

## Assessing the Regulatory and Healthcare Environment in the Middle East

### Key Messages

In 2001, CMR International conducted a study amongst eleven of the world's leading pharmaceutical companies in nine major countries of the Middle East: Bahrain, Egypt, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia and United Arab Emirates (UAE), and seven Ministries of Health to assess the regulatory and healthcare environment.

The greatest difficulty faced by Ministries across the Middle East is a lack of internal resources. The requirement for a Certificate of Pharmaceutical Product (CPP) legalised by the consulate of the certifying country is the most important issue of concern for pharmaceutical companies.

The majority of companies find that a legalised CPP from the source country is required at the time of Marketing Authorisation (MA) application. However, although Ministries will not grant final approval until a CPP has been received from companies, a number are now willing to accept CPPs at the time of MA.

Both pharmaceutical companies and Ministries of Health in the Middle East need to increase their dialogue in the future and take a proactive approach to address the current difficulties that are delaying patient access to medicines.

### Ministry participants

|                     |                          |   |
|---------------------|--------------------------|---|
| <b>BAHRAIN</b>      | Layla Abdul Rahman       | Director, Pharmacy & Drug Control   |
| <b>EGYPT</b>        | Moustafa Ezzat El Hadary | Former Chairman, Drug Policy and Planning Center                                    |
| <b>JORDAN</b>       | Maisa Al Saket           | Director, Drug Directorate  |
| <b>KUWAIT</b>       | Ghaya N. Al-Saad         | Director, Pharmaceutical & Herbal Medicines Registration and Control Administration |
| <b>OMAN</b>         | Sawsan Ahmed Jaffar      | Director General of Pharmaceutical Affairs  |
| <b>SAUDI ARABIA</b> | Hajed Mohamed Hajed      | Director, Pharmaceutical Affairs  |
| <b>UAE</b>          | Easa Ahmed Al Mansoori   | Director, Drug Control Department   |

## Perspective

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### Authors:

Gina Isherwood  
Neil McAuslane  
Stuart Walker

### References:

- 1) Lambert, G, Anderson, CA & McAuslane, JAN (2000). The registration of pharmaceuticals in the Middle East. CMR99-108R2.
- 2) World Health Organisation. Guidelines on the implementation of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce. Available at: <http://www.who.int> (July 2001).
- 3) Trading into the future: The introduction to the WTO. The organisation. Members and observers. Available at <http://www.wto.org> (accessed February 2002).
- 4) Davidson, A, Grace, AJ, Schwarz, EW & Vickers, C (2002). The Value of Certificate of Pharmaceutical Product in Registration of Medicinal Products. DIA Journal p163-167.

a Participating companies were members of the PhRMA Middle East/North Africa LAWG, which provided financial support for the study.

b The following countries in the region are currently members of the WTO: Bahrain, Egypt, Jordan, Kuwait, Oman, Qatar & UAE. Observer countries are Lebanon (Working Party established 14-04-99) and Saudi Arabia (Working Party established 21-07-93). These countries must start accession negotiations within five years of becoming an observer country (3).

Initiatives established in the mid 1990s, such as the Middle East Regulatory Conferences (MERC), have helped to promote successful dialogue between the international pharmaceutical industry and Ministries of Health across the Middle East. These initiatives have led to an increased understanding of the regulatory requirements for successful registration in the region and have provided local Ministries with a greater awareness of recent harmonisation initiatives developed in other areas such as, the EU and associated European countries.

A recent survey conducted by CMR International in 1999 (1), identified a number of difficulties that international pharmaceutical companies faced during the registration of new medicines across the Middle East. However, the difficulties and perceptions for Ministries of Health in the region were not addressed. The current study was conducted by CMR International in 2001 to identify the key factors for both the pharmaceutical industry and Ministries of Health that currently influence patient access to medicines in nine major countries of the Middle East: Bahrain, Egypt, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia and United Arab Emirates (UAE).

Questionnaire-based responses were provided by eleven of the world's leading pharmaceutical companies<sup>a</sup> and data from seven key Ministries of Health across the region (Table 1) were collected through interview with CMR International personnel.

**Table 1. Ministry participants**

|                     |  |
|---------------------|--|
| <b>BAHRAIN</b>      | <b>Layla Abdul Rahman</b><br>Director, Pharmacy & Drug Control   |
| <b>EGYPT</b>        | <b>Moustafa Ezzat El Hadary</b><br>Former Chairman, Drug Policy and Planning Center                            |
| <b>JORDAN</b>       | <b>Maisa Al Saket</b><br>Director, Drug Directorate  |
| <b>KUWAIT</b>       | <b>Ghaya N. Al-Saad</b><br>Director, Pharmaceutical & Herbal Medicines Registration and Control Administration |
| <b>OMAN</b>         | <b>Sawsan Ahmed Jaffar</b><br>Director General of Pharmaceutical Affairs                                       |
| <b>SAUDI ARABIA</b> | <b>Hajed Mohamed Hajed</b><br>Director, Pharmaceutical Affairs   |
| <b>UAE</b>          | <b>Easa Ahmed Al Mansoori</b><br>Director, Drug Control Department   |

## Key Issues

### Key issues currently affecting patient access to medicines

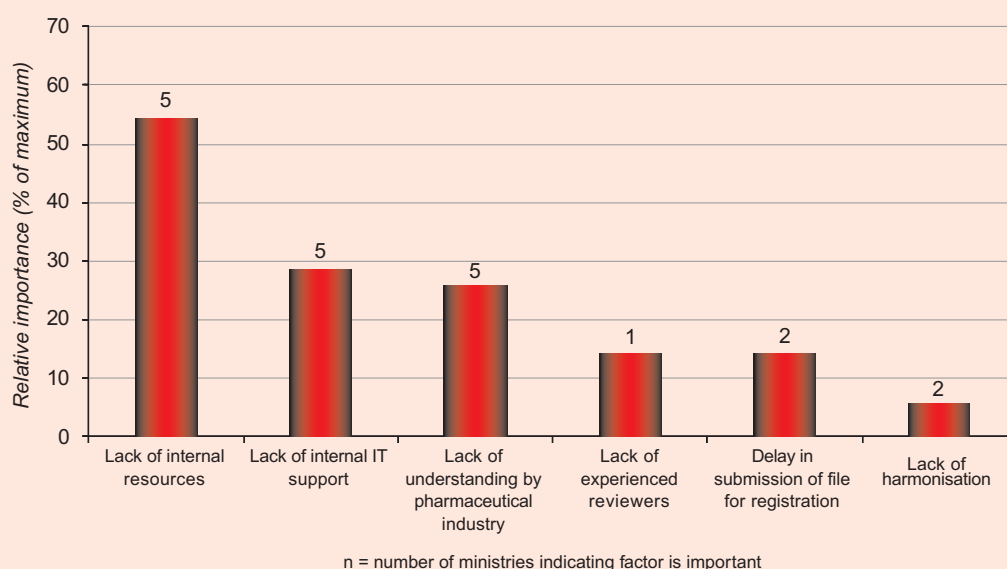
#### Ministries

When Ministries were asked to identify the current difficulties that cause delays in patient access to new medicines in their country, a lack of internal resources was seen as the greatest issue of concern (Figure 1). Over 70% of Ministries believed that their current difficulties could be overcome through increased internal resources and IT support, and greater training of Ministry personnel. Most Ministries believed that the international pharmaceutical industry could also help to resolve their difficulties through an increased understanding of the problems that Ministries across the region currently face. Companies could also help to resolve these difficulties by participating in educational workshops with Ministries to debate and discuss key topics such as the drug development process and harmonisation of regulatory requirements.

#### Companies

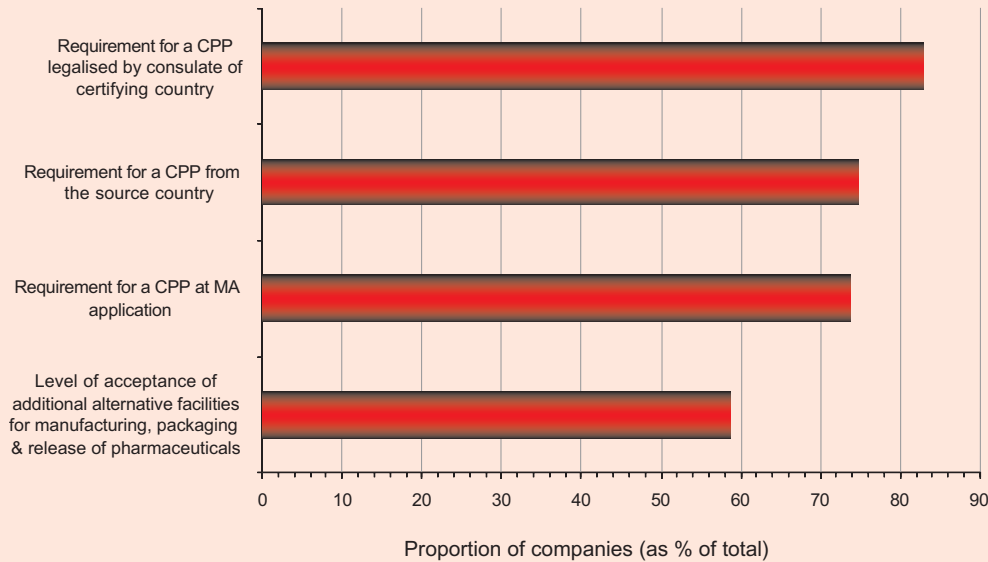
For pharmaceutical companies, the requirement for a CPP legalised by the consulate of the certifying country is seen as the greatest issue of concern across the Middle East (Figure 2a). Two other issues identified for companies also relate to the timing and acceptance of CPPs (Figure 2a). Companies are clearly facing greater difficulties in some countries e.g. Saudi Arabia and Egypt, compared with other countries in the region e.g. Bahrain and Kuwait (Figure 2b).

**Figure 1. What are the major difficulties faced by Ministries of Health across the Middle East that delay local patient access to medicines?**



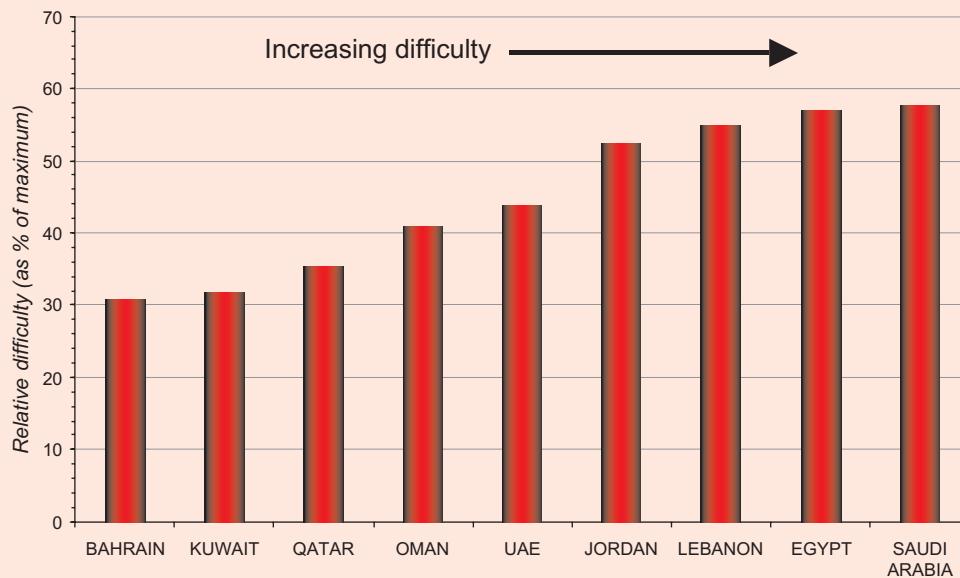
Ministries were asked to identify from a list of six factors those that represented a current difficulty in their country. Respondents were also asked to rank the importance of each identified difficulty in causing delays in patient access to new medicines. The results are shown as the relative importance of each difficulty as a percentage of the maximum response. The n values refer to the number of Ministries indicating that the factor was important. However, not all of participants provided a ranking for the identified factors.

**Figure 2a: What are the major difficulties for international pharmaceutical companies that delay patient access to medicines in the Middle East?**



Source: CMR International

**Figure 2b: Where within the Middle East are the difficulties for international pharmaceutical companies that delay local patient access to medicines?**



Source: CMR International

Companies were asked to identify from a list of eighteen factors, those that represented a major issue of concern in each country of the region regarding patient access to medicines. Figure 2a (top panel) presents the four most commonly cited issues of concern for companies across the region. The results in Figure 2a are shown as the proportion of companies identifying the factor as an issue of concern. Figure 2b (lower panel) shows companies' current level of concern in each country of the Middle East. The results in Figure 2b are shown as the relative difficulty for companies in each country of the region. Source country: Country where product was originally manufactured.

## Current review times and registration processes

In the current study, data was collected on companies' MA application and authorisation activities in the Middle East between 1999 – July 2001. Comparison of this information with data from 1995 – 1998, collected in the previous CMR International study (1), reveals decreases in review time in some of the countries in the Middle East, most notably in Qatar (Figure 3).

Since 1995, review times have remained relatively short in Bahrain and Kuwait, at less than 6 months, but have remained static or have increased to over 1.5 years in Egypt and Saudi Arabia (Figure 3). Several Ministry participants also provided estimates of their current review times, which are outlined in Table 2. All Ministries have a specific department responsible for conducting the registration process in their country and update their requirements for registration on a regular basis. Some Ministries across the region such as Jordan, Egypt and Kuwait utilise a priority review system for important 'breakthrough' products.

Almost all Ministries publish their registration requirements in Arabic or in English and five Ministries communicate their requirements directly to international pharmaceutical companies. Interestingly, the registration requirements of two Ministries are currently published on a Government website and a further four Ministries are developing a website in their country, where registration requirements will be made available to international pharmaceutical companies in the future.

Most Ministries believe that the registration processes in their country are viewed 'positively' [5/7 Ministries] or 'very positively' [1/7 Ministries] by the international pharmaceutical industry, whilst only one Ministry thought the pharmaceutical industry held a negative view of their registration processes.

Table 2. Estimates of review times by Ministries of Health in the Middle East

|               |   |
|---------------|---|
| <b>EGYPT</b>  | Ministry aims to finalise registration of new medicines in 12 months  |
| <b>JORDAN</b> | Current average regulatory review time is between 6 - 12 months   |
| <b>KUWAIT</b> | For a well-organised dossier with FDA or EMEA approval, the current average review time is between 3 - 6 months   |
| <b>UAE</b>    | Ministry is keen for new medicines to be registered in 2 - 3 key countries before registration locally, since the Ministry relies on their expert reviews |

Figure 3. What is the time from MA application to MA in the Middle East?

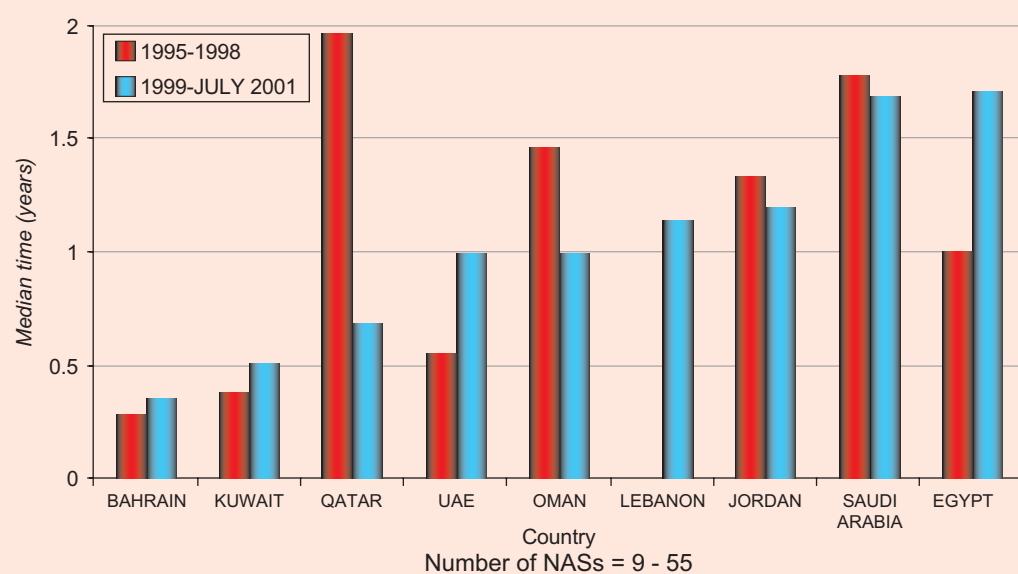
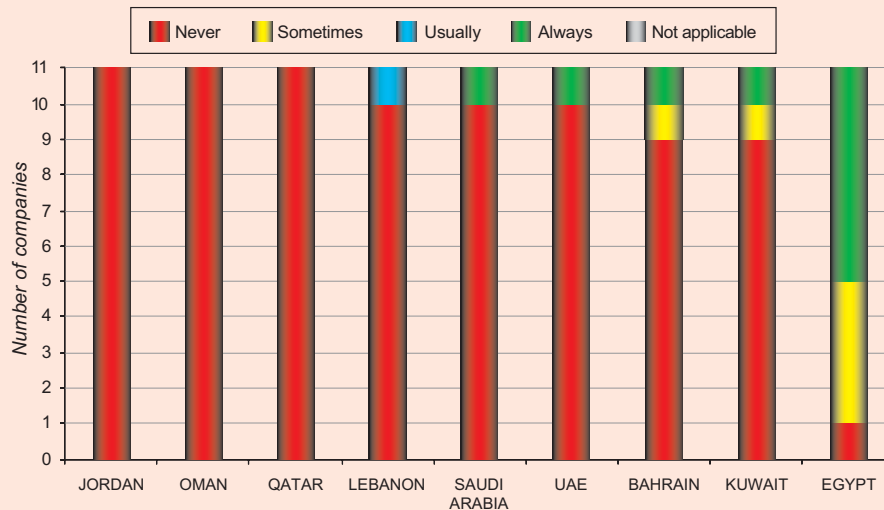


Figure 3 shows the median time in years from MA application to authorisation for pharmaceuticals that were granted MA in the countries of the Middle East between 1995–1998 and 1999–July 2001. Data from the 1995–1998 cohort were collected by CMR International as part of the previous Middle East survey (1). However, for the purposes of comparison, only data that were provided by the participants of the current study were included in these analyses. Since Lebanon was not included in the previous survey by CMR International (1), data is shown for the 1999–July 2001 cohort only.

## Requirements and timing of Certificates of Pharmaceutical Product (CPPs)

Over 80% of companies find that Ministries of Health, with the exception of Egypt, do not accept a CPP at the time of MA (Figure 4). In Egypt, six companies have found that a CPP is 'always' accepted at MA and only one company has 'never' experienced a CPP being accepted at the time of approval (Figure 4).

Figure 4: According to company experience, are Ministries in the Middle East currently accepting CPPs at the time of MA?



Source: CMR International

Companies were asked to indicate from their experience whether local authorities in the Middle East 'always', 'usually', 'sometimes' or 'never' accept a CPP at the time of MA.

The timing of submission of CPPs is clearly not the only issue for companies in relation to the current requirements for CPPs in the Middle East (Figure 2a). Legalisation is an additional step required by the authorities for CPPs, which causes further delays to MA applications, but the WHO (2) guideline recommends that legalisation is not necessary. Over 80% of companies find that a legalised CPP is always required in each country of the Middle East.

A second issue for companies is the requirement for a CPP from the manufacturing source country, which does not provide additional assurances to the quality, safety and efficacy of the medicine. At least 70% of companies indicated that a CPP from a non-source or reference country is never accepted in a number of countries across the Middle East, although companies find that the authorities in Kuwait and Egypt may be more willing to accept a CPP from a reference country. Interestingly, a number of Ministries, shown in Table 3, indicated that they are now willing to accept a CPP at the time of MA, but final approval will not be granted until a CPP has been submitted.

Table 3. Comments by Ministries of Health on requirements and timing of CPP submission

### INDICATED WILLINGNESS TO ACCEPT A CPP AT THE TIME OF MA

|                |  |
|----------------|--|
| <b>BAHRAIN</b> | Ministry is supportive, but had not received requests from companies for CPP submission to be delayed until the time of regulatory approval  |
| <b>EGYPT</b>   | Current law requires that a CPP must be submitted from the country of origin   |
| <b>JORDAN</b>  | In an exceptional circumstance, Ministry accepted a file with FDA approval only (without a CPP) for a product that was needed by patients in Jordan.   |
| <b>KUWAIT</b>  | Ministry agrees that requesting a CPP from the country of origin may not always be appropriate. Ministry may be willing to nominate a list of countries from which a CPP can be provided         |
| <b>UAE</b>     | Since 2000, files have been accepted without a CPP. The Ministry will conditionally approve the file before requesting a CPP, but will not grant final approval until the CPP has been provided. |

## Pricing procedures

Over 60% of companies indicated that Jordan, Lebanon and Saudi Arabia currently publish their pricing procedures, whereas only around 40% of companies find that these procedures are published in other countries of the region. Most companies indicated that Ministries throughout the Middle East require pricing information from the country of origin and other countries in the region at the time of MA application. The current pricing procedures in the Middle East, however, have led almost all participating companies to delay launch of pharmaceutical products in the region. Several Ministries provided comments on their current pricing procedures, which are summarised in Table 4.

Table 4. Comments by Ministries of Health on pricing procedures

|                |   |
|----------------|---|
| <b>BAHRAIN</b> | <p>Pricing is linked to registration and Ministry does not believe that these processes should be separated in the future</p> <p>Companies are expected to provide comparative pricing information from other countries, particularly the country of origin &amp; other countries in the region</p> <p>Companies should be prepared to provide data to the Ministry that is already in the public domain</p>  |
| <b>EGYPT</b>   | <p>Companies may be able to achieve increased prices for their medicines if they are willing to help to further develop Egypt, e.g. by making additional investments within the country</p>   |
| <b>JORDAN</b>  | <p>Requests pricing details from the Near East countries and the EU &amp; USA</p> <p>Does not always require pricing information from the country of origin</p>   |
| <b>KUWAIT</b>  | <p>Registration is separate from the pricing review and a Certificate of Registration is issued before pricing commences</p> <p>Prices for Kuwait are compared with other countries, e.g. the country of origin, USA, 2 EU member states and other countries within the Gulf</p> <p>The price of other similar types of products is also reviewed, but a price premium is permitted for innovative products or those with improved properties of safety or efficacy</p> |

## Intellectual Property (IP)

Over 60% of companies indicated that unlicensed copies of their products have been manufactured or marketed in the Middle East since 1999. Current data and patent protection provided in the region represents a number of issues of concern for companies such as, the lack of effective enforcement of IP laws. Parallel importation of products was also identified as an issue of concern for over 70% of companies, particularly in Lebanon.

Most Ministries provided their perception of how intellectual property protection currently influences patient access to medicines in their country. Ministries clearly have mixed views with three believing that intellectual property has a 'very positive' influence on patient access in their country, whilst two Ministries view the influence as 'negative'.

Several Ministries provided comments on the current IP laws in their country, which are summarised in Table 5.

Table 5. Comments by Ministries of Health on IP laws

|                |   |
|----------------|---|
| <b>BAHRAIN</b> | IP laws have been implemented since 1999<br>Ministry will continue to respect these laws in the future  |
| <b>EGYPT</b>   | Current IP laws respect data protection, but not patent protection of final products<br>New IP laws will be implemented in 2005, which will include patent protection for products, as required by the WTO's (3) agreement on TRIPS   |
| <b>JORDAN</b>  | Data protection has been provided since May 2000<br>Ministry believes that current IP laws allow pharmaceutical companies to register new products more quickly in Jordan compared with other countries in the region                 |
| <b>KUWAIT</b>  | The Health Minister issued a decree in 1998 to apply IP laws, which have been implemented since 1999<br>Ministry has joined discussions with industry to address how IP protection should be implemented most appropriately in Kuwait |
| <b>UAE</b>     | Since 2000, non-patented products that are similar to other medicines covered by patents will not be registered for the duration of the patent term   |

## Recommendations for the future

A number of factors have been identified that lead to delays in patient access to new medicines in the Middle East. Both pharmaceutical companies and Ministries of Health in the region can help to resolve these difficulties through:

- Effective use of the CPP scheme by adopting the following initiatives that are consistent with recommendations previously suggested by the pharmaceutical industry (4):
  1. Rapid implementation of acceptance of CPPs at MA.
  2. Accepting a CPP from a reference country
  3. Removing the requirement for CPPs to be legalised by the consulate of the certifying country (also a WHO recommendation).
- Acceptable increase in registration fees to help to resource Ministries if this will lead to a more efficient and rapid review.
- Implement exchange programmes for local reviewers to aid education.
- Undertake small educational workshops for Ministries
- Wider publication and easier access of registration requirements by Ministries.
- Provision of appropriate data and patent protection laws by Ministries as outlined in TRIPS.
- Increased dialogue between:
  1. Ministries
  2. Companies
  3. Ministries and companies.

Both the pharmaceutical industry and Ministries of Health in the Middle East should seek to increase their dialogue in the future and take a proactive approach to address the current difficulties that are delaying patient access to medicines, which is in the best interest of patients and the general public.

### For further information please contact:

CMR International Institute for Regulatory Science  
 Novellus Court 61 South Street Epsom Surrey KT18 7PX UK  
 Tel: +44 (0)1372 846100 Fax: +44 (0)1372 846101 Email: [cmr@cmr.org](mailto:cmr@cmr.org) Web: [www.cmr.org](http://www.cmr.org)