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Original Article

An Overview on Development, Approval and Post Registration Activities for Pharmaceuticals in European Union

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ABSTRACT

Bringing a new medicine from concept to market is costly and complex. Years of study and development go into it. Product development operations should be carried out in line with applicable regulatory standards to save time and money when bringing innovations to the marketplace. While the information on regulatory requirements is readily accessible, navigating the regulatory system is complex and becomes considerably more difficult when working with many countries. The primary goal is to improve regulatory awareness and achieve regulatory compliance in product development. An excellent place to start is with one of these ideas. The guide is not a list of laws but a discussion of the foundational ideas and principles governing regulatory policymaking and enforcement in the European Union. Throughout the drug's lifespan, these rules are consistent. Companies may standardise their processes and keep track of every action at every step of the lifecycle by developing a workflow and adhering to its stages of lifecycle compliance for each set of guidelines. Because of the current pharmaceutical market's complexity, more efficient drug research and manufacturing are required. This review article is based on the information collected from various sources from EMA and ICH websites and the articles mentioned. Despite the extreme complexity, Product Lifecycle Management has the potential to make pharmaceutical manufacturing more efficient and less risky. Pharmaceutical product lifecycle management during various phases such as research and development, regulatory submission and approval, commercialisation and marketing plays a significant role.

Keywords: Product Lifecycle Management, Navigation Pathway, New Product Development, Post Approval Changes, Regulatory Review, European Union.

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INTRODUCTION

The pharmaceutical industry is currently one of the most strictly regulated industries, with regulators requiring significant data before releasing a medical product. In each country, there is a separate regulatory agency. Europe's regulated market highly values product lifecycle in this context.[1]

The development of an innovative medicine from the development phase to the commercialisation phase is a costly and time-consuming process that requires extensive resources. It is the culmination of years of research and development. Product development operations should be carried out in line with applicable regulatory standards to save time and resources when bringing innovations to the marketplace. These factors help marketplace. These factors help produce a high-quality, safe, and effective product that meets regulatory requirements.

Information on regulatory needs is publicly available, but navigating the regulatory system is complex, primarily when operating with multiple countries. Pharmaceutical products are regulated by national regulatory agencies in terms of drug development, licensing, registration, manufacturing, marketing, and labelling. Regulators encourage a wide range of efforts to assure pharmaceuticals' safety, efficacy, and quality.[2]

The concept of Life Cycle Management can be termed as a more predictable and efficient manner of governing the post-approval CMC changes throughout the product lifecycle. It would thereby promote an uninterrupted improvement and innovation, which in turn would sustain the quality and reliability in the supply of the product and proactive planning of supply chain adjustments. Henceforth, these changes will enable the regulators (inspectors and assessors) to understand better and uphold

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faith and assurance for the management of post-approval CMC changes in a company's Pharmaceutical Quality System (PQS). A harmonised approach to regulatory and technical considerations for Life Cycle Management is currently lacking. Wide gaps in knowledge hinder the full realisation of intended benefits, due to which "Operational Flexibility" for post-approval changes has not been achieved.[3]

Implementing Life Cycle Management from an industrial perspective will promote a quality improvement paradigm.

DISCUSSION

Product Development

Determining the regulatory path for a healthcare product begins with correctly classifying it as a medication, biologic, medical device, or combination product. The next stage is to figure out the healthcare product's claim is, to conduct the proper research to back up the claim and the label. Regulators may have different oversight requirements if the claim changes; the medical device categorisation is one example. To design a regulatory strategy after the therapeutic claim has been established, it is necessary to identify specific regulatory requirements and the possible pathways to take. The implementation of the regulatory strategy will be guided by in-depth knowledge of these requirements. A medical product development plan is the next step, translating product requirements into actions. Milestones, critical paths and periodic decision reviews should be included and updated regularly.[4]

The complete process for developing a drug product is described in Figure 1.

The strategy for product development must be implemented. Production, quality control, regulatory, clinical and non-clinical operations, and collaboration with external parties necessitate relevant expertise. The next step is to implement the clinical plan. As a pre-requisite to the submission of a licensing application, the clinical investigation should follow Good Clinical Practice (GCP) and comply with other requirements, including approval from the ethics committee and regulatory approvals. A pre-submission meeting with a regulatory agency helps address specific issues before submitting a clinical trial application. Compile the data in preparation for regulatory filing. These reports and data must be compiled for inclusion in the product approval once they are available from the product design and production, quality control, and non-clinical and clinical studies. Regulatory submission should be compiled per applicable regulatory rules for specific submission type and ensure that the submission is thorough and complete. Prepare to respond to inquiries from the authority during the review process. Before filing the licensing application, pre-submission meetings with the regulatory board are generally recommended for novel healthcare products. The final stage ensures the product is safe to use and all post-marketing requirements are met.[5]

Life Cycle Management of Pharmaceutical Product

Product Lifecycle Management (PLM) is the systematic approach to manage the lifecycle of a pharmaceutical product from idea conception through development, production commercialisation and disposal. PLM is the systematic coordination of operations such as planning, execution and effective data management and its application, cross-functional and cross-organisational control, and timely improvement across the product's lifecycle.

Because of the current pharmaceutical market's complexity, more efficient drug research and manufacturing are required. Despite the extreme complexity, PLM can potentially make pharmaceutical manufacturing more efficient and less risky. Product innovations, lower research costs and speedier market entry are all possible benefits of PLM for pharmaceutical companies. Other advantages include the ability to extend the useful life of pharmaceuticals, improved regulatory compliance and more effective data management. It also increases patent life and pricing strategy, better patient compliance, revenue growth, and improved clinical benefits are among the benefits of product lifecycle management.[6]

Clinical trials and findings have traditionally been the focus of drug development efforts. However, the industry is now looking at more holistic techniques to optimise the processes of bringing new products to market, which can speed up product development while decreasing operational costs. One holistic approach is PLM to manage products and related information in the pharmaceutical industry.[7]

This lifecycle usually involves the following stages:

1. Discovery and research.

2. Development.

3. Regulatory review and approval.

4. Commercialisation and marketing.

Discovery and research

In general, pharmaceutical development can be categorized as either "novel" or "generic," with "improvement of current pharmaceutical products" serving as a middle ground (either changes in formulation or administration methods). From product identification to commercialisation, developing a new medicinal product (i.e., a novel medicine or biologic) is a lengthy, challenging, and costly process that generally takes 10 to 12 years (sometimes longer). These development operations are resource-intensive due to lengthy timetables, strict regulatory supervision, and substantial investment requirements.[8]

New Product Development (NPD) is a complex and time-consuming process, which entails more dangers than initially seems. Throughout the life cycle of a product, a business must maximise the novelty and productivity of new product development while minimising development expenses and preserving profitability and sustainability. To sustain the proficient and monetary life expectancy of new pharmaceuticals at its pinnacle, the pharmaceutical companies are implementing PLM to effectively manage the entire product portfolio of an enterprise, from concept to development to commercialisation to market withdrawal.

Development

New drug product development

Non-clinical testing is often the first step in developing a novel therapeutic product, followed by phases of human clinical trials to support licence application. In order to aid these investigations, CMC operations (Chemistry, Manufacturing, and Controls) are being carried out in parallel. Through the Innovation Taskforce, innovative treatment developers can address their drug's scientific, legal, and regulatory implications with the EMA at an early stage of development.[9]

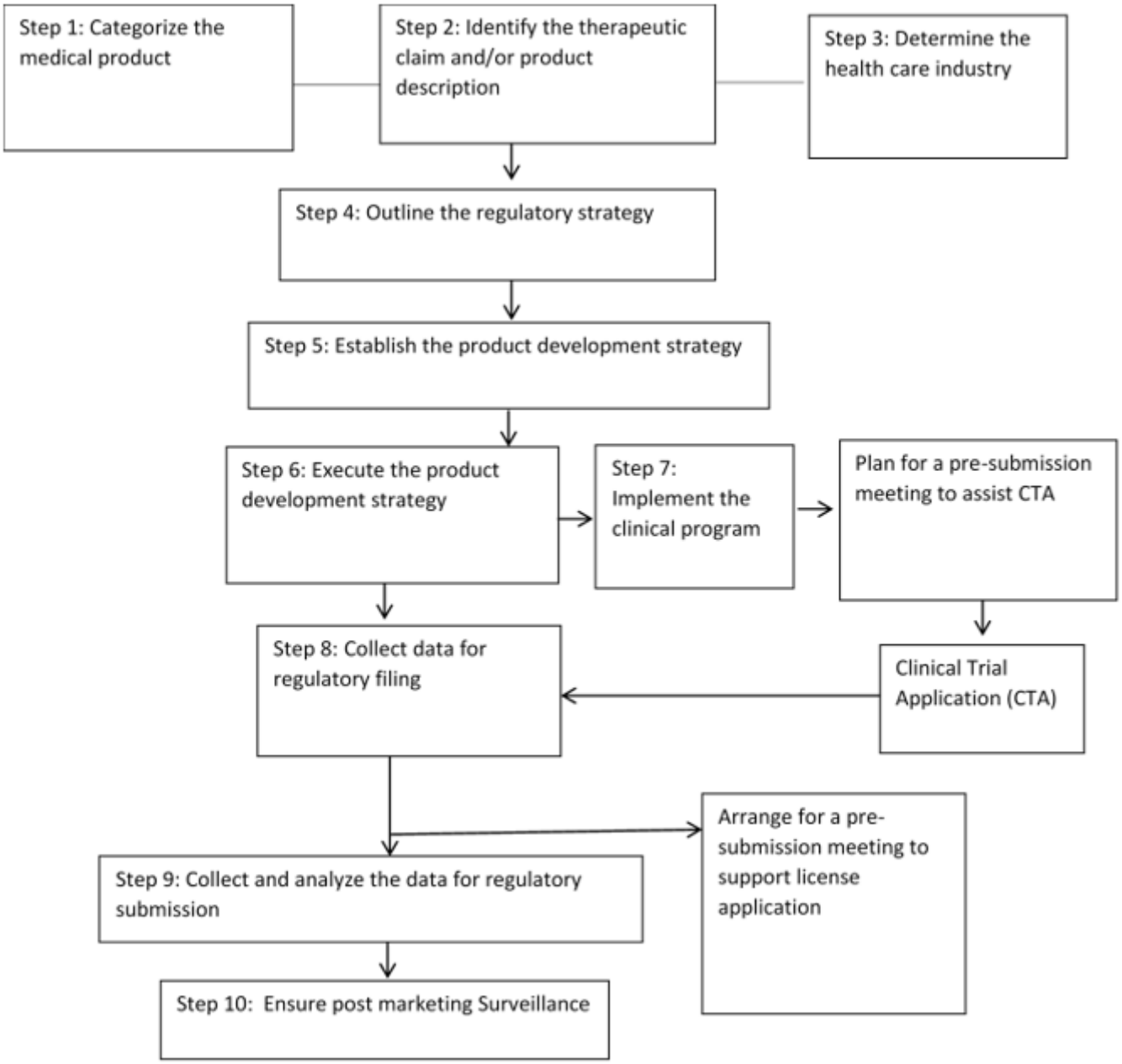

Figure 1: Key steps for pharmaceutical product development.

Preclinical Studies

Before moving into human studies, conducting non-clinical studies such as experimental research and animal testing is necessary to assess a pharmaceutical product's therapeutic properties and demonstrate its reasonable safety. Additional long-term studies such as reproductive and carcinogenicity studies may also be conducted after the clinical trial has begun. Good Laboratory Practices (GLP) must be followed in non-clinical studies. This testing phase includes significant *in vitro* and *in vivo* studies that generate preliminary efficacy, Pharmacodynamics and Pharmacokinetics (PD and PK), safety, and toxicity data. Guidance documents from regulatory authorities and the International Conference on Harmonization [ICH] are reviewed before experimental studies are conducted.[10]

Clinical trials

Clinical trials are human investigations conducted under scientific control to demonstrate or verify the safety and efficacy of Investigational Medicinal Products (IMPs). Regulation (EU) No 536/2014 governs clinical trials in the European Union (EU) and the European Economic Area (EEA), which came into effect on 31 January 2022. Clinical trials are regulated to protect clinical trial participants' rights and safety and for the accuracy and usefulness of clinical trials' results. The European Medications Agency (EMA) bases its opinions on the approval of medicines on the outcomes of clinical trials conducted by pharmaceutical companies and regulatory submission is given in Figure 2.[11]

The EMA is critical in creating and maintaining IT platforms for clinical trial coordination throughout the EU. A typical clinical trial consists of four phases and must adhere to regional requirements and GCP. Phases I through III studies are done to obtain information on safety and effectiveness to support licence application. Phase IV is performed after commercialisation when the medicinal product reaches the market. The Submission pathway for clinical trial is presented in Figure 3.[12]

Phase I – Human pharmacology studies

First-in-human trials are a crucial stage in developing new medications. A drug evaluated *in vitro*, on animals, or in other preclinical research is administered to humans for the first time. These trials often involve healthy volunteers or patients if cytotoxic medications are used.[13]

Typically, this research has non-therapeutic purposes. The study design may include randomisation and blinding techniques to ensure the validity of the observations.[14]

Phase 1 clinical trials may include the following studies:

An evaluation of the drug's initial safety and tolerance, encompassing both single-dose and multiple-dose delivery.

- Determination of dosage and potency.
- Studies on pharmaco- and toxicokinetics.
- Studies on pharmacodynamics.
- Early measurements of product activity.

Phase II – Therapeutic exploratory studies

Phase II investigates the medication efficacy in trial patients, utilising designs that include continuous controls and baseline status comparisons. Typically, the trial population is selected using stringent criteria. An important goal is to assess the dose(s) and regimen appropriate for the Phase III trial. In addition, exploratory analyses, assessing data subsets, and utilizing multiple endpoints in clinical trials can be used to evaluate possible study endpoints, therapy regimens, and target groups (e.g., moderate versus severe disease).[15]

Phase III – Therapeutic confirmatory studies

The primary objective of phase 3 trials is to establish and corroborate the preliminary evidence gained from prior trials that the medicine is a safe, effective, and helpful therapy for the specified indications. These are crucial studies designed to give a sufficient foundation for marketing authorisation.[16] The purpose of Phase III studies is to evaluate the effectiveness of the novel treatment to that of the standard treatment. These are the most extensive and rigorous sort of scientific clinical evaluations of novel medicine.[17]

Phase IV – Therapeutic use or post-marketing surveillance studies

Phase IV studies are conducted after a drug or medication has been commercialised to collect data on the drug's effect on various demographics and any long-term adverse effects. Typically, post-registration or post-licensure trials provide further information about a pharmaceutical's long-term effectiveness or safety profiles.[18] Phase IV commences following product approval. It may involve post-approval research designed to address concerns raised during the regulatory assessment process. In addition to investigating drug-drug interactions, dose-response, and safety, further studies are commonly conducted (e.g., mortality/morbidity analyses, epidemiological studies) to support use under the agreed objectives. [19]

CMC – Chemistry, Manufacturing and Controls

To properly manufacture medicinal products or biologics, specific manufacturing procedures, product attributes, and quality control must be determined to ensure the product's safety, efficacy, and batch-to-batch consistency. These tasks are called CMC, or chemistry, manufacture, and control. CMC is involved in all phases of the pharmaceutical development process following drug discovery.[20]

Extensive CMC operations are required to determine the quality of the medicinal component. Initial substance characterisation

PRODUCT	Drugs	Drugs
COUNTRY	EU	EU
TYPE OF APPLICATION	Clinical Trials	MAA
LIFECYCLE PHASE	R&D	MAA
REGULATORY DEPARTMENT	Science Medicine Health	Science Medicine Health
REGULATORY AGENCY	European Medicines Agency	European Medicines Agency
DIVISION	Committee for Medicinal Products for Human Use (CHMP)	Committee for Medicinal Products for Human Use (CHMP)
REGULATORY CLASSIFICATION	Chemicals	Chemicals

Figure 2: Regulatory submission for drug products in EU.

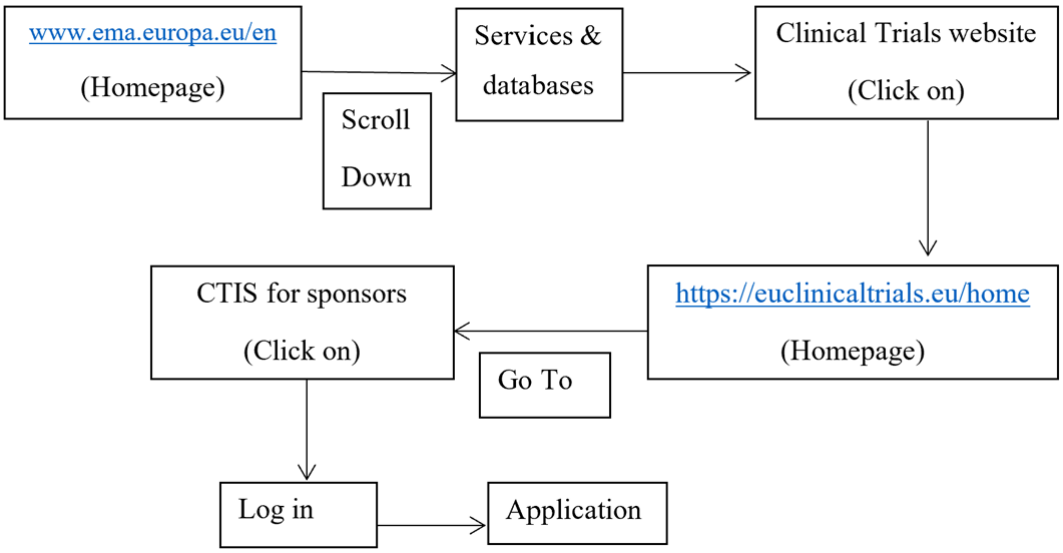

Figure 3: Submission pathway for clinical trial.

permits a comprehensive understanding of the material's structure, stereochemistry, contaminants, and chemical and physical properties.

It is necessary to collect data to establish the product's stability. All activities must conform to Good Manufacturing Practices (GMP) and must be meticulously created and organised to support considerable research's non-clinical and clinical phases.[21]

Regulatory review and approval

Before a novel medication or biologic may be introduced to the market, a dossier must be produced and submitted to the relevant regulatory agencies for assessment and, eventually, regulatory approval. Drug approval is standardised throughout the EU. Except for a few national characteristics, the European Union's Directives and Regulations are the foundation for the approval process.

Effective drug regulation necessitates the accountability of regulatory bodies in order to ensure pharmaceutical safety, effectiveness, and quality, as well as the accuracy and appropriateness of publicly available medication information. For obtaining the medication-related information, one must know where the regulated information, i.e., Act/Regulations/Guidance, is parked on the regulatory websites.[22]

One must know the correct information parked at specified regulatory sites to access the correct information. This can be accomplished with a "navigation pathway" to obtain regulatory approval from a specific agency. We need to apply for a specific product. They are submitted to their respective authorities to advertise their products and guarantee that they are safe and effective to persons worldwide. So, we need a distinct navigation method for particular applications or pharmaceutical products. Implementing a solid Regulatory Information Management (RIM) solution offers an elementary answer to various complex challenges. Regulatory agencies are becoming more safety

concerned and requesting more data, which leads to growth in the need for navigation pathways. Globally, the fundamental objectives of regulatory bodies and organisations are to protect pharmaceuticals' safety, quality, and efficacy, harmonise legal procedures associated with drug discovery, and monitor and evaluate compliance with applicable requirements.[23]

Pre-submission meeting

Although optional, a pre-submission meeting is valid, especially for novel products, to resolve issues before submission and ensure compliance with all applicable legal and regulatory requirements. This meeting also gives the agency information regarding the product, allowing them to allocate their resources accordingly.[24]

Appointment of rapporteurs

The scientific assessment is conducted by experts appointed by the Pharmaceutical Risk Assessment Committee (PRAC) and the Committee for Medicines for Human Use (CHMP). During the pre-authorization phase of a Marketing Authorization Application (MAA), two rapporteurs are appointed (a rapporteur and a co-rapporteur).

Common Technical Document Compilation (CTD)

The CTD was created to standardise the technical documentation involved in a human pharmaceutical product registration application throughout Europe, the United States, and Japan. Its primary goal is to prepare and verify the entire Module1-5 CTD dossier for submission in Europe, which is valid for all marketing authorisation applications.[25]

CTD has the following five distinct components or modules:

Regional Requirements of the EU or Module 1 of the EU CTD:

The administrative data required by the EU are contained in this module. The CTD for EU Module 1 CTD has the following sections mentioned in Figure 4.

Module 2 is a comprehensive quality overview summarising Modules 3, 4, and 5. This section includes a brief description of

1.0 1.1	Cover Letter Comprehensive table of content
1.2 1.3	Application Form Product Information
1.3.1	Summary of Product Characteristics, Labelling and Package Leaflet
1.3.2 1.3.3	Mock-up Specimen
1.3.4 1.3.5	Consultation with Target Patient Groups Product Information already approved in the Member States
1.3.6	Braille
1.4 1.4.1	Information about the Experts Quality
1.4.2 1.4.3	Non-clinical Clinical
1.5	Specific Requirements for different types of applications
1.5.1 1.5.2	Information for bibliographical applications Information for Generic, "Hybrid" or Bio-similar Applications
1.5.3 1.5.4	(Extended) Data/Market Exclusivity Exceptional Circumstances
1.5.5	Conditional Marketing Authorisation
1.6 1.6.1	Environmental risk assessment Non-GMO
1.6.2 1.7	GMO Information relating to Orphan Market Exclusivity
1.7.1	Similarity
1.7.2 1.8	Market Exclusivity Information relating to Pharmacovigilance
1.8.1 1.8.2	Pharmacovigilance System Risk-management System
1.9	Information relating to Clinical Trials Responses to Questions

Figure 4: Module 1 CTD sections.

the product. Module 2 consists of an introduction, overall quality summary, non-clinical overview, clinical overview, and clinical summary.

Module 3 contains the product's chemical, production, and quality control reports. Module 3 should be prepared according to ICH M4Q guidelines. Drug Substance (DS) and Drug Product (DP) are the two critical components of Module 3.

Module 4 investigates the drug and its formulation in a non-clinical setting. It includes animal research on pharmacokinetics and pharmacodynamics as well as toxicology. Module 4's structure and content are outlined in the ICH M4S recommendations.[26]

Clinical studies of the drug and its formulation are the focus of Module 5. Safety and effectiveness have been studied in humans, as well as pharmacokinetics and pharmacodynamics. The ICH M4E standards outline the organisation and contents of Module 5.

Marketing authorization submission

The sponsor of a pharmaceutical product must select one of four potential approaches to market authorisation for a new drug: the National Authorization Procedure; Decentralized; Mutual Recognition; and Centralised procedure. The submission pathway may be chosen depending on the medication category, how many nations plan to market it, and the expected timeframe for approval. Medical products can be sold in the European Union only when they have been approved for marketing by the competent authority of a Member State (national authorisation) or by the European Union's No. 2309/93 regulation. The list of guidance documents are listed in Table 1.[27]

Centralised procedure

Single marketing authorisation allows sponsors to advertise and distribute medicines throughout Europe under a "Centralised procedure" and is given by the European Commission following the evaluation of the submission by EMA. Upon submission of a legitimate application, the examination may take up to 210 days, after which the Committee for Medicinal Products for Human Use (CHMP) must offer a scientific opinion regarding whether or not the drug may be authorised. An identical marketing authorisation application is concurrently filed to the relevant authorities of the Reference Member State and the Concerned Member States. The CHMP evaluates centrally authorised goods with assistance from the Pharmacovigilance Risk Assessment Committee (PRAC) and the Committee for Advanced Therapies (CAT) for advanced-therapy drugs.[28]

One Member State is designated as the Rapporteur (reviewer) for a specific application and leads the CHMP evaluation process. After the procedure, the Reference Member State's recommended final assessment report, Supplementary Protection Certificate (SPC), labelling, and package leaflet are authorised. A manufacturer may only get one marketing authorisation per medical product under the centralised system.[29]

Biologic pharmaceuticals derived from recombinant technology, Orphan medicinal supplies or treatments for rare illnesses, and Medicinal products containing novel active ingredients for indications such as cancer, neurological disorders, diabetes, and autoimmune conditions are eligible for centralised review.[30]

DCP-Decentralized procedure

Sponsors can concurrently apply for market authorisation in multiple EU states for products that have not previously been approved in any EU state and do not fall within the mandated centralised process. A written assessment report, a summary of the product's features, a labeling and packaging leaflet may be requested from one or more member states in 210 days. Applicants seeking a decentralized approach ask one state to serve as the reference state, which reviews the application and conducts an assessment. The other member nations may provide feedback on the report of the evaluation. After acknowledging their agreement with the Assessment Report and other documents, the relevant authorities of the Reference Member State (RMS) and Concerned Member States (CMS) decide within 30 days. After completion of

Table 1: List of guidance documents.

Sl. No.	Guidance Description	Directive	Link
1.	The requirements set forth in Annex 1 must be followed for all clinical trials submitted as part of an application for marketing authorization for human medicine in the European Economic Area.	Directive 2001/83/EC	https://eurlex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32001L0083&from=en
2.	Clinical trials regulations and clinical trial information system.	Regulation No. 536/2014	https://eurlex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:32014R0536&from=EN
3.	A clinical trial conducted outside the European Economic Area must adhere to ethical principles equivalent to those established in the European Economic Area.	International Good Clinical Practice	http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html
		The Declaration of Helsinki	https://www.wma.net/wp-content/uploads/2018/07/DoH-Oct2008.pdf

the national phase, a marketing authorisation will be awarded to each participating member state after the procedure.[31]

MRP-Mutual Recognition Procedure

In this approach, EU nations may accept the decision taken by another EU country regarding a pharmaceutical product. The pharmaceutical manufacturer sends its application to the nation selected for the evaluation, which accepts or rejects the application. Within ninety days, the other nations must determine whether they accept or reject the choice made by the initial nation.

The two committees which contribute to the working of the mutual recognition procedure are:

1. For human medicinal products, the CMD (h)-Coordination group for mutual recognition and decentralised procedures (human);

2. For veterinary medicinal products, the CMD (v)-Coordination group for mutual recognition and decentralised procedures (veterinary).

During the 60-day pre-referral procedure, if the member states are unable to reach a settlement, a request for intervention may be filed through the CHMP's secretariat at the EMA.

Independent National procedure

The registration process is country-specific and is dependent on the requirements of that country. In contrast to the MRP and DCP, there are no specified or conventional timelines for the duration of the national procedure. To receive marketing authorisation in a nation, the application must be filed in the native language of the country's Competent Authority. This process has a duration of 210 Days. (Free of stop clock inquiries).[32]

MA grant/Approval

Pharmaceutical companies evaluate applications filed by EMA's CHMP, which then makes recommendations on whether or not a product should be given marketing authorisation. The protection of public health is the fundamental goal of regulations controlling pharmaceuticals. Innovations in the pharmaceutical industry must not be hindered in pursuing this goal. For this reason, Europe's pharmaceutical laws have constantly sought to protect public health while allowing for the free circulation of medicines. Information on regulatory needs is publicly available, but navigating the regulatory system is complex, primarily when operating with multiple countries. Understanding laws, guidance documents and international standards are essential to improve regulatory awareness and achieve regulatory compliance in product development.

COMMERCIALIZATION AND MARKETING

There is a need for cardinal focus in the post-marketing phase to fill the gaps in the implementation. The primary attention has always been centralised on the development and launch phases of the product lifecycle. For example, inevitable confusion exists due to a lack of alignment of the necessary detail and information in the dossier and its impact on regulatory reporting and change management. Perpetual improvement and innovation in biotechnology and pharmaceuticals sectors can be retarded by the shortcoming of harmonised approaches for both regulatory and technical aspects of Life Cycle Management. The Submission

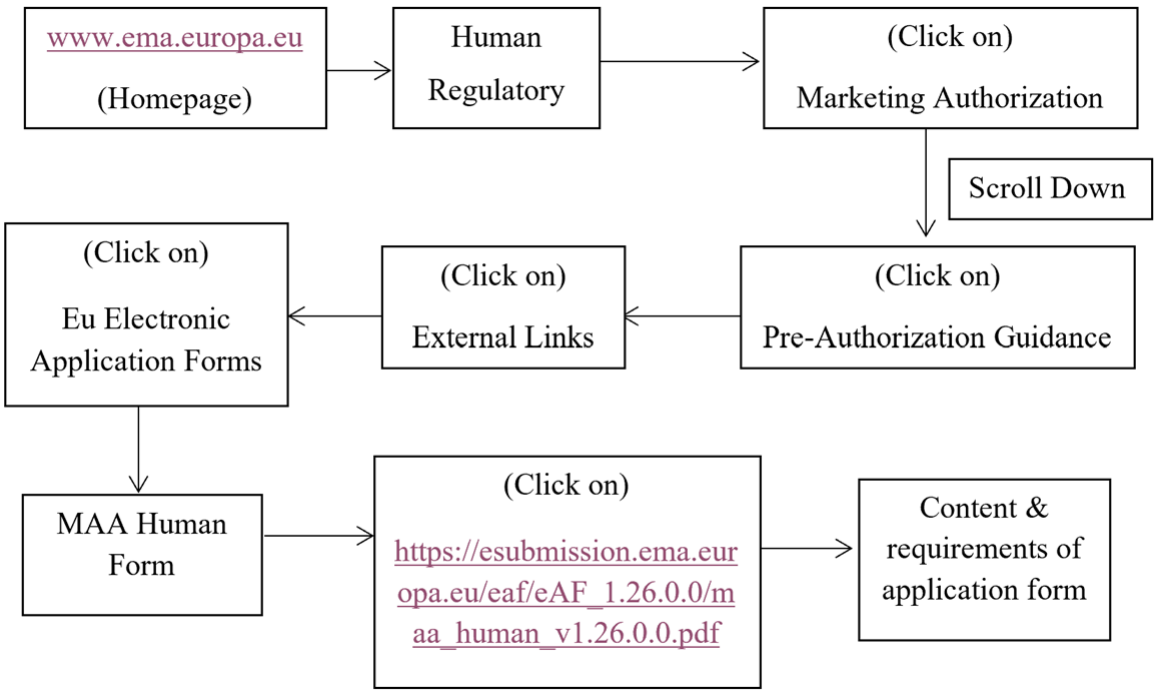

Figure 5: Submission pathway for EMA for authorisation of a medicine.

Figure 6: Types of variations.

pathway for EMA for authorisation of a medicine is represented in Figure 5.

As per the regulatory aspect, it is the applicant's responsibility to apply for seeking approval for a change. The terminology and classification of changes differ from country to country.

Variations

In the European Union, a variation specific to marketing authorisation is an alteration to the dossier's contents. Before circulating a drug product finished with a change to the approved application, the possessor of an approved application must evaluate the effects of the change. Information decided by EMA to be suitable for each change should be included in the variation application. Evaluation of post-approval changes is generally carried out for administrative changes, manufacturing quality improvements, better bioavailability, improved tolerability and simplified dosing.[33]

Changes that can occur after approval of application include improvements to the equipment and manufacturing process, transfer to a new manufacturing/other sites, batch size scale up, source changes, formulation development changes, packaging changes, Pharmacopeial updates, administrative changes, changes to new sites, changes to specifications, analytical method changes, etc. Post approval changes must be filed to meet the regulatory requirements: For example, updated regulations and guidance, updates to the pharmacopoeia, and safety-related warnings, The various types of variations are represented in Figure 6.[34]

Types of variations

Type IA Variations

These are modest alterations that have low or no influence on the pharmaceutical product's quality, safety, or efficacy and do not require clearance prior to the initiation ("Do and Tell" procedure).[35]

Minor variations are classified into:

Type IA Variation that requires immediate notification (IA IN).

Type IA Variation" that does not requires immediate notification (IA) (within one year following imposition).

After implementation, a minor Type IA variation must be reported immediately to ensure that the drug is under ongoing observation. This should be filed quickly and often within two weeks after the change's implementation.

Type IB Variations

Before implementation, the Market Authorization Holder (MAH) must advise the EMA of these modifications. However, to ensure that the agency accepts the notice, the MAH must wait 30 days before implementing the modification (Tell, Wait and Do procedure). Type IB alterations have a little to moderate impact on product quality (Tell, Wait and Do procedure).

Type II Variations

These variations are not "extensions" but significantly impact a pharmaceutical product's Efficacy, Safety, or Quality. Type II Variations have a significant impact on the quality, safety, and effectiveness of the product.

Extension (New Application)

A new dossier should be presented when changes are crucial that they change the conditions of the currently approved dossier and cannot be treated as changes.

Such applications will be evaluated the same way the preliminary marketing authorisation will be granted. If the extension is included in the preliminary marketing authorization, it can be granted as a new marketing authorization.[36]

CONCLUSION

Establish a Navigation Pathway for accessing critical regulatory information for Life-Cycle Management of the selected product, i.e., Drugs. A detailed Factsheet and comparison table have been prepared to access the critical regulatory information for the products above from the various authority websites. The current study provides detailed regulatory information management of the act/regulations and guidelines for the EU Market.

In the pharmaceutical industry, a drug product's post-approval maintenance is challenging. The most important aspect of

the maintenance phase is performing the CMC change. Every regulatory authority has its guidelines and requirements for making post-approval changes. Therefore, it is necessary to refer to specific guidelines of each country and comply with those guidelines to obtain quick approval of the change. In this present study, an attempt was made to study Post Approval Changes regulations of the European Union. The study mainly covers the changes related to the manufacturing site, manufacturing process, and formulation. Specification, stability and container closure system and labelling.

Insight into these will enable the sponsor to develop the CMC strategy to implement change successfully in European Union and Canada-regulated markets. This will eliminate excess time and workforce required to plan, strategize, and file the Post Approval Changes. It will enable industries to develop necessary information and the level of detail required in the dossier for regulatory reporting.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

PQS: Pharmaceutical Quality System; **GCP:** Good clinical practice; **PLM:** Product lifecycle management; **NPD:** New product development; **CMC:** Chemistry, Manufacturing, and Controls; **GLP:** Good Laboratory Practices; **PD:** Pharmacodynamics; **PK:** Pharmacokinetics; **ICH:** International Conference on Harmonization; **EU:** European Union; **EEA:** European Economic Area; **EMA:** European Medications Agency; **GMP:** Good Manufacturing Practices; **RIM:** Regulatory Information Management; **PRAC:** Pharmaceutical Risk Assessment Committee; **CHMP:** Committee for Medicines for Human Use; **MAA:** Marketing Authorization Application; **CTD:** Common technical document compilation; **DS:** Drug Substance; **DP:** Drug Product; **CAT:** Committee for Advanced Therapies; **SPC:** Supplementary Protection Certificate; **MRP:** Mutual Recognition Procedure; **DCP:** Decentralized procedure.

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