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COMPARISON AND COMPILATION OF THE VACCINATION APPROVALPROCEDURE IN THE USA AND THE EU: A ROAD MAP FOR THE COVID 19 EMRGING AND DEVELOPING NATIONS

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ABSTRACT

The use of vaccines has considerably improved worldwide public health by preventing and controlling infectious disease. The development of vaccinations has advanced significantly over the years, resulting in the discovery and production of numerous safe and efficient vaccines. This abstract describes recent developments in vaccine research and development and emphasizes significant factors that have influenced the development of contemporary vaccines. In order to fulfill the problems outlined by COVID-19, the present research set out to analyze the procedures utilized by two significant worldwide regulating bodies for pharmaceutical organizations to approve vaccines and to create a roadmap for vaccine advancement in developing countries. **Methods:** This article provides a brief update on the regulatory clearance processes participating in the registration of vaccines in the throughout the United States of America (USA) and the EU, or the European Union. The comparative analysis aids in elucidating the regulatory issues that surface during the corresponding vaccination authorization processes in both in the EU and the USA. In **conclusion**, this paper offers a thorough account of recent developments in vaccine development, illuminating the growth of both conventional and cutting- edge platforms and their contributions to the fight against infectious diseases. Additionally, emphasize the significance of continued studies and cooperation in order to face problems in vaccine development and international health security.

Keywords: Marketing authorization (MA), Vaccine, COVID-19

INTRODUCTION

The unusual corona virus illness (COVID-19), caused by the recently discovered corona virus SARS-CoV-2, initially surfaced in China in mid-December 2019, shocking the whole globe. Most of the world's population has been affected by this virus, which is also causing respiratory illnesses. Several pharmaceutical businesses and research institutions across the world are presently working to create effective COVID-19 medications and vaccines through preclinical and clinical research **[1-3]**.

An infectious or malignant disease specific active acquired immunity is provided by a biological preparation called as a vaccine. The effectiveness and safety of vaccines have been rigorously examined and verified. Vaccines usually contain a substance that mimics a disease-causing bacterium; this substance is often constructed from weaker or dead types of the bacterium, one of its surface proteins, or one of its toxins. As a result of the chemical, the immune system recognises the substance as a threat, destroys it, and then is able to identify and eliminate any further germs linked to the substance that it may come into contact with in the future **[4-7]**.

Before a vaccine is made widely available to the public, its safety and effectiveness must first be established through the European Union (EU) and US approval processes. Both areas have developed regulatory structures and organisations in charge of approving and reviewing vaccinations **[8-11]**.

Procedure for EU vaccine approval

The centralised process is the main route for vaccination approval in the European Union. The regulatory organisation in charge of conducting vaccine scientific evaluations and approving vaccinations is the European Medicine Agency (EMA). The procedure starts with the vaccine producer submitting a thorough dossier that includes preclinical and clinical data, production information, and information on safety and efficacy. The EMA committee for medicinal goods for human use (CHMP) thoroughly assesses the data, it also takes into account the vaccine's effectiveness, safety, and quality profile. The CHMP evaluation is supported by input from impartial specialists and is based on scientific knowledge marketing permission **[12]**.

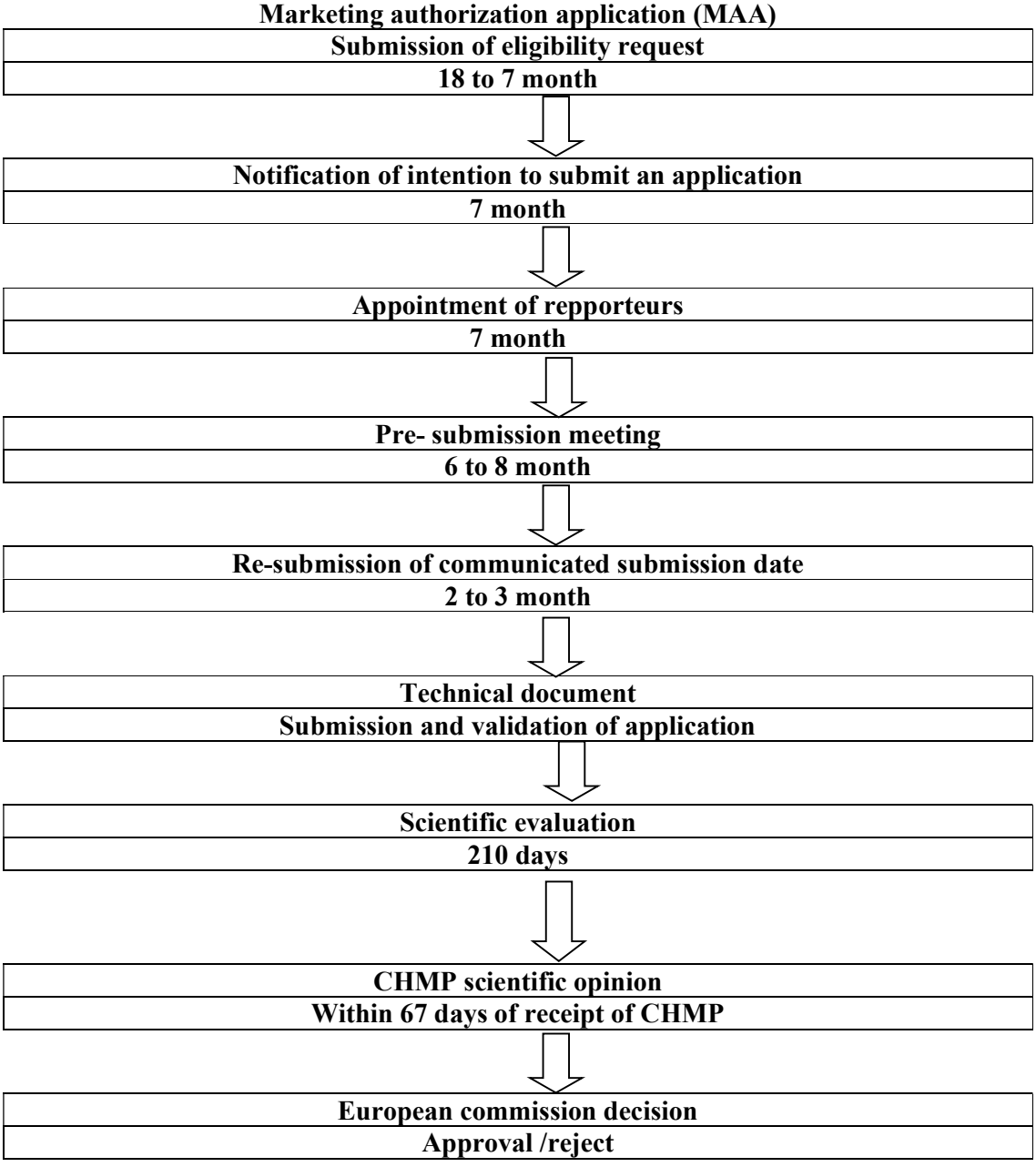
Marketing permission

The Committee for Medicinal Products for Human Use (CHMP) grants marketing permission following a thorough assessment of the product's quality, safety, effectiveness, and risk-benefit ratio **[13]**.

Registration

Through centralised, nationalised, decentralised, mutually recognised, and process-based methods, the EU authorises

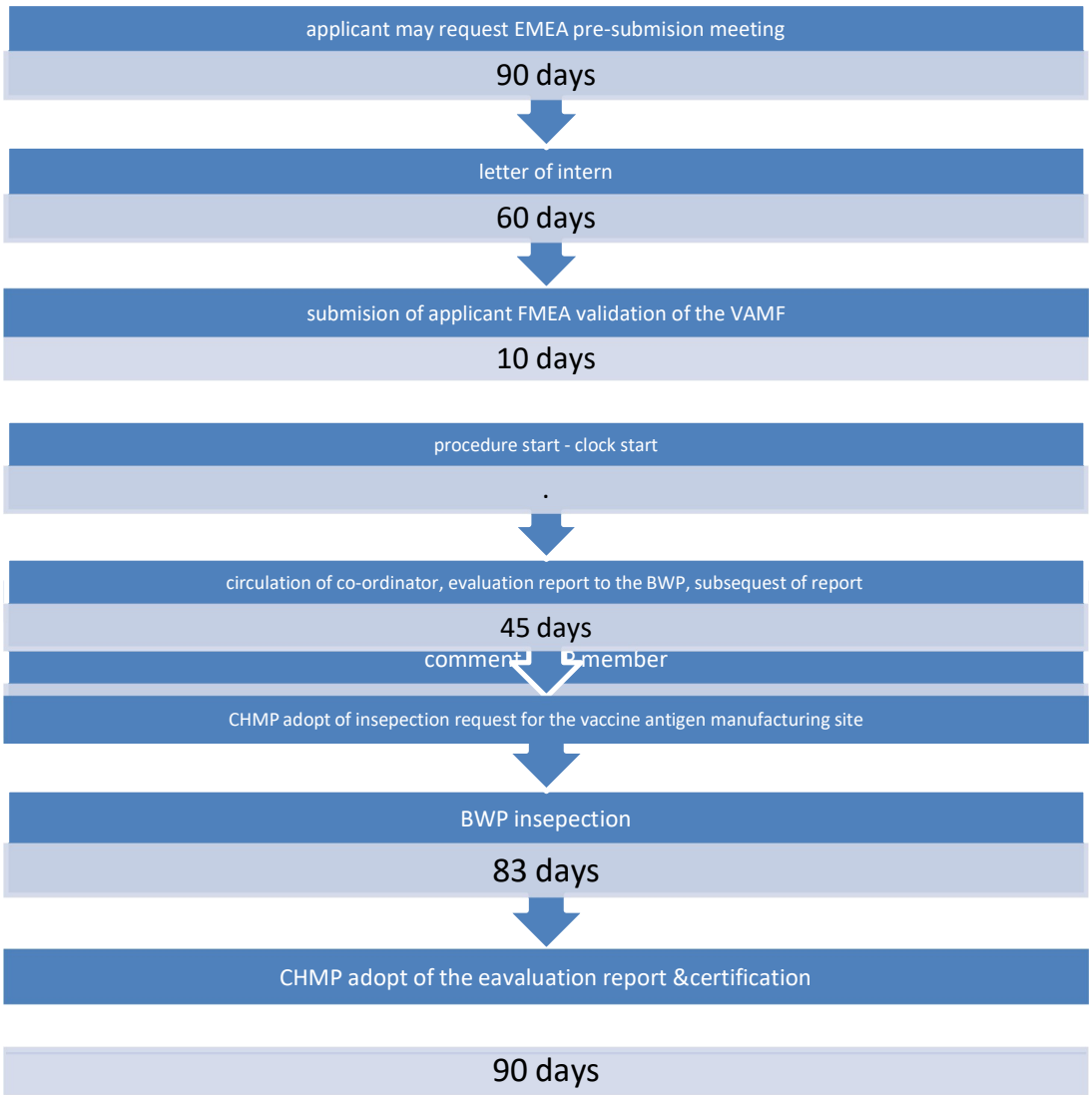
vaccines. The manufacturer normally favours the centralised method when getting a marketing license for a vaccine product. Patients and the healthcare system can readily get vaccinations since there is just one marketing authorization approval process for vaccine goods within the EU. The European Medical Agency (EMA) will receive the single application for the commercialization of a vaccine product across the EU after CHMP has examined it **[14-17]**.



Quality evaluation

Before being administered, immunisations will go through quality control after receiving marketing authorisation. Become available on the market. The European Pharmacopoeia Secretariat is a division of the European Directorate for Quality of Medicines (EDQM), establishes a recognised European control laboratory, and simplifies the method of quality assessment. Vaccines are examined for unfavorable side effects after being put on the market to ensure they adhere to the safety profile established as the product was being developed. Finding uncommon events that would not have been obvious during clinical development was the aim of the risk management plan **[18-20]**.

VAMF approval process



Vaccine Antigen Master File (VAMF)

When a centralised system is use, the vaccine manufacturer is required to submit a Vaccine Antigen Master File (VAMF) certification application the European Medicines Agency's clearance (EMA, 2005). When the scientific committees and you met before submitting, The VAMF filing procedure and the marketing authorisation process will be available as options for the manufacturers. The given dossier will be subject to a scientific analysis by the CHMP, and centralised methods are generally advised (EMEA, 2005). In the EU, the Eudra Vigilance system is used to monitor the negative side effects of vaccinations. The manufacturer could report a negative incident.either the patient or the doctor. The report will be evaluated in accordance with the Eudra Vigilance system, and CHMP will take necessary action as a result, instance include denying the product's request or approving its removal from the market (European Medicines Agency, 2003). It is easier to understand the variations and similarities between the marketing authorization procedures for vaccines in the EU and the USA.

Vaccination restrictions brought on by the EU's COVID-19 crisis

Unlike prior restrictions, the European Medicines Agency quickly approves the immunisation, which occasionally took 18 to 24 months for the EU to approve medicines. The following are the two primary processes for authorising pandemic influenza vaccinations:

The following are the two basic processes for approving pandemic influenza vaccines:

- Using a **mock-up approach,** a vaccine can be created and licenced in advance of a pandemic using the data generated by a particular virus strain.
- **Emergency procedure** Using this emergency method, a vaccine can be licenced rapidly after the pandemic starts. These vaccinations require shorter time for permission than traditional immunisations. The information provided by the manufacturer is assessed over a shorter period of time. The rule states that companies developing new vaccines must gather more data in order to alter the strain of virus in a fake vaccination. Instead of waiting until they have a dossier of information by employing the rolling review procedure, firms will use this strategy to provide information on vaccines that are in development as it becomes available.
- **US control of vaccines**

  The CBER is in responsible of upholding section 351 of the Public Health Service Act, which governs

immunisations and associated items. The process for registering a vaccine is carried out by submitting a BLA in an FDA Form 356h.

Regulatory evaluation and endorsement

The company must file a CBER of USFDA in FDA Form 356h, a biologics licence application, when the Phase 3 trials are concluded in order to get permission to make and distribute the vaccine to a large population. Depending on whether the application is being reviewed as a priority or under a regular review, it can take anywhere between 6 and 12 months to complete. Phase 4, often known as post-marketing monitoring, will start after the approval procedure. Within 15 days of receiving the immunisations, any adverse event or effect must be reported to the vaccine adverse event reporting system (VAERS).

Application for a Biologic License (BLA)

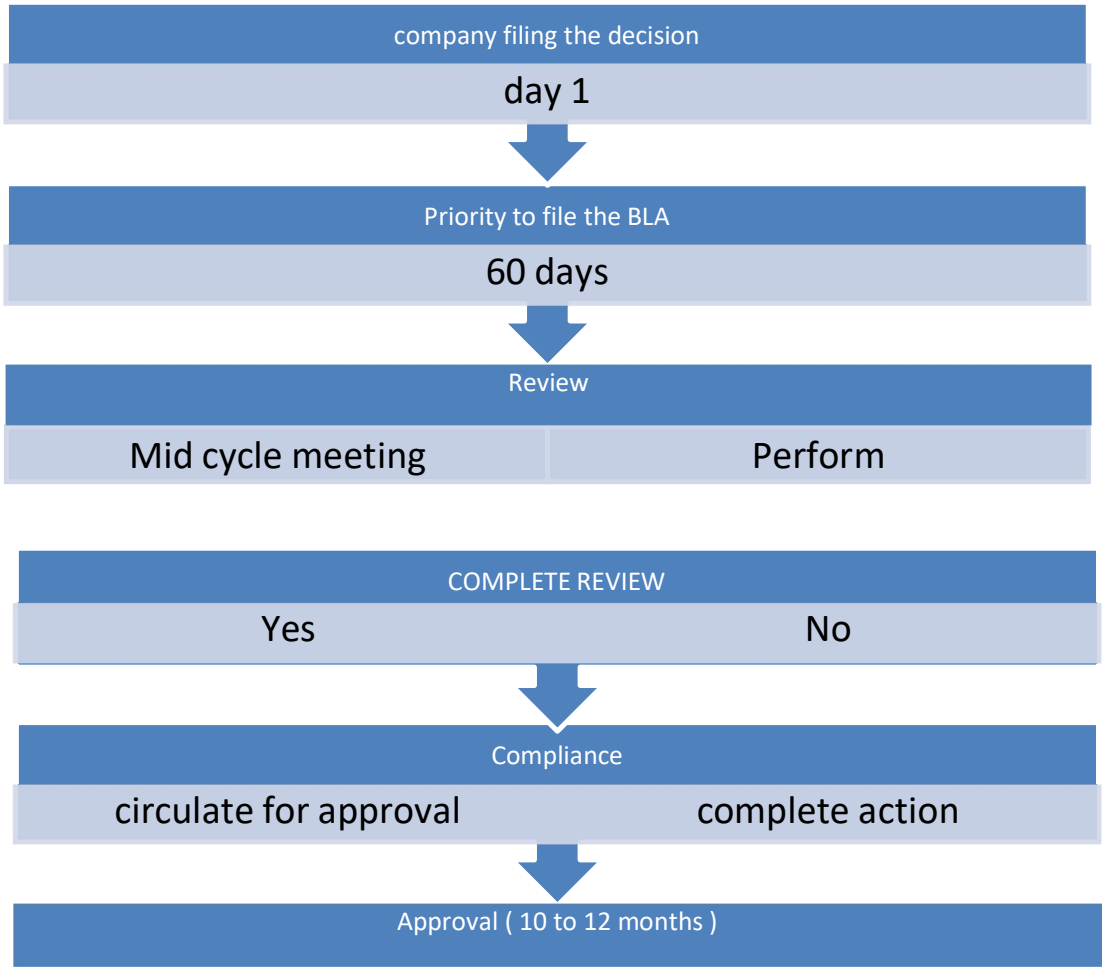
The biological licence application will be used to commercialise the produced vaccine product in the US. In accordance with Section 351 of the Public Health Service Act, this application must be submitted on FDA Form 356h. The application procedure begins when a BLA is decided to be submitted on day 1. Within 45 days of the application submission procedure, meetings must be scheduled. The manufacturer will have 60 days to submit the BLA and other required dossier papers, as well as to set the inspection window. Whether a candidate is eligible for a priority or routine evaluation will be decided by the FDA. If the immunisation has a considerable positive impact on public health, the corporation may also request priority consideration. In contrast to the ordinary review, which may take up to 12 months to investigate a vaccination product, the priority evaluation could take up to 6 months. In addition, if the FDA chooses to give the application priority consideration, they will let the applicant know within 60 days. It will be known whether there is a standard review by day 74. By Day 75, the FDA will inform the firm if it discovers any potential problems with the immunisation product. A midcycle meeting of the VRBPAC (Advisory Committee on Vaccines and Related Biological Products) should be attended by the manufacturer. Minimizing the risk posed by the vaccine product and informing FDA of any necessary corrective measures. An inspection will be carried out and a comprehensive evaluation will be documented during this review period. The immunisation product's compliance will be carefully examined. After distribution, the application will be examined and accepted.

ADR reporting of vaccines

The VAERS form is used to record vaccine adverse drug reactions (ADRs), which are any bad experiences related to the use of immunisation products. Together with the FDA, the Centres for Disease Control and

Prevention (CDC) support VAERS, a nationwide vaccine safety surveillance initiative. Vaccine adverse event reporting can be done online, via fax, or by mail. Within 15 days of being found, the unfavorable incidence must be recorded.

Biological license application flow chart



Vaccine restrictions as a result of the COVID-19 situation in the USA

By providing guidelines to those creating COVID-19 vaccinations, the FDA has in the current situation taken crucial efforts to guarantee the speedy production of safe and effective immunisations to prevent COVID-19.

• The FDA publishes updated guidance recommendations for developing a safe and effective COVID-19 vaccine by providing considerations for Emergency Use Authorization (EUA) of an experimental vaccine. The FDA cannot provide an EUA for a specific product unless the Secretary of Health and Human Services declares an emergency or identifies a threat that warrants the permission of emergency use.

According to Section 351(a) of the Public Health Service Act (PHS Act), which is codified at 42 U.S.C. 262, vaccines that are licenced in the United States must abide by all applicable legal and regulatory requirements for vaccine development and licensure as well as for vaccine quality, production, and control. The Secretary made this decision about COVID-19 on February 4, 2020.

• The immunisation product must adhere to current good manufacturing practise (cGMP) as defined in section 501(a)(2)(B) of the FD and C Act (21 U.S.C. 351(a)(2)(B) and 21 CFR Parts 210, 211, and 610).

First-stage research and development - 1

The coronavirus vaccine was made fairly fast since the Chinese government provided the virus' genetic sequence, which usually takes 2 to 4 years to produce.

Pre-clinical Stage 2

Following the first testing, the Plants and animals are used in vaccination testing to see how effectively it affects their immune systems.

Clinical Stage 3

This stage of the vaccine's development is the most significant and vital since it involves assessing the vaccine's efficacy in humans. This process has three steps. Phase 1 entails delivering the

Vaccinating a small number of people and checking on them to determine if their bodies have produced antibodies. Phase 2 of the vaccine programme, which might last 6 to 8 months, involves hundreds of people. The candidates' capacity to mount an immunological defense against the illness is evaluated. The immunisation may need to be administered to thousands of Phase 3 patients over the period of six to eight months.

Comparing the regulation and approval processes for vaccines in the USA and Europe			
Sr. No.	**Parameter**	**USA**	**EU**
1.	**REGULATORY AGENCY**	**Federal food and drug administration {USFDA}**	**European Medicine agency {EMA}**
2.	**REGULATING MINISTER**	**Department of human and health service**	**National competent authority of member state of European union {EU}**
3.	**REGULATION**	**Public health service {PHS}Act**	**European directive**
4.	**TYPES OF SUBMISSION**	**Biological license application {BLA}. Electronic regulatory submission and review : E-CTD submission**	**Marketing authorization application {MAA}** **E-submission gateway and web-client.**
5.	**FORMAT OF SUBMISSION**	**ICH-CTD and e-CTD format**	**Country specific**
6.	**GUIDELINE**	**21 CFR 600- Biological Product general** **21 CFR 601- licensing** **21 CFR 610- General biological product standard** **Guidance for Industry – content and format for CMC {Chemistry, manufacturing, and control } information and descriptive information related to biological product**	**EU Directives** **Directive 2001/83/EC** **Regulation (EC) No 726/2004** **Guideline on quality aspects included in the product information for vaccines for human use** **Guideline on dossier structure and content for Pandemic Influenza Vaccine Marketing Authorization Application**
7.	**CLASSFICATION OF VACCINE**	**Live attenuated** **Inactivated** **Subunit** **Toxoid** **Conjugated** **DNA recombinant variants**	**Live attenuated** **Killed inactivated subunit**
8.	**APPLICATION FORM**	**FDA form 356h**	**Marketing authorization application {MAA}**
9.	**OUTPUT LICENSE**	**New vaccine approval**	**Marketing authorization of vaccine**
10.	**MODE OF PAYMENT**	**$4,154,664**	**€286,900**
11.	**TIME FOR REVIEW**	**6 to 12 month**	**210 days**
12.	**MAA VALIDITY**	**Continuing for long period of time**	**5 years**
13.	**ADVISORY COMMITTEE**	**Vaccine related biological product advisory committee {VRBPAC}**	**Scientific Advisory Group on Vaccine (SAG-V)** **Vaccine Working Party**
14.	**DEFINATION**	**A preparation that is used to stimulate the body's immune response against diseases. Vaccines are usually administered through needle injections, but some can be administered by mouth or sprayed into the nose.**	**A biological treatment known as a vaccine increases immunity to a specific illness.**
15.	**QUALITY CERTIFICATE**	**NA**	**VAMF {vaccine antigen master file}**
16.	**ADR REPORTING**	**Vaccine adverse events reporting system {VAERS}**	**Eudravigilance sustem**
17.	**POST MARKETING REQUIREMENT**	**It include studies and clinical trial that sponsor require to conduct under one or more statutus and regulation**	**Plan for phamacocovigilance and risk manangement**

A SUMMARY OF THE PATHWAY FOR VACCINE DEVELOPMENT IN EMERGINGCOUNTRIES

- In this industry, developed or mature markets and emerging or developing markets are the two key market segments.
- An emerging market, country, or economy is one that has characteristics with an established market but departs from its norms.
- Egypt, Indonesia, Mexico, South Korea, Saudi Arabia, Taiwan, and Turkey are among the top ten largest emerging and developing economies by nominal or PPP-adjusted GDP, as are four of the five BRICS countries: Brazil, Russia, India, China, and South Korea.

Emerging manufacturers, for example, are taking an active role.

INDIA: Serum Institute of India, Panacea Biotech, Shantha Biotechnics, Bharat Biotech, and Biological E Ltd are all based in India.

CHINA: Shenzhen AVP, Shenzhen Kangtai, Chengdu, Shanghai (SIBP) Sinovac.

Brazil has Bio-Manguinhos and Butantan Institute, whereas Birmex and Instituto Finlay are located in Mexico and Cuba, respectively. Berna Green Cross (Berna) and LG Life Sciences are located in South Korea; Bio-Manguinhos and Butantan Institute are located in Brazil.

Country centered

Ensuring that vaccination and immunisation are accessible and available in all areas of the world without restriction Each nation is in charge of creating and promoting the immunisation programme required to safeguard its population's health.

Data-driven

With assistance for cutting-edge vaccination technology and information sharing, utilizing resources efficiently and based on evidence will be easier with the immunisations that were developed and researched. It will be simpler to understand the data and apply the study to any illness issues with the help of evidence-based practices.

❖ CONCLUSION

The vaccine approval process in both the European Union (EU) and United State (US) have been rigorous and focused on ensuring the safety and efficacy of vaccine. Although there are some similarities in the general framework, there are also notable difference in the specific requirement and procedures. The EU tends to rely more on the centralized evaluation by EMA, while the USFDA involve external exports committee in their decision-making process.

Emerging countries face unique challenges in their vaccine approval processes, primarily due to limited resource, infrastructure, and expertise. To ensure the safety and effectiveness of vaccines, these nations must build robust regulatory

systems. Here the general roadmap that emerging countries should follow:

1. Strengthen the infrastructure
2. Collaborate with international agencies
3. Adapt existing guideline
4. Establish clinical trial standard
5. Post marketing surveillance
6. Public communication and trust building

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