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# A COMPREHENSIVE REVIEW ON DRUG REGULATORY GUIDELINES IN MIDDLE EAST AND THE NORTH AFRICAN COUNTRIES

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## ABSTRACT

The Middle East and North Africa (MENA) region presents a mix of opportunities and obstacles for drug companies seeking to register their products. Despite economic growth and a large population, navigating regulatory requirements and political complexities proves challenging but critical for accessing this important market. This analysis aims to evaluate registration procedures for pharmaceuticals in MENA countries, understand their constraints and potential, and provide insights for companies. While the drug market shows diversity, sustainability, and expansion driven by population size, oil wealth, higher incomes, education, a larger middle class, and disease burden, regulations and uncertainties curb progress. Regulatory bodies administer separate healthcare systems, but written laws are limited, mostly in local languages, open to interpretation, and hindered by lack of transparency or instability in some countries. Demand for advanced drugs and medical goods will likely increase, but navigating complex regulations and requirements presents difficulties. Each country issues guidelines for health authorities and export/import medication. Requirements encompass export applications, checklists, renewal registrations, lab standards, supplement registrations, application receipts, and appointment sheets. Public health services are managed differently, requiring country-specific knowledge. Opportunities abound for addressing health needs, but political and economic realities significantly impact regulations and companies' ability to access this market. Improving standards are dampened by ongoing

challenges. MENA remains an important yet complicated market for pharma companies to understand for registration and entry.

**KEYWORDS:** Regulations guidelines, MENA countries, Market access, Regulatory constraints, Common technical document.

## INTRODUCTION

Pharmaceuticals have become increasingly important on international agendas as health indicators are linked to a country's development. Laws and regulations surrounding pharmaceuticals have become more complex and politicized due to the rise in global trade. To protect public health, comprehensive laws and regulations need to be approved by governments, and national regulatory authorities established to ensure the appropriate regulation of medicines and access to accurate information. [1] The Middle East and North Africa (MENA) region (shown in Fig. 1), which consists of three sub-regions - Arabian Peninsula, Western Asia, and North Africa - has a diverse healthcare market with emerging market-type growth due to a growing population of 400 million people, increased Gross Domestic Product (GDP)/capita income, an improved literacy rate, and a larger middle class. [2] However, the main diseases in the region are metabolic in nature, such as obesity, hypertension, hyperlipidemia, and diabetes, resulting in high demand for medical treatment. The Gulf Cooperation Council (GCC) countries have a high prevalence of cardiovascular diseases, diabetes, cancer, obesity, tuberculosis, and other respiratory ailments. The late identification of fatal diseases such as colon cancer and breast cancer is due to a lack of disease awareness and prudery in the region. Healthcare spending as a percentage of GDP is estimated to be 6.4% in the Middle East/Africa, with spending expected to rise by an average of 10% annually in the coming years. Healthcare is one of the fastest-growing sectors worldwide, and the Middle East and Africa are expected to be the fastest-growing region in the future.[3]

This review article aims to examine the regulatory guidelines and challenges for pharmaceutical product registration in MENA countries, specifically in Saudi Arabia, Yemen, and Oman. Additionally, this article aims to explore the unique opportunities and prospects for international manufacturers in this market. The objective of this review article is to provide an overview of the roles and responsibilities of health authorities, requirements for drug registration, and the challenges faced by international manufacturers in the MENA market, with a focus on Saudi Arabia, Yemen, and Oman. Furthermore, this article aims to

analyze the findings of the study conducted on drug product registration in these three countries and provide insights into the regulatory environment's impact on the growth of the pharmaceutical and medical products market in the MENA region.

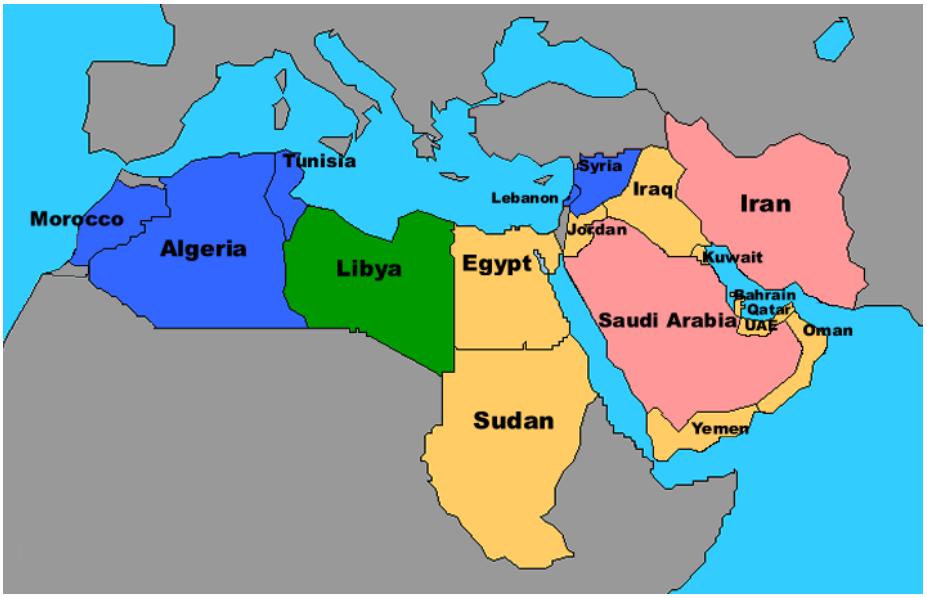


**Fig. 1: Map showing MENA countries.**

## PHARMACEUTICAL REGULATIONS IN MENA COUNTRIES

In MENA Region a study was conducted on Drug Product registration in 3 Different Countries viz., Saudi Arabia, Yemen, and Oman. Different modules and profiles related to pharmaceutical product registration in the MENA regions (shown in Fig. 2) are:

- Module 1 refers to administrative information, which includes details such as the name of the product, the manufacturer, and the intended use.
- Module 2 is the quality overall summary, which provides an overview of the quality of the product.
- Module 3 is the quality module, which includes information on the manufacturing process, specifications, and controls.
- Module 4 includes non-clinical study reports, which provide information on the safety and efficacy of the product in animals.
- Module 5 includes clinical study reports, which provide information on the safety and efficacy of the product in humans.

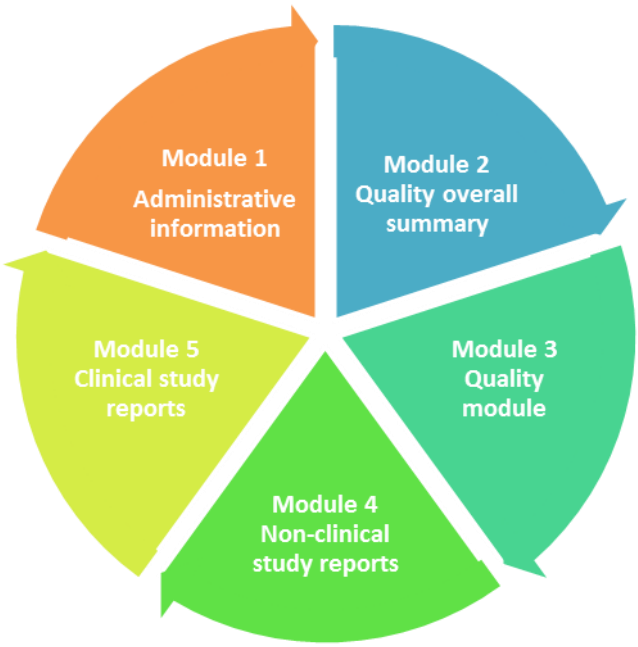


**Fig. 2: Different modules and profiles related to pharmaceutical product registration in the MENA regions.**

**Saudi Arabia**

Saudi Arabia seeks to approve an electronic dossier (eCTD dossier) for a medicinal product to be marketed in the region. The stability conditions required for the dossier are Zone IVb, with a temperature of $30^0$C ± $2^0$C and relative humidity of 75% RH ± 5% RH. A minimum of 12 months of stability data is required.[4]

The dossier of Saudi Arabia shall have the following modules:

**Module 1:** It contains the essential administrative documents and information specific to product registration in the kingdom. A cover letter addresses SFDA submitting the dossier for evaluation and approval of the product. A comprehensive table of contents with page references facilitates easy navigation and assessment of the dossier by regulators.

The application form provided by SFDA for registration of medicinal products in Saudi Arabia is duly completed with relevant details of the product including name, dosage form, strength, route of administration and description of the container closure system.[5]

A summary of quality, safety and efficacy of the product in the form of Summary of Product Characteristics (SPC) complies with Saudi guidelines ensuring proper usage of the product.

Product labelling including inner and outer labels in Arabic and English conforms to Saudi regulations.

Patient Information Leaflets (PILs) in Arabic and English educate patients about correct usage of the product. Separate PILs in the two languages are provided. Mock-ups or specimens of the proposed packaging demonstrate conformity to approved designs.

Samples of the product, reference standards, container closure and other materials are submitted as required for comprehensive evaluation by SFDA experts. Information on the qualifications and experience of experts involved in quality, non-clinical and clinical assessment of the product is detailed.[6]

Summaries of quality, non-clinical, clinical and other information as specified in Modules 3 to 5 provide essential details for evaluation of the product. Information on environmental risk assessment, use of non-GMO technologies, presence of GMO and pharmacovigilance including the system for safety monitoring post approval is included. The risk management plan addresses potential risks associated with the product.

Certificates of analysis, GMP certificates, free sale certificates and other documents from manufacturing and testing sites confirm compliance with approved standards ensuring quality, safety and efficacy of the product.

Module 1 collates all essential administrative details, documents and information related to registration and approval of the medicinal product in Saudi Arabia. The module facilitates comprehensive evaluation of the product by SFDA experts.[7]

**Module 2:** It contains the overall quality summary that outlines essential quality information of the drug substance and drug product to provide regulators an overview of the details presented in Module 3. The introduction specifies the proprietary name, non-proprietary name, dosage forms, strengths, route of administration and proposed indications of the product.[8]

Information on the manufacturer of the drug substance including general details and manufacturing process with flow diagram, source materials, critical steps, process controls, acceptance criteria and process validation is summarized. Major manufacturing changes, their assessment and studies using affected batches are cross-referenced.

Evidence of drug substance structure, isomerism including stereoisomers used in development and marketing is discussed along with tabulated characterization data and graphs. Specifications, analytical procedures, validation and batch analyses with graphs justify controls.

Reference standards and materials are listed in tabular form. The container closure system is briefly described and discussed.

Stability study details (conditions, batches, analytical procedures), results, conclusions on storage conditions and shelf life along with post approval stability protocol are summarized. Tabulated stability results and graphs demonstrate product stability.[9]

For the drug product, its description, composition, pharmaceutical development including formulations used in trials, dissolution profiles and manufacturing process with flow diagram, process validation, excipient quality, product specifications, analytical procedures, validation, characterization of impurities, reference standards, container closure system, stability studies and post approval protocol are discussed to establish quality, safety and efficacy.

Tabulated analyses with graphs under different sections justify controls while approving the medicinal product for marketing in Saudi Arabia. Overall, Module 2 presents a comprehensive yet summarized quality overview of the drug substance and drug product according to Saudi guidelines.

**Module 3**

This module contains the quality data including details of the active pharmaceutical ingredient (API) and finished pharmaceutical product (FPP). Module 3 specifies the API name, manufacturer, nomenclature, structure, properties, manufacturers, manufacturing process controls, material controls, critical step controls, validation, development, characterization, impurities, specifications, analytical procedures, validation, batch analyses, justification of specifications, reference standards, container closure, stability summary, commitments and data.[10]

A similar structure is provided for the FPP with details of description, composition, development, container closure, microbiology, compatibility, manufacturers, batch formula, process controls, critical step controls, validation, excipients controls, specifications, analytical procedures, validation, batch analysis, characterization impurities, justification of

specifications, reference standards, container closure and stability summary, commitments and data.

**Modules 4**

This module 4 establishes a standard structure for organizing nonclinical data in regulatory submissions. It specifies how the nonclinical information should be presented, but does not mandate which nonclinical studies are required. It only provides a template for organizing the nonclinical findings that have been obtained.[11]

**Module 5**

This module recommends organizing clinical study reports and related information in regulatory submissions to simplify preparation and review. It establishes a standard structure for arranging reports and data, specifying how biopharmaceutic studies, pharmacokinetics using human biomaterials, human pharmacokinetic studies, pharmacodynamic studies, efficacy and safety studies, post-marketing experience, case report forms, literature references, and a tabular study listing should be presented. Though it mandates no particular studies, it aims to facilitate submission and review by indicating an appropriate organization. Reports should only appear in one section, with cross-references used when objectives differ. Explanations are provided where information is missing. This structured approach streamlines the process of compiling and evaluating clinical data for regulatory approval of pharmaceutical products.[12]

**Yemen**

The Ministry of Public Health and Population of the Republic of Yemen seeks to approve a CTD dossier for a medicinal product. The required stability conditions are Zone IVb, temperature of $30^0$C ± $2^0$C and relative humidity of 75% RH ± 5% RH. A minimum of 12 months of stability data is necessary.[13]

The dossier of Yemen will comprise the following modules:

**Module 1**

This module collects the administrative documents required in each region for approving a pharmaceutical product. It includes information such as product details, manufacturer details, a copy of the manufacturing license, evidence of good manufacturing practice compliance, a

free sale certificate, product artwork, a power of attorney, a declaration of prohibited ingredient avoidance, and qualitative/quantitative formulations.[6]

The precise content and format of the module is specified by regulatory authorities based on regional requirements. Module 1 ensures all necessary administrative prerequisites for approval and marketing have been met. It establishes the legitimacy and standards compliance of the product and its manufacturer through compiled information and supporting documents.

**Module 2**

This module provides an overview of the pharmaceutical product, including details of its pharmacologic class, mode of action, proposed use, and a brief introductory paragraph. It contains sections on the CTD table of contents, introduction, Quality Overall Summary, nonclinical overview, clinical overview, nonclinical summaries, and clinical summary.[7]

The Quality Overall Summary (QOS) compiles key information from Module 3 on product quality into an integrated summary. It should only include data, justification and details also found in Module 3 and other CTD sections. The QOS gives reviewers enough Module 3 information to understand the product, emphasizes critical parameters, provides justification where guidelines differed, and discusses key issues integrating information from quality and other Modules, including cross-references.

The QOS aims for 40 pages to succinctly summarize most products, up to 80 pages for complex products like biologics. It gives quality reviewers an overview of the product's development, quality, and standards compliance evidence. The summary synthesizes details on manufacturing, specifications, controls, justification for non-standard approaches, and key data facilitating quality assessment and approval decisions.

**Module 3**

This module specifies the API name, manufacturer, nomenclature, structure, properties, manufacturers, manufacturing process controls, material controls, critical step controls, validation, development, characterization, impurities, specifications, analytical procedures, validation, batch analyses, justification of specifications, reference standards, container closure, stability summary, commitments and data.[8]

The FPP section details description, composition, development, container closure, microbiology, compatibility, manufacturers, batch formula, process controls, critical step controls, validation, excipients controls, specifications, analytical procedures, validation, batch analysis, characterization impurities, justification of specifications, reference standards, container closure and stability summary, commitments and data.

**Module 4**

This module establishes a standard format for organizing nonclinical reports submitted to regulatory authorities. It specifies how nonclinical information should be presented but does not indicate required studies. It merely provides a template for the nonclinical findings obtained.[9]

**Module 5**

Module 5 establishes a standardized and comprehensive structure for organizing clinical data submitted to support product approval. It recommends compiling a table of contents, tabular listing of all studies, and detailed reports categorized as follows:

Biopharmaceutic studies evaluate drug release and absorption, including bioavailability, comparative bioavailability/bioequivalence, in vitro-in vivo correlation, and bioanalytical methods. Pharmacokinetic studies using human biomaterials assess distribution, metabolism, excretion, protein binding and interactions. Human pharmacokinetic studies in healthy and patient populations consider influencing factors and population PK. Human pharmacodynamic studies evaluate dose-response and PK/PD relationships. [10]

Efficacy and safety studies include controlled trials for the claimed indication, uncontrolled trials, integrated analyses across studies, and other reports. Post-marketing experience documents utilization and any identified risks. Case report forms provide original patient data, and individual patient data may also be included. Literature references cite any relevant published research.

The placement of each study depends on its primary objective, with cross-references linking related studies. Explanations justify any missing information. This comprehensive yet standardized structure simplifies preparation for submission while enabling complete and efficient review. It thus facilitates the evaluation and approval of clinical data demonstrating

the product's safety, effectiveness, quality, and compliance with standards to support public access.

The objectives of Modules 4 and 5 are to standardize the organization and presentation of nonclinical and clinical study reports/data submitted for regulatory review and approval of pharmaceutical products.

**OMAN**

The Ministry of Health - Sultanate of Oman seeks to approve an eCTD dossier for a medicinal product. The required stability conditions are Zone IVb, temperature of $30^0$C ± $2^0$C and relative humidity of 75% RH ± 5% RH. A minimum of 12 months of stability data is necessary.

The dossier of Oman will comprise the following modules:

**Module 1**

This module compiles administrative documents required to approve a pharmaceutical product in each region. This includes a cover letter, table of contents, application form, product information, summary of product characteristics, labels, patient information leaflets in local languages, artwork/mock-ups, samples, expert information, and various certificates and declarations.

Quality-related documents certify GMP compliance, specifications, controls, purity, and stability across manufacturing, excipients, drug substance and finished product, considering alcohol content, pork content, TSE suitability, diluents/colorants in the formula, and patent information. They include a GMP certificate, certificate of pharmaceutical product (CPP), free sale certificate, certificates of analysis for drug substance, product, and excipients, declarations on alcohol, pork, TSE, etc.[12]

Regulatory submissions necessitate information on non-clinical, clinical and environmental risk assessments, pharmacovigilance systems and plans, letters of access to DMFs, price lists, and other relevant documents.

The submission also details the manufacturing facility's pharmacovigilance system, risk management plan, and any GMO-related information.

The content and format of Module 1 depends on specific regional requirements as administrative details and supporting evidence vary in each context. The module compiles all documents required to authorize marketing a pharmaceutical product in a given region before approval can be granted.

**Module 2**

This module provides essential context and guides reviewers to key information on a pharmaceutical product's quality and development. It begins with a high-level introduction summarizing the product, including name (proprietary/non-proprietary/common), company, dosage forms, strengths, routes of administration, pharmacologic class, mode of action, proposed use(s), and indication(s). Module 2 then outlines 7 sections compiling comprehensive yet standardized quality information: a CTD table of contents; introduction; Quality Overall Summary (QOS); nonclinical overview; clinical overview; nonclinical summaries; and clinical summary.

The QOS synthesizes Module 3 details into an integrated summary of 40-80 pages for most/complex products, outlining quality information without new data or justification. It ensures sufficient depth for quality reviewers to understand the product; emphasizes critical quality parameters; justifies non-standard approaches; and discusses key issues across quality and other Modules, including cross-references.[13]

Module 2 and its QOS provide a roadmap, facilitating efficient yet complete review of information demonstrating product quality, development, standards compliance, safety, and effectiveness for approval and marketing authorization. The comprehensive yet streamlined submission establishes legitimacy and substantiates applications enabling regulatory decisions regarding access.

**Module 3**

Module 3 comprehensively outlines the quality information required to approve a pharmaceutical product. It begins with a table of contents and then presents the "Body of Data" in outline format, indicating where information should be located without specifying extent or support. Content follows ICH guidelines as available but depends on regulatory guidance for all areas.

This module focuses on the drug substance, including general information, nomenclature, composition, properties, manufacturers, production sites/facilities, manufacturing process description/controls, reprocessing justification/data, specifications, analytical procedures, batch analyses, justification for specifications, container closure system, stability data, and container closure specifications/description.

General information specifies recommended INN, other names (compendial, chemical, company code), structures (NCE: formula, stereochemistry, molecular formula/weight; biotech: amino acid sequence, modifications, molecular weight), and properties (physicochemical, biological activity for biotech), Manufacturers list names, addresses, responsibilities and production sites/facilities involved, including contractors.[14]

The manufacturing process description commits to the described process for manufacturing the drug substance. It provides a flow diagram including formulae, weights, yields, starting materials, intermediates, reagents, chemical structures reflecting stereochemistry, operating conditions and solvents. A sequential narrative covers quantities of raw materials, solvents, catalysts and reagents for a representative batch, critical steps, process controls, equipment, operating conditions (temperature, pressure, pH, time). Alternate processes and any reprocessing justification with supporting data are provided.

Specifications, analytical procedures and batch analyses ensure quality and compliance. Justification is provided for release and shelf-life acceptance criteria.

The container closure system, stability data and related specifications/description also pertain to drug substance quality and safety. Module 3 specifies the API name, manufacturer, nomenclature, structure, properties, manufacturers, manufacturing process controls, material controls, critical step controls, validation, development, characterization, impurities, specifications, analytical procedures, validation, batch analyses, justification of specifications, reference standards, container closure, stability summary, commitments and data.

The FPP section details description, composition, development, container closure, microbiology, compatibility, manufacturers, batch formula, process controls, critical step controls, validation, excipients controls, specifications, analytical procedures, validation,

batch analysis, characterization impurities, justification of specifications, reference standards, container closure and stability summary, commitments and data.

**Module 4**

This module organizes non-clinical study reports to simplify preparation and review, ensuring completeness without specifying required studies. It indicates an appropriate format for included non-clinical data and evidence.[15]

**Module 5**

This module similarly organizes clinical study reports and related information to facilitate applications while remaining flexible. It recommends placing each report in one section, cross-referencing as needed, and explaining any exclusions.

Module 5 begins with a table of contents for included reports. It then specifies a tabular listing of clinical studies including information like objectives, design, location, duration, sample size/characteristics, treatments, endpoints/measures, results, and conclusions. Studies are listed in the sequence described for report placement. Deviations from this sequence are noted and justified.[16]

Organized reports include biopharmaceutical studies (bioavailability, comparative bioavailability/bioequivalence, in vitro-in vivo correlation, related bioanalytical methods), studies using human biomaterials (plasma protein binding, hepatic metabolism, drug interactions, other materials), human pharmacokinetic studies (healthy subject PK/tolerance, patient PK/tolerance, intrinsic/extrinsic factor effect, population PK), human pharmacodynamic studies (healthy/patient PD/PK-PD), efficacy and safety studies (controlled clinical studies for a claimed indication, uncontrolled studies, integrated analyses across studies, other reports), post-marketing experience, and case report forms/individual patient data. Literature references are also provided.

**Similarities and differences in drug product registration in Saudi Arabia, Yemen, and Oman**

Saudi Arabia seems to follow ICH guidelines most closely, as Module 2 specifies following ICH guidance where available for content and and Modules 4 and 5 indicate ICH recommendations for organizing non-clinical and clinical information. Saudi Arabia may thus have the most aligned and streamlined process, though still tailored to its needs.[14]

Yemen's guidelines are the least specific, merely indicating an appropriate format and organization for included information without specifying details. This could make the Yemen process more flexible but also less transparent or predictable. Applicants would need to determine requirements through consultation.[15]

Oman provides some intermediate level of detail, outlining required information and recommended structures, but not citing ICH guidelines. Its process may be reasonably straightforward but require more effort to compile all necessary evidence and align with expectations.[16]

In summary, Saudi Arabia likely has the most straightforward and transparent guidelines, enabling easier navigation and compliance. Oman would require moderate additional effort, while Yemen's process could potentially be the most challenging to work with given limited published guidelines. The key similarities and differences between these countries are listed out in Table 1.

**Table 1: Similarities and differences in drug product registration in Saudi Arabia, Yemen, and Oman.**

| Similarities | Differences |
|---|---|
| **Stability conditions:** Zone IVb climate, 30°C ± 2°C temperature and 75% RH ± 5% RH humidity across Saudi Arabia, Yemen and Oman.<br>**Minimum stability data requirement:** 12 months stability data required for approval in all 3 countries.<br>**Dossier structure:** The dossier includes Administrative Information (Module 1), Quality Overall Summary (Module 2), Quality (Module 3), Non-clinical study reports (Module 4) and Clinical study reports (Module 5) for all products registered in Saudi Arabia, Yemen and Oman. | **Type of dossier:** Saudi Arabia and Oman require eCTD dossier while Yemen requires CTD dossier.<br>**Requiring health authority:** Saudi Food & Drug Authority (SFDA) in Saudi Arabia, The Republic of Yemen Ministry of Public Health and Population (MoPHP) in Yemen and Ministry of Health –Sultanate OF Oman (MoH) in Oman.<br>**Detailed requirements:** The specifications, analytical procedures, validation requirements, characterization of impurities etc. under Module 3 may differ in the 3 countries based on their guidelines.<br>**Timelines:** The timelines for submission, review and approval of dossiers can vary in Saudi Arabia, Yemen and Oman based on their regulatory review processes.<br>**Fees:** The registration and approval fees applicable would depend on the regulations in Saudi Arabia, Yemen and Oman. |

**MENA countries versus other countries in drug product registration**

Process requirements tend to vary based on a country's regulatory capacity, priorities and standards alignment. More established agencies like US FDA, UK MHRA, EU EMA generally have the most comprehensive, science-based processes aligned with international norms (ICH). Emerging agencies often have more limited guidance, relying more on discretion or adapting other countries' frameworks.[17]

The scope and standards of evidence demanded for approval can differ substantially based on factors like a country's economic development, health system capabilities, disease burden, risk tolerance, etc. This impacts things like requirements for non-clinical/clinical studies, post-approval reporting, etc. More limited health systems may demand less data for access. Developed systems expect more substantial evidence of safety, effectiveness and quality.

Bureaucracy and resource constraints can also impact a country's ability to implement and consistently apply regulation. Clear guidelines alone do not guarantee a transparent, streamlined and objective process if overburdened staff have limited capacity to properly review complex applications and evidence. Corruption also poses risks to regulatory integrity in some contexts.[18]

Mutual recognition of registrations can help facilitate global access, e.g. WHO prequalification helps accept some registrations in developing countries. But regulatory harmonization requires significant investments of time, expertise and coordination. Bilateral/multilateral agreements provide another path to leveraging other rigorous reviews rather than each country developing its own standards anew.[19]

The balance of flexibility versus consistency also depends on a country's priorities and abilities. More flexibility may be preferred when capacity is limited, enabling tailoring of huge evidence demands. But too much subjectivity risks lack of transparency, objectivity or predictability which are key regulatory aims. Consistency helps ensure integrity, fairness and a "level playing field".

## CONCLUSION

It can be concluded that obtaining global marketing approval and launch in all regions simultaneously is impractical due to differences in regulatory requirements. Manufacturers should carefully assess market interest, costs, target regions, and regulatory requirements

before developing drugs, and define a clear regulatory strategy based on different patent terms, application possibilities, data requirements, and deadlines for launching products in different regions. Harmonization of requirements is necessary to avoid duplication of work and waste of resources. Examining markets individually can lead to improvements in regulatory barriers and ensure access to safe and effective medicinal products, which is the critical purpose of drug registration.

## REFERENCES


1. K. Anilkumar, K.I. Anitha, 18 Clinical Research—History of Regulations, Clinical Aspects of Functional Foods and Nutraceuticals, 2014; 257.
2. A. Arouri, The evolving clinical research environment in MENA region, 2014.
3. C. Breen, C. El Safadi, H. Huigens, S. Tews, K. Westley, G. Andreou, R.O. Vazquez, J. Nikolaus, L. Blue, Integrating cultural and natural heritage approaches to Marine Protected Areas in the MENA region, Marine Policy, 2021; 132: 104676.
4. S. Colombo, 'Principled Pragmatism'Reset: For a Recalibration of the EU's Diplomatic Engagement with the MENA Region, IAI Papers, 2021; 39.
5. S. Colombo, E.S. i Lecha, M. Otte, A Half-Empty Glass: Limits and dilemmas of the EU's Relations to the MENA Countries, MENARA Working Papers, 2019; 32.
6. A. Deep, G. Khurana, J. Kumar, A. Monga, Comparison of regulatory requirements for registration of pharmaceutical drugs in ASEAN and GCC regions, Applied Clinical Research, Clinical Trials and Regulatory Affairs, 2019; 6: 62–70.
7. N. Dellepiane, B.D. Akanmori, S. Gairola, S.S. Jadhav, C. Parker, C. Rodriguez, S. Srivastava, Regulatory pathways that facilitated timely registration of a new group A meningococcal conjugate vaccine for Africa's meningitis belt countries, Clinical Infectious Diseases, 2015; 61: S428–S433.
8. N. Dellepiane, S. Pagliusi, R.E.W. Group, Challenges for the registration of vaccines in emerging countries: differences in dossier requirements, application and evaluation processes, Vaccine, 2018; 36: 3389–3396.
9. D.A. Diaz, M. Lynch, M. McMahon, R. Oblessuc, S.T. Colgan, Science and Risked-Based Stability Testing Strategies—a Test Case on the Global Implementation and Regulatory Reception, The AAPS Journal, 2020; 22: 1–11.
10. A. Djeflat, National systems of innovation in the MENA region, World Bank Institute Report, Washington, 2004.

11. G. Faour, M. Mhawej, A. Fayad, Detecting changes in vegetation trends in the Middle East and North Africa (MENA) region using SPOT vegetation, Cybergeo: European Journal of Geography, 2016.
12. A. Fasseeh, R. Karam, M. Jameleddine, M. George, F.B. Kristensen, A.A. Al-Rabayah, A.H. Alsaggabi, M. El Rabbat, M.S. Alowayesh, J. Chamova, Implementation of health technology assessment in the Middle East and North Africa: comparison between the current and preferred status, Frontiers in pharmacology, 2020; 11: 15.
13. D.W. Harron, Technical requirements for registration of pharmaceuticals for human use: the ICH process, The Textbook of Pharmaceutical Medicine, 2013; 447–460.
14. V.S. Janjal, S.R. Dhamodkar, Y.P. Jadhao, S.B. Manmode, A.K. Pawar, H.R. Khandelwal, Recent drug regulatory affair and CTD module progress review for submission of pharmaceuticals product, GSC Biological and Pharmaceutical Sciences, 2021; 16: 200–221.
15. K. Kausch, Competitive multipolarity in the Middle East, The International Spectator, 2015; 50: 1–15.
16. E. Mashaki Ceyhan, H. Gürsöz, A. Alkan, H. Coşkun, O. Koyuncu, S. Walker, The Turkish medicines and medical devices agency: comparison of its registration process with Australia, Canada, Saudi Arabia, and Singapore, Frontiers in Pharmacology, 2018; 9: 9.
17. P. Patel, J.K. Badjatya, M. Hinge, Comparative study of Regulatory requirements of Drug Product in Emerging market, International Journal of Drug Regulatory Affairs, 2019; 7: 48–62.
18. A.S. Rathore, A. Bhargava, Regulatory considerations in biosimilars: Middle East and Africa regions, Preparative Biochemistry & Biotechnology, 2021; 51: 731–737.
19. N. Sahoo, P. Manchikanti, Herbal drug regulation and commercialization: an Indian industry perspective, The Journal of alternative and complementary medicine, 2013; 19: 957–963.