The European Pharmacopoeia has legal force among the EU Member States. The organization, a Council of Europe Directorate that was founded in 1994, is made up of four Departments and five Divisions **[7]**.

Sections of the Directorate for the Quality of Drugs in Europe [7]

The various sections are,

1. European Pharmacopoeia Department (EPD)
2. Department of Journals and Hypermedia
3. Department of Research laboratory (D Lab)
4. Department of Healthcare, Biological Standardization.

Sections of the Directorate for the Quality of Drugs in Europe's Divisions [7]

1. Division for Substance Certification (DCEP)
2. Division of Reference Standards and Samples (DRS)
3. Group for Documentation and Public Relations
4. Accounting and Finance Division
5. Division for Environment, Safety, and Quality

EU CLINICAL TRIALS [8]

Clinical trials are research projects that examine the effectiveness of novel medical treatments on human subjects. Each study may provide answers to scientific queries and seeks to identify more effective methods for disease prevention, detection, diagnosis, and treatment. The new treatment may be compared to the current treatments in clinical trials.

EU clinical trial guidelines [8]

Guidance materials for clinical trials are included in Volume 10 of Eudralex.

Application Forms and Applications [8]

1. Complete instructions on how to ask competent authorities to approve clinical trials for human use, as well as how to notify them of noteworthy changes and test findings.
2. Detailed instructions on the application format and supporting materials needed to get an Ethics Committee opinion for clinical research involving pharmaceuticals for human use.
3. The European Medical Experimental Database offers thorough advice (EudraCT).

Safety Reporting [8]

1. Detailed instructions on how to gather, verify and deliver reports of adverse events and reactions resulting from human medical trials.

2. Reference Guidelines for Development Security Update Reports ICH Guidance E2F.

The investigational drug's level of efficacy

Proper developed procedures aimed at creating experimental remedial items. Information about the specifications for chemical and pharmaceutical quality records pertaining to medical products tested in clinical trials **[8]**.

INSPECTIONS [8]

The aspectual guidance involved in European Union clinical trials is

a. Advice for getting ready for the GCP inspections.

b. Instructions for conducting GCP inspections.

c. For guidance on conducting GCP studies, see Appendix VII-Biological Analysis Part, Statistical Analysis of Pharmacology, and Bio Equilibrium Tests.

Legislation

The Assembly and the European Legislature signed 2001/20/EC Order Approving Laws, Regulations, and Administrative Rules on April 4, 2001.

The Commission's Directive 2005/28/EC of April 8, 2005, established principles and specific recommendations for good clinical practice in relation to investigational medical goods for human use as well as the criteria for obtaining a license to manufacture or import such products **[8]**.

Eudract (EU Clinical Trials Register)

A database called EUDRACT, which was created in accordance with the EUDRACT Database Order 2001/20/EC, contains all clinical trials that have been conducted in the European Community since May 2004 **[9]**.

A. Support for medical tests should access the EUDRACT application by going to the EUDRACT website.
B. Get EUDRACT quantity.
C. To identify an experimental study, send the clinical trial submission form to appropriate organizations and ethical review boards.

Arrangements for Mutual Recognition (MRA) [10]

Partner nations of the MRA and the EC have developed Mutual Authorization Agreements (MRAs):

1. By facilitating market access and protecting consumers from inferior products, lower trade barriers to trade.
2. Mutual recognition of documents issued by regulatory bodies, including reports, accreditations, and compliance scores.
3. Inform one another about the stages compliance assessment systems take to make sure the requirements are being followed.
4. Encouraging sectoral collaboration on GMPs for veterinary and human products, as well as global synchronous agreements on mutual recognition of compliance evaluation of regulated items.

Issuance of Certificate and Package of Eligible Person

Typically, a qualified person (QP) is an accredited chemist, pharmacist, or biologist. (Or another licensed educator) with years of experience working in the pharmaceutical industry. A qualified individual must certify each batch of completed medications. This documentation must clearly specify the matters for which this confirmation for other Q.P. is made **[11]**.

Drug Safety and Risk Management Agency

Pharmaceutical monitoring, or monitoring of a medical product's safety, is sternly governed by EU laws and regulations throughout its entire existence on the market. In accordance with EU law, member states are required to set up national pharmacological monitoring organizations to gather and assess data on the side effects or adverse effects of medical products and to take appropriate action where necessary. The MAHs report should be on the lookout for unfavorable responses to regulatory authorities under specified circumstances and within a given window of time. Applicants and MAHs must also submit **[12, 13]**.

A description of the pharmacological monitoring methods used by the firm for its numerous goods, as well as qualified officers with it. In order to control the pharmacy monitoring organization in the EU, the EC, EMA, and member nations work together. Regional centers are managed by a national competent authority in some member countries, per the EMA Pharmacovigilance System EMA Pharmacological Surveillance System Guide **[14]**.

Regulation (EC) No. 726/2004, Order 2001/83/EC, and C all summarize the legislative criteria for the EMA Pharmacological Monitoring Scheme for Human Drugs **[12, 14]**.

BEST PRACTICES IN PHARMACOVIGILANCE

In EU member states, marketing accreditors (MAHs), agencies, and drug regulatory bodies are subject to Good Pharmacological Monitoring Practices (GVP). Includes medicines that have been nationally and clinically approved by the firm **[15]**.

Eudravigilance: EMA created Eudra Vigilance in 2001 to keep track of the marketing authorization of medicinal products in the EEA. Eudra Vigilance is a security information handling web and management organization. Its goal is to detect and evaluate suspicious reactions while a project is being developed **[15]**.

Eudra Vigilance network (EVWEB): The Eudra Vigilance system offers a web-based application that enables the creation of protection and response messages and the

development of medical product intelligence via a border termed EVWEB, in addition to automatic note production and handling **[15]**.

Risk Management Plan (RMP)

A risk management plan, or RMP, is an article that describes the security profile of a medication, describes how possibilities should be avoided as well as reduced in patients, strategies aimed at education, and supplementary actions intended toward learning more about safety and efficiency of drugs, risk features aimed at increasing side effects and evaluates the success of risk-reduction methods.

209 Companies in the EU are required to acquiesce an RMP to the Organization when requesting a marketing license. Any application that entails a major change in marketing recognition for medications without RMP will be required **[16]**.

PATENT, DATA PRIVACY, AND DATA PROTECTION IN EUROPE:

Patents: Drug patents are not the responsibility of the EMA or nationally competent authorities; those matters fall outside the purview of the agency **[17]**. Member nations that participated in the 2000 European Patent Conference. The European Patent Office only issue patents for patented inventions, which are those that are original, amenable to further development, and have industrial applications (EPO). If governmental patent agencies or the EPO receive patent claims, the patent will be granted to the owner in each contracting state beginning on the day that the notice of its grant is published and will confer the same rights as the national patent awarded in that state. The filing date marks the start of the 20-year protection period **[18]**.

Data Privacy: If the MAH receives recognition for one or more new treatment symptoms before they have undergone a thorough scientific evaluation and are believed to be able to resolve the problem and provide a clinical benefit, the effective 10-year market exclusivity period may be extended for a maximum of one year, during the first eight years of those ten. The new EU Drug Act, introduced in 2004, also included an additional two-year market exclusivity condition and provided a comparable eight-year EU data exclusion requirement **[19]**.

Additional Protection Certificates (APC): The Supplementary protection certificates are an extension of a patent right and constitute an Intellectual Property Right (IPR). They apply to specific pharmaceutical products that have regulatory body authorization. A patent can only be extended up to a maximum of five years by an SPC. The purpose of auxiliary safety certifications is to prevent the extensive testing and clinical research that

must be done on these goods before they can gain regulatory marketing clearance from infringing on the patent for a drug. Regulation (EC) No. 1901/2006 permits a further six-month extension if the SPC relates to a pediatric pharmaceutical product and data is provided in accordance with the PIP. To approve pediatric drugs, 210 supportive PIPs are necessary. They make sure that enough information is gathered about how the drug affects kids **[20]**.

CONCLUSION:

The European Pharmaceuticals Association (EMA) provides highly effective scientific methods for monitoring and evaluating medications for the EU's benefit of both human and animal health. Health and health systems are both impacted by EU health policy. Although it contains unusual and bad-form features, procedures, and priorities, most policy sectors in any democratic system have these characteristics. This document provides an explanation of the European Medical Agency and its different pharmaceutical laws **[21]**.

REFERENCES:

[1] About the European Union < Principles, countries, history (europa.eu)>

[2] Ra¨go L, Santoso B. Drug regulation: history, present, and future. In: van Boxtel CJ, Santoso B, Edwards IR, editors. Drug Benefits and Risks: International Textbook of Clinical Pharmacology. 2nd ed. Amsterdam and Uppsala: IOS Press and Uppsala Monitoring Centre; 2008. p. 65-76

[3] European Union. 50 years of landmarks in EU therapeutic guideline;2014 Medicinal products for human use - European Commission (europa.eu)

[4] Medicines Agency of Europe. about us,2016 < About us - EN (europa.eu)>

[5] Organigram for the European Medicines Agency; 2017 < EMA Organisational Chart (europa.eu)

[6] Heads of pharmaceutical organizations about HMA;2016 < Heads of Medicines Agencies: About HMA >

[7] European Directorate for the Quality of Medicines and Healthcare - European Directorate for the Quality of Medicines & HealthCare (edqm.eu)

[8] Commission Europe. Volume 10 of EudraLex: Clinical Trials Regulations; 2017 EudraLex - Volume 10 (europa.eu)>

[9] Union of Europe. Clinical Trials in the EU Register;2016 EU Clinical Trials Register - Update

[10] Mutual Recognition Agreements between the European Remedies Organization;2016 European Medicines Agency | (europa.eu)

[11] Europe's planning. EU Guidelines for GMP for Pharmaceuticals for Human and Veterinary Use, Volume 4 of Eudralex, Annex 16: Batch Release and

Certification by a Qualified Person Final version sent to EC (europa.eu)

[12] Drug Enforcement Agency of Europe. user's manual for minor and medium-sized businesses (EMA/860940/2011); July 2016 User guide for micro, small and medium-sized enterprises (europa.eu)

[13] Agency for European Medicines. Pharmacovigilance; 2015 Pharmacovigilance (europa.eu)

[14] Agency for European Drugs. version 1.2 of the EMA pharmacovigilance system manual (EMA/623550/2013);October 13, 2016 Microsoft Word - EMA pharmacovigilance system manual _12 (europa.eu)

[15] EudraVigilance from the EMA; 2016 EudraVigilance | European Medicines Agency (europa.eu)

[16] Guidelines for appropriate pharmacovigilance procedures (GVP) and Module V-Risk management systems, both from the European Drug Agency; April 15, 2014 Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) (europa.eu)

[17] Agency for European Medicines. often posed issues;2016 Frequently asked questions | European Medicines Agency (europa.eu)

[18] European Patent Office; 2016 EPO - FAQ - Patent & IP basics

[19] According to the European Medicines Agency's guidance (EMEA/CHMP/225411/2006), individuals using the centralized process for generic/hybrid applications should follow the right protocol; August 4, 2016, Microsoft Word - Pre-Submission Guidance generics - track changes - Jan 2021 (europa.eu)

[20] Certificates of additional protection for medicinal and plant protection goods from the European Commission, January 18, 2017, Supplementary protection certificates for pharmaceutical and plant protection products (europa.eu)

[21] Conclusion - Everything you always wanted to know about European Union health policies but were afraid to ask - NCBI Bookshelf (nih.gov)