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An Appraisal of Good Regulatory Review Practices in the Gulf Cooperation Council States

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Abstract

The aim of this study was to evaluate how each Gulf Cooperation Council (GCC) regulatory authority is building quality into the assessment and registration process and to establish opportunities for the exchange of best practice between the GCC states. A questionnaire was completed by the 7 Gulf States (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates [UAE], and Yemen), which provided details of the quality attributes that characterize the extent of the scientific assessment in the region. The results showed that each authority has its unique practices that characterize their 7 milestones in comparison with the other GCC authorities. Bahrain uses good review practice (GRP) guidelines and has placement arrangements in competent authorities, while Kuwait has separate pricing and registration departments. Oman engages external audit programs from accredited bodies, while Saudi Arabia and UAE conduct formal training for their assessors.

Keywords

good review practice; regulatory review; quality measures; assessment templates

Introduction

Drug regulatory authorities are constantly challenged to develop and improve their capacity to regulate pharmaceutical products. Therefore, it is critical to develop regulations based on 2 broad objectives: firstly, to provide technical assistance in establishing and implementing effective strategies for monitoring quality and correcting deficiencies[1]; and secondly, to refine existing methods to ensure optimal regulatory services through an applied quality management program. The regulations must be broad enough to address all the essential issues, but flexible enough to be applied to specific problems.[2]

In the world of medicine regulations, the term *quality* is normally associated with data on the pharmaceutical characteristics of the medicinal product and the processes for chemical and manufacturing control (CMC).[3] Increasingly however, *quality* is also being used in discussions of the drug regulatory process itself. It is not enough to measure regulatory performance in terms of timelines and the speed of the review process. The quality of the process, from the construction of the dossier to the ultimate regulatory decision, must also be monitored.[4] Regulators have different definitions of *quality*, but they all agree that the term is defined in the light of the provider's standards and patient's expectations. The degree of quality is the extent to which quality of care is expected to achieve the most favorable balance of benefits to risks.[5]

This study assesses and compares the quality of the review process conducted in the 7 Gulf States that comprise the Gulf Cooperation Council (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates [UAE], and Yemen). It provides a clear understanding of the current situation and a valuable insight into aspects of their good review practices.

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Methodology

Study Instrument

A questionnaire was designed to examine the activities that contribute to the quality of the review processes and measures adopted to improve consistency, transparency, timeliness, and competency. The questionnaire was piloted with 2 regulatory authorities, Kuwait and Saudi Arabia, to ensure its practicality and appropriateness for the region.

All authorities were able to complete the questionnaire on time. The data were then standardized into a document file, and the resulting reports were sent to the authorities for auditing, correction, and comment in 2010. The participating authorities were contacted by email to confirm the accuracy of the information contained in the respective country reports.

The questionnaire consists of 6 sections: general measures used to achieve quality, quality management tools, communication as an element of quality, training and continuing education, transparency of the review procedure, and the drivers and barriers to achieving a quality review. Moreover, open- and close-ended questions were used, and the study participants provided detailed explanations to clarify points related to the individual questions.

Results

General Measures Used to Achieve Quality

Six quality measures were considered critical in the evaluation of the regulatory review process in the GCC states, namely, quality policy, good review practice (GRP), standard operating procedures (SOPs), assessment templates, peer review (external and internal), and joint and shared reviews. The measures currently used by each regulatory authority in the region to achieve a high quality review process are shown in Figure 1, and the results indicated that a joint review is the only quality measure shared by all 7 GCC authorities.

Quality Policy

An organization's quality policy is its overall intention and direction related to quality as formally expressed by top management. It aims to improve the performance of the reviewers, to establish whether the outcome of the review process is acceptable, and whether the registration procedure fulfils the desired quality standard. Four out of 7 authorities stated that they have quality policies (Bahrain, Kuwait, UAE, and Yemen), whereas the other 3 are planning to introduce them in the foreseeable future.

Good Review Practice (GRP)

The 7 authorities were asked whether they implement a GRP, defined as a code about the process and documentation of review procedures that aims to standardize and improve the overall documentation and ensure timeliness predictability, consistency, and high quality reviews and review reports. Only Bahrain stated that they implement a GRP system, while Kuwait explained that the Ministerial Decree 302/80 is being used as an appropriate guidance for both assessors and the industry throughout the scientific assessment process.

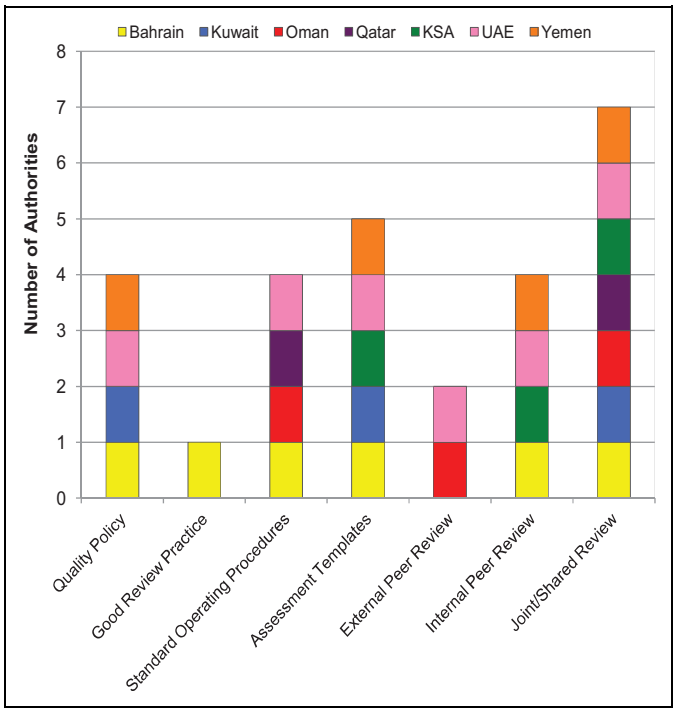

Figure 1. The current measures used to achieve quality in the Gulf Cooperation Council review processes.

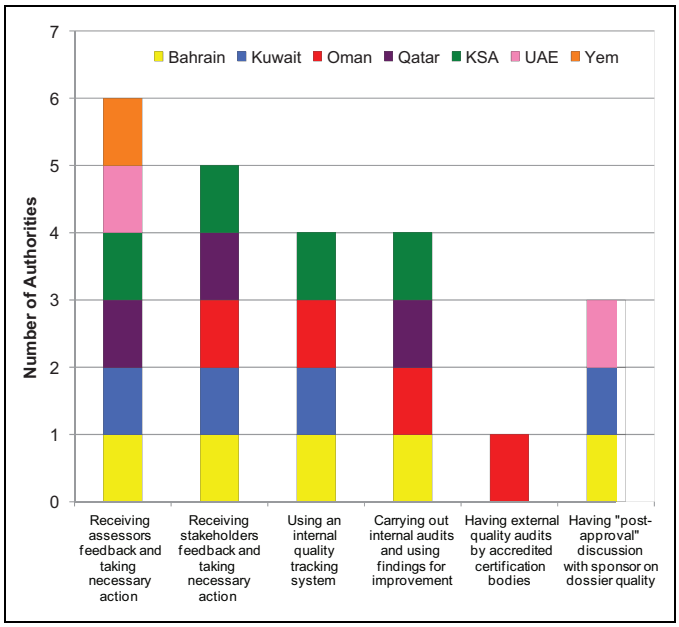

Figure 2. The quality audit and feedback activities in the Gulf Cooperation Council states.

Table 1. Description of the Scientific Committees in 5 Gulf Cooperation Council Authorities

Description	Bahrain	Oman	Saudi Arabia	UAE	Yemen
Committee	RC	TCR&P	SAC	SC + HRC	TCR
Meeting frequency	Once a month	Every 2 weeks	Once a week	Every 2 months	Once a week
Number of members	8	8	19	5 (average)	14
Committee reviews all applications (NASs/EASs)	×	✓	✓	✓	✓
Committee reviews selected applications (NASs/EASs)	✓	×	×	×	×
Committee review complete dossier	×	×	✓	×	✓
Committee reviews assessment reports from reviewers	✓	✓	×	✓	×
Committee makes the final approval decision	✓	✓	✓	×	✓

EAS, existing active substance; HRC, Higher Registration Committee; NAS, new active substance; SAC, Scientific Advisory Committee; SC, Scientific Committee; RC, Registration Committee; TCR, Technical Committee for Registration; TCR&P, Technical Committee for Registration of Pharmaceutical Companies and their Products and Pricing.

Table 2. Electronic Facilities for Registering and Tracing Applications in the Gulf Cooperation Council States

Electronic facilities	Bahrain	Kuwait	Oman	Qatar	Saudi Arabia	UAE	Yemen
Electronic system for registering and tracking application available	×	×	✓	×	✓	✓	✓
Tracking application that are under review and identifying the stage in the process	×	×	✓	×	✓	✓	✓
Signaling that target review dates have been exceeded	×	×	✓	×	✓	×	×
Recording the terms of the authorization once granted	×	×	✓	×	✓	✓	✓
Archiving information on applications in a way that can be searched	×	×	✓	×	✓	✓	✓

Table 3. Interactive Relationship Between the Sponsor and the Gulf Cooperation Council Authorities

	Bahrain	Kuwait	Oman	Qatar	Saudi Arabia	UAE	Yemen
Methods of communicating regulatory information and guidelines to the industry							
Through the authority's official website	×	×	✓	×	✓	×	✓
On-request	×	✓	×	✓	×	✓	✓
Through official publications	✓	×	×	×	×	✓	×
Presubmission advice is provided	✓	✓	×	×	×	✓	×
Applicant receives details of the technical staff that can be contacted to discuss the application during the review process	✓	×	×	×	×	✓	✓
Level of contact with the authority's staff during the review process							
Extensive formal contact (including scheduled meetings)	✓	✓	×	×	×	✓	×
Extensive informal contact (frequent telephone or email contacts)	✓	×	×	×	×	✓	×
Some formal contact (possibly of meetings)	×	×	×	✓	✓	×	✓
Some informal contact (possibly of telephone or email contacts)	×	×	✓	✓	✓	×	×

However, Kuwait as well as the other Gulf States are planning to implement a full GRP system in the future.

Standard Operating Procedures (SOPs)

This measure is defined as the formal documents that clearly and accurately describe how an individual or organization should be performing a certain task. The purpose of a SOP is to carry out the procedures correctly and always in the same manner, and it should be available at the place where the work is done. In the GCC states, 4 out of 7 countries (Bahrain, Oman, Qatar, and UAE) use SOPs for the guidance of scientific reviewers, whereas the other 3 expressed their intentions to implement this quality measure in the future.

Assessment Templates

Five out of the 7 authorities in the region (Bahrain, Kuwait, Saudi Arabia, UAE and Yemen) used assessment templates for reports on the scientific review of a new active substance (NAS) and an existing active substance (EAS). These templates are an important quality measure that set out the content and the

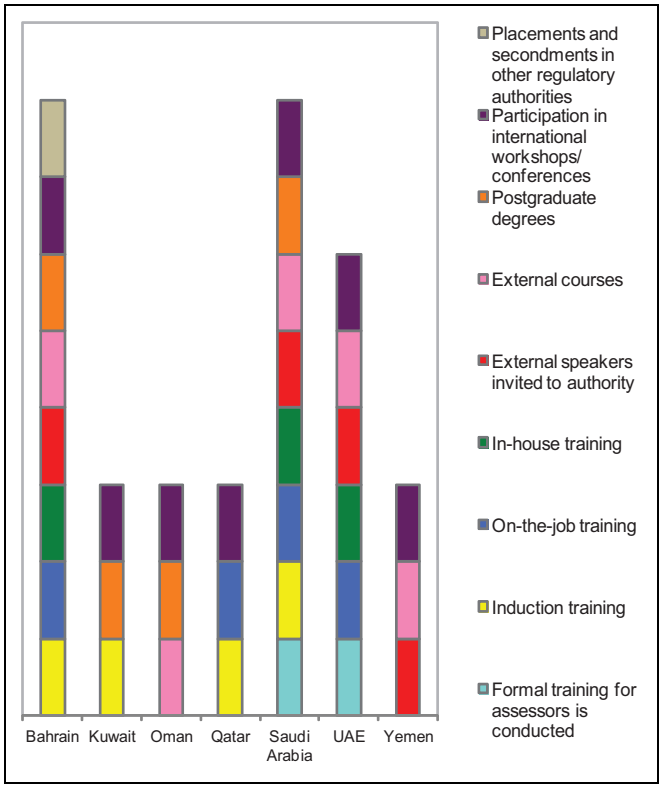

Figure 3. Training and continuing education in the Gulf Cooperation Council regulatory authorities.

format of the written scientific assessment reports. Oman and Qatar indicated that they intend to introduce assessment templates in the near future. These, coupled with SOPs, form an essential component for the implementation of GRPs.

Peer Review

Four out of 7 authorities (Bahrain, Saudi Arabia, UAE, and Yemen) stated that they performed internal peer reviews through their established scientific committee, which evaluates the reviewer's assessment reports, while only 2 authorities stated that they, in addition, carry out external peer reviews to ensure that the registration dossier is of the desired quality. Kuwait and Qatar did not perform peer reviews, as they were totally dependent on the qualification and experience of the reviewer. However, Qatar has a registration committee that makes the final approval decision if the assessment report shows a positive outcome. In Kuwait, the drug registration and release superintendent (DRRS) reviews the scientific report made by the assessor and makes the final decision.

Joint/Shared Reviews

A *joint review* was described as a procedure where the whole dossier is reviewed by each authority and the outcome discussed before the decision is taken by agreement between the 7 member states. The Gulf States adopted this initiative from the European centralized procedure, where joint reviews of the registration dossier are carried out by the EU member states. All the authorities stated that they conduct joint reviews as part of the GCC central drug registration (GCC-DR) system. In a

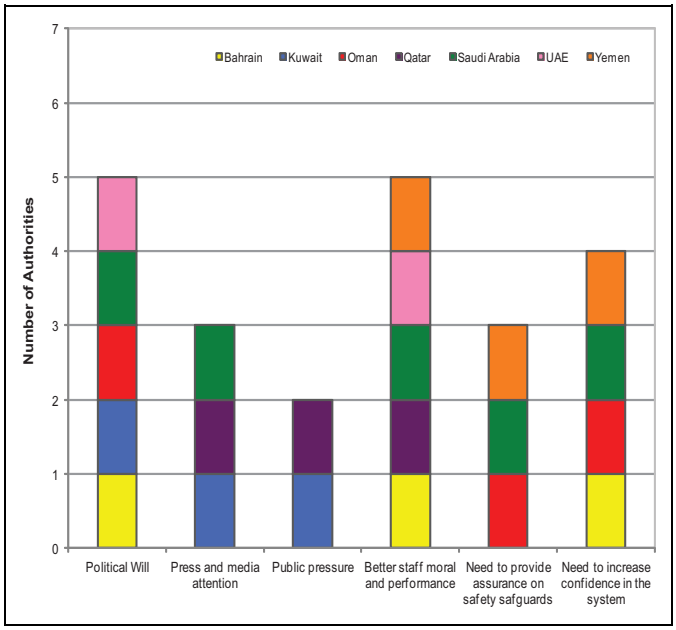

Figure 4. Transparency as an element of quality in the Gulf Cooperation Council regulatory review procedure.

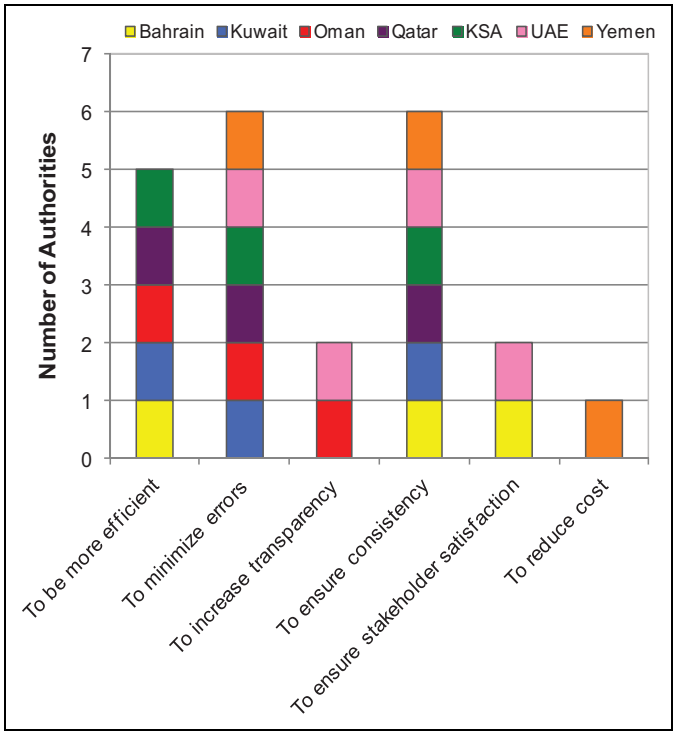

Figure 5. Reasons for introducing quality measures in the Gulf Cooperation Council review procedures.

Table 4. Drivers and Barriers to the Quality Review Process in the Gulf Cooperation Council States

Country	Drivers	Barriers
Bahrain	Easy access Good communication Clear guidelines	No accreditation from trusted drug authorities Inadequate PMS studies Marketing status in the country of origin
Kuwait	Well-established system Supportive government Variety of scientific qualifications	No QA policy system in place No project management planning No electronic handling for product dossier
Oman	Good tracking system Following a scheme of assessment Good management plan Reviewers are well qualified	Shortage of experience and personnel No independent budget No internal quality policy
Qatar	Need of access of new drugs to patients Emergence of new diseases The desire for advancement	Shortage in manpower Increasing workload due to growing market Weak follow-up
Saudi Arabia	E-communication with applicants E-environment (EURS ECTD).	Delayed response of companies Inappropriate responses from companies
UAE	Utilizing reference countries' approvals Flexibility and understanding	Lack of human resources Lack of laboratory technical resources. Complex administrative and hierarchy structure and appointments systems
Yemen	Well-trained, qualified persons Written SOPs for reviewers Archiving information database	Current programs need updating Registration department and QC laboratory are overloaded with products and applications. Shortage in working facilities (eg, computers, technical references)

EURS ECTD, European Review System, Electronic Common Technical Document; QA, quality assurance; QC, quality control; SOP, standard operating procedure.

shared review, however, each authority takes responsibility for reviewing a separate part of the dossier.[6] This approach is not carried out in the GCC regulatory system.

Quality Management Tools

Quality Audits and Feedback

The Gulf States implemented a number of measures for continuous improvement, including quality audits and feedback activities as described in Figure 2. Internal audits typically involve the organization auditing different units or processes. External audits are normally carried out by accredited certification bodies, for example the International Organisation for Standardisation (ISO) and the European Foundation for Quality Management (EFQM). These quality audits are essential to provide the authorities with the feedback required to improve the quality of the review process. Four authorities carry out internal audits (Bahrain, Saudi Arabia, UAE, and Yemen) whereas only 1 authority performs an external audit (Oman). In addition, 3 authorities (Bahrain, Kuwait, and UAE) conduct "post-approval" discussions with the sponsor, which is an effective way to provide feedback on the quality of the dossier and obtain the company's comments. This is an important practice to exchange constructive feedback between the 2 parties for the benefit of the review outcome.

Quality Assurance Infrastructure

Only Kuwait and Yemen stated that they had dedicated departments or units for the quality assurance of the assessment and registration process. Kuwait has a small unit consisting of 2 pharmacists, although its functions are not fully regulated or enforced in the current organization. UAE stated that its quality assurance department was not limited to assessment and registration processes, and covers all aspects of medical practice and licensing.

Scientific Committee Procedure

Committees are a necessary aspect of organizations of any significant size, and they formally draw together people of relevant expertise from different parts of an organization to share information and coordinate activities resulting in the widening of viewpoints and sharing of responsibilities. Kuwait and Qatar do not have scientific committees, whereas Qatar does have a registration committee that makes the final approval decision (Table 1). In 4 authorities (Saudi Arabia, Yemen, Oman, and Bahrain), the committees are responsible for assessing the applications and making the final approval decision. In UAE however, separate scientific committees exist for each area (e.g., stability, quality control, Good Manufacturing Practice, bioequivalence studies, minor variations, internal peer reviews, and external screening committee). All reports of the scientific

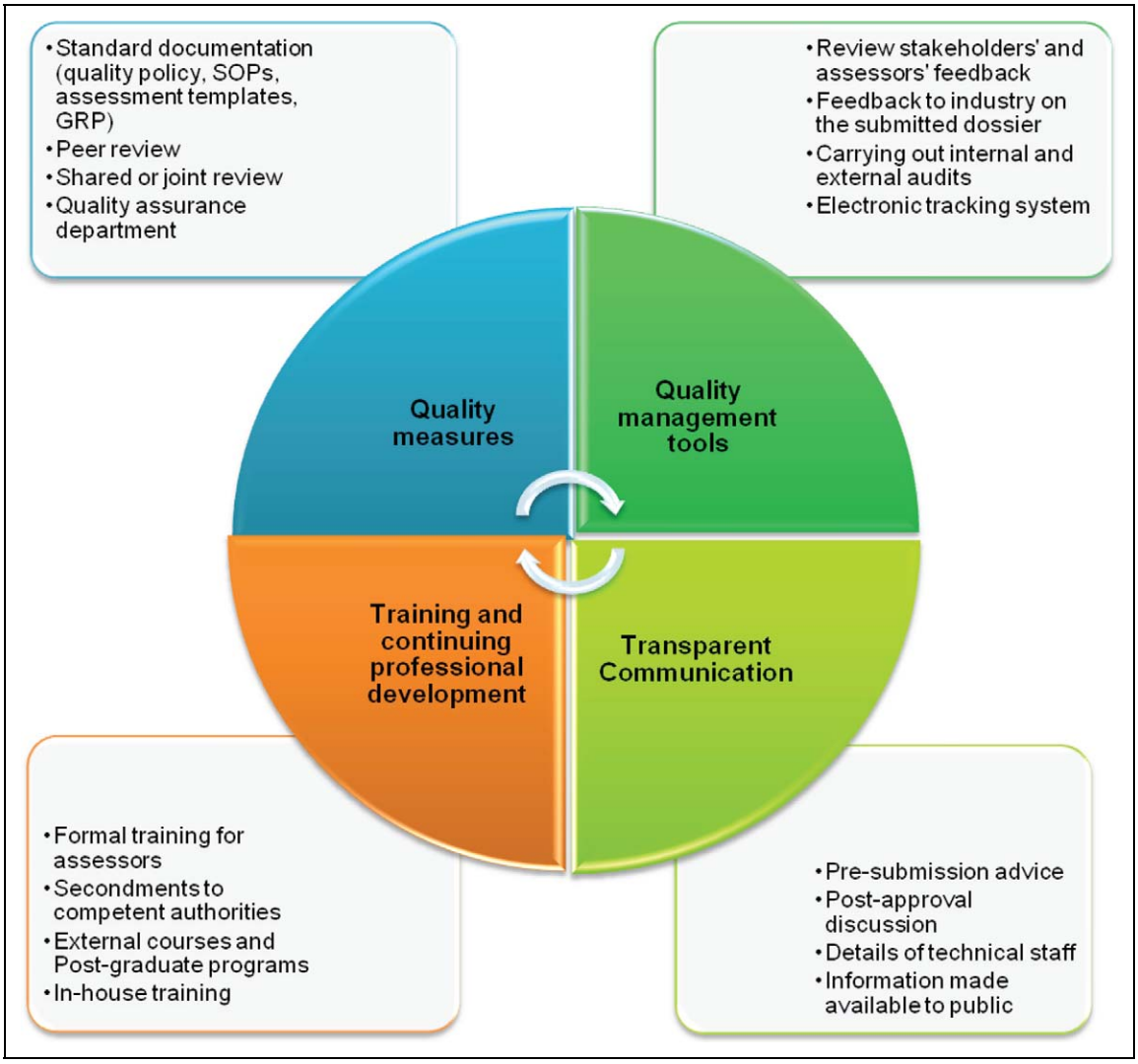

Figure 6. Balanced scorecard framework for the types of quality measures and activities included in the study on the Gulf Cooperation Council regulatory authorities.
Source: Template adopted from www.bscdesigner.com.

committees are then discussed in the higher registration committee after the scientific committees have given their opinions, and it is this committee that makes the final approval decision.

Information Technology (IT) Infrastructure

Four authorities (Saudi Arabia, Oman, UAE, and Yemen) already have in place an electronic system for registering and tracking applications, recording the terms of the authorization once granted, and archiving information on applications in a way that can be searched (Table 2). Saudi Arabia is the only authority in the region that is placing considerable effort and resources to improve the quality of the review process such as electronic common technical document (eCTD) and electronic tracking systems.

Even though these facilities are available, the sophistication and the know-how of the system can differ between the 4 authorities. Only 2 authorities (Saudi Arabia and Oman) have an electronic system that signals delays in the review process; this is an important tool to control and monitor the approval timeline for pharmaceutical products.

Communication as an Element of Quality

The most prevalent method for providing official information and guidelines to assist the industry in the registration of medicinal products is "on request." UAE provides the guidelines in the customer service desk, as they are available during official office hours on a purchase basis. Three authorities provide official guidelines through the official authority's website, which is the most convenient method for the companies.

In general, formal contact through scheduled meetings and official letters as well as informal contacts through telephone, email, or fax occurred between the sponsors and the authorities (Table 3). It may be an extensive form of contact, as occurs in Bahrain, Kuwait, and UAE; or less extensive, as occurs in Oman, Saudi Arabia, Qatar, and Yemen. The importance of keeping the lines of communication between the 2 parties cannot be overemphasized, and a successful and timely completion of the review process largely depends on the degree and quality of the communication. This is particularly useful when presubmission advice is required by the sponsor to have a better understanding of the registration system and the associated requirements to approve their pharmaceutical product. This occurs in Bahrain, Kuwait, and UAE. Furthermore, a rational practice to enhance communication is to allow it to occur between the pharmaceutical company and the authority's internal staff. This practice is carried out in Bahrain, UAE, and Yemen. However, the other authorities apply restrictions to such practices to prevent the culture of corruption from creeping into the system.

Training and Continuing Education as an Element of Quality

To maintain and improve the quality of the review process, it is essential that reviewers are involved in training or refresher courses as part of their continuous professional development (CPD) needs. In certain cases it may be worthwhile to second someone to another authority for a certain period to get in-service training and experience in a different regulatory culture. Ideally, after training or attending a course, the reviewer should report and convey his/her experience or knowledge to colleagues and top managers and make proposals for any change to existing procedures or adoption of new practices to improve the overall performance of the reviewing staff. Tests to assess the proficiency of the reviewer are another method to ensure that the required knowledge and skills have been successfully absorbed by the reviewer.

Training the reviewers in the Gulf authorities is essential to ensure the work is carried out in a professional manner. Only Saudi Arabia and UAE have formal training for the assessors. Most of the Gulf authorities believe that they have continuing education programs, but these programs are not necessarily focused on the review process. Saudi Arabia is believed to be the first country to take a positive initiative toward properly training the reviewers in the new Saudi Food and Drug Authority (SFDA) (Figure 3).

Transparency of the Review Process

Transparency is an important element to ensure that the review process is moving toward the desired direction and producing the quality standards that are acceptable to both the authority and other regulatory stakeholders. All the authorities believed that transparency is essential in their relationships with the public, professionals, and the industry (Figure 4). It was found that no one incentive for transparency was shared by all 7 Gulf States and that the 3 most prevalent incentives in the region were political will, better staff moral and performance, and the need to increase confidence in the system.

Drivers and Barriers

The most important reasons for the introduction of quality measures and the activities performed by the 7 authorities to bring about improvement in their regulatory review processes is shown in Figure 5. The most commonly stated reasons were to minimize errors, to ensure consistency, and to increase efficiency in the GCC review systems.

Understanding the drivers and barriers to achieving a quality regulatory review process can promote innovative and creative ideas and practices to help reviewers assess new products and underline the importance of monitoring the quality of the review process. This provides the regulators with the information to continuously educate themselves to establish a wealth of knowledge and professionalism that increases confidence in the regulatory system and stimulates transparency to the public, health care professionals, and the industry.

Each of the 7 authorities were asked to list 3 unique factors that contribute to the effectiveness and efficiency of its review procedures and 3 that act as barriers to making new medicines available in a timely manner. In reviewing the responses from each of the Gulf States, a variety of factors emerged, as listed in Table 4, related to the authority's distinctive environment, current political situation, and the governmental level of autonomy. In general, the major barrier was identified as shortage of manpower and resources, whereas the major driver was good communication.

Discussion

This study is particularly important in underlining that limited data available on review timelines does not necessarily imply a poor performance level. It is increasingly recognized that determination of quality management tools is a more appropriate indicator of regulatory performance.[7] Therefore, in order for the GCC authorities to build quality into their regulatory practices, they need to create a balance between 4 quality assurance attributes, namely, quality measures, quality management tools, training and continuing professional development, and transparent communication. This can be achieved using a balanced scorecard framework, shown in Figure 6.

Quality measures, such as SOPs, assessment templates, GRPs, internal and external peer reviews, and shared and joint reviews, are the first aspect in the proposed balanced scorecard framework that are considered essential practices for ensuring consistency, accuracy, competency, and efficiency of the

review process. These can be secured if the respective authority has an independent quality assurance (QA) department. Furthermore, the GCC authorities need to focus their efforts on the quality management tools which comprise activities that ensure the achievement of best outcomes from the managerial and technical staff by using them effectively and efficiently.[8] These activities include reviewing stakeholders' and assessors' feedback, providing feedback to the pharmaceutical companies on the submitted dossier, carrying out internal and external audits, and establishing an electronic tracking system for monitoring the approval process in each of the 7 authorities (Figure 6).

Training and CPD programs involve engaging experts in association with the authorities' staff to improve the quality of their assessment through knowledge and skill transfer.[9] These programs are critical for the advancement of the GCC regulatory systems because they motivate the employees to be more efficient, increase their capacity to adopt new technologies and methods, reduce staff turnover, and enhance creativity and innovation. This can be achieved by conducting formal training programs for assessors, providing placements and secondments to competent authorities, attending external courses and postgraduate programs, and carrying out in-house and/or on-the-job training (Figure 6). Lastly, transparent communication is an important aspect for building quality into the GCC regulatory systems. Effective communication ensures knowledge transfer, saves resources and enhances the relationship between the sponsor and the authority, increases the employees' confidence and job satisfaction, and prevents confusion and misunderstanding of the delivered message regarding sensitive issues. Transparency builds trust between the 2 parties through sharing knowledge, continuous follow-up, consistency, and predictability of outcomes.[10] These can be achieved by providing presubmission advice and increasing the level of information made available to the public. Furthermore, postapproval discussion between the sponsor and the authority is a critical practice to improve the quality of the review process and the submitted dossier, which will enhance the level of trust between the 2 organizations. This improves the assessors' knowledge and skills in handling a quality review more efficiently and effectively.

Conclusion

The 7 GCC states have well-established authorities that demonstrate their experience in the registration process, a good degree of communication, a cooperative attitude, and the desire for continuous development. These positive characteristics provide the basic groundwork for the implementation of critical quality management systems that can achieve standardized good review practices in the region. The authorities should consider adopting a standardized assessment template and SOPs to minimize variations in their assessment procedures. However, to improve the performance of the assessor in carrying out a good quality review, the authorities should implement standard training and CPD programs as well as engage external quality audits by accredited certification bodies for the exchange of improved knowledge and expertise in reviewing the registration dossiers. An electronic tracking system is another critical quality management tool which should be developed to monitor the review milestones and approval timelines. Finally, the authorities should further improve the level of transparency and communication with the public and the pharmaceutical industry as well as with each other to increase confidence in their review systems.

Declaration of Conflicting Interests

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