What are the attributes that companies believe would help agencies to make quality regulatory review decisions?

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Background

The function and activities of review processes across all regulatory agencies are very similar in terms of the mission, procedures and steps required to assess a medicine for safety, quality and efficacy. Regulatory systems vary across countries as well as over time. However the characteristics that reflect the activities of a well-developed regulatory agency are recognised through four domains that are embedded into their process and procedures: transparency, timeliness, process predictability and quality reviews. These form than basis of Good Review Practices, which have been characterised for selected agencies.[1,2] However, not all agencies implement activities that facilitate a quality review process.

This study was conducted to characterise the processes that pharmaceutical companies believe can drive improvements in company-agency interactions thereby improving quality review processes implemented by agencies. CIRS conducted this study to identify "best practices" in terms of activities, process and procedures, which if adopted by an agency would enable good agency review practices in terms of timeliness, predictability, transparency and good-quality reviews. Furthermore, this study provided the first global assessment of companies' perceptions of the ability of agencies to meet these characteristics.

Objectives

- Characterise the regulatory practices which from a company perspective, enable agencies to reflect Good Review Practices that can be used by emerging market (EM) agencies to ensure quality decisions
- Identify activities believed to add value to the regulatory process by recognising key attributes that enable a transparent, timely, predictable and good-quality review
- Understand how companies believe regulatory agencies rate with regard to the attributes that underpin transparency, timeliness, process predictability and quality reviews

Methods

Between June and September 2011, Microsoft Word©-based surveys were sent to the senior managerial regulatory affairs contact at the following 12 multinational research-based companies: Abbott, Allergan, AstraZeneca, Bayer, Celgene, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Novartis, NovoNordisk, Pfizer and Roche.

Part 1 - Enablers of the Regulatory Review

In order to identify processes and practices that enable or hinder an efficient and effective review, companies rated attributes identified by the authors. These attributes were determined by an iterative review process initiated by CIRS and through feedback by invited external reviewers. The attributes were organised by the following 8 categories: *Guidance and Registration; Dialogue and Negotiation; Transparency; User Fees; Submission Methods; Management Systems; Training* and *Other*

Methods (cont)

Attributes were rated by companies as follows:

Barriers to agency activities: **1** = a barrier to enabling a timely, predictable, transparent good-quality review; **2** = not a barrier but has no value in enabling a timely, predictable, transparent good-quality review; **3** = has undetermined value in enabling a timely, predictable, transparent, good-quality review; *Enablers of agency activities:* **4** = low value in enabling a timely, predictable, transparent good-quality review; **5** = is extremely valuable in actively enabling a timely, predictable, transparent, good-quality review.

All attributes that were rated a 5 were further identified as being a primary contributor to one of the following 4 domains of good agency review practices that facilitate an efficient and effective dossier review: timeliness, process predictability, transparency, and quality reviews (Fig1).

Figure 1. Process for rating good agency practices that enable an efficient and effective review

Guidance/ Regulations Attributes	Rating					If you have rated an attribute as *5*, please tick only 1 descriptor that is enabled			
	1	2	3	4	5	Transparency	Timeliness	Predictability	Quality
Type – Limited, administrative (eg, number of dossier copies, number of samples, etc)									
Type – Detailed (technical, therapy area guidance)									
Type – Decision frameworks (eg, benefit-risk)									
Delivery/availability – English as well as local language									
Delivery/availability – Electronic /Available on website									
Publication of established guidelines used by reviewers									

Part 2- Company ratings of agencies

Companies rated 20 regulatory agencies on the attributes that enable good review practice. These attributes were organised according to four domains representing factors that characterise timeliness, process predictability, transparency and quality reviews.

Attributes were rated by companies as follows:

1 = **Unsatisfactory**: The elements do not meet the minimum standard required. Most elements are not available or have limitations, such as incomplete sections, missing information and or inconsistencies; **2** = **Poor**: The majority of elements do not meet the expected standard. Many elements have a number of deficiencies, where improvements can be made; **3** = **Satisfactory/fit for purpose:** The elements adequately meet the expected standard. By and large, they were sufficiently detailed, clear, consistent and accurate; however there is room for improvement; **4** = **Good:** The elements highly meet the expected standard. Most elements were clear, consistent and accurate; **5** = **Excellent:** The elements exceeded expected standards. Most elements were clear, consistent and accurate and considered as best practice.

Results

Response rate: For both parts of the study, 9 companies (75%) responded to the survey. Not every company provided answers for each country; the number of respondents per item is shown parenthetically.

Part 1 - Enablers of the Regulatory Review

The most important attributes that enable the review process (determined by items that received a rating of 4 or 5 by more than 80% of respondents) are listed in Table 1.

Table 1. Top ten attributes rated by companies that enable the review process	Companies %
Ability for dialogue with assessor to clarify issues raised in deficiency letter	100
Pre-submission dialogue	100
Detail of approval process: Detailed description of each stage of the approval process including target times	92
Adherence to target timelines during the review	92
Agencies' adherence to international standards for requirements	92
Summary basis of previous approvals: Detailed information	92
Ability to negotiate timing of CPP submission	92
Availability of different assessment routes, eg, priority, orphan status, standard, abridged or full review	83
Availability of timelines: Detailed target times for each stage of the review process	83
Ability to contact person at the agency	83

A number of factors were identified that enable the 4 domains of Good Review Practice (Fig 2).

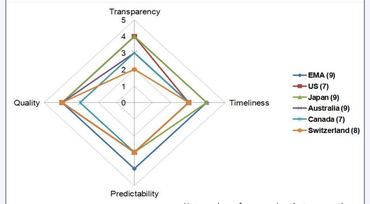
Figure 2. Attributes that enable the review process

Part 2- Company ratings of agencies

Ratings data were provided for 20 countries. The results for these countries are organised by geographic region. No country received a rating of 5 (Excellent) for any attribute (Figs 3-6)

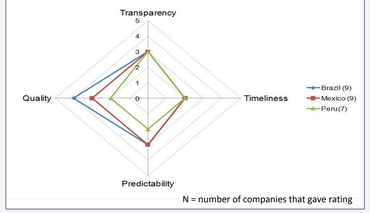
Results cont

Figure 3. Comparative ratings: ICH countries



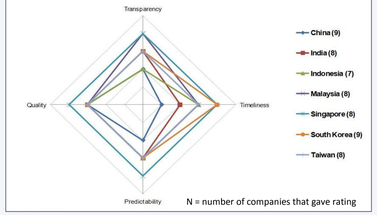
N = number of companies that gave rating

Figure 4. Comparative ratings: Latin American countries



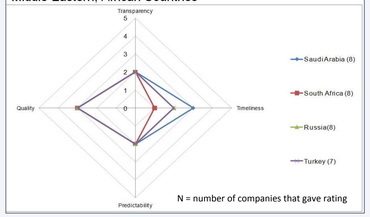
N = number of companies that gave rating

Figure 5. Comparative ratings: Asia Pacific countries



N = number of companies that gave rating

Figure 6. Comparative ratings: Eastern Europe, Middle Eastern, African Countries



N = number of companies that gave rating

Conclusions

- Key enablers of a quality review process were identified; the most important was the ability for companies to maintain a dialogue with agencies through the review process.
- Other key enablers were that the agency be able to provide details describing the submission process and requirements, that these requirements be consistent with international standards, that agencies adhere to published timelines, offer a summary basis for approval or equivalent document illustrating their review finings, and the ability for agencies and companies to negotiate the timing of submission of the Certificate of Pharmaceutical product (CPP).
- Companies rated agencies as "satisfactory/fit for purpose" or "good" for most of the 4 domains of transparency, timeliness, process predictability and quality reviews.
- Agencies developing their regulatory systems tended to be rated lower.
- The methodology was found to be simple and understandable and the findings serve as a baseline against which changes over time can be assessed.

Considerations

- This pilot survey represents the opinions of a small number of multinational companies, but we believe the responses are reflective of the top-tier pharmaceutical companies.
- Since this study was conducted, some agencies have implemented new processes to enhance their adherence to Good Review Practices and hence, moving toward quality review processes. These improvements are not reflected in the results provided herein.
- Some responses were completed by the central office while others came from country-based affiliates. An analysis of responses categorised by the location of the responder may suggest differences in rating (ie, affiliates that have good local relations with an agency may rate that agency highly, while interactions through a central office may not be as constructive).
- A companion survey of agencies' self-rating of transparency, timeliness, process predictability and quality reviews is being undertaken by CIRS.
- CIRS is providing agencies with the results of this study to drive conversations around suggestions for processes and performance optimisation, with a focus on the key enablers.

Disclosures

The authors have no disclosures.

References

1. McAuslane, N. Streamlining review processes in the Asian Pacific Region: The importance of good review practices. *DIA Global Forum* **4**, 15-17 (2012).
2. Al-Essa, R., Salek, S., Walker, S. An appraisal of good regulatory review practices in the Gulf Cooperation Council States. *Drug Info. J.* **46**, **57-64 (2012).**