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Review Article

The Role of Investigational New Drugs Applications in Emergency Use Authorization (EUA) of New Drug Molecules

Harsh Pandey*, Anubhav Shukla, Farhan Hasan, Ashutosh Gupta, Gaurav Shukla

Maharishi School of Pharmaceutical Sciences, MUIT, Lucknow, Uttar Pradesh, 226013, India.

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ABSTRACT

The demand for effective and adaptable authorization processes increased as a result of the COVID-19 pandemic's extraordinary global health catastrophe, which altered regulatory frameworks for drug development. In order to guarantee the safety and scientific integrity of experimental treatments, the Investigational New Drug (IND) application has long been a vital entry point for clinical trials in the US. However, the Emergency Use Authorization (EUA) mechanism offered a supplemental regulatory tool to enable the quick deployment of potentially life-saving medical measures during public health emergencies, like the COVID-19 pandemic. The complex relationship between IND filings and EUA approvals is highlighted in this review, which also shows how early-phase IND data was crucial in facilitating EUA decisions for important medications and vaccines. In addition to discussing how these data sets were repurposed to meet EUA standards under the U.S. Food and Drug Administration (FDA) and international agencies, the paper examines the structural framework of the IND process, including preclinical data, manufacturing quality, and clinical trial protocols. Remdesivir, monoclonal antibodies, and mRNA-based vaccines are notable examples of case studies that highlight the importance of IND-backed data in bolstering EUA approvals under COVID-19. The study assesses the effects on future disaster preparedness of regulatory flexibilities used during the pandemic, including adaptive trial designs, rolling reviews, and the utilization of real-world evidence. In the context of rapid authorizations, ethical factors such as informed consent, data openness, and public trust are also investigated. By proposing the creation of a hybrid IND-EUA paradigm to expedite future responses to global health issues, these offer a forward-looking viewpoint. Stakeholders can improve the responsiveness, safety, and effectiveness of future drug approval pathways during emergencies by taking lessons from the regulatory agility seen during COVID-19.

INTRODUCTION

The unprecedented global health crisis brought on by the COVID-19 pandemic placed immense pressure on the pharmaceutical industry and regulatory bodies to rapidly develop, test, and distribute safe and effective therapeutics and vaccines. Drug development is often a systematic, multi-phase procedure that is intended to guarantee patient safety and product efficacy over an extended period of time. But given the pandemic's urgency, a quicker but more dependable route for access to medications and vaccines was required. The Emergency Use Authorization (EUA) and the Investigational New Drug (IND) application were two crucial regulatory tools in this situation. *(Bhimraj et al., 2022)* The EUA method offered a way to approve the use of unapproved medicinal items in emergency situations when conventional approval deadlines were impractical, while the IND approach permitted the start of human clinical studies based on encouraging preclinical findings. The

***Corresponding Author:** Harsh Pandey

Address: Maharishi School of Pharmaceutical Sciences, MUIT, Lucknow, Uttar Pradesh, 226013, India.

Email ✉**:** harshpandey7802@gmail.com

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intersection of these frameworks demonstrated a unique synergy during COVID-19, enabling faster deployment of critical interventions without compromising safety. *(Chattopadhyay et al., 2024)*

Global health systems have been significantly impacted by the COVID-19 pandemic, which has shown weaknesses and led to important changes in regulatory frameworks and healthcare delivery. The disruption of regular healthcare services, particularly a sharp drop in cancer diagnosis and treatments, has been one noteworthy effect. According to a study by the International Agency for Research on Cancer (IARC) of the World Health Organization, there was a 23% drop in new cancer diagnoses in 2020. The report attributed this to supply chain problems, less access to healthcare, and fear of catching COVID-19. This decrease highlights the indirect impact of the pandemic on health outcomes that are not related to COVID-19. *(Chattopadhyay et al., 2024)*

Telemedicine and digital health technologies have been rapidly adopted in response to the pandemic's challenges. Telemedicine, which was previously neglected, became crucial for providing medical care while following physical distance regulations. This change removed long-standing obstacles and made it possible to continue providing patient care in the face of lockdowns and limitations on healthcare facilities. *(Hazell & Shakir, 2006)* Significant gaps in access to medical countermeasures worldwide, especially in low- and middle-income countries (LMICs), were also brought to light by the epidemic. The difficulty that many LMICs had obtaining vaccines and necessary medical supplies highlights the necessity of bolstering regulatory frameworks to guarantee fair access to safe and efficient medical items. Improving regulatory readiness has emerged as a key element of pandemic response and global health security initiatives. *(Bowes et al., 2012)*

The pandemic also revealed the vulnerability of the world's supply systems for medical supplies. Essential medications and medical equipment became scarce as a result of border closures, trade restrictions, and transportation delays. These difficulties highlighted how crucial it is to create robust supply chain plans and encourage domestic production in order to lessen reliance on foreign markets. *(Hopkins & Groom, 2002)* The importance of regulatory frameworks like Emergency Use Authorizations (EUA) and Investigational New Drug (IND) applications has grown in light of these difficulties. Throughout the pandemic, these methods have made it easier to develop and implement medical countermeasures quickly. Through an analysis of their roles in accelerating access to vital medical therapies during public health emergencies and the extraction of lessons to improve future pandemic preparedness, this paper seeks to examine the synergy between IND applications and EUAs. *(Dahlin et al., 2015)*

The main goal is to critically analyze how crucial Investigational New Drug (IND) applications are to the Emergency Use Authorization (EUA) process, especially as the COVID-19 epidemic has shown. The purpose of this study is to clarify how IND procedures have been modified and used to expedite the creation and distribution of critically needed medications and vaccines in emergency situations while maintaining safety and scientific integrity. The review aims to demonstrate the dynamic synergy between IND submissions and EUA pathways in promoting quick clinical trials, data evaluation, and conditional approvals by examining regulatory tactics, case studies, and lessons learned from the worldwide pandemic response. In order to increase readiness for upcoming public health emergencies, it seeks to identify regulatory innovation gaps, obstacles, and opportunities. The paper's ultimate goal is to offer practical advice to legislators, regulatory bodies, and pharmaceutical researchers on how to best strike a balance between rapid access and careful assessment of experimental medications in emergency situations. *(Recovery Collaborative Group et al., 2020)*

Framework of Investigational New Drug

A regulatory submission known as an Investigational novel Drug (IND) application is made to organizations like the FDA to request permission to start human clinical trials for a novel medication or biologic. An IND is primarily used to verify that the clinical trial procedures are created to protect the rights and welfare of participants and that the investigational product is reasonably safe for initial use in human beings. By offering regulatory monitoring before human exposure and linking preclinical findings with clinical evaluation, the IND framework acts as a crucial checkpoint in the drug development process. *(The investigational new drug application, 2016)*

Investigator INDs and Commercial INDs are the two primary categories into which INDs are often divided. Pharmaceutical businesses or sponsors who want to create and eventually launch a new drug product usually submit a commercial IND. *(Lipinski, C. A. et al. 2001)* With the ultimate objective of receiving regulatory clearance for marketing, these INDs are frequently a component of a strategic strategy for comprehensive clinical development, which includes substantial Phase III trials as shown in Figure 1. Long-term safety monitoring, manufacturing uniformity, and the thorough clinical development program are the responsibilities of commercial IND sponsors. *(The investigational new drug application, 2016)*

An individual investigator, frequently a clinical practitioner or academic researcher, submits an Investigator IND when they plan to examine a medication primarily for research reasons or for unapproved uses. Investigator INDs often have a more constrained scope and concentrate on pilot or proof-of-concept trials, which are smaller clinical studies. Researchers may try new compounds with no commercial intent or examine an approved medication for a new indication. Under the IND, the investigator is in charge

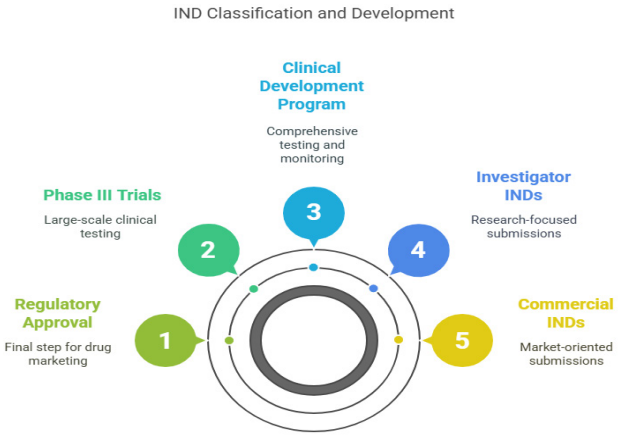

Figure 1: Development and working of INDs

of the trial's conduct and adherence to regulations. *(The investigational new drug application, 2016)*

These categories are crucial, particularly during emergency scenarios like the COVID-19 pandemic, when investigators and commercial sponsors used the IND pathway to quickly start trials that served as the evidence-based foundation for Emergency Use Authorizations (EUAs). This collaboration demonstrated how IND regulations are both structured and flexible, allowing for prompt access to potentially life-saving treatments. *(Vandenbossche et al., 2013)*

Stages in IND Application Process

A key component of the regulatory process for drug development is the Investigational New Drug (IND) application. It guarantees that clinical studies are carried out with the proper level of safety precautions and scientific rigor. Preclinical research, Chemistry, Manufacturing, and Controls (CMC), as well as the clinical trial protocol, are some of the crucial steps in the IND process. Every step is essential to facilitating the safe and prompt transition from lab research to human testing, which is particularly important in times of public health emergencies like the COVID-19 epidemic. *(Drews et al., 2000)*

Preclinical Studies

Preclinical studies constitute the foundation of the IND application and are designed to generate initial data on the safety, efficacy, pharmacokinetics, and toxicology of a new drug candidate before human trials begin. *(Gupta et al., 2010)*

- *In-vitro and In-vivo Testing*

These studies involve laboratory-based cell assays and animal models to assess biological activity and potential toxic effects. Pharmacodynamics and pharmacokinetics are characterized to understand the drug's mechanism of action, absorption, distribution, metabolism, and excretion (ADME). *(Patrick et al., 2017)*

- *Toxicology studies*

Acute, sub-chronic, and chronic toxicity studies are conducted to evaluate dose-related adverse effects. Genotoxicity, carcinogenicity, and reproductive toxicity are also assessed, ensuring human safety. *(Patrick et al., 2017)*

- *Pharmacology and dose selection*

Data derived from preclinical studies inform the selection of starting doses and dosing regimens for first-in-human trials. During COVID-19, accelerated preclinical evaluation was crucial to fast-track promising antivirals and vaccines. *(Mullard et al., 2016)*

Chemistry, Manufacturing and Controls (CMC)

CMC documentation is a regulatory requirement within the IND to ensure drug product quality, consistency, and safety.

- *Drug substance (Active pharmaceutical ingredient, API) characterization*

The IND must detail the chemical structure, physicochemical properties, and synthesis pathways of the API, ensuring reproducibility and purity.

- *Manufacturing process and controls*

A robust manufacturing process description, including scale-up and validation, is necessary. Controls for impurities, contaminants, and batch-to-batch consistency are mandatory to prevent variability that might impact safety or efficacy.

- *Formulation development*

Details of the drug formulation, including excipients and dosage form, are documented to guarantee stability and bioavailability. For COVID-19 vaccines, novel platforms such as lipid nanoparticles (LNPs) required comprehensive CMC evaluations to meet IND standards rapidly.

- *Stability studies*

Stability data ensure that the drug maintains its integrity and potency under various storage conditions, crucial for maintaining efficacy throughout distribution, especially under emergency circumstances.

Clinical Trial Protocol for INDs

The clinical trial protocol submitted within the IND outlines the planned human studies, providing a detailed roadmap for safety, efficacy, and ethical oversight.

- *Study design and objectives*

The protocol defines trial phases, participant eligibility criteria, dosing strategies, endpoints (primary and secondary), and statistical methods. Adaptive designs became a hallmark during COVID-19, enabling modifications based on interim data to accelerate development.

- *Safety monitoring and risk management*

Plans for adverse event reporting, Data Safety Monitoring Boards (DSMBs), and stopping rules ensure participant protection. In the EUA context, balancing rapid data generation with participant safety was a major regulatory focus. *(Tralau-Stewart et al., 2009)*

- *Informed consent and ethical considerations*

Ethical conduct is maintained through detailed informed consent processes, respecting participant autonomy despite the urgency of public health needs.

- *Site selection and investigator qualifications*

Selection of experienced clinical sites and qualified investigators assures protocol compliance and data integrity.

Components of Investigational New Drugs Application

The Investigational New Drug (IND) application is a comprehensive regulatory dossier submitted to the U.S. Food and Drug Administration (FDA) to seek authorization for administering a new drug or biologic to humans *(U.S. Food and Drug Administration, 2010)*. The IND serves to protect human subjects during clinical trials and ensures scientific integrity. It includes a detailed collection of data and documentation across multiple modules. The following are the major components as shown in Figure 2.

- *FDA form 1571 – The regulatory cover sheet*

The official cover document for all IND filings is Form FDA 1571. Important details including the sponsor's name, the investigation's phase (e.g., Phase I, II, or III), and whether the IND is commercial or research-focused are all outlined. Along with a legal commitment by the sponsor to adhere to FDA standards under 21 CFR Part 312, it also contains a checklist of all submitted components. The regulatory basis for any subsequent communications with the FDA is provided by this form. *(Unger et al., 2016)*

- *Investigational brochure (IB)*

A thorough synopsis of all available clinical and nonclinical data on the experimental medication is provided in the Investigational Brochure (IB). The chemical structure, formulation, pharmacokinetics, toxicological profile, and any previous human experience are usually included. The IB helps guarantee that the medication is administered consistently and with knowledge by acting as a reference manual for investigators. Because experimental research is dynamic during emergencies, the IB was regularly updated with new clinical data during the COVID-19 pandemic. *(Unger et al., 2016)*

- *Study protocols*

Comprehensive clinical study protocols must be included with every IND filing. The goals, design, patient eligibility

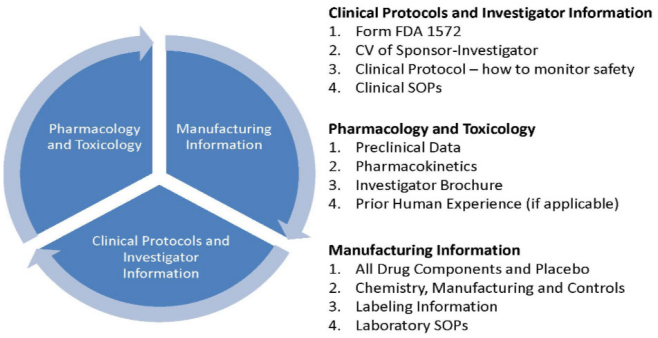

Figure 2: The key components of the INDs application

requirements, dosage schedule, and safety monitoring methods of the study are all specified in these protocols. They also describe the statistical techniques to be used when examining the findings of the investigation. The FDA allowed protocol changes to expedite subject recruitment in emergency scenarios, like the COVID-19 pandemic, while upholding ethical and scientific requirements.

- *Chemistry, manufacturing and controls (CMC)*

Important details regarding the production, testing, and storage of the investigational product are provided in the CMC section. It contains information about the drug's ingredients and final product, as well as manufacturing facilities, analytical testing procedures, and formulation components. The FDA is reassured in this part that the investigational product can be manufactured with reliable quality and safety standards. In order to speed up the start of clinical trials, the FDA notably introduced regulatory flexibilities during the COVID-19 crisis by permitting rolling filings and conditional acceptances of CMC data. *(Swinney et al., 2011)*

- *Pharmacology and toxicology data*

Nonclinical studies that assess the drug's safety profile prior to human exposure are included in this section. It includes safety pharmacology, animal pharmacokinetics, and toxicity investigations. These investigations are essential for detecting possible hazards and establishing the safe initial dosage for human trials. The pandemic's urgency made it necessary to expedite clinical evaluations by using preclinical data that was already available and, in certain situations, animal effectiveness studies conducted in accordance with the FDA's Animal Rule. *(Swinney et al., 2011)*

- *Clinical investigator information (Form FDA 1572)*

Every investigator taking part in the clinical research has their qualifications, affiliations, and agreements to adhere to regulatory and Good Clinical Practice (GCP) criteria gathered on Form FDA 1572. This guarantees that the trial will only be conducted by qualified experts. Alternative verification methods, like remote site inspections

and virtual audits, were used to expedite investigator approvals during the pandemic. *(Menda et al., 2011)*

- *Institutional review board (IRB) approval*

Sponsors are required to provide proof that the study protocol and consent forms have been examined and approved by an IRB in order to protect the rights and welfare of clinical trial participants. Even in times of need, this ethical lapse cannot be avoided. Many IRBs used expedited review procedures in response to COVID-19 in order to address the pressing demand for experimental treatments.

- *Informed consent documents*

A draft of the Informed Consent Form (ICF), which describes the study's goals, methods, possible risks, advantages, and participant rights, must be included with the IND. Given the experimental character of many COVID-19 treatments and the requirement for quick participant recruitment, informed consent—a fundamental component of ethical clinical research—became even more crucial during the pandemic. *(Lee B. et al., 2005)*

- *Previous human experience*

Disclosure is required if the investigational product has been used in humans before, either in international research or under other INDs. *(Mullard, A. et al. 2016)* This influences dosing techniques and aids the FDA in weighing possible hazards and benefits. Drugs like hydroxychloroquine and remdesivir were repurposed in the context of COVID-19 based on prior data from other indications, which had a big impact on EUA considerations.

- *Additional attachments and safety reporting*

Finally, the IND should include other relevant documentation such as financial disclosures, safety reporting plans, and environmental assessments. A robust system for adverse event reporting under 21 CFR 312.32 is crucial, especially during emergencies when unexpected toxicities may arise due to expedited trial timelines and limited prior data. *(Lee B. et al., 2005)*

Concept of Emergency Use Authorization (EUA)

During public health emergencies, medical products may be made more quickly available through the Emergency Use Authorization (EUA) regulatory system. The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 improved the EUA framework, which was first created in the US under the Project BioShield Act of 2004. When specific statutory requirements are satisfied, such as the lack of suitable, approved, and accessible alternatives and a finding that the known and potential benefits outweigh the known and potential risks, the U.S. Food and Drug Administration (FDA) may use this mechanism to permit the use of unapproved medical products or unapproved uses of approved products. *(Hackam et al., 2006)*

Similar accelerated procedures have been implemented by other regulatory bodies worldwide to handle emergent medical emergencies. For example, the Emergency Use Listing (EUL) process was introduced by the World Health Organization (WHO) to evaluate the appropriateness of new medical items in the event of a public health emergency. The EUL seeks to expedite the release of medications, vaccines, and diagnostics while guaranteeing that strict safety, effectiveness, and quality standards are fulfilled. Data from late-phase clinical trials and other pertinent information are rigorously evaluated during this procedure. *(Ellenberg et al., 2001)*

Regulation 174 of the Human Medicines Regulations 2012 was used by the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom to temporarily authorize COVID-19 vaccinations, allowing for their quick distribution throughout the pandemic. In a similar vein, the European Medicines Agency (EMA) used conditional marketing authorizations to provide early access to medications with a favorable benefit-risk balance, while Health Canada implemented interim orders to speed up the authorization of COVID-19-related treatments. During the COVID-19 epidemic, these regulatory flexibilities played a pivotal role in expediting the availability of vital medical interventions. *(Grein et al., 2020)*

The significance of worldwide cooperation among regulatory agencies was highlighted by the COVID-19 pandemic as shown in Table 1. In order to accelerate the development, approval, and accessibility of COVID-19 therapies and vaccines globally, groups like the International Coalition of Medicines Regulatory Authorities (ICMRA) were essential in promoting strategic coordination and information exchange. *(Grein et al., 2020)*

The necessity of international regulatory harmonization to speed up the creation, assessment, and dissemination of medical countermeasures was highlighted by the COVID-19 pandemic. International regulatory organizations realized this and stepped up their joint efforts to expedite procedures and guarantee prompt access to safe and efficient medications and vaccines around the globe.

The International Coalition of Medicines Regulatory agencies (ICMRA), a platform for strategic collaboration among international medication regulatory agencies, was a key participant in this effort. In order to promote regulatory convergence and address regulatory considerations for COVID-19 vaccine candidates, ICMRA organized frequent virtual sessions that brought together more than 100 participants from 29 member agencies. The goal of these talks was to simplify regulatory monitoring during the epidemic and standardize procedures for first-in-human clinical studies. *(Recovery Collaborative Group et al., 2020)*

Apart from ICMRA's endeavors, the World Health Organization (WHO) initiated the Access to COVID-19

Table 1: Comparisons between EUA and traditional approval process

Parameter	*Emergency Use Authorization (EUA)*	*Traditional Approval (e.g., NDA/BLA)*
Regulatory Authority	U.S. FDA under Section 564 of the Federal Food, Drug, and Cosmetic Act	U.S. FDA under 21 CFR Parts 314 (NDA) and 601 (BLA)
Trigger for Use	Declared public health emergency	No specific emergency required
Objective	Rapid access to potentially life-saving medical products	Comprehensive evaluation for long-term use
Application Type	EUA Request (no formal IND/NDA required, but supportive data often submitted)	New Drug Application (NDA) or Biologics License Application (BLA)
Data Requirements	Reasonable evidence of safety and potential efficacy (Phase I/II data may suffice)	Full preclinical + clinical data (Phases I–III) demonstrating safety and efficacy
Review Timeline	Rapid – typically days to weeks	Lengthy – often 10–12 months (standard)
Product Labeling	Includes disclaimer on investigational status and emergency use	Full prescribing information based on completed clinical trials
Informed Consent Requirements	Simplified patient information fact sheets	Detailed patient information and full labeling
Manufacturing Standards	cGMP compliance expected but may allow flexibility	Full compliance with cGMP (Current Good Manufacturing Practices) required
Market Exclusivity	No exclusivity granted	Market exclusivity and patent protection apply
Duration of Authorization	Temporary – ends with termination of emergency declaration	Permanent approval unless withdrawn or suspended
Examples (COVID-19)	Remdesivir (initial EUA), Moderna and Pfizer-BioNTech vaccines (early 2020)	Remdesivir (fully approved in Oct 2020), COVID-19 vaccines post full data review
Post-Authorization Monitoring	Required under EUA (e.g., pharmacovigilance plans)	Required (Risk Evaluation and Mitigation Strategies - REMS, post-marketing studies)
Revocation Possibility	Can be revoked at any time based on emerging evidence or end of emergency	Withdrawal only upon substantial safety or efficacy concerns

Tools (ACT) Accelerator, a worldwide partnership aimed at expediting the creation, manufacturing, and fair distribution of COVID-19 diagnostics, treatments, and vaccinations. The COVAX program was created within this framework to guarantee fair vaccination distribution, especially to low- and middle-income nations. 184 nations had joined COVAX by October 2020, demonstrating a common worldwide commitment to vaccine fairness. *(Farne et al., 2020)*

Additionally, national regulatory bodies adjusted to the difficulties presented by the pandemic. For example, the National Health Surveillance Agency (ANVISA) in Brazil developed expert committees to prioritize applications relevant to COVID-19, performed remote Good Clinical Practice inspections, and instituted flexible submission and evaluation procedures. These actions were intended to preserve strict safety regulations while accelerating the availability of essential medical supplies. *(Yao, X. et al. 2020)* To meet the problems posed by the epidemic, the U.S. Food and Drug Administration (FDA) collaborated with other countries. The Center for Biologics Evaluation and Research (CBER) of the FDA stepped up its global efforts, taking part in research and regulatory partnerships pertaining to COVID-19 treatments and vaccines. Additionally, CBER improved worldwide pharmacovigilance efforts by facilitating the interchange of inspection information with partners throughout the world. *(U.S. Food and Drug Administration [FDA], 2010)*

The significance of regulatory harmonization in response to public health emergencies is underscored by the coordinated international efforts during the COVID-19 epidemic. In order to ensure readiness for upcoming global health concerns, the cooperative frameworks and adaptable methods created during this time frame serve as a basis for future international regulatory collaboration.

Transitions of Post- Emergency Use Authorization (EUA)

It takes extensive clinical evidence and stringent manufacturing assessments to move from Emergency Use Authorization (EUA) to full FDA approval. For example, after undergoing thorough safety and effectiveness testing, Novavax's COVID-19 vaccine, which was first approved under the EUA, received full approval for certain populations in May 2025. The FDA's dedication to

rigorous review, even after the EUA, is demonstrated by this approval. Similar to this, after submitting solid clinical trial results, medications like remdesivir moved from EUA to full approval. These incidents demonstrate how important it is to maintain data collecting and regulatory oversight in order to guarantee the efficacy and safety of medical products outside of emergency situations. *(Farne et al., 2020)*

Regulatory Expectations for Continued IND-Supported Data

The U.S. Food and Drug Administration (FDA) expects sponsors to continue gathering and submitting thorough data to support a complete Biologics License Application (BLA) or New Drug Application (NDA) after an Emergency Use Authorization (EUA) has been issued. EUAs are not a replacement for complete approvals, even though they provide for quicker access to medicinal supplies in times of public health emergencies. To move from EUA to full approval, the FDA requires sponsors to submit strong clinical trial results, manufacturing details, and quality control procedures. Investigational New Drug (IND) applications, which enable the methodical collecting of safety and efficacy data over long periods of time, frequently facilitate this continuous data collection. The FDA emphasizes the importance of this continued data submission to ensure that the benefits of the product outweigh any potential risks in the broader population. *(Farne et al., 2020)*

Timeline and Case Studies of EUA-to-BLA/NDA Transitions

Several COVID-19 treatments and vaccines have served as examples of the shift from EUA to full approval. For example, the COVID-19 vaccine developed by Pfizer-BioNTech was fully approved by the FDA as Comirnaty in August 2021 after being first approved under an EUA in December 2020. Extensive evidence from more than 44,000 participants, including six months of follow-up data showing 91% efficacy in preventing COVID-19, served as the basis for its approval. Spikevax, a vaccine produced by Moderna, also went from EUA to full approval in January 2022. *(Yao et al., 2020)*

Regarding medicines, the FDA fully approved Paxlovid (nirmatrelvir and ritonavir) in May 2023 after it was approved under an EUA in December 2021 for the treatment of mild-to-moderate COVID-19 in high-risk people. By requiring the switch to an NDA-labeled medicine by March 8, 2024, the FDA amended the EUA to phase out the distribution of Paxlovid under the EUA label. These changes demonstrate the FDA's dedication to making sure that goods first approved under EUAs fulfill the stringent requirements needed for complete approval, such as thorough clinical data and evaluations of manufacturing quality. *(Duong, 2020)*

Implications for Long-Term Pharmacovigilance and Label Updates

Pharmacovigilance and labeling are significantly impacted when a product moves from EUA to full approval. The extent of post-marketing surveillance is constrained under an EUA. However, strong pharmacovigilance plans are required for complete approval in order to track the product's effectiveness and safety in the broader population. This involves submitting periodic safety update reports (PSURs) and, if required, putting Risk Evaluation and Mitigation Strategies (REMS) into practice. During this shift, labeling also receives important improvements. The enhanced data gathered during the post-EUA phase is used to refine information about adverse reactions, contraindications, and usage guidelines. For instance, Comirnaty's label was revised to incorporate details on the risks of myocarditis and pericarditis found during post-marketing surveillance. *(Wang et al., 2020)* Additionally, the FDA anticipates that sponsors will carry out additional research to assess long-term results, efficacy against new variations, and use in certain demographics including youngsters and expectant mothers. These studies help guide future label changes and guarantee that patients and healthcare professionals have access to the most up-to-date information about how to use the medicine. *(Grein et al., 2020)*

Challenges and Ethical Considerations

Significant difficulties arise from the accelerated process of Emergency Use Authorizations (EUAs), especially when compared to the more stringent Investigational New Drug (IND) procedure. The fact that there is less safety data available under EUA than in conventional IND-supported clinical trials is one of the main issues. In order to evaluate safety and efficacy over time, IND applications necessitate comprehensive preclinical data and phased clinical studies; yet, EUA judgments are frequently based on interim or preliminary results. When interventions are implemented on a large scale, as is the case with COVID-19 vaccinations and treatments, this can raise the possibility of unidentified negative effects. During emergencies, informed consent becomes yet another crucial ethical concern. There is frequently pressure under EUA to implement interventions quickly, which may jeopardize the caliber and comprehensiveness of the information given to patients. EUA interventions may be carried out without thorough patient education on potential dangers and alternatives, in contrast to IND trials, where informed consent is carefully controlled and monitored in accordance with Good Clinical Practice (GCP) principles. Public trust is called into question, particularly when unfavourable outcomes occur after authorization. Sustaining trust in regulatory agencies and public health initiatives requires maintaining openness and unambiguous communication. Access and distribution

equity continue to be major ethical conundrums. Despite its speed, the EUA process might unintentionally provide preference to populations and places with greater resources because of differences in infrastructure, political clout, and logistics. Unfair vaccination availability during the COVID-19 pandemic brought to light structural injustices, especially in low- and middle-income nations. The disparity in EUA-enabled access continued despite international efforts such as COVAX, raising concerns about the equity of international emergency response systems. Strong post-marketing surveillance, open policymaking, and international cooperation are necessary to address these issues and guarantee that rapid approvals under EUA adhere to the same moral principles as those required under the IND framework.

CONCLUSION

The COVID-19 epidemic presented previously unheard-of difficulties that necessitated an immediate and well-coordinated international response. Of the several lessons learnt, the strategic and regulatory significance of Investigational New Drug (IND) applications in supporting Emergency Use Authorizations (EUAs) was one of the most important. The conventional IND framework, which was originally intended for systematic drug development, was quickly modified to meet pressing public health demands. This allowed for the quick evaluation of manufacturing quality, safety, and efficacy. This development demonstrated the IND process' adaptability when paired with emergency regulatory procedures, in addition to confirming its resilience. The early and well-organized IND filings played a major role in the successful EUA of important treatments and vaccines, including Remdesivir, monoclonal antibodies, and mRNA-based vaccines. These applications made guaranteed that regulatory agencies had access to enough preclinical and early-phase clinical data to make risk-reduction, science-based choices in a timely manner. Additionally, rolling review procedures, real-time data monitoring, and adaptable trial designs—all carried out in accordance with IND protocols—became essential components of regulatory innovation. Transparency, informed consent, and fair access to EUA products are just a few of the ethical challenges that were made clear by the experience. These difficulties highlight the necessity of globally standardized frameworks and regulatory readiness that can be effectively implemented in future crises. The next phase of regulatory science will probably be characterized by the incorporation of real-world evidence, AI-supported analytics, and digital health tools into IND-supported EUA pathways. Future outbreaks or pandemics may benefit from a hybrid approach that combines the reactivity of EUAs with the rigor of INDs. To guarantee prompt access to safe and efficient interventions, it will be essential to invest in regulatory agility and strengthen international collaboration. In the end, the combination of IND and EUA procedures marks a significant change in pharmaceutical regulation that may influence future developments in global health readiness.

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