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Evaluation of the Performance of the Iraqi Regulatory Authority: Recommendations to Optimize Patients' Access to Medicines

Alhasan Zalzala[1], Orooba Ibrahim[2]

Abstract

The Iraqi Regulatory Authority (IRA) has been a key player in the pharmaceutical industry, focusing on improving patients' access to medicines. The agency's organizational structure includes accreditation of manufacturing facilities for Good Manufacturing Practices (GMP), advertising regulation, laboratory examination of sample data, price control, marketing authorizations, and product licenses. The registration process involves a hybrid review procedure that uses type 1 and type 2 requirements and verification methods. The study has shown an urgent need to develop a unified national guideline to regulate all pharmaceutical product registration and marketing authorization in Iraq. Using identical analyzing and verification approaches when assessing new pharmaceutical products, especially in veterinary versus human products. Separating the regulatory body from the executive body to eliminate the main source of bias in the decision-making process. Creating a specialized auditing body to review the implementation of SOPs and to develop the gaps in guideline creation and evolution. Endorsing a continuous learning system where new staff regularly receive sufficient information on requirements and duties of each function, thus creating a sustainable environment within the regulatory body. Harmonize the process by aligning our operations with leading global agencies (stringent health authorities) to enhance workflow and optimize patients' access to care.

Keywords: *Regulatory Authority; NDA Submission; marketing authorizations; Patients' Access.*

1. INTRODUCTION

The earliest code of rules governing medicines and human treatments was created by Hammurabi, who reigned between 1795 and 1750 BC in Babylon and Mesopotamia. This is where the first model of health authority was seen. This was regarded as one of the oldest recorded laws [1]. The Hippocratic Oath makes it apparent that similar medical rules and regulations were also established in the Greek and Roman eras. History is replete with incidents that show how eager people have been to advance medical and pharmacology to increase patients' access to better care, even as healthcare authorities focus on regulating and ensuring a balance between the risks and benefits.

"The pharmaceutical industry and Health Technology Assessment (HTA)" agencies have shown an increased interest in patients' access to medications in recent years [2]. One main article that changed the perspectives of many was "Thalidomide and Congenital Abnormalities" [3], a new controlled age started in the 1960s. This was seen as a

[1] Department of Pharmacology and Toxicology, College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq, Alhassam.zalzala@gmail.com
[2] Department of Pharmacology and Toxicology, College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq, auroba.m@covm.uobaghdad.edu.iq

significant issue for the Health Authorities (HA), national governments, and international healthcare organizations like the World Health Organization (WHO). HA play a crucial role in evaluating the safety of pharmaceuticals in addition to their quality and efficacy prior to marketing authorizations, so the WHO made Multiple efforts and issued determinations to support health systems in developing their own local guidelines to optimize healthcare and patients' access to care since 1975 [4].

Health authorities' attention has shifted from quality to effectiveness since the 1960s, from safety measurements alone to a mindset of benefit-risk analysis, later on, to the value-added of licensed medications. The pharmaceutical business, distinguished as being highly dynamic, fast-evolving, and the most regulated of all industries, has seen a continual change in the regulatory environment due to the shifting and demanding emphasis on health authorities [5].

2. MATERIAL AND METHODS

2.1 Data Collection

the Biologics and Biosimilar Registration Committee (BBRC) helped enable this investigation. The registration department provided data about yearly submission and evaluation timelines. The information concerned NASs, including the quantity of marketing authorization requests and the general review and approval schedules [6].

2.2 The questionnaire's format

The agency's organizational structure and resources were described in the first part. Organization of the Agency. To ascertain whether the registration department thoroughly evaluated outcome data or if a different review model de-pendent on the outcomes that validate the review assessments of other authorities—was used, it also investigated the evaluation protocol for different products.

In Part II, Significant Achievements in the Registration of Drugs. This section focused on evaluating and licensing novel active substances (NASs). To make data collection and illustration easier, a uniform process map with milestones was created, making it easier to compare regulatory agencies.

In Part III Improving the evaluation scheme' Quality as the section looked at the important components of “Good Re-view Practices (GReP)” which affect the decisions and the steps made by the RA to increase constancy, clearness, cor-rectness, and capability.

Finally, a conclusion is made to identify the relationships between RA functions and relevant stakeholders. It also made it known whether an assessment framework and procedures were available for use by the internal staff of the agency and/or the external reviewers after completing the questionnaire [7].

3. RESULTS AND DISCUSSION

3.1. Part I: The Regulatory Authority's Organizational Structure

The registration department's range of responsibilities also includes the accreditation of manufacturing facilities for Good Manufacturing Practices (GMP) and the regulation of advertising, laboratory examination of sample data, price control, marketing authorizations, and product licenses. There are 108 employees total, and more than 25% of them have medical backgrounds as doctors or pharmacists. Additionally, 47 employees of the regulatory authority are charged with reviewing requests for product licenses and marketing authorizations. The regulatory authority is a paid service provider by the fees it charges from applicants [9].

3.1.1 Assessment and Requirements for Data

According to local pharmaceutical regulations, any pharmaceutical product must receive marketing authorization permission from the regulatory authority before it may be marketed in Iraq. Therefore, pharmaceutical firms must meet various regulatory standards to receive regulatory approval. Initially, the candidate must be an approved com-pany located in Iraq. After that, a request should be sent to the registration department along with the supporting pa-perwork indicated in the licensing regulation. All NDAs are currently presented in accordance with regional licensing specifications. Additionally, the applicant must create comprehensive record in accordance to "Common Technical Document (CTD)", which must be supported by the international commission of Harmonization requirements covering API and the finished product. The MAA must be formatted and organized in accordance with the checklist, proposed and approved labelling claims, and non-clinical and clinical data. When applying for registration in Iraq, the CPP is not necessary. Prior to final approval, a CPP of the evaluated product labelling; however, other proof, such as an e-CPP or the official online database, can be acceptable. Most notably, the Iraq Regulatory Authority only conducts a hybrid review procedure using type 1 and type 2 requirements and verification methods [8].

3.2. Part II: Important Aspects for Iraqi Review Process

A roadmap for the entire approval process and its turning points is a general, streamlined flow chart that depicts the key actions taken within the registration department throughout the product approval submissions, initially with the pilot assessment of the dossier to the final stages when the file is approved. As a result, the map does not depict all phases and procedures involved in denying a submission. Additionally, the map does not outline the preliminary ac-tions that must be taken as part of the GMP accreditation procedure before applying for marketing permission [10].

3.2.1 Requirements for Pre-submission and the GMP Procedure

Before applying for an MAA, the product's manufacturing facilities are required by local law to obtain GMP accredita-tion. Facilitated the submission and review of a marketing authorization application for high-priority goods (orphan and life-saving goods) concurrent with an ongoing GMP procedure. These goods can also be qualified for an expedited registration review if carried out concurrently with the GMP procedure, subject to a Prioritization Assessment Commit-tee decision. The first stage in becoming registered is to submit a thorough GMP dossier, which contains information on the facilities' quality and manufacturing capabilities as well as the goods produced there. After that, Good Manufac-turing Practice submission goes through a procedure and is classified to establish the order of priority for each product. The candidate is advised of the potential timelines for reviewing all manufacturing steps for a given product and en-suring the application of GMP. The timeline for the GMP inspection process is unpredictable, and there is currently no established time frame dedicated to the process. A segmentation concerning priority and requirements for the 4 primary prioritized classifications determines how quickly the GMP process is completed. A benefit-risk analysis and phar-macoeconomic considerations determine the product's GMP priority category. Products categorized as priority 1 as "orphan" or "lifesaving products" gain importance, and finishing the GMP will take approximately one year, whereas priority 4 medication, such as the inclusion to different production facilities medication, possess a lower level of priority from RA and for that reason, a 3 years deadline is made for that category. Afterwards, GMP audit is concluded, the submeter should contact RA and immediately carry out any remedial procedures. The "GMP certificate" will be grant-ed according to the evaluation. The same certification procedure must be followed to renew GMP certificates in Iraq before their three-year expiry date [11].

3.2.2 Medical Assessment

The effectiveness data for an application are evaluated scientifically, and the need for medicine is evaluated sepa-rately. The National Board for the Selection of Medicines (NBSD), which includes reviewers formally appointed by the Ministry of Health based on Clinical proficiency, conducts the primary scientific evaluation. Therefore, scientific as-sessment approval of the proposal is regarded as the most important milestone in the evaluation process. Other com-mittees start the review process after this stage is finished.

3.2.3 Specialist Committees

Numerous committees (totalling nineteen) under the MoH conduct various scientific evaluations. Additionally, external specialists' major duties are offering a thorough judgment testimony, approval, and employees' guidance on certain matters. Consequently, it was required to implement the panels' recommendations. Furthermore, there is no written agreement requiring exterior reviewers to meet agency timeframes. As a result, the committee review schedules are not consistent.

3.2.4 Merchandise Labelling

After the scientific evaluation is complete but before the RA grants approval, on the other hand, an established discus-sion for the leaflet, which includes "the Summary of Product Characteristics (SmPC)" and "Patient Information Leaflet (PIL)". Therefore, before MA approved, the proposed SmPC and PIL are examined by the Pharmacological Commit-tee. Additionally, the final product sample, packaging, and labelling are all reviewed throughout the sales license appli-cation and authorized as necessary. Data for the four years (2019–2021) were examined, and the findings indicated a general tendency for growth in the number of new molecules being addressed to RA. As a result, there were more NAS applications (Figure 1). Additionally, Figure 3.4 displays the volume of new molecules MA that RA authorized and re-fused in 2019, 2020, and 2021 [12].

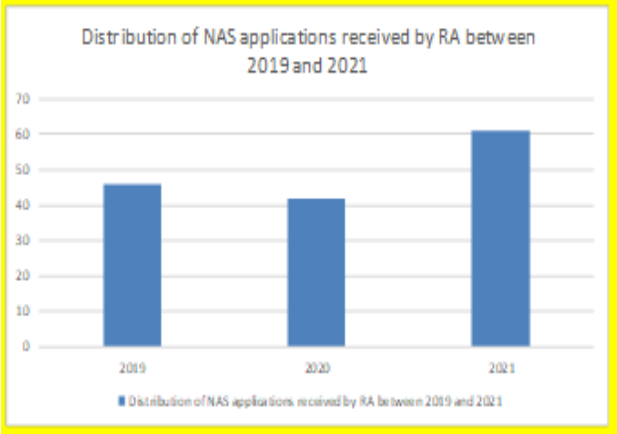

Figure 1: Distribution of NAS applications received by RA between 2019 and 2021

The approval timelines (mean for 3 randomly chosen dossier) for NASs from 2019 through 2021 are shown in (Figure 2)

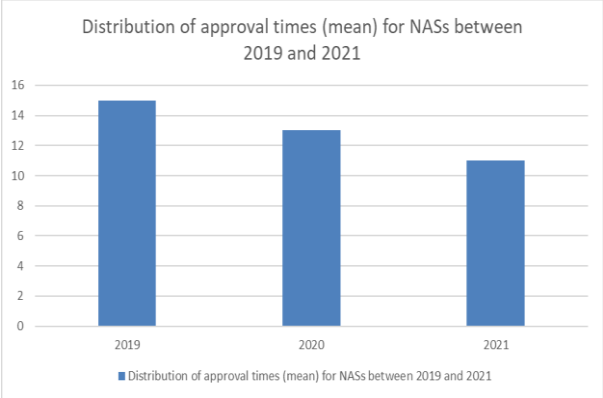

Figure 2: Distribution of approval times (mean) for NASs between 2019 and 2021 (in months)

A mean submission period of 11 months, the major approval was in 2021 and 61 NDA. These statistics showed that the RA's accomplishment throughout the evaluation period significantly developed after 2020, most likely because of the rise in committees and reviewers. However, if the GMP requirement were carried out concurrently for all NAS ap-plications, the review's effectiveness may be increased even more.

3.3. Part III: GxD in the Evaluation and Approval Process

Regulatory agencies place a premium on quality for approval pathways because it promotes uniformity, transparency, speed, and competence in the approval queue. Regulatory agencies are constantly creating and putting various measures into practice to enhance and reach greater quality standards and match businesses' needs. As a result, the CTD file, which describes product attributes and "chemical and manufacturing control (CMC)" procedures, typically determines the quality level of pharmaceutical products [13]. The process of making a decision, in addition to time-lines, has recently emerged as a critical element that must be closely monitored and assessed to assess the RA execu-tion and competence. The 3rd portion of the survey was used to get a perception of plans, programs, and resources used to create the standard of the evaluation procedures. Outcomes showed organizations appear to have a thorough and formal quality policy, which is "defined as the overall intentions and direction of the organization related to quali-ty". However, the results showed that "Good Review Practice (GReP)" remains absent, despite commitments to do so.

Nevertheless, various "standard operating procedures (SOPs)" are employed primarily for leaflet evaluation, pharma-covigilance evaluations, and to provide advice for expert's committees. It is not common practice to conduct a peer review or a second examination of the initial assessment by a third party or committee. The fundamental obstacle re-mains the lack of a universal SOP with a set schedule for each process stage.

The common assessment is the RA preferred method for examining a different dossier section. Each authority reviews the dossier as part of a collaborative evaluation, and the results are discussed before making a decision. Training and lifelong learning as components of excellence. Training and ongoing education are essential elements that guarantee the agency employees have knowledge of relevant SOP regulations and processes and preserve uniformity in perfor-mance. Insufficient hands-on instruction, internal training programs, assistance for graduate studies in relevant fields, attendance at international meetings and seminars, and postings and assignments at other regulatory agencies are the primary areas that need improvement to achieve a better level of compliance.

The Ministry of Health's Registration Department is a reputable organization dating back to 1923, when it was orga-nized as the MoH's Medicines Directorate and began

regulating the pharmaceutical business. As a result, it is widely acknowledged that Iraq has an extensive RA scheme that has long allowed for approving of patients and their access to medications following their introduction in advanced nations like EMA and FDA. However, recent local develop-ments have severely impacted the clearance process and deadlines.

4. CONCLUSION

In conclusion, the study conducted by surveying the registry department within MoH provided valuable insights into the submission and evaluation timelines in Iraq's regulatory authority. The registration department oversees various aspects, including manufacturing facilities, advertising, laboratory examinations, marketing authorizations, and prod-uct licenses. The evaluation process involves scientific assessments conducted by the National Board for the Selection of Medicines and specialist committees, focusing on reviewing labeling and ensuring compliance with manufacturing facility standards.

Notably, recent years have witnessed an increase in approvals and improved timelines, which can be attributed to the involvement of more committees and reviewers. However, there is a need to further enhance the quality of the evalua-tion process by implementing Good Review Practices and standard operating procedures. These measures would con-tribute to uniformity, transparency, and efficiency in the approval queue.

The Registration Department in Iraq is crucial for regulating the pharmaceutical industry and ensuring patient medica-tion access. Emphasizing training, education, and standardization can improve compliance and operational excellence. A robust regulatory framework and continuous improvement are essential for optimizing patient care and facilitating timely access to safe medications..

5. RECOMMENDATIONS

An urgent need to develop a unified national guideline to regulate all pharmaceutical product registration and market-ing authorization in Iraq. Using identical analyzing and verification approaches when assessing new pharmaceutical products, especially in veterinary versus human products. Separating the regulatory body from the executive body to eliminate the main source of bias in the decision-making process. Creating a specialized auditing body to review the implementation of SOPs and to develop the gaps in guideline creation and evolution. Endorsing a continuous learning system where new staff regularly receive sufficient information on requirements and duties of each function, thus cre-ating a sustainable environment within the regulatory body. Harmonize process by aligning our operations with leading global agencies (stringent health authorities) to enhance workflow and optimize patients’ access to care

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7. COMPETING INTEREST

The authors declare there is no conflict of interest

8. AUTHOR CONTRIBUTIONS

Both authors have done the research article proposal, experiment design, explaining the findings, article writing, Statistical analysis, and review & editing.

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