Regional Alignment in Asia Pacific:

What needs to be in the regulatory **science "toolkit" to enable good** regulatory decision making

WORKSHOP
26 – 27 January 2011
Tokyo, Japan

Workshop Synopsis

CMR International
INSTITUTE FOR REGULATORY SCIENCE

The following is a high-level summary of key points from a Workshop conducted by the CMR International Institute for Regulatory Science (the Institute; currently known as the Centre for Innovation in Regulatory Science) on 26-27 January, 2011, in Tokyo, Japan.

Background to the Workshop

Regulatory agencies are rising to meet the challenge posed by the reality in which companies are not only undertaking global clinical trials but are also looking to make their products available to patients worldwide in a timely, often almost simultaneous fashion. In the developing pharmaceutical markets this has put pressure on the evolution of regulatory policy, infrastructure and resources, while in established markets resource implications along with the duplicative nature of some of the work is resulting in an increasing emphasis on collaboration and sharing of resources where possible. As more agencies look to take a science-based approach to regulation and risk-based decision making, a common regulatory language is being developed as well as clarity around the resources required to approve and monitor new medicines. This has lead agencies to begin to discuss and work out how to cooperate in order to share information and activities, such as safety data and inspections, as well as exchange of staff. In addition, some agencies are looking to the exchange of assessment reports. Challenges to collaboration include differences in skill sets, experience and processes between agencies. The key question therefore is, what are the underpinning components of good regulatory decision making and what are the regulatory science tools that can be used to ensure a timely, high-quality, predictable and transparent process whilst ensuring an effective and efficient use of resources?

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The objectives of this Workshop were to:

- **Discuss good risk-based regulatory decision making** and what the components are that need to be built into the review process
- **Identify current initiatives/approaches** and understand how these are enabling the decision making process from companies and agencies perspective
- **Recommend what should be in the regulatory science "toolkit"** and how best this can be used as part of the regional alignment initiatives

The Workshop and its Syndicate Discussion Sessions provided a comprehensive look at and recommendations for the use of three key tools that can form the basis of a good regulatory decision making strategy: a Quality Scorecard for the assessment of dossiers and their reviews, a simple, standardised benefit-risk framework, and the foundational elements that can underpin the sharing of assessment reports among stakeholders. Each of these was addressed within the broader context of moves towards regionally harmonised regulatory activities.

Good Regulatory Decision Making: Key components that build predictability

Dr Satoshi Toyoshima, *Senior Advisor, Pharmaceuticals and Medical Devices Agency (PMDA), Japan* reported on the status of the five components of the PMDA four-year action programme for new drug reviews: improving the consulting service and review system; promoting global drug development; improving measures for ensuring public safety and reassurance; strengthening international programs including collaboration with Asian regulators; and advancing regulatory science within the agency, industry and academia.

The holistic paradigm of the United States Food and Drug Administration for ensuring the safety and efficacy of drugs throughout their life cycles was described by **Dr Christopher Hickey**, *Director, China Office, U.S. Food and Drug Administration (FDA), China* which consisted of good review management principles and practices, oversight of post-market drug safety and harmonisation and collaboration with other regulatory authorities

Noting that the quality of regulatory decisions are dictated by their accuracy, predictability and transparency, **Dr Zili Li,** *Emerging Markets Regulatory Strategy and Policy Lead, Merck & Co Inc, USA* detailed the quality measures, continuous improvement initiatives, training and education of assessors and communication efforts being undertaken by thirteen regulatory authorities in the Emerging Markets to meet these goals.

As the Chair of the Asia Pacific Economic Cooperation (APEC) Regulatory Harmonization Steering Committee (RHSC), **Mike Ward,** *Manager International Programs Division, Health Canada* detailed important new developments taking place within APEC in advancing regulatory harmonisation and cooperation, including the ratification of a multi-year strategic plan, moving from individual effort to more collective, coordinated and more effective action. A project plan to be implemented during 2011-2012 includes the development of a training program, a good review practice toolkit and a framework for the use and exchange of regulatory information.

According to **Dr Won Shin,** *Division Director, Korea Food and Drug Administration,* good review practices, training and international and regional cooperation are the most important platforms on which to build trust and partnership across agencies. This partnership is particularly important in the development of the rapidly growing Asian pharmaceutical market, which represents both the largest portion of the global population and an environment that highly encourages research and development.

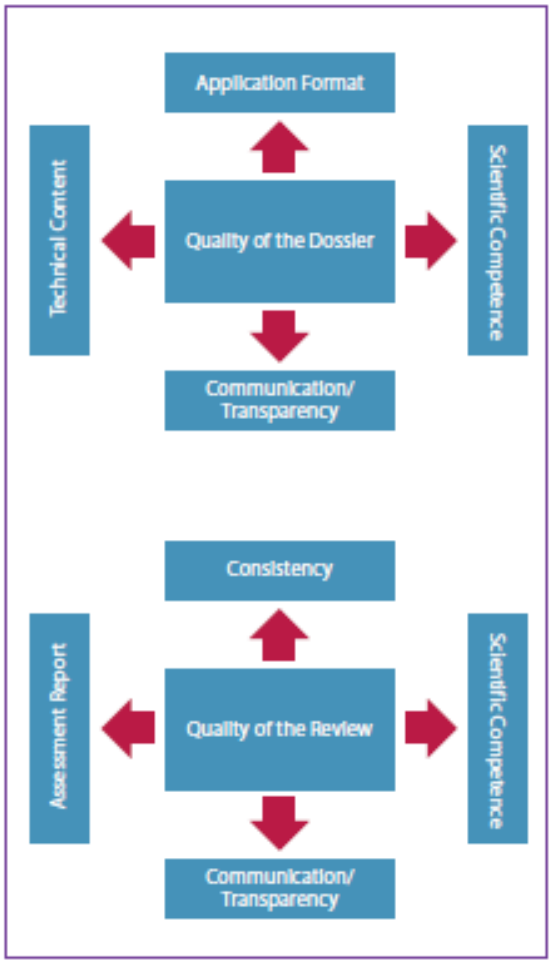
Dr Supriya Sharma, *Director General, Therapeutic Products Directorate, Health Canada* discussed the contribution of Good Review Practices (GRPs) to a well-functioning regulatory review system and to inter-agency cooperation. Although *good regulatory review* is a highly subjective concept for which there is no easy measure, there are ten hallmarks that point to an independent, objective, scientific and timely analysis of information relevant to a marketing application. A good review is knowledge-based, uses critical analyses, identifies signals, investigates issues, makes linkages, considers context, involves consultation, is balanced, thorough, and well documented.

Following the Scientific Advice obtained from a regulatory agency is one of the strongest predictors of regulatory success yet identified; how to best provide this advice in a consistent manner that can drive both regulatory and reimbursement decisions remains a matter of discussion. As the former Chair of the Scientific Advice Working Party (SAWP) of the Committee for Medical products for Human Use (CHMP) **Professor Bruno Flamion**, *Chairman, Belgian Committee for Reimbursement of Medicines (CTG/CRM), Belgium* reported that receipt of unfavourable scientific advice from the SAWP is a negative factor toward achieving marketing authorisation in the EU if the company does not change its development plans accordingly. The SAWP would welcome the opportunity to provide parallel scientific advice with other regulatory bodies and expects that it would be provided in collaboration with key European HTA and payers organisations in the near future.

MEASURING PERFORMANCE ACROSS REGULATORY AGENCIES: IMPROVING PREDICTABILITY AND REGULATORY DECISION MAKING THROUGH THE USE OF BENCHMARKING AND QUALITY SCORECARDS

Dr David Jefferys, *Senior Vice President, Global Regulatory and Healthcare Policy, Eisai. Europe Ltd, UK* provided an industry wish list for regulatory performance by an agency: rapid assessment and outcome determination; pragmatic, proportionate, justified decisions; balanced and transparent benefit-risk assessment; and predictability. Judging an agency's performance by metric benchmarking, however, is complicated by the fact that performance targets reflect different country regulatory systems and involve different definitions.

Improving predictability and regulatory decision making regulatory research programme : Scorecards. The Institute has developed two scorecards – one to measure the quality of the sponsor's submission and the second to measure the quality of the regulatory review.



Dr Neil McAuslane, Scientific *Director,* *CMR International Institute for Regulatory Science*, explained that because no agency works in isolation and because they are being judged by their stakeholders, timely, high-quality, predictable and transparent processes for the measurement of performance such as the Institute's Regulatory Benchmarking and Quality Scorecard programmes can help underpin good regulatory decisions, create a basis for improvement and aid in more predictable decision making**.**

For example, at Swissmedic, performance measurement is directly related to strategic goals and they have measures related to employees, process, finance, stakeholders and mandate, the results of which are reported as a balanced scorecard. **Dr Petra Dörr,** *Head of Management Services and Networking* reported that benchmarking information can used to support strategic planning discussion with stakeholders, and at Swissmedic such data have been used to support requests for additional resources to maintain global competitiveness.

KEY POINTS FROM THE SYNDICATE DISCUSSIONS

- **Scorecards and the Emerging Markets dossier:** Although the general consensus was that Scorecards are an appropriate element of the regulatory toolkit, issues must be considered relative to their application, transparency among agencies and industry and their relative place in the review process.
- **Added complexity of scorecard approach in Emerging Markets**: In addition to rating the quality of the dossiers received from sponsors, health authorities may need to rate the quality of information received from other health authorities (assessment reports).

APPLYING A STANDARDISED BENEFIT-RISK FRAMEWORK TO THE ASSESSMENT OF NEW MEDICINES

This is a clear need for a better understanding of why different agencies come to different conclusions when faced with essentially identical application data; this is a particularly challenging issue for regulatory agencies which are under growing pressure to increase transparency and accountability for their decision making. **Professor Stuart Walker,** *Founder of the Institute,* described the efforts underway to develop an international, structured, systematic and standardised benefit-risk framework as an essential part of the regulators' transparency armamentarium. He presented a summary of the seven steps of such a framework currently being developed by the Institute.

KEY POINTS FROM THE SYNDICATE DISCUSSIONS

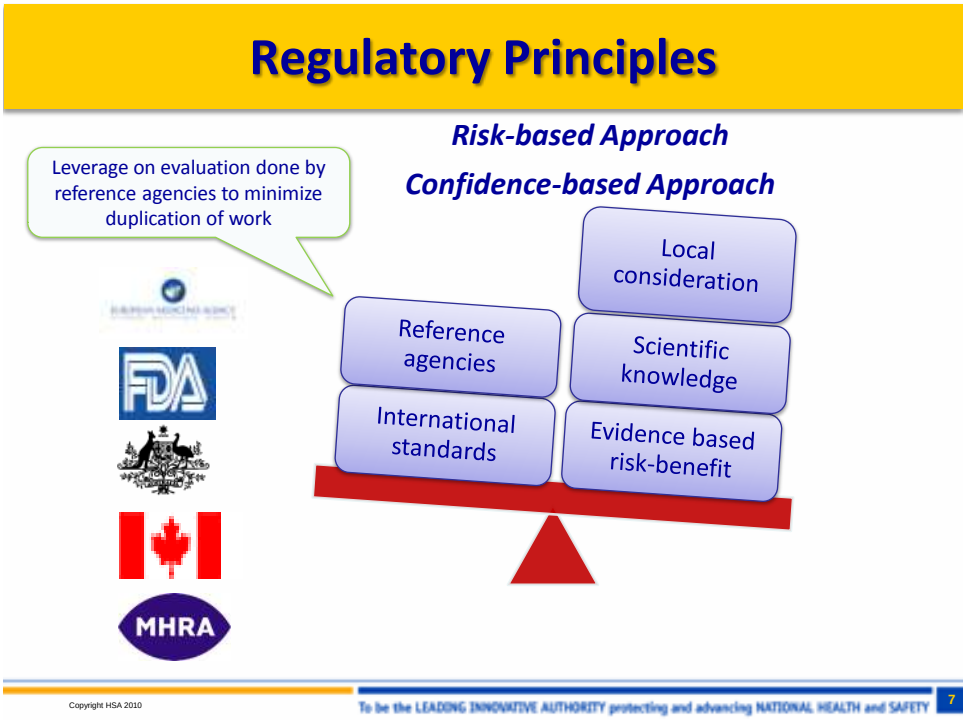
- **A proactive Emerging Markets benefit-risk plan:** Although benefit-risk evaluations are currently part of the regulatory review process in many Emerging Market countries, a formal codification would add structure, could improve overall assessment and facilitate inter-agency exchange of assessment reports. Countries with developing pharmaceutical markets should not wait for the United States FDA and the European Medicines Agency to implement a benefit-risk framework before initiating work in this area,
- **Integrating benefit-risk throughout a product life cycle:** To better understand a medicine's effectiveness, there should be a post-marketing plan to study benefit-risk in "real-world" settings.

SHARING REGULATORY ASSESSMENT REPORTS

During the course of this Workshop, it became clear that streamlining the regulatory process by sharing regulatory assessment reports is a win-win proposition for agencies in the Asia Pacific region. According to **Dr Meir-Chyun Tzou,** *Director, Division of Drugs and New Biotechnology Products, Food and Drug Administration, Chinese Taipei,* such collaboration will save resources, lead to better review quality and earlier approval of and access to medicines. A pilot study of best regulatory practice will be conducted by APEC in 2011-2012 and is co-sponsored by 10 other countries.

Joseph Scheeren, *SVP, Head of Global Regulatory Affairs. Bayer Healthcare, Pharmaceuticals Inc, USA* agreed that regulatory dialogue and sharing regulatory reports has many advantages and will allow a more efficient use of resources and earlier access to medicines. The chief challenges to this sharing will be language and standardisation barriers and a framework for partnership is required.

Dr Christina Lim, *Deputy Group Director, Health Products Regulation Group, Health Sciences Authority (HSA), Singapore* explained that although HSA does use information from other agencies in their decision making, the primary challenges in obtaining the best value for the exchange of regulatory reports are a lack of access to the data set submitted to other agencies in support of an application, the lack of avenues to seek clarification, and industry's expectation that regulatory approval in other countries would lead to HSA approval.



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- **Differences in format and content of assessment reports:** Assessment reports are highly variable in substance, level of detail. The extent of decision rationale and the details of the question and answers can be lacking.
- **Timing of global applications:** It was felt that although it is the sponsors' intent to achieve approval as quickly as possible, use of completed assessments could lead to delay of submission and approval. Challenges include varying levels of agency development, different visions, and language. Implementation of the sharing of reports requires agency and industry commitment and incentives for both sponsors and regulators should be defined.

CONCLUSION

Professor Robert Peterson, *Executive Director, Drug Safety and Effectiveness Network. Canadian Institute of Health, Canada* concluded the Workshop presentations by reminding the audience that the primary objective of regulatory agencies is the timely, predictable review of new medicines, permitting market entry of products with a positive benefit-harm profile while demonstrating value to national or regional healthcare systems. Strategies to accomplish this objective successfully in an increasingly complex global environment include regional harmonisation, scientific advice prior to submission, measuring performance, and use of GRP and a benefit-risk framework. Strategies for efficiencies meanwhile, include sharing regulatory assessment reports, parallel reviews, multinational regulatory consortia, use of other regulator's decisions and regional safety surveillance

SPECIAL THANKS TO:

The Workshops Chairs

Dr Thomas Lönngren, *Former Executive Director, EMA*
Professor Sir Alasdair Breckenridge *Chairman, MHRA, UK*
Professor Robert Peterson, *Executive Director, Drug Safety and Effectiveness Network. Canadian Institute of Health, Canada*

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A complete Workshop Report including full presentation summaries and syndicate recommendations will be available shortly.

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