INTRODUCTION
CIRS has collected regulatory assessment data for over 20 years, initially with ICH and ICH-observing countries. The OpERA programme, “Optimising Efficiencies in Regulatory Agencies (OpERA)”, was initiated through CIRS in 2013 with agencies from Asia, Latin America, Africa and the Middle East. Since then, CIRS has expanded this programme to over 20 countries and several regional alignment initiatives. OpERA is a global programme, available to all regulatory agencies irrespective of their size, mission or maturity.

OpERA combines qualitative (process mapping; Figure 1) and quantitative (performance metrics; Table 1) information to provide a detailed picture of the regulatory assessment activities of agencies at any stage of maturity. As the regulatory landscape evolves and to put performance metrics into local context, CIRS developed a systematic questionnaire completed by agencies to map regulatory processes and procedures. The resultant Country Report has been linked to metrics provided by each agency.

OBJECTIVES OF OpERA
• Help regulators integrate a practice of tracking and measuring regulatory performance and promote continuous improvements in review and approval times while ensuring safety, efficacy and quality
• Understand the regulatory processes that drive approval times
• Identify qualitative and quantitative regulatory indicators of performance.

Table 1. Performance metrics

<table>
<thead>
<tr>
<th>Target time</th>
<th>Definition</th>
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<tr>
<td><strong>Overall Approval Time</strong></td>
<td>The time between the date stamped on Receipt of Dossier when received by authority and the Date of Legal Marketing (date of the product licence)</td>
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<tr>
<td><strong>Dossier Validation</strong></td>
<td>The time between the date stamped on Receipt of Dossier when received by authority and the Date of &quot;Acceptance (or Refusal) to File&quot; (letter was sent)</td>
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<td><strong>Scientific Assessment Time</strong></td>
<td>Amount of time spent actively reviewing the dossier or additional information provided</td>
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<td><strong>Sponsor Time</strong></td>
<td>Time during which the clock was stopped during the review whilst the authority awaited additional data provision by the company</td>
</tr>
<tr>
<td><strong>Other Regulatory Authority Time</strong></td>
<td>Time taken up by the authority during the review for administration, queuing, Advisory Committee time etc.</td>
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Key Milestone Dates
1. Receipt of the dossier
2. Acceptance to file
3. Start of Primary Scientific Assessment
4. Completion of Primary Scientific Assessment
5. Secondary assessment following deficiency letter response (if applicable)
6. Advisory Committee Review (if applicable)
7. Marketing Authorisation Granted /Rejected
For REC: Final Acceptance by member state
OUTPUTS AND METHODS
There are two components to the OpERA Programme: The Country Report (process) (Figure 2) and specific metrics collections (Figure 3).

THE COUNTRY REPORT (PROCESS)
The Country Report is created by CIRS with information provided by each agency through the Country Questionnaire. More than 15 years ago CIRS developed a standardised reporting approach to identify key characteristics that may impact regulatory performance. Using this mature process, CIRS uses information provided by an agency via the Country Questionnaire to create the agency-specific Country Report.

This report:
• allows accurate interpretation of the quantitative metrics to be evaluated according to the review process
• permits global comparisons to similar agencies open to sharing their profile
• encourages sharing and adopting of Good Review Practices.

The report captures:

- Part 1: Organisation of the agency
- Part 2: Types of review models
- Part 3: Key milestones in the review process (Figure 1)
- Part 4: Good Review Practices (GRevP)
- Part 5: Quality Decision-Making Processes
CIRS works closely with each agency to verify collected data and prepare the Country Report (Figure 4).

**Figure 4. How the country report is produced**

1. Pre-filled by CIRS and Completed/Verified by Agency
2. Converted to Standardised Draft Country Report by CIRS
4. CIRS creates Final Country Report

**Practical Use of the Country Report**
The Country Report can be used by the agency internally, cited within publications or to conduct a gap analysis to identify where improvements can be made. Figure 5 is a case study described in “The Saudi Arabia Food and Drug Authority: An Evaluation of the Registration Process and Good Review Practices in Saudi Arabia in Comparison with Australia, Canada and Singapore” (Hashan H., Aljuffali I., Patel P., Walker S. Pharmaceut Med. 2016; 30: 37–47).

**Figure 5. Case Study – Saudi Arabia – Gap analysis (in collaboration with agency)**

- Internal utilisation of country report
- Gap analysis
- Publication-recommendations
- Introduction to risk stratification routes**

Compared to these agencies: SFDA, TGA, HC and HSA*

* SFDA: Saudi Food and Drug Authority; TGA: Australia Therapeutic Goods Administration; HC: Health Canada; HSA: Singapore Health Sciences Authority.

** As a result, other agencies in the region have also introduced risk stratification in their review process (Jordan, UAE)
REGULATORY PERFORMANCE METRICS: LINKING THE APPROVAL PROCESS TO METRICS

The product characteristics requested for each submission and key milestone dates are illustrated in Figures 2 and 3 and Table 1. Data can be provided to CIRS by the agency in two ways (Figure 6):

- Via the secure OpERA online data collection portal
- Using a password-protected Excel spreadsheet provided by CIRS

Using the OpERA Metrics Report

The metrics report helps to identify the major components of the Regulatory Review and opportunities for optimisation. Results can be used to monitor yearly changes. OPERA profiles can help agencies raise questions on their optimal process and identify both what is working and what is not in terms of effectiveness. Participating agencies can also understand how they compare to other agencies doing similar activities, and identify opportunities for improvement.

The below analysis with fictitious data (Figure 7) shows the summary of the main components of the review process and their associated timelines. These are outlined using a box and whiskers analysis, with median time and variability of each component.

Figure 6. How the metrics report is produced

Figure 7. Summary of Review Process Timeline Components

(n1) = number of drug applications, (n2) = number of companies
COUNTRIES COVERED TO DATE

Figure 8 and 9 show countries for which data are included in the OpERA programme.

Figure 8. Countries covered in country reports

![Map showing countries covered in OpERA programme]

Regional Regulatory Initiatives:
- Completed Caribbean Regulatory System, Gulf Health Cooperation
- In discussion ZAZIBONA (Zambia, Zimbabwe, Botswana, Namibia)

Figure 9. Countries engagement in performance metrics

![Map showing countries engaged in performance metrics]

Regional Regulatory Initiatives:
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HOW DOES OpERA COMPARE TO OTHER REGULATORY STRENGTHENING INITIATIVES?

The OpERA Programme is focused on the details of marketing authorisation activities. Therefore, it is synergistic with other regulatory strengthening projects, such as the ones listed below with their main objectives:

- **WHO Global Benchmarking Tool**: Evaluates regulatory systems across all functions within an agency
- **AMRH/NEPAD monitoring & evaluation tool**: Provides information for decision-making and program planning
- **Pan American Health Organization (PAHO) Indicators**: For the assessment of core health indicators, health analysis, and other health topics in the national regulatory systems.

OpERA is focused on the regulatory assessment process (including decision making and Good Review Practice indicators) and monitoring the assessment process performance (Table 1).
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CIRS - The Centre for Innovation in Regulatory Science Limited - is a neutral, independently managed UK based subsidiary company, forming part of Clarivate Analytics (UK) Limited. CIRS’ mission is to maintain a leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and HTA policies and processes. CIRS provides an international forum for industry, regulators, HTA and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy through the innovative application of regulatory science and to facilitate access to medical products through these activities. This is CIRS’ purpose. CIRS is operated solely for the promotion of its purpose. The organisation has its own dedicated management and advisory boards, and its funding is derived from membership dues, related activities, special projects and grants.

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