WORKSHOP REPORT

Regulatory agency collaboration and system strengthening – How is this enabling national, regional and continental models and improving medicines availability for patients?

26-27th February 2025
Marriot Melrose Arch,
Johannesburg, South Africa

CIRS Centre for Innovation in Regulatory Science

Executive Summary

Background

The increasing complexity of new products creates regulatory challenges for national regulatory authorities (NRAs) with limited resources. NRAs must therefore strengthen their regulatory systems, alongside ensuring the best use of resources and expertise.

Most countries are implementing risk-based approaches to medicines regulation, using various models including unilateral reliance through abridged review, work sharing and collaborative procedures. These exist at the national level and increasingly within regions, such as Asia (ASEAN), Eurasia (EAEU), Middle East (GHC), and Africa (EAC, WAHO, SADC, IGAD), as well as across regions (e.g. Access Consortium and Project Orbis).

Regional models, such as those in Africa, provide learning and information exchange platforms and enable further collaboration at a continental level; however, apart from Europe, continental models are few in number. As Africa looks to build a continental system through the establishment of the African Medicines Agency (AMA), there needs to be support from strong NRAs within different regions and collaborative regional models that can provide early availability to good quality medicines.

CIRS has been promoting regulatory system strengthening in Africa at the jurisdictional level and conducting studies assessing the effectiveness and efficiency of the regional work-sharing initiatives, ultimately supporting the foundations for a continental model. CIRS has also supported jurisdictional and regional work in Asia and Latin America.

This multi-stakeholder workshop built on this work to discuss how jurisdictional system strengthening and regional regulatory collaboration can underpin the development of efficient and effective regulatory systems, which in turn builds competency and capacity, ensuring the availability of high-quality medicines to patients globally.

Objectives

- Identify the critical success factors and activities that agencies need to put in place to strengthen their regulatory systems for the registration of medicines and how this is being carried out at a jurisdictional (national) level and through regional work-sharing initiatives.
- Discuss the opportunities, challenges and lessons learned from current initiatives and practices that enable jurisdictions and regional work-sharing initiatives to move from concept to practical implementation.
- Make recommendations on how jurisdictional system strengthening and regulatory collaboration can drive continental models across agencies and improve medicines availability for patients globally.

Key points from presentations and open-floor discussions

Jurisdictional regulatory strengthening: A foundation for regional and continental collaboration

NRAs must have autonomy, strong regulatory frameworks supported by legal instruments and commitment from leadership to ensure effective collaboration at regional and continental levels. Comprehensive benchmarking, such as through the WHO Global Benchmarking Tool (GBT), is important for NRAs to assess the strength of their regulatory systems and identify where improvements can be made. This has been demonstrated by the achievements of Singapore (attained Maturity Level 4 (ML4) in 2022, then WHO-Listed Authority (WLA) in 2023), South Africa (attained ML3 for vaccines in 2022) and Ghana (attained ML3 for medicines and vaccines in 2020, working to achieve ML4 by the end of 2025).

Building trust and enhancing transparency helps to enable collaboration between NRAs. However, there can be a challenge with resource allocation between national duties and supporting other NRAs, such as through regional centres of excellence.

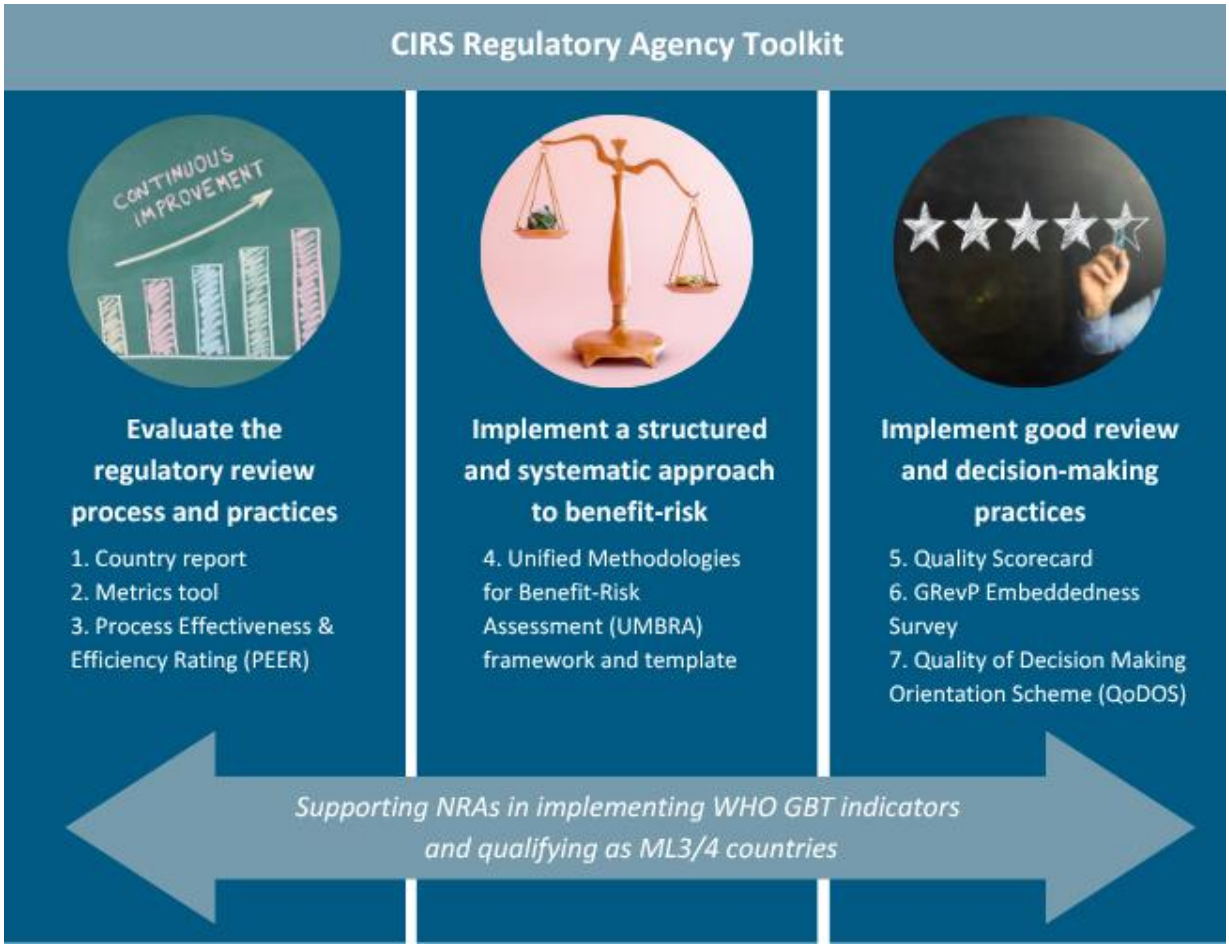
Key components of regulatory strengthening

Tools

Regulatory science tools are key to strengthening regulatory systems and to improve efficiency and effectiveness of NRAs, irrespective of maturity. These include tools to evaluate regulatory capacity e.g. WHO GBT, as well as tools to evaluate review timelines or ensure a structured approach to decision making e.g. CIRS toolkit (pictured).

The WHO GBT assessment process includes nine regulatory functions and evaluates elements like legal provisions, organisation, quality management and regulatory processes. As of February 2025, 50% of benchmarked WHO Member States are at maturity level 1, 19% at level 2, and 31% at levels 3-4. The institutional development plan in the GBT methodology provides context-specific actionable steps countries can take to advance their system's functionality and maturity.

The CIRS Optimising Efficiencies in Regulatory Agencies (OpERA) Programme provides tools that help NRAs integrate a practice of tracking and measuring performance. There are tools for process mapping and metrics, assessing embeddedness of good review practices, benefit-risk assessment and supporting quality decision making. These tools are linked to WHO GBT indicators and can help agencies achieve and maintain ML3 or ML4 status by providing frameworks for measuring timelines, documenting procedures and ensuring quality decision making.



Metrics

Case studies from Zambia and Brazil highlighted the importance of using metrics to measure agency performance. To support its progression to ML3 status, the Zambia Medicines Regulatory Authority (ZAMRA) conducted a study using CIRS OpERA tools to assess its review process. Recommendations from the study included establishing clear timelines for both regulatory authority reviews and industry time, publishing public assessment reports and providing more internal training on structured benefit-risk assessment methodologies.

The Brazilian Health Regulatory Agency (ANVISA) has also used CIRS OpERA tools to establish a baseline for measuring performance. More recently, as it works towards WLA status, ANVISA has been enhancing transparency of its metrics. While this brings challenges, such as higher stakeholder expectations and dependency on analytical tools, there are many benefits, including fewer information requests, better public image and clear justification of decision making.

From an industry perspective, agencies should report overall approval timelines, review milestones, company response timelines, common types of queries raised by the agency and agency adoption of harmonisation. An agency assessment of company compliance with regulations, transparency and post-market surveillance (e.g. a trust index) allows for transparent discussion between companies and agencies and provides background on agency decisions taken.

Quality decision making

Case studies from Canada and South Africa demonstrated the value of decision-making tools and resources in supporting regulatory decisions. Health Canada developed a Regulatory Decision Guide to improve internal documentation of decision-making processes, reduce litigation risk and strengthen/maintain the integrity of its decisions. The guide includes sections on roles and responsibilities, types of decisions, decision-making excellence and handling diversity of views, with practical case studies in administrative law.

The South African Health Products Regulatory Authority (SAHPRA) conducted a series of studies to investigate the value of a structured benefit-risk assessment of new chemical entities using the Universal Methodology for Benefit-Risk Assessment (UMBRA) framework. Use of the UMBRA template alongside the SAHPRA template enhanced the quality of the benefit-risk assessment and justification for the review outcomes. Completion of the UMBRA template based on public assessment reports led to shorter review timelines, suggesting that UMBRA could be a useful tool for reliance.

Reliance

Case studies from Australia and South Africa focused on the practical implementation of reliance and its economic impact, respectively. The Therapeutic Goods Administration (TGA) has relied on information from comparable regulators for decades, building confidence that has been key to recent implementation of work sharing through the Access Consortium. There needs to be early and strong buy-in from those directly impacted by and involved in reliance, with clear communication of the rationale and potential benefits. Governance arrangements supporting reliance must be continually reviewed and feedback from those working within the system listened to.

Research from SAHPRA's Backlog Clearance Project showed significant cost savings (77-81% reduction in assessor costs) through implementing reliance. This demonstrates that reliance is a tool to safeguard NRA resources and could help to offset the financial efforts required to attain higher WHO GBT maturity levels. Furthermore, an industry survey indicated support for potentially higher fees for reliance reviews, provided NRAs adhere to published timelines.

Navigating complexities of regional and transregional collaboration

Learnings from the Access Consortium and ASEAN Joint Assessment were shared. Trust and transparency among participating agencies are essential for successful collaboration. Within agencies, strong leadership and fostering a culture of learning can help to prevent potential inefficiencies in a work-sharing arrangement, for example, where reviewers may conduct a peer review of their own work before sharing it externally with partnering agencies for their peer review. Regulators should consider stronger advocacy work to promote awareness and adoption of collaborative models among industry.

From an industry perspective, there are several barriers to effective regional/transregional collaboration including limited benefit vs other procedures, lack of transparency and inefficient use of reliance. The vision should be for a single harmonised global dossier, with scientifically justified requirements and predictable timelines across countries. Measuring impact with standardised Key Performance Indicators (KPIs) is also key to refining models.

Moving from regional to continental collaboration in Africa

Africa is moving from regional to continental collaboration through the African Medicines Agency (AMA), under the leadership of the African Medicines Regulatory Harmonisation (AMRH) initiative. AMA will complement, not replace, aspects of the work of regional economic communities (RECs) and NRAs, improving efficiency and effectiveness through work sharing and reliance, and increasing capacity to assess complex medical products.

The RECs are important coordination structures that have helped to harmonise standards across African NRAs. Key challenges include varying decision-making timelines by NRAs following recommendations and the availability of competent experts to support technical work. There are plans to pilot continental technical standards, benchmarking against international ones, as well as continuing capacity development and strengthening more African NRAs towards ML3.

Vaccine manufacturing projects in Africa are progressing but face commercial, technical and regulatory challenges. Regional initiatives are key to supporting capacity for vaccine regulation in Africa. Greater focus on collaboration is needed, utilising facilitated regulatory pathways, reliance, work sharing and information sharing among vaccine regulators.

Leveraging digital solutions to support collaboration

Case studies from regulatory and industry experts were shared on the challenges and opportunities for implementing digital solutions, such as information management systems, cloud-based submission/review platforms and artificial intelligence (AI) tools, within jurisdictional and collaborative regulatory models. Cloud-based platforms enable multiple NRAs to have access to the same dossier, giving assurance of sameness and facilitating reliance and work sharing. However, individual country queues may prevent timely handling of applications. AI can automate tasks such as technical screening and report generation and potentially enhance regulatory decision making by providing actionable insights aligned with best practices.

There are several challenges for implementing digital regulatory solutions including cost, technical competencies, data security, data governance and for AI in particular, ethical issues. Nevertheless, these may be outweighed by the opportunities to improve regulatory efficiency and transparency, and in turn, enhance trust and collaboration.

Recommendations from breakout discussions

Key components of regulatory strengthening

- Investigate reference agencies' practices in providing unredacted assessment reports:
  - What are current practices?
  - What role do companies play?
  - What are the limitations in each agency's jurisdiction?
- Characterise different countries' regulatory frameworks that support national implementation of regional/collaborative procedures:
  - What does the end-to-end process look like?
  - What are best practices?
- Explore whether the UMBRA benefit-risk framework can facilitate reliance implementation.
- Study non-scientific country-specific requirements:
  - How divergent are they across countries?
  - What is their purpose?
  - Can they be harmonised/streamlined?

Qualitative and quantitative metrics underpinning regulatory strengthening

- Share case studies to support change management in agencies.
- Support the development of KPI systems and tools including:
  - Investing in capacity building / training.
  - Develop an IT solution (once metrics are known), embedding KPIs into the system operations.
  - Design decision dashboards and iterate with feedback loops.
- Publish KPIs from ML3+ countries, showcasing best practices - these can be used as a case for change by other NRAs.
- Support KPI and metrics capacity by:
  - Investigating who is using which metrics and why.
  - Establishing common terminology for KPIs and metrics.
  - Conducting pilots and publishing results from NRAs.
  - Allowing KPIs to be flexible and evolve with time.

Reliance/workshare review model for generics

- Identify lessons learned from agencies and industry who have experienced reliance in practice.
- Evaluate risk-based models implemented in different countries; this could be covered as part of WHO GBT assessments.
- Enable regulatory systems to allow transparency and information sharing.
- Implement unique manufacturing facility identifiers.
- Explore how AI can enable better reliance practices by different agencies.
- Agencies should develop, implement and publish criteria for prioritising applications based on public health needs, medicine shortages and multiplicity.

GRAPHIC SUMMARY

CIRS brought together regulators, pharmaceutical companies, academics and non-profit organisations to discuss **success factors** for **strengthening regulatory systems** to support the implementation of **collaborative models**.

Workshop Programme

Please click on a section of interest to find that section in the report.

Day 1: Wednesday 26th February 2025

Session 1: Why jurisdictional regulatory strengthening is key to underpinning regional and continental collaboration	
09:00	**Chair's welcome and introduction** **Dr Steffen Thirstrup,** Chief Medical Officer, European Medicines Agency (EMA)
09:05	**Country welcome and keynote presentation** **The importance of individual agency regulatory strengthening within a region - Is this a key cornerstone for a strong regional model/continental model?** **Dr Boitumelo (Tumi) Semete,** Chief Executive Officer, South African Health Products Regulatory Authority (SAHPRA)
09:25	**Discussion**
09:30	**Case studies on regulatory strengthening - What do agencies need to consider and what are the particular challenges and rewards?** **Singapore – Attaining ML4 and WLA listing – Agnes Chan,** Director, Therapeutic Products Branch, Health Sciences Authority, Singapore [Pre-recorded presentation] **Ghana - Moving from ML2-ML3-ML4 – Joseph Ofosu Siaw,** Acting Director, Business Development and International Partnerships, Food and Drug Administration, Ghana
10:00	**Panel discussion – Why is there a need for strong jurisdictions as a centre of excellence within a region?** **Dr Boitumelo (Tumi) Semete,** Chief Executive Officer, SAHPRA **Joseph Ofosu Siaw,** Acting Director, Business Development and International Partnerships, and Head, Quality Management Systems, Food and Drug Administration Ghana **Richard Rukwata**, Director-General, Medicines Control Authority, Zimbabwe **Ginny Beakes-Read**, VP and Head, Global Regulatory Policy, Johnson and Johnson, USA
10:45	**Break**
Session 2: Key components of regulatory strengthening - How can agencies improve step wise and what should they concentrate on to build capacity?	
11:15	**What are the tools, practices and agency activities that build capacity and competency?** **WHO Global Benchmarking Tool - Does this provide a workable framework for jurisdictional regulatory strengthening?** **Dr Tariro Sithole,** Technical Officer – Health Products Regulation, World Health Organization (WHO), Ethiopia **CIRS tools – How do they support agencies in preparation for the WHO GBT assessment?** **Prof Stuart Walker,** Senior Advisor and Founder, CIRS
11:55	**Discussion**

12:05	**Focus on performance metrics** **Utilising quantitative and qualitative metrics to aid ZAMRA to measure its performance** **Constance Chisha**, Senior Registration Office Human Medicines, Medicines Regulatory Authority, Zambia **Transparency of performance metrics: Pros and cons** **Raphael Sanches Pereira**, Deputy General Manager, Drugs Office, ANVISA, Brazil **What key measures should an agency report and why are these important to companies?** **Puvi Naidoo,** Regulatory Lead, SSA Cluster, Pfizer, South Africa
12:50	**Discussion**
13:00	**Lunch**
Session 3: Case studies relating to regulatory strengthening activities to improve process or meet GBT standards	
14:00	**Chair's introduction** **David Mukanga,** Deputy Director Africa Regulatory System, Gates Foundation, Kenya
14:05	**Focus on quality decision making practices** **Embedding quality decision-making practices within an agency** **Dr Supriya Sharma,** Chief Medical Adviser, Health Canada **Implementing a systematic structured approach to benefit risk assessment and decision making - does this improve the efficiency and effectiveness of the review?** **Dr Star Khoza,** Clinical Evaluator, SAHPRA
14:35	**Discussion**
14:45	**Focus on reliance** **Changing reviewer's mindset to enable practical implementation of reliance within and agency – What are the practical steps needed and how can this be best achieved?** **Mr Michael Wiseman,** Assistant Secretary, International Regulatory Branch, Therapeutic Goods Administration, Australia **Economic impact of implementing reliance – Is there an economic benefit for agencies?** **Lorraine Danks,** Senior Program Officer, Gates Foundation, South Africa
15:20	**Discussion**
15:30	**Break**
Session 4: What frameworks do agencies need to practically use regional/transregional models?	
16:00	**Moving from regional to continental collaboration – What is the approach for Africa and how is this going to be practically implemented?** **Chimwemwe Chamdimba,** Head of the African Medicines Regulatory Harmonisation, African Union Development Agency (AUDA-NEPAD)
16:20	**Discussion**
16:25	**Implications of local vaccine manufacturing – How does regulatory thinking or ways of working need to change?** **Prof John Skerritt,** Enterprise Professor for Health Research Impact, University of Melbourne, Australia

16:45	**Discussion**
16:50	**Panel discussion – How can regulatory agencies better navigate complexities of regional and trans regional collaboration to improve access to high quality safe and effective medicines?** **Access Consortium – Dr Eveline Trachsel,** Head of Medicinal Products Approval and Vigilance, Member of the Management Board, Swissmedic **ASEAN Joint Assessment Procedure – Dr Azuana Ramli,** Director, National Pharmaceutical Regulatory Agency, Malaysia **Industry perspective – Nevena Miletic,** Regulatory Policy and Science Chapter Leader, F. Hoffmann-La Roche
17:40	**Introduction to breakout discussions**
17:45	**End of Day 1**
18:30	**Reception, followed by dinner**

Day 2: Thursday 27th February 2025

Session 5: Breakout discussions	
08:30	**Breakout A: Key components of regulatory strengthening for the review of medicines – What are the building blocks of an effective jurisdictional regulatory review process and how to maximise this for collaborative resource sharing?** **Chair: Dr Steffen Thirstrup,** Chief Medical Officer, EMA **Rapporteur: Nevena Miletic,** Regulatory Policy and Science Chapter Leader, F. Hoffmann-La Roche **Breakout B: Qualitative and quantitative metrics can underpin regulatory strengthening – What should be measured and how this can be best integrated into an agency process, practice and mindset?** **Chair: Dr Murray Lumpkin,** Lead for Global Regulatory Systems Initiatives, Gates Foundation, USA **Rapporteur: John Mwangi,** Regulatory Policy Science Lead, Bayer, Kenya **Breakout C: Reliance/workshare review model for generics - Same or different considerations compared to new medicines?** **Chair: Dr Tariro Sithole**, Technical Officer – Health Products Regulation, WHO, Ethiopia **Rapporteur: Amira Younes,** Director, Global Regulatory Policy, Europe, Middle East and Africa, MSD, United Arab Emirates
10:00	**Break**
10:30	**Breakout discussions continue**
12:00	**Lunch**

Session 6: New ways of working – Key to success in a resource constrained environment	
13:30	**Chair's Introduction - Dr Boitumelo (Tumi) Semete,** Chief Executive Officer, SAHPRA
13:35	**Feedback by breakout rapporteurs, followed by discussion**
14:30	**The importance of leveraging a robust Information management system (IMS) – What is being planned and what are the challenges?** **Dr Nancy Ngum,** Programme Officer - Public Health, AUDA-NEPAD
14:45	**Discussion**
14:50	**Use of digital/cloud-based sharing (Accumulus) - What are the principles and how could this aid agencies as they look to increase efficiency and effectiveness?** **Dominique Lagrave,** Senior Vice President, Innovation, Accumulus Synergy, USA **Company case study on the utilisation of cloud-based sharing: Challenges and opportunities** **Mike Abernathy,** Executive Director, Global Regulatory Affairs/Digital Regulatory Innovation Lead, Amgen, USA **Agency case study on the utilisation of cloud-based sharing: Challenges and opportunities** **Suraiya Suliman,** Manager: PEM Post-registration, SAHPRA
15:30	**Discussion**
15:40	**Regulation meets innovation: Leveraging AI for health product safety** **Christelna Reyneck,** Chief Operations Officer, SAHPRA
16:00	**Discussion**
16:10	**Chair's summary**
16:20	**Close of workshop**

Session summaries

Please note that the following summaries represent the views of the individual presenters and do not necessarily represent the position of the organisation they are affiliated with. Included slides are attributed to the individual presenters and have been reproduced with their permission.

Session 1: Why jurisdictional regulatory strengthening is key to underpinning regional and continental collaboration

The importance of individual agency regulatory strengthening within a region - Is this a key cornerstone for a strong regional model/continental model?

Dr Boitumelo (Tumi) Semete, Chief Executive Officer, South African Health Products Regulatory Authority (SAHPRA)

There are four key elements that national regulatory authorities (NRAs) should focus on to strengthen their regulatory systems and thus enable strong regional and continental models.

1) Legal frameworks and autonomy

Countries must have robust legal frameworks that enable medicine regulation, by supporting collaborative and reliance practices, but most importantly, NRA autonomy. Many African countries lack these frameworks, hindering their NRAs from achieving Maturity Level 3 in the WHO Global Benchmarking Tool (GBT).

Building on these legal foundations are national regulations and guidelines. NRAs must ensure that these align with global best practices and standards, such as International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines.

2) Collaboration at national, regional and international levels

NRAs need to be able to collaborate with partners at the national level, particularly regarding post-market activities like pharmacovigilance and post-market surveillance. For example, SAHPRA worked with national partners to launch the WHO National Action Plan for the management of substandard and falsified products, a key issue that cannot be tackled by NRAs alone.

Regional and international collaborations are also essential, whether through collaborative reviews, worksharing, information sharing or observing other NRA assessments. Through the EU-M4All procedure, SAHPRA has been exposed to EMA practices, benefitting not only SAHPRA's assessors but also South African patients, who have gained faster access to high priority medicines.

3) Improving capability

Improving NRA capability is a key part of regulatory system strengthening. SAHPRA has piloted the rigorous WHO Competency framework process as a mechanism to assess internal capabilities, identify skills gaps and initiate structured training plans. This has helped with individuals' career development, hopefully helping to improve staff retention.

4) Digitalisation to build capacity

NRAs must digitalise their processes to improve efficiency and address capacity challenges. SAHPRA has recently implemented a Regulatory Information Management System (RIMS) and developed three artificial intelligence proof-of-concept tools for specific tasks of a repetitive nature, such as technical screening for dossiers and GMP assessments.

Attaining ML4 and WLA – Singapore's journey of regulatory strengthening and innovation

Agnes Chan, Director, Therapeutic Products Branch, Health Sciences Authority (HSA), Singapore

As Singapore is a small country, HSA continuously endeavours to maximise the use of its scarce resources through innovation. Validation through external evidence-based assessments, such as the WHO Global Benchmarking Tool (GBT), not only helps to advance public health but also strengthens public trust and promotes regulatory cooperation, convergence and transparency globally.

GBT assessment

The GBT uses a rigorous, structured approach to assess key regulatory functions. It is an extensive tool comprising of over 250 indicators to objectively assess the level an NRA is operating at. For example, key assessments of the marketing authorisation function include autonomy and legality; integration of Good Regulatory Practices; evaluation team competency; and accessibility of online resources.

HSA began GBT assessment in March 2020 and despite the challenges of the COVID-19 pandemic, attained Maturity Level 4 (ML4) status in January 2022. HSA adopted WHO's recommendations following the benchmarking audit and implemented improvements, including enhanced tracking of internal timelines and establishing mechanisms for sharing evaluation and inspection reports with other NRAs.

While the GBT provides overarching principles and global standards, it is important to recognise that each country has unique circumstances that need to be considered. For some GBT indicators, HSA has tailored its approach to meet stakeholder needs, which WHO accepted after open discussions.

Journey towards WLA

HSA continued its regulatory strengthening journey by participating in the WHO-Listed Authority (WLA) pilot between 2022-2023. Following a rigorous process involving multiple onsite and virtual assessments, HSA attained WLA Listing for medicines in October 2023, with an additional requirement for the market surveillance function. WLA status for all functions was attained in May 2024. The WLA status helps to promote HSA as a reference agency for reliance-based reviews.

The WLA Performance Evaluation indicators under the marketing authorisation function relate to compliance with procedures and timelines, transparency, resources for stakeholders, use of an advisory committee, KPI tracking and access to evaluation reports, including for rejected applications. To improve transparency, HSA enhanced its website to include information on pre-submission consultation, summary reports of benefit-risk assessment, listing of approvals and post-registration actions. These features were devised to enhance access to information and facilitate industry stakeholders to seek regulatory advice.

Challenges and opportunities

For HSA, the WLA process was a balancing act of exceptional staff dedication and efficient resource allocation. While there were several challenges, such as obtaining consent to share confidential information and coordination with various third parties, there were also valuable opportunities. The synergy and robust exchange of ideas with WHO assessors enabled constructive insights and opportunities for contextualising the WHO's requirements to the local context, ensuring that Singapore's system is globally aligned and locally optimised. The WLA process also helped to improve HSA's communication with its stakeholders and cultivated strong teamwork internally and externally.

Conclusions

- We emerged stronger and more resilient through remaining steadfast in our vision, and committed in preparatory efforts supported by strong team work and collaborative approach with WHO

Vision

- Set goal to achieve WLA
- Developed a plan
- Worked closely with WHO and MOH to achieve the goal

Preparation & Action

- Conducted multiple internal reviews against benchmark tools & performance evaluation indicators
- Refined & improved our processes

Team Attributes

- Strong coordinated team with passion & perseverance
- Openness of WHO & International assessors in understanding HSA's risk-based approach
- Continually improve & adapt

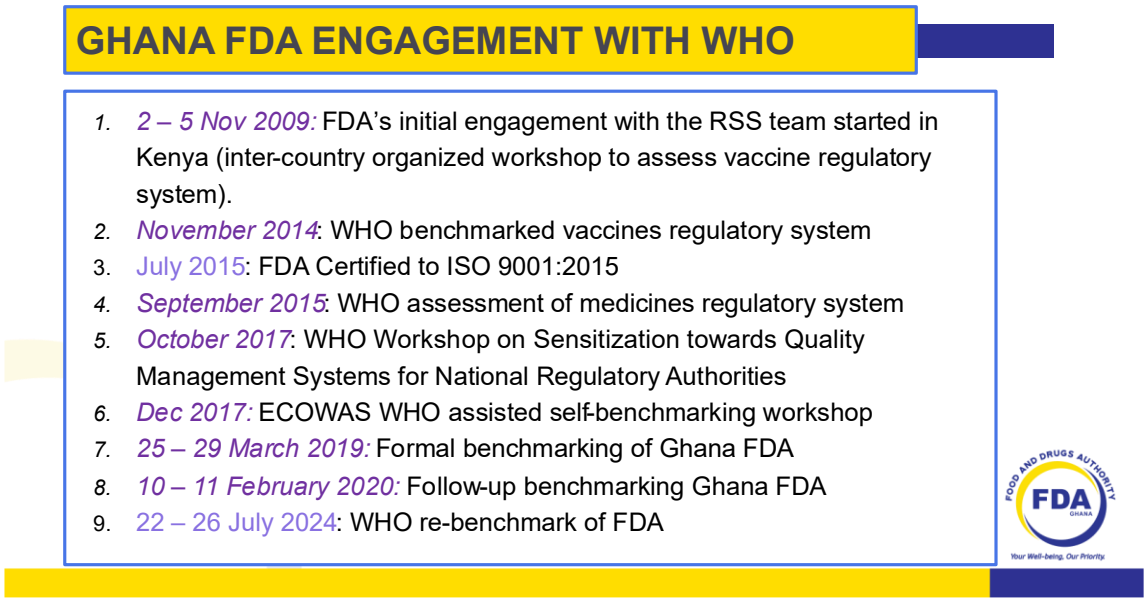
Ghana's Journey to WHO GBT Maturity Level 3

Joseph Ofosu Siaw, Acting Director, Business Development and International Partnerships, and Head, Quality Management Systems, Food and Drug Administration Ghana

Food and Drugs Authority (FDA) Ghana is a WHO Global Benchmarking Tool (GBT) maturity level 3 (ML3) agency, with its pharmacovigilance function being designated ML4. FDA is also a Regional Centre of Regulatory Excellence (RCORE) in medicines registration, safety monitoring and pharmacovigilance, and clinical trial oversight.

GBT assessment

FDA Ghana underwent GBT assessment to enhance regulatory capacity and become a Global Centre of Excellence for food and medical product regulation. Over 15 years, FDA Ghana engaged with WHO in a stepwise approach to obtain system certifications (see below). At the time of the first benchmarking visit in 2019, FDA did not meet 27 ML3 sub-indicators and received institutional development plans to work on. By 2020, only four ML3 sub-indicators remained unmet, and FDA was granted ML3 status.



Key processes for achieving ML3

1. **Strategic initiative**: Commitment from FDA's management and board.
2. **Request for benchmarking**: Expressing interest and communicating with WHO.
3. **Resource allocation**: Providing necessary resources (human, financial, equipment, information systems) to support the benchmarking process.
4. **Multi-disciplinary team**: Establishing a team from relevant regulatory functions.
5. **Quality manager**: Assigning a focal point for WHO contact and information sharing.
6. **Roadmap adherence**: Following timelines for benchmarking activities.
7. **Documentation**: Completing the GBT with relevant evidence and uploading to WHO's platform.
8. **Stakeholder engagement**: Involving national stakeholders including the Ministry of Health.

9. **WHO interaction**: Regular communication with WHO staff and the benchmarking team.
10. **Monitoring and motivation**: Continuously monitoring and motivating the implementation team.

Strengths and recommendations

The GBT process highlighted many strengths in FDA's regulatory system, including having a strong legal basis, reliance policy for key regulatory functions, risk-based approach to regulatory decision making, established relationships with other government institutions, competent staff and integrated quality management system. Between 2020-2024, FDA implemented WHO's recommendations for improvement, which included enhancing its documentation system, addressing human resource gaps, establishing a national ethics committee, enhancing internal communication and implementing a risk-based post-marketing surveillance programme.

Summary

The WHO GBT process leads to many benefits such as more stable, well-functioning and integrated regulatory systems, improved service delivery, better customer satisfaction, increased recognition at national, regional and international levels, and improved collaborations with other NRAs. FDA Ghana achieved ML3 status in July 2020 through key processes including senior management commitment and regular communication with WHO. The agency is working to achieve ML4 status by the end of 2025 and is using its experience and knowledge to help other African NRAs to achieve ML3 through its role as an RCORE.

Panel discussion: Why is there is a need for strong jurisdictions as centres of excellence within a region?

Dr Boitumelo (Tumi) Semete, Chief Executive Officer, SAHPRA

Joseph Ofosu Siaw, Acting Director, Business Development and International Partnerships, and Head, Quality Management Systems, Food and Drug Administration Ghana

Richard Rukwata, Director-General, Medicines Control Authority, Zimbabwe

Ginny Beakes-Read, VP and Head, Global Regulatory Policy, Johnson and Johnson, USA

Key discussion points

- **Regulatory system strengthening**: While pursuing regional collaboration, NRAs must maintain strong regulatory systems to ensure patient safety, product quality and efficacy. The goal is to build strong NRAs capable of making independent decisions while collaborating with other NRAs for support and guidance.
- **International standards and harmonisation**: Adhering to international guidelines and standards, such as those from ICH and WHO, is key.
- **Predictability and transparency**: Both regulators and companies must adhere to clear timelines, processes and guidelines.
- **Centres of excellence**: Regional centres of excellence have a role in supporting regulatory capacity and training. All member states should be represented in regional and continental decision-making processes, even if not all contribute equally.
- **Reliance**: NRAs must retain autonomy while relying on assessments from other regulators.
- **Digitalisation**: Implementing electronic systems and automating processes are key to enhancing regulatory transparency and efficiency.

Challenges and potential solutions

- **Post-market activities**: Need for more focus and investment into post-market surveillance to ensure ongoing product safety and quality.
- **Change management**: Strategies to shift mindsets within NRAs may facilitate adoption of new practices like reliance and digitalisation.
- **Resource management**: Balancing resources between national duties and supporting other NRAs is challenging. NRAs should explore partnership and funding opportunities to support capacity building and resource sharing.
- **Regulatory autonomy**: Politicians may need to be convinced of the importance of maintaining NRA autonomy and not just relying on assessments from other NRAs.

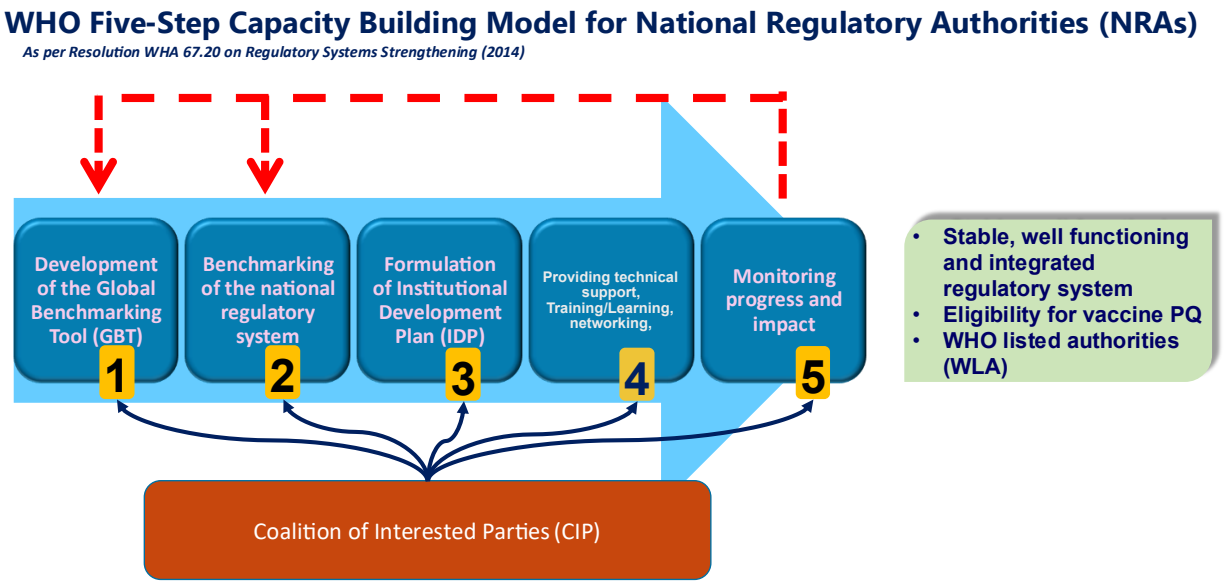
Session 2: Key components of regulatory strengthening - How can agencies improve step wise and what should they concentrate on to build capacity?

WHO Global Benchmarking Tool – Does this provide a workable framework for jurisdictional regulatory strengthening?

Dr Tariro Sithole, Technical Officer, Health Products Regulation, World Health Organization (WHO)

NRAs in low- and middle-income countries (LMICs) are often overburdened and under-staffed, with fragmented structures or insufficient legal frameworks. This leads to major challenges such as disparate regulations, unclear regulatory pathways, delays in processing applications and limited transparency. Other challenges are the prevalence of substandard and falsified medical products and the lack of regulatory preparedness for public health emergencies.

WHO was mandated by Member States to support them in reaching and sustaining effective regulatory oversight of medical products through its Regulatory Systems Strengthening (RSS) programme. One of the RSS programme's key activities is regulatory capacity building, which follows a five-step approach (see below). The Coalition of Interested Parties supports this by promoting a unified, coordinated approach to strengthening regulatory systems, aiming for greater effectiveness.



What is the Global Benchmarking Tool?

The Global Benchmarking Tool (GBT) is a global standard for objectively assessing capacity for regulatory oversight for medicines and vaccines. It has also been expanded to blood and blood products (GBT + Blood) and medical devices (GBT + Medical Devices). The GBT incorporates principles in WHO guidelines on Good Reliance Practices, Good Regulatory Practices, Good Review Practices and implementation of quality management systems, as well as other standards like ISO 9004.

The GBT assesses nine regulatory functions i.e. National Regulatory System, Registration & Marketing Authorization, Vigilance, Market Surveillance & Control, Licensing Establishments, Regulatory Inspection, Laboratory Testing, Clinical Trials Oversight and NRA Lot Release (for vaccine producing countries), covering cross-

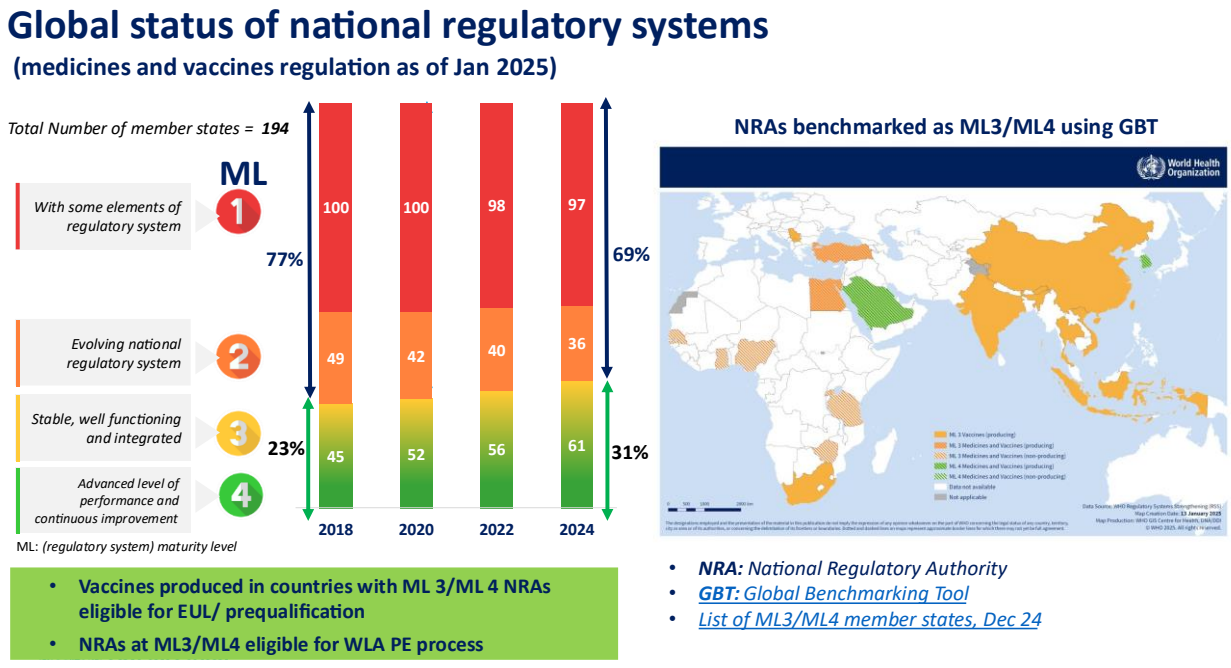
cutting elements such as legal provisions, governance, policy, leadership, transparency, quality management, regulatory processes, resources and progress monitoring.

How does the GBT process work?

The GBT process usually begins with a pre-visit from the WHO. Next, the NRA conducts self-benchmarking and creates an initial institutional development plan (IDP). The IDP in the GBT methodology identifies gaps and weaknesses and provides context-specific actionable steps that countries can take to advance their system's functionality and maturity. The WHO then verifies the self-benchmarking and carries out a formal visit to evaluate the regulatory functions and evidence of implementation before finalising the IDP, ensuring that it is effective and workable. The WHO then monitors the NRA's implementation of the IDP and continually provides support until the NRA reaches maturity level 3, which is defined as a stable, well-functioning and integrated regulatory system.

Which countries have been assessed using the GBT?

As of January 2025, 97 out of 194 Member States have been benchmarked using the GBT (both self-benchmarking and formal benchmarking), representing 77% of the world population. The global status of national regulatory systems determined using the GBT and other evaluation tools shows that 50% of Member States are at Maturity Level (ML) 1, 19% at ML2, and 31% at ML3-4. The number of ML3-4 Member States has been steadily increasing since 2018 (see below).



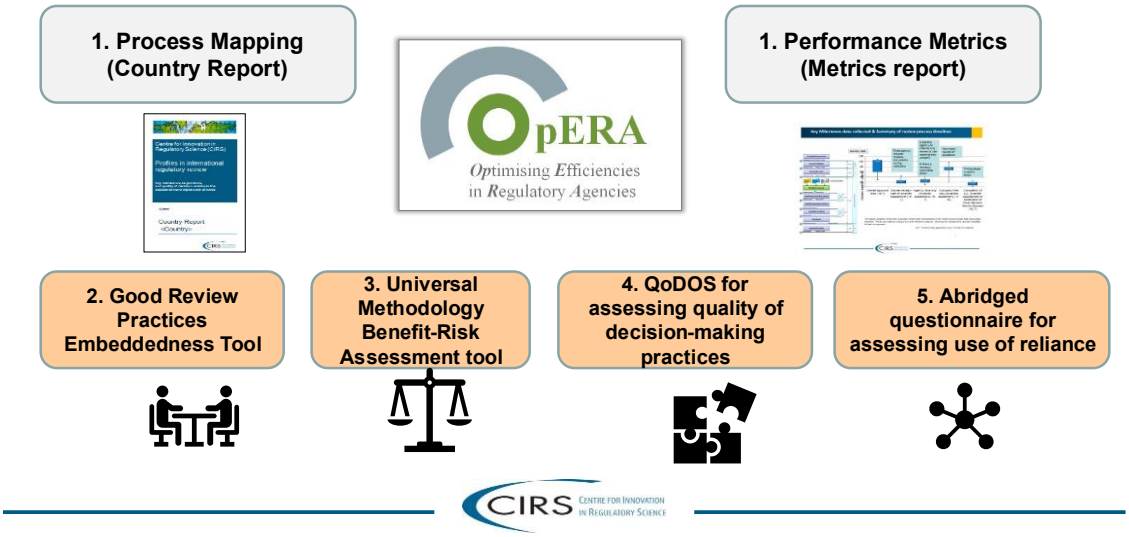
Summary

The WHO GBT is a workable framework for strengthening regulatory systems that also helps to foster regulatory reliance and harmonisation. However, regulatory strengthening remains a country-driven process that requires political will, supportive legal frameworks for independent NRAs, committed leadership, resources, infrastructure, partnerships, and continuous monitoring and improvement.

CIRS tools – How do they support agencies in preparation for the WHO GBT assessment?

Prof Stuart Walker, Senior Advisor & Founder, CIRS

CIRS has developed several regulatory strengthening tools that have been validated in collaboration with regulatory agencies. These tools form part of a comprehensive toolkit to support the Optimising Efficiencies in Regulatory Agencies (OpERA) Programme, a global programme available to all regulatory agencies irrespective of their size, mission or maturity. There are tools to provide evidence-based insights into agency performance (grey boxes below), and tools to support decision making (orange boxes below). The goal is to encourage a culture of benchmarking and self-assessment within agencies, driving continuous improvement.



Assessing performance using CIRS tools

The CIRS Country Report and Metrics Tool give insight into an agency's regulatory performance. The Country Report helps agencies to understand where time is spent in the regulatory process and identify process limitations. It is generated by CIRS following the agency's completion of a comprehensive questionnaire made up of five parts: organisation of the agency; types of review models; key milestones in the review process; Good Review Practices; and quality decision-making processes. Combined with the agency's metrics on approval timelines, validation and queuing time, and scientific assessment and registration time, observations can be made about the effectiveness and efficiency of the regulatory process and areas for improvement can be identified.

Questions that can be answered using the Country Report and Metrics Tool include:

- How much of the total approval time/scientific assessment time is agency vs company time?
- How much of the 'pick up' time is validation vs queue?
- What is the impact of activities prior to approval e.g. advisory committees, label negotiations, pricing?
- What are the drivers for time e.g. capacity issues, redundancy and ineffective practices?

CIRS tools in support of GBT indicators

CIRS' regulatory strengthening tools are linked to WHO GBT indicators and can help agencies achieve and maintain maturity level 3 or 4 status by providing frameworks for measuring timelines, documenting procedures and ensuring quality decision making. For example, the Metrics Tool links to GBT MA06 and the MA06.02, which

require the establishment and implementation of performance indicators for registration and/or marketing authorisation activities. The Universal Methodology Benefit-Risk Assessment (UMBRA) tool links to MA0401, which specifies that documented procedures and tools need to be implemented to assess different parts of the application i.e. safety, efficacy and quality. The Quality of Decision-Making Orientation Scheme (QoDoS) tool links to MA04.10, which ensures that regulatory decisions are adequately documented and there is consistency throughout the review process in terms of requirements and criteria for registration.

Summary

Regulatory system strengthening is imperative for all agencies irrespective of maturity and should include the use of metrics to assess performance and help optimise the review process. CIRS has been benchmarking regulatory authorities globally with tools to support efficient, effective and fit-for-purpose regulatory systems. CIRS tools help to incorporate a culture of process measurement and provide a starting point to assess regulatory performance for those agencies that aspire to become a WHO-Listed Authority.

Utilising quantitative and qualitative metrics to aid ZAMRA to measure its performance

Constance Sakala Chisha, Senior Registration Office Human Medicines, Medicines Regulatory Authority, Zambia

Introduction

A study was carried out under the CIRS Optimising Efficiencies in Regulatory Agencies (OpERA) Programme to assess the regulatory performance of the Zambian Medicines Regulatory Authority (ZAMRA). The objectives were to:

- Assess ZAMRA's current regulatory review process.
- Identify the key milestones and target timelines achieved in the review process.
- Evaluate the overall performance for the review models and different product types approved in Zambia during 2020–2023.

Methodology

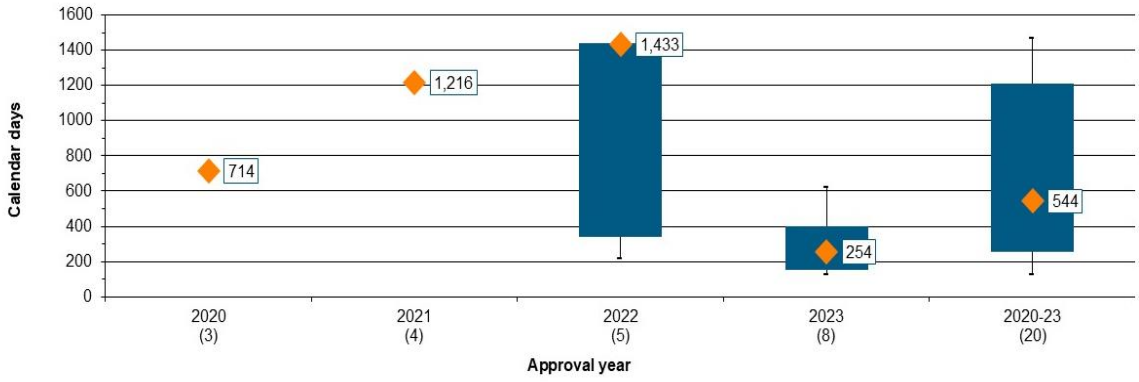
The OpERA questionnaire was used to generate the Country Report, which outlined the organisation of the agency, types of review models, key milestones in the review process, adoption of Good Review Practices (GRevP) and quality decision-making processes. The Metrics tool was used to outline the key milestones and review models used for the different types of products approved during 2020 to 2023.

Results

At the time of the study, ZAMRA had 14 assessors, with 10 additional assessors employed through support from a cooperating partner. Four review models were used: verification, abridged, fast track and full review. The following GRevP indicators had been implemented: internal quality policy, standard operating procedures, joint reviews (as part of the ZaZiBoNa initiative), feedback to industry on submitted dossiers, internal peer reviews and induction training.

From 2020 to 2022, the overall median approval time for new active substances (NAS) increased (see below). This was attributed to the COVID-19 pandemic, which slowed the review process and delayed submission of responses by applicants. In 2023, the median approval time for NAS reduced significantly due to the easing of COVID-19 pandemic pressures.

Approval timelines for new active substances approved by ZAMRA (2020-2023)



Data are shown for applications that were approved ("Marketing Authorisation Granted Date") between 01/01/2020 and 31/12/2023. (n) = number of drug applications.

◆ = Median. Where (n) is less than 5, only the median is displayed.

Taken from Chisha CS et al. 2024

ZAMRA mostly receives generic applications. The median approval time for generics during 2020-2023 was 1055 days, considerably higher than the NAS approval time of 544 days. Analysis of the review milestones indicated that the extended approval times for generics were due to lengthy queues and slower sponsor responses.

Recommendations for ZAMRA

- **Target timelines**: These need to be established for each milestone based on the review model and the type of the product.
- **GRevP**: These need to be standardised for the review process.
- **Transparency**: This could be enhanced by publishing public assessment reports.
- **Reliance**: To shorten the review times and ultimately the overall approval time, there is need to implement a reliance model especially for NAS that have been approved by stringent regulatory authorities or ML-4 agencies.
- **Benefit-risk assessment**: A structured approach should be included in the review process.
- **Quality of decision making**: A systematic quality decision-making framework would support consistency in the review process.

Transparency of performance metrics – Pros and cons

Raphael Sanches Pereira, Deputy General Manager, Drugs Office, ANVISA, Brazil

Public decisions and queues

Since its establishment in 1999, ANVISA has been required by law to publish all final decisions (both approvals and withdrawals) in the Official Gazette. This facilitates the issuing of reports to provide context on the agency's performance metrics e.g. percentage of reprovals or total analysis time.

The queue of requests waiting for analysis is also public, and is organised by class (registration of generics, innovative products, post-approval changes etc). All stakeholders can therefore check whether they are being treated equally by ANVISA. When enhancing transparency, agencies need to be ready to be questioned and to explain if/why they are treating stakeholders differently.

Lifecycle panel

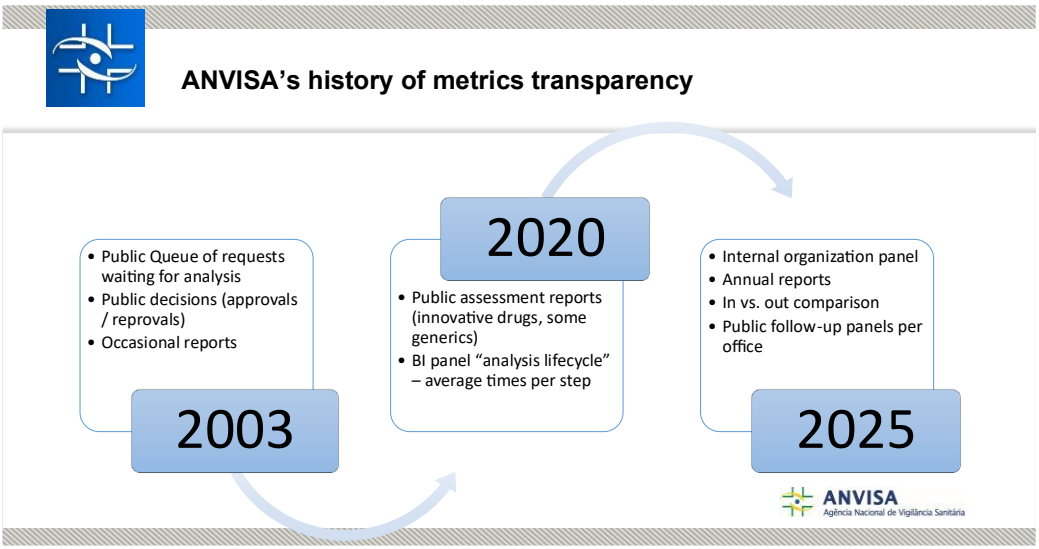
In 2020, ANVISA launched a Business Intelligence (BI) panel that enables lifecycle analysis of review times, such as lead times per evaluation step (queue, analysis, scientific evaluation, finalisation etc) and agency vs company time. The panel can be filtered by date, allowing monitoring of ANVISA's performance over time. The panel can also be filtered by the offices within ANVISA, which helps to identify internal bottlenecks and gives companies more predictability of response time e.g. when they can expect to receive CMC or bioequivalence related questions.

APIs of drugs waiting for decision

ANVISA often receives queries from patients or the media asking if there are any registration requests relating to a particular Active Pharmaceutical Ingredient (API). In 2024, a public BI panel organised by APIs was launched. This not only facilitates information sharing to patients and the medic but also allows generic companies to identify market trends.

In and out comparisons

Agencies must have an overview of how many requests they have received and how many decisions they are making. These 'in and out comparisons' can facilitate internal trend analysis, for example, to monitor whether a backlog is forming, and make decisions about workforce capacity.



Summary

- Transparency means publishing 'the good' as well as 'the bad'.
- Transparency is important for meeting some WHO Global Benchmarking Tool performance indicators.
- Benefits of transparency:
    - Better justification of decision making
    - All stakeholders have access to the same data
    - Improved public image and trust
    - Fewer transparency requests e.g. Freedom of Information requests.
- Challenges of transparency:
    - Dependency on BI tools
    - Frequent need for data checking and cleaning
    - Higher stakeholder expectations
    - Potential for misunderstandings by some stakeholders.

What key measures should an agency report and why are these important to companies?

Puvi Naidoo, Sub-Saharan Africa Regulatory Cluster Lead, Pfizer, South Africa

As medicines regulatory agencies evolve and the partnerships between agencies and companies are enhanced, there are several key measures that are important for both companies and regulatory agencies.

Key measures	Importance
Overall approval timelines for new chemical entities and generic applications, per pathway (annually)	• Companies can utilise this data to advocate for specific pathways to be used and to justify additional document requirements. • Can be used to evaluate regulatory agency and company efficiencies (year on year improvement).
Timelines for review within each of the process steps	• For agencies, this facilitates resource monitoring, identification of bottlenecks and process improvement. • For companies, this facilitates predictability by providing expected timelines within the regulatory process.
Company response timelines including number of requests for extension to respond (as allowed by regulatory agency) as well as reasons for extension requests	• Allows companies to critically evaluate their internal processes for regulatory agency responses. • Companies should respect the timelines to respond and provide the information required. • These measures allow for better discussion between agencies and companies on industry trends.
Common types of queries raised by the agency	• Assists with guideline development/enhancements. • Can focus in on the types of queries being raised during reliance to assess the agency's utilisation of reliance. • Gives companies better transparency for dossier improvement.
Agency assessment of company compliance, transparency, post market surveillance, track record and history e.g. a 'trust index'	• Allows for transparent discussion between companies and agencies. • Provides companies with background on the decisions taken by regulatory agencies.
Agency adoption of harmonisation e.g. tracking timelines and types of queries across countries in a region.	• Allows for assessment of agency adoption of harmonisation. • Facilitates planning of dossier submissions across multiple countries.

Summary

Regulatory performance measures can help both agencies and companies improve efficiency, transparency, and planning. Key measures include tracking approval timelines, review steps, company responses, agency queries, compliance assessments, and harmonisation efforts to support better decision making and collaboration.

Sessions 3: Case studies relating to regulatory strengthening activities to improve process or meet GBT standards

Embedding quality decision-making practices within an agency - Development and implementation of a Regulatory Decision Guide

Dr Supriya Sharma, Chief Medical Advisor, Health Products and Food Branch, Health Canada

As the national body responsible for regulating health products and food, the decisions a national regulatory authority makes are vital to the lives of its citizens. Therefore, it is very important that regulatory decisions, and the bases for those decisions, are transparent, reasonable, procedurally fair, and demonstrate due diligence in how they are documented and communicated.

Regulatory Decision Guide

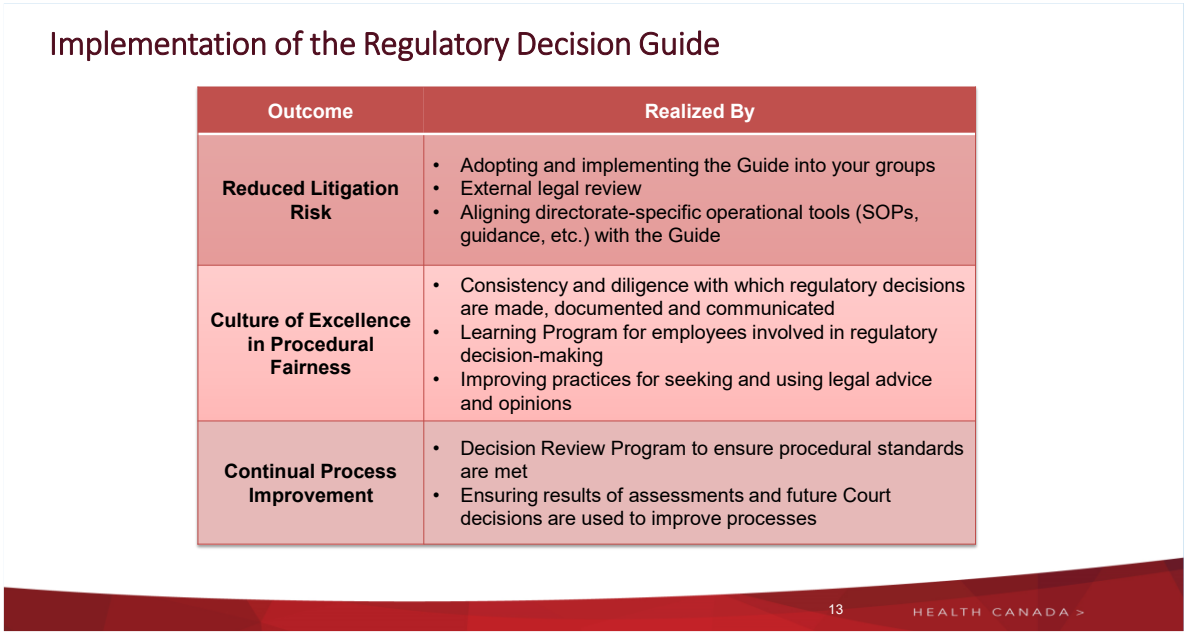
Health Canada's Health Products and Food Branch developed a Regulatory Decision Guide to improve internal documentation of decision-making processes, reduce litigation risk, strengthen and maintain public confidence in the regulator, and strengthen the integrity of decisions. The guide was developed by a Working Group comprised of junior and senior members from each regulatory Directorate within the Health Products and Food Branch. The guide includes sections on responsibilities, types of decisions, who makes the decisions, decision-making requirements, diversity of views, and decision-making excellence. Each section contains a practical case study to illustrate key administrative law points.

Handling diversity of views

Diversity of views is a healthy component of decision making and is inevitable in medicine regulation as decisions rely on information and opinions from various levels of management and reviewers. The primary goal should be to openly resolve differences in opinions, but if this is not possible, there should be a formal resolution process for staff to follow. The Health Products and Food Branch is currently updating the Standard Operating Procedure (SOP) for its formal resolution process, implementing learnings from the first phase of Regulatory Decision Guide implementation.

Implementation of the guide

Health Canada is monitoring implementation of the Regulatory Decision Guide using outcomes related to litigation risk, procedural fairness and continual process improvement (see below).



The Regulatory Decision Guide training is mandatory for all staff at the Health Products and Food Branch. Most staff who have taken the training have less than two years of work experience in the branch. Several staff, including managers, have taken the courses a second time as they found them helpful towards their day-to-day work. A new SharePoint page and e-mail inbox has been set up to further support staff with using the Regulatory Decision Guide.

Summary

Health Canada's Health Products and Food Branch developed a Regulatory Decision Guide to improve internal documentation of decision-making processes, reduce litigation risk and strengthen the integrity of decisions. Revisions are being made following learnings from the first phase of implementation of the guide, including an updated SOP for resolving diversity of views, improving clarity on the guide's scope, and exploring the potential for a separate section on reliance and work-sharing decision making.

Implementing a systematic structured approach to benefit-risk assessment and decision making – SAHPRA experience with the UMBRA framework

Dr Star Khoza, Clinical Evaluator, South African Health Products Regulatory Authority (SAHPRA), and Associate Professor, Pharmacology and Clinical Pharmacy, University of the Western Cape

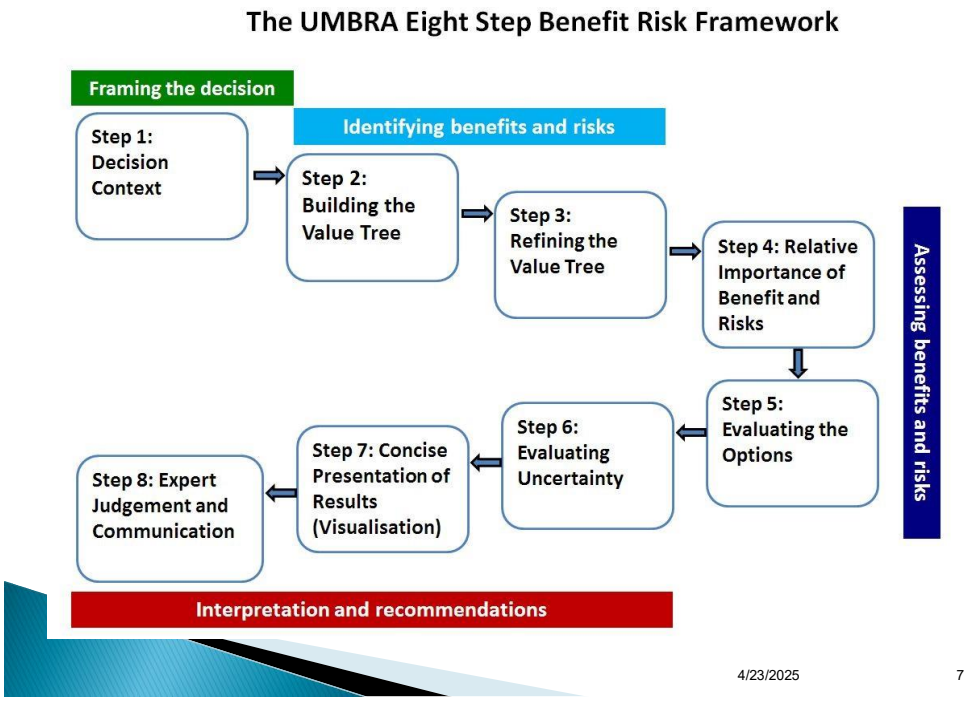
Background

SAHPRA inherited a large backlog of applications from a former agency, the Medicines Control Council. While it was important to clear the backlog, SAHPRA also had to ensure that those decisions were quality decisions following a standardised process. There were concerns about the potential for subjective and inconsistent decision-making processes at SAHPRA, especially regarding prescribing information. The UMBRA pilot conducted in collaboration with CIRS was an opportunity to reflect and review how to enhance the quality of the decision-making process and benefit-risk assessment.

UMBRA framework

Having a benefit-risk framework supports a better understanding of outcomes and why different agencies may come to different decisions and conclusions, often based on the same data. Without one, decisions can be challenged as they rely on the expertise of reviewers rather than a standardised decision-making process.

The Universal Methodology for Benefit-Risk Assessment (UMBRA) framework, developed by CIRS, consists of eight steps designed to frame the decision, identify the benefits and the risks, assess those benefits and risks, and interpret them to make recommendations (see below).



UMBRA project

SAHPRA conducted a series of studies in 2021-2022 to evaluate the value of the UMBRA template in making benefit-risk decisions and investigate whether it could enhance the quality of SAHPRA's decision making. Six new chemical entity applications from the backlog were reviewed by three SAHPRA assessors (two applications each). Each assessor conducted a retrospective review of a previously evaluated application (the UMBRA template was completed using the evaluation report), and a prospective review of a new application (the UMBRA template was completed alongside the SAHPRA clinical evaluation template).

Results

The UMBRA template's approach of assigning weights to benefits and risks identified in the clinical trial was found particularly useful by the SAHPRA assessors. Use of the UMBRA template alongside the SAHPRA template enhanced the quality of the benefit-risk assessment and justification for the review outcomes. Use of the UMBRA framework also led to recommendations that were more aligned with the EMA and/or US FDA for the prescribing information (SmPC, Professional Information). In addition, completion of the UMBRA template based on public assessment reports led to shorter review timelines, suggesting that UMBRA could be a useful tool for reliance.

Summary

The study showed that using the UMBRA template alongside SAHPRA's standard template could improve SAHPRA's decision-making processes, providing better rationalisation for decisions and facilitating alignment with other regulatory authorities while allowing for local contextualisation. The value of the UMBRA tool is in facilitating data-driven/evidence-based decision making for benefit-risk assessment.

Changing reviewer's mindset to enable implementation of reliance within an agency: What are the practical steps needed and how can this be best achieved?

Michael Wiseman, Assistant Secretary, International Regulatory Branch, Therapeutic Goods Administration (TGA), Australia

TGA's experience with reliance

TGA has a long history of undertaking reliance activities, including information sharing (e.g. Project Orbis that provides real-time information sharing), report sharing (e.g. Comparable Overseas Regulators (COR) process) and work sharing (e.g. Access Consortium). It is almost impossible to go straight to work sharing without first going through information and report sharing to build confidence and trust. A key principle for enabling reliance is to work with regulators with similar values and approaches to critical decision making.

Building and confirming trust

To build trust internally, the agency, not just evaluators, needs to have a clear understanding of the 'why' behind reliance; the rationale for doing reliance as well as its potential benefits and value. Once the 'why' is understood, the 'what' and 'how' questions need to be addressed and continually reviewed.

Governance is key to influencing the evaluator mindset for successful implementation of reliance. Internally there needs to be a culture where evaluators see themselves making a decision on behalf of the organisation, rather than individuals making decisions. Practical elements need to be in place, such as a quality management system, SOPs and templates. Agencies must have their 'own house in order' before entering any reliance arrangements, as a certain level of capability and capacity will be required.

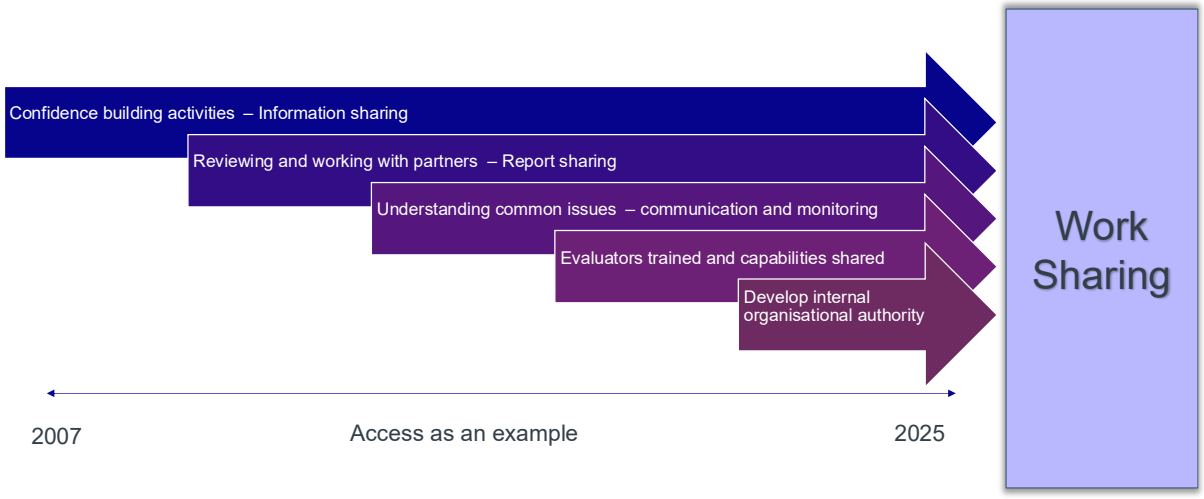
Learnings from the Access Consortium

While the agency heads and technical staff are fully engaged in the Access Consortium, there is a gap in middle management engagement that needs to be addressed by strengthening governance. Evaluator training is also an area that needs more support; there are currently considerations for evaluator exchange between the Access Consortium agencies and periodic parallel review to ensure ongoing alignment of outcomes and trust building.

Summary

TGA has relied on information from comparable regulators for decades, building confidence and relationships that have been key to the implementation of work sharing through the Access Consortium. There needs to be early and strong buy-in from those directly impacted by and involved in reliance, with clear communication of the rationale and potential benefits. Governance arrangements supporting reliance must be continually reviewed and feedback from those working within the system listened to.

Building trust through reliance



Therapeutic Goods Administration – tga.gov.au

Is there an economic benefit to agencies for undertaking a reliance review?

Lorraine Danks, Senior Program Officer, Gates Foundation, South Africa

Background

While WHO's Global Benchmarking Tool (GBT) identifies requirements for mature medicines regulatory systems, some African national regulatory authorities (NRAs) struggle to meet these due to compromised resources, infrastructure deficiencies and lack of internal expertise, compelling them to rely on external partnerships to achieve their WHO GBT goals. Implementation of reliance practices could be an answer to NRA sustainability, as agencies pursue higher WHO maturity levels.

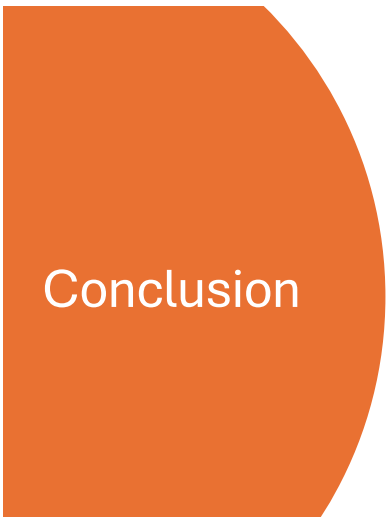
The South African Health Products Regulatory Authority (SAHPRA) inherited a backlog of 16,000 medicines applications, which was cleared through facilitated review pathways that included reliance on prior work by trusted regulators. Research was conducted to determine the economic impact of reliance on NRAs in terms of assessors' costs, especially to offset the financial efforts required to attain a higher GBT maturity level, and understanding the way fees can sustain NRA activities. The study consisted of an economic case study focusing on SAHPRA, a review of African NRA fee structures, and a survey of the pharmaceutical industry.

Results

Time-cost metrics analysis showed that reliance assessments saved SAHPRA $277,413 across 188 applications compared to full reviews (77-81% reduction in assessor costs). The NRA fee structure review revealed outdated fees with little differentiation between full and reliance assessment. While NRAs lack the financial resources to strengthen regulatory systems, the pharmaceutical industry was willing to pay increased fees for reliance reviews when authorities adhere to published timelines. More expensive fast-track services were cited, making an argument for higher fees for reliance assessment when this enables medicines to reach markets quicker.

Summary

This study illustrates the return on investment of reliance for NRAs and, if optimally implemented, benefits for industry and patients too. Reliance is a tool to safeguard NRA resources and could help to offset the financial efforts required to attain higher WHO GBT maturity levels.



- Investing in reliance practices not only enables expedited medicine access, but also allows NRAs to **utilise financial resources more effectively**
- By implementing reliance, **cost-savings could be re-invested** by NRAs to sustain/enhance maturity levels, but also for:
  - Improved service delivery through more expert evaluators (cutting-edge biological therapies, digital health technologies (DHTs) & AI-based health products)
  - Optimised, integrated data management system
  - Enhanced market surveillance & control
  - Accurate tracking of NRA performance
- **Reliance is a tool to safeguard NRA resources** and supports regulatory & information systems strengthening. Study illustrates ROI of reliance for NRAs and, if optimally implemented, benefits for Industry and patients as well

Session 4: What frameworks do agencies need to practically use regional/transregional models?

Moving from regional to continental collaboration – What is the approach for Africa and how is this going to be practically implemented?

Chimwemwe Chamdimba, Head of the African Medicines Regulatory Harmonisation, African Union Development Agency (AUDA-NEPAD)

Approach to regional harmonisation

The African Medicines Regulatory Harmonization (AMRH) programme was initiated in 2009 to help address common challenges faced by the 55 national regulatory authorities (NRAs) in Africa. These challenges include varying regulatory capacity, differences in requirements, minimal transparency and underleveraging reference evaluations. The approach to harmonisation was based on leveraging governance structures already in place: the eight Regional Economic Communities (RECs). The AMRH programme took a stepwise approach, beginning with harmonising standards, then implementing joint assessments and inspections, followed by work sharing and streamlining decision-making processes. So far 25 standards and guidelines have been harmonised, over 530 products approved jointly, and a pool of continental regulatory experts has been established. A key achievement of the AMRH programme has been the building of trust between African NRAs.

Moving from regional to continental harmonisation

The AMRH programme has a key role in establishing the African Medicines Agency (AMA) through the work of Technical Committees. The RECs will remain important coordination structures at the regional level, while the NRAs will be responsible for providing the RECs and AMA with expertise and technical leadership, as well as using the regional and continental recommendations to inform their regulatory decisions. The more mature NRAs are expected to provide expertise to lead technical work, support strengthening of other countries through mentorship, participate in continental and regional pilots, and champion continental reliance.

The approach to continental harmonisation will continue to be stepwise, as not all Member States have yet signed the AMA Treaty (currently 29 out of 55 have signed). Progress has been made on the implementation of AMA, including the establishment of the AMA Board in 2024 and initiation of the recruitment process for the AMA Director General.

Challenges and lessons learned

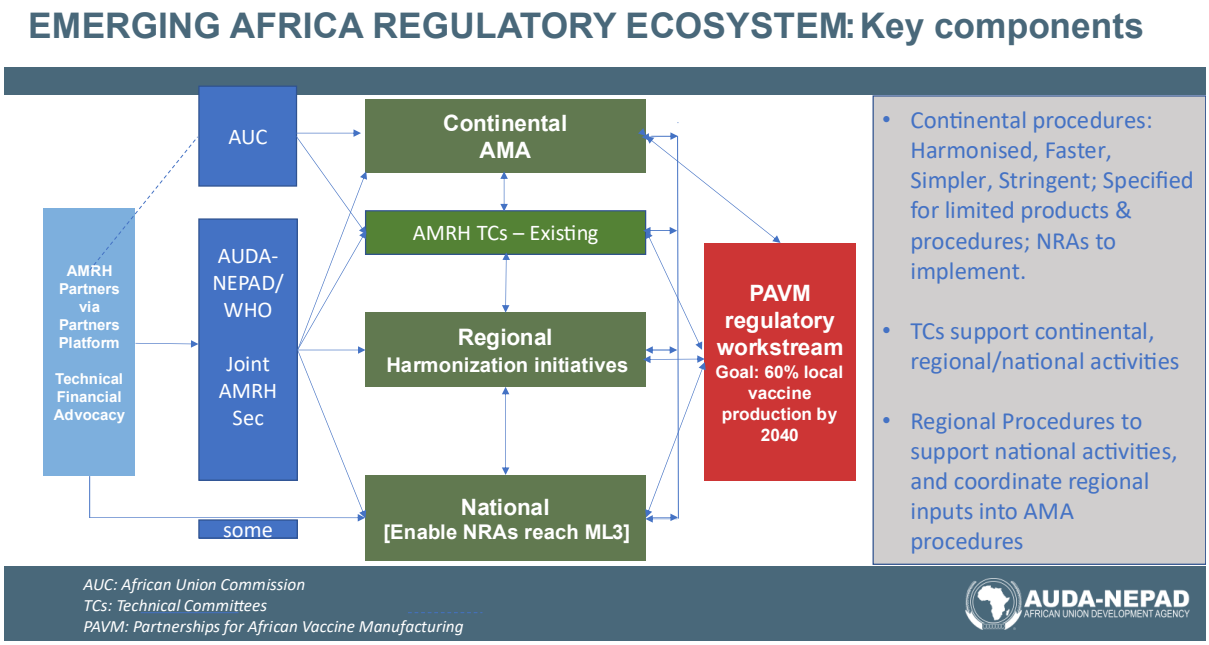
Through the journey of moving from regional to continental harmonisation, there have been several challenges and lessons learned along the way. A key issue has been the varying timelines in decision making by NRAs following regional recommendations. To help overcome this, a forum to facilitate implementation of decisions has been established, a continental reliance framework developed, and electronic information sharing platforms implemented. To minimise duplication at the continental, regional and national levels, a guidance document for selecting priority products has been developed. A competency framework and electronic pool of experts have also been set up to improve the availability of competent experts to support technical work.

Next steps

- Piloting continental technical standards and processes – benchmarking on international standards
- Capacity development - Ecosystem to depend on experts to undertake scientific work
- Strengthening NRAs - towards more ML3s & above
- Increasing use of reliance
- AMRH transition to AMA
- Establish strategic partnerships – AMRH Partnership Platform & technical benchmarking and capacity building partnerships
- Identify a sustainable financing mechanism.

Summary

Africa is moving from regional to continental collaboration through AMA, under the leadership of the AMRH initiative. AMA will complement, not replace, aspects of the work of RECs and NRAs, improving efficiency and effectiveness through work sharing and reliance, and increasing capacity to assess complex medical products. Key challenges include varying decision-making timelines by NRAs following recommendations and the availability of competent experts to support technical work. There are plans to pilot continental technical standards, benchmarking against international ones, as well as continuing capacity development and strengthening more African NRAs towards ML3.



Implications of local vaccine manufacturing: How does regulatory thinking or ways of working need to change?

Prof John Skerritt, Enterprise Professor in Health Research Impact, University of Melbourne, Australia

Plans for African manufacturing of vaccines are gaining in momentum due to the efforts of multiple organisations and initiatives. However, there are several challenges linked to political will, capacity and commercial issues. The focus of this presentation was however more specifically on regulatory challenges and opportunities for vaccines, particularly in an African context.

Regulatory challenges

Different types and levels of regulatory oversight are required for various vaccine development and manufacturing approaches, such as oversight of fill and finish facilities versus drug substance manufacture. Some of the regulatory challenges for vaccines are as follows:

- **Regulatory guidance and capacity** - Comprehensive regulatory guidance is not available for many of the newer vaccine types, even in developed countries. Furthermore, agency resources for vaccine evaluation and the technical capacity of evaluators in assessing newer vaccine technologies can be limited.
- **Clinical evaluation** – Vaccine clinical trials are challenging to perform given the large participant numbers in studies of natural infection and to determine less common safety signals. A more supportive regulatory environment and clinical infrastructure is needed to encourage a greater number of vaccine clinical trials to be conducted in Africa.
- **Preclinical development and evaluation –** Preclinical data for vaccines is typically less extensive than for medicines, but there are differing views on regulatory data requirements. Animal studies may not always predict rare or unusual vaccine safety outcomes.
- **Chemistry, manufacturing, and controls (CMC)** – As vaccines are labile biological products, it can be difficult to ensure that quality is consistently maintained for different vaccine batches, and to meet stringent export requirements. Only two African countries are operating at WHO Maturity Level 3 (vaccine manufacturing) level, as assessed by the WHO Global Benchmarking Tool. A simple but aligned lot release system across Africa would help to avoid the need for re-testing by individual countries.
- **Good Manufacturing Practice (GMP) –** As local vaccine manufacturing increases, there needs to be stronger GMP assurance. Capacity in GMP needs to be built across African regulators, enabling more to become members of the Pharmaceutical Inspection Cooperation Scheme (PIC/S). Mutual recognition of GMP clearances and multi-regulator inspections should be encouraged.

Regulatory opportunities

Developers and regulators are now exploring the use of platform approaches for vaccines. A platform approach enables vaccines to be quickly updated to the strain (or even new pathogen) that is causing an outbreak, or more broadly enable development and regulatory experience with one vaccine to be adapted for other related products. This can simplify regulatory evaluation without compromising product quality, safety or efficacy.

Another opportunity lies within collaborative review models, including work sharing and reliance. There is less experience in collaborative review of vaccines than of other medicines. Establishing trust and confidentiality agreements to facilitate information sharing is key. Simplifying pre-submission processes and developing a public database of reference and relying countries and their processes would help to enable reliance.

Facilitated regulatory pathways are also less commonly used for vaccines than medicines, despite criteria for priority or provisional review of particular products apparently often being met. It is important to ensure that each regulator in manufacturing and purchasing countries has a legal basis to use facilitated pathways, and that regulatory processes and criteria are aligned across countries as much as possible.

Conclusions

- **Plans for African manufacturing of vaccines** have gained in momentum – but there are many commercial, technical and regulatory challenges
- **Vaccine manufacturing is often more complex** than medicines manufacturing, which has implications for regulatory capacity
- **African regional initiatives to support regulatory capacity** will play a major role
  - Greater focus on collaboration on vaccine regulation needed
  - More African countries must achieve ML 3 as vaccine producers
  - Need more African countries to join PIC/S and build GMP regulatory capacity
- Must **avoid country-specific regulatory requirements** e.g. lab testing
- **Potential for greater use** of facilitated regulatory pathways, regulatory reliance, worksharing and information sharing among vaccine regulators

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Panel discussion - How can regulatory agencies better navigate complexities of regional and transregional collaboration to improve access to high quality, safe and effective medicines?

Each participant was asked to provide their reflections on lessons learnt from regional and transregional collaborative approaches.

Agency perspective - Dr Eveline Trachsel, Head of Medicinal Products Approval and Vigilance, Member of the Management Board, Swissmedic

- The Access Consortium involves five like-minded agencies working together to promote greater regulatory collaboration and alignment of requirements.
- Benefits of the Access work-sharing procedure:
    - Reduced submission gaps (as shown in CIRS R&D Briefing 97), which is especially important for smaller markets like Switzerland.
    - Simultaneous market access in several countries.
    - Consolidated List of Questions.
    - Predictability: evaluation plan specified in advance.
    - Regulatory convergence.
    - Saving resources.
    - Sharing and expanding scientific expertise.
- Trust and transparency among participating agencies are essential for successful collaboration.
- Mindset change is a key challenge within agencies when implementing collaborative procedures.
    - Fostering trust and a culture of learning is key; this can help to prevent potential inefficiencies in a work-sharing arrangement, for example, where an agency may conduct an additional internal peer review of their own work before sharing it externally with partnering agencies for their peer review.

Agency perspective - Dr Azuana Ramli, Director, National Pharmaceutical Regulatory Agency (NPRA), Malaysia

- The ASEAN Joint Assessment (AJA) covers 10 countries with a total 700 million population and has evolved from focusing on priority diseases in ASEAN to including biologicals, products under maternal and reproductive health, rare diseases, autoimmune diseases and oncology products.
- Key challenges facing the AJA include:
    - Resource constraints.
    - Logistics of coordination and communication e.g. different languages, conflicting schedules.
    - Varying regulatory frameworks and requirements.
- To navigate these challenges, the AJA needs to continuously improve through:
    - Regular training, engagement and discussion among participating regulators.
    - Enhancing the information management system.

- Expansion to include post-approval changes, line extensions and first wave products in ASEAN.
- Formalising the AJA procedure as an additional pathway at the country levels.
- Further harmonisation of regulatory standards within ASEAN.
- Stronger advocacy work to promote awareness and adoption of the AJA among industry.

Industry perspective – Nevena Miletic, Regulatory Policy and Science Chapter Leader, F. Hoffmann-La Roche

- Industry currently navigates approximately 20 collaborative procedures globally, requiring complex decision making for filing strategies.
- There are several barriers to effective collaborative procedures including limited benefit vs other procedures, lack of transparency and inefficient use of reliance.
- The vision should be for a single harmonised global dossier, with scientifically justified requirements and predictable timelines across countries.
- Digital tools, AI, and interoperable systems should be leveraged by agencies for efficiency.
- Measuring impact with standardised Key Performance Indicators (KPIs) is key to refining collaborative models.

Session 5: Breakout discussions

Workshop participants were assigned to a breakout group and provided with a background document developed by CIRS, containing information and questions for discussion. The Chairs and Rapporteurs of each breakout were asked to facilitate and document the discussion, respectively. The Rapporteurs then fed back to all workshop participants in the main plenary session.

Breakout A: Key components of regulatory strengthening for the review of medicines – What are the building blocks of an effective jurisdictional regulatory review process and how to maximise this for collaborative resource sharing?

Chair: Prof Steffen Thirstrup, Chief Medical Officer, European Medicines Agency

Rapporteur: Nevena Miletic, Regulatory Policy and Science Chapter Leader, Roche, Switzerland

1) Key components of regulatory strengthening for the review of new medicines

- **Political support:** Essential for health authorities to enhance maturity levels and engage in regulatory strengthening activities.
- **Legal framework:** Provides a mandate for health authorities to work on regulatory strengthening and supports collaboration.
- **Global standards**: Adoption of global standards at the national level aids in regulatory strengthening.
- **Human resources**: Adequate competencies and training programmes for reviewers and cross-regional learning.
- **Fee structures:** Suitable and transparent fee structures, outlining who are the fee recipients and how are the fees distributed.
- **Processes:** Transparent, predictable processes with defined timelines, supported by a common language across health authorities.
- **Digital infrastructure:** Implementation of digital systems to facilitate collaboration.
- **Contingency planning:** Preparedness for emergencies, including health crises.
- **Stakeholder engagement:** Involvement of broader stakeholders, including industry, in scientific discussions and new approaches.
- **Openness to new approaches**: Piloting of new concepts and ways of working.

2) Challenges and solutions to build regulatory strengthening into agency processes and practices

Top 3 challenges	Possible solutions
Regulatory framework including harmonisation of requirements, global standards adoption; also common tools to be able to collaborate	– Collaboration, networking, participation in global platforms (e.g. ICH, IPRP) – Standard procedures and common tools – Technology – AI-based solutions
Competencies of regulators	– Training (e.g. secondments, exchange programmes with mature agencies) – Collaboration and stakeholder engagement – Pilot studies

Resources (financial, human resources, time to implement)	– Dedicated budgets – Political advocacy with all the participants in the healthcare systems – Clear communication strategies (e.g. on advantages of regulatory system strengthening) – Annual reports on progress to ensure continuous support

3) Key building blocks that build in regulatory strengthening and ensure an effective and efficient jurisdictional regulatory review

- **Regulatory and legal framework**: Mandating transparency and efficient operation (e.g. on stakeholders' engagement, fee structure and allocation, timelines, processes/procedures, outcomes of assessment). Memoranda of Understanding and confidentiality agreements are essential.
- **Competencies and resources**: Dedicated resources for collaborative assessments and work sharing.
- **Harmonised guidelines/agreements**: Implemented within global standards, supported by common language and tools.

4) Recommendations for further work and research to support further regulatory strengthening:

- Investigate reference agencies' practices in providing unredacted assessment reports:
  - What are current practices?
  - What role do companies play?
  - What are the limitations in each agency's jurisdiction?
- Characterise different countries' regulatory frameworks that support national implementation of regional/collaborative procedures:
  - What does the end-to-end process look like?
  - What are best practices?
- Explore whether the UMBRA benefit-risk framework can facilitate reliance implementation.
- Study non-scientific country-specific requirements:
  - How divergent are they across countries?
  - What is their purpose?
  - Can they be harmonised/streamlined?

Breakout B: Qualitative and quantitative metrics can underpin regulatory strengthening – What should be measured and how this can be best integrated into an agency process, practice and mindset?

Chair: Dr Murray Lumpkin, Lead for Global Regulatory Systems Initiatives, Gates Foundation, USA

Rapporteur: John Mwangi, Regulatory Policy Science Lead, Bayer, Kenya

1) Importance of qualitative and quantitative performance metrics to enabling regulatory strengthening

- **Accountability -** By measuring timelines and other performance indicators, agencies can ensure that they and the industry meet their obligations.
- **Decision making –** Metrics enable data-driven decision making by agencies and politicians.
- **Standardisation –** Metrics help to standardise performance and terminology across the regulatory process e.g. clarifying 'approval' vs 'time to NRA decision'. This may help tackle mis/disinformation.
- **Quality-driven performance –** Metrics allow for a holistic view of NRAs' processes beyond timelines, building quality into the process and ensuring transparency.
- **Outcome-based focus –** It is important to shift the focus from output (e.g., number of applications received) to outcomes (e.g., number of approvals leading to timely availability). This ensures that the regulatory process is efficient and effective in achieving its goals.
- **Efficiency –** Metrics help to identify where time/resources are used/lost.
- **Training and awareness -** Metrics provide opportunities for training and continuous improvement. By analysing trends, comparing with peers and putting data in context, agencies can identify areas for improvement and make necessary adjustments.

2) Key regulatory activities or processes that metrics should be established for

- **Timelines -** Including decision time, validation time, scientific assessment time, applicant stop clock time and total time taken.
- **Applicant submission quality** – Including extent of guideline understanding, cycles to approval, number of major queries, outputs of pre-submission meetings. These metrics will help to ensure guidelines and pre-submission meetings improve the quality of applications.
- **NRA decision quality** – Including decisions validation, quality scoring, trends identification. The aim is to measure NRA's "accountability for reasonableness".
- **Predictability, consistency and transparency of NRA decisions and processes -** Measuring the accuracy and reliability of decisions.
- **Flexibility (NRA and applicants) –** Including the number of out-of-process decisions e.g. on unmet medical need products, accuracy of NRA horizon scanning/applicant estimates e.g. for NRA planning purposes.

3) Changes needed within an agency to integrate appropriate metrics as part of regulatory strengthening

Area of change	Key changes/needs	How to make the change
Strategy	– KPIs as part of organisational strategy – Link KPI achievement to reward system at NRA and with applicants	– Appropriate metrics to keep track of performance – KPIs that speak to all e.g. transparency and predictability is important to industry
Resource/people	– Showcase success – Demonstrate reason to measure – Set aspirational but achievable targets	– Peer to peer comparison – Best practice sharing
Process/practice change	– Performance management function – Project management approach – Performance tools – Dashboard for management	– Introduced as an enabler not for policing people – Tools that are easy to use and embedded in daily work e.g. running in the background of the information management system
Mindset changes	– Change management process – Change 'champions'	– Promote awareness of change and reasons behind it – Training to support staff with new processes/tools – Reinforce culture of openness to change
Industry engagement	– Industry as one of the drivers for change	– Consider point-based system to incentivise good behaviour – Regular stakeholder sessions

4) Challenges and solutions to building metrics into the processes and practices within agencies

- **Resistance to change by NRA and industry**: Overcome by implementing internal change management programmes, change ambassadors etc, and engagement with industry.
- **Fragmented and outdated systems**: Define the metrics before creating new systems/tools, which should be simple to use and integrated into daily work. Encourage adoption of new systems and allocate resources to the set KPI areas.
- **KPIs linked to outcomes/public health benefit**: Ensure they are 'SMART' KPIs and ideally linked between applicants and NRAs i.e. as a "social contract between stakeholders".

5) Reasons to embed a culture of continual measurement into agencies

Embedding an internal culture of measurement helps agencies to drive efficient use of resources, build trust, provide accountability and continuously improve their performance. Agency self-measurement is important for industry as it provides transparency, predictability and consistency. It is also important to patients and politicians, as gives more confidence in agency decisions and their use of public health resources.

6) Recommendations for further work and research on agency metrics

- Share case studies to support change management in agencies.
- Support the development of KPI systems and tools including:
    - Investing in capacity building / training.
    - Develop an IT solution (once metrics are known), embedding KPIs into the system operations.
    - Design decision dashboards and iterate with feedback loops.
- Publish KPIs from ML3+ countries, showcasing best practices - these can be used as a case for change by other NRAs.
- Support KPI and metrics capacity by:
    - Investigating who is using which metrics and why.
    - Establishing common terminology for KPIs and metrics.
    - Conducting pilots and publishing results from NRAs.
    - Allowing KPIs to be flexible and evolve with time.

Breakout C: Reliance/workshare review model for generics – same or different considerations compared to new medicines?

Chair: Dr Tariro Sithole, Technical Office – Health Products Regulation, World Health Organisation, Ethiopia

Rapporteur: Amira Younes, Director, Global Regulatory Policy, Europe, Middle East and Africa, MSD, UAE

The group considered the following questions. Key points from the discussions are summarised below.

1) Challenges facing regulators with respect to generics - why could a reliance or risk-based model be of value?

Major challenges	**How will a reliance or risk-based model be of value?**
Lack of risk-based approach models to inform **prioritisation** of products and allocation of resources.	– Learning from reference agencies on how to apply and adapt risk-based approaches.
Capacity & capabilities: – Multiple applications of the same molecule results in high volume capacity challenges e.g. in African markets, the majority of applications are generics. – Long review timelines & long queuing time leads to backlog issues. – Different maturity systems across countries results in different regulatory systems. – Capacity for quality control testing, GMP inspections and bioequivalence assessments.	– Reliance will prevent duplication, accelerating timelines & freeing up resources. – Work sharing & training initiatives can build capacity for regulators. – Rely on ML3 /ML4/ WLA countries to support capacity building to improve maturity.
Data quality: – Issues with data integrity. – Poor quality submissions & long sponsor response time. – Challenges applying international best practices and requirements to local applicants due to political issues.	– Data transparency incentivises higher quality data. – Lack of harmonisation hinders the ability of agencies to use reliance, thus harmonising international standards is required.
Country-specific requirements hinder work sharing / different labelling requirements across countries & shared pack challenges.	– Harmonisation of requirements can enable better usage of risk-based models.

2) Key considerations for developing a risk-based approach for generics

Considerations for **unilateral reliance**:

- Identify **criteria for selecting reference agencies**, ensuring they apply the same regulatory standards and requirements.
- Develop **risk-based framework** to apply reliance.
- Define what is needed to confirm **sameness.**
- Understand and implement **Good Reliance Practices and Good Review Practices**.
- For generics, there is no requirement for clinical package or consideration of local context. The variability in standards for generics can make it difficult to implement reliance.

Considerations for **work sharing**:

- **Language** barriers.
- Need to have a **mechanism for information exchange** among agencies.
- Different national **timeframes** / fitting international timeframes into national processes.
- Complexity in **coordination and communication**.
- Application of different standards of evaluation - **trust/confidence building** takes time.
- Need to ensure p**redictability** and **flexibility**.
- Understand and implement **Good Reliance Practices and Good Review Practices**.

Considerations for **collaborative reviews**:

- Same considerations as for unilateral reliance and work sharing.

3) Changes needed within an agency to integrate risk-based approaches for generics

Strategy:

- Secure organisational commitment through endorsement from higher management and buy-in from all stakeholders.
- Provide training and ensure commitment to implementing the strategy.

People and mindset changes:

- Implement change management principles and provide transparency on the reasons for change.
- Foster a cultural shift to embrace risk-based models.
- Ensure staff are trained and committed to the new approaches and to continuously improving.

Processes:

- Review existing processes to incorporate risk-based approaches.
- Implement AI initiatives to support and facilitate the new models.

4) Recommendations for further work and research on reliance/work-sharing models for generics

- Identify lessons learned from agencies and industry who have experienced reliance in practice.
- Evaluate risk-based models implemented in different countries; this could be covered as part of WHO GBT assessments.
- Enable regulatory systems to allow transparency and information sharing.
- Implement unique manufacturing facility identifiers.
- Explore how AI can enable better reliance practices by different agencies.
- Agencies should develop, implement and publish criteria for prioritising applications based on public health needs, medicine shortages and multiplicity.

Session 6: New ways of working – Key to success in a resource constrained environment

The importance of leveraging a robust information management system – what is being planned and what are the challenges?

Dr Nancy Ngum, Public Health Officer, African Union Development Agency (AUDA-NEPAD)

A Regulatory Information Management System (RIMS) provides a centralised platform for storing and sharing information. A robust RIMS can streamline evaluation and approval processes; enhance communication, coordination and monitoring; and support training and capacity building.

Journey towards a continental RIMS

In 2022, with assistance from the World Bank, the African Medicines Regulatory Harmonisation (AMRH) programme conducted an assessment of the implementation of RIMSs across Africa. The findings indicated that only 36% of African national regulatory authorities (NRAs) had a fully functional digital RIMS, while 23% were using manual systems and 41% were using a combination of manual and digital systems.

To support the continental digitalisation agenda of the African Medicines Agency (AMA), the Information Management System (IMS) Technical Committee was established. This committee comprised IT experts from African NRAs, representing all regions involved in the AMRH initiative. The IMS Technical Committee recommended that an African Union (AU) Model RIMS should be developed and adapted for implementation at the continental, regional and national levels.

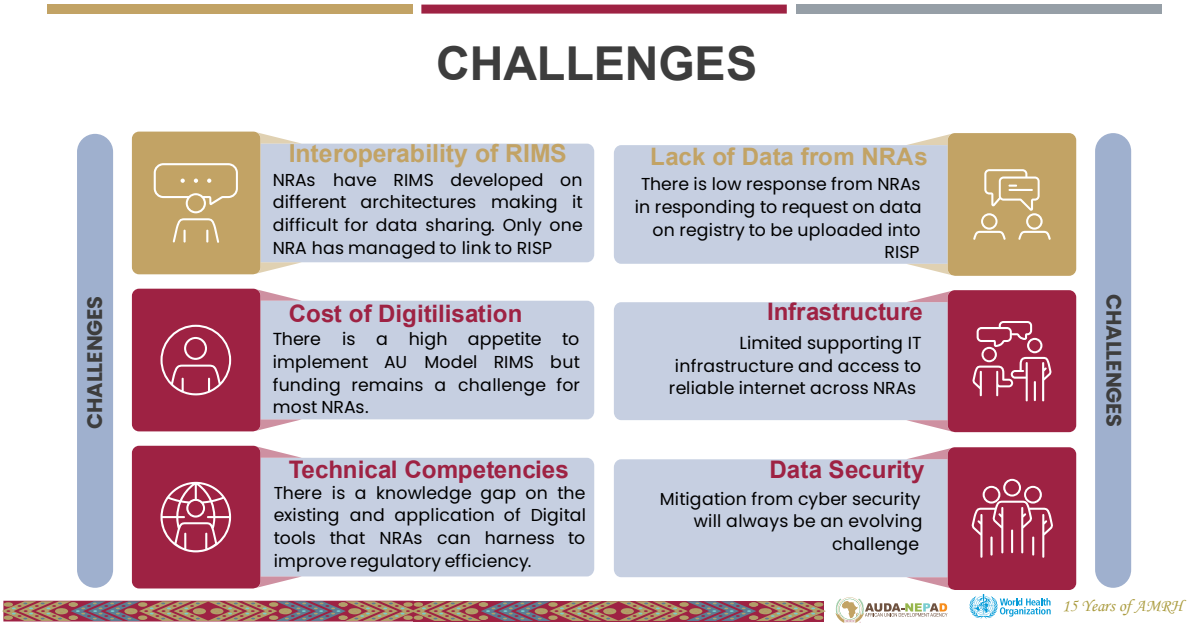
Achievements of the IMS Technical Committee

1. **AU Model RIMS**: A prototype for the AU Model RIMS has been developed, aimed at facilitating the digitalisation of regulatory systems. This model is designed to be adaptable and cost-effective for low and middle-income countries.
2. **Digitalisation Strategy**: A strategy has been developed to guide countries in implementing their first RIMS or enhancing their existing RIMS, ensuring interoperability and information sharing.
3. **Regulatory Information Sharing Portal (RISP)**: This was designed to facilitate the exchange of regulatory data, policies and compliance information among African NRAs, regional regulatory bodies, healthcare stakeholders and industry. RISP aims to enhance cross-border collaboration, pharmacovigilance and safety monitoring, and access to medicines and regulatory data.
4. **Continental eCTD**: The Technical Committee is advocating for a Continental Electronic Common Technical Document (eCTD) to standardise submissions across Africa. This will simplify the submission process for manufacturers and regulatory authorities.
5. **Continental API Database**: A central repository for approved and certified Active Pharmaceutical Ingredients (APIs) has been developed. This will improve access to API information for evaluators and inspectors, facilitating reliance activities.
6. **Electronic Document Management System**: An Electronic Document Management System (eDMS) has been developed to support AMRH and its structures to manage, store and track electronic documents and other content.
7. **Electronic Continental Regulatory Experts Solution:** This platform serves as a central hub for experts involved in the regulation of medical products, providing a unified space for collaboration, sharing of

insights and knowledge exchange. This will help to improve the efficiency and effectiveness of regulatory processes across Africa.

Challenges to implementing RIMS

Several challenges in the journey towards robust RIMS implementation have been identified, relating to interoperability, cost, technical competencies, data collection, infrastructure and data security (see below).



Next steps

Future plans include integrating all Technical Committees into the eDMS and developing continental eCTD specifications. More countries will be encouraged to adopt or adapt the digitalisation strategy, and the AMRH website will be enhanced, including providing a link to RISP.

Summary

A robust RIMS is key to enhancing regulatory processes, improving collaboration and ensuring better access to medicines across Africa. While there are several challenges, such as variable digital architectures, high costs and limited technical competencies, significant progress has been made, and plans are in place to continue advancing the digitalisation agenda across Africa.

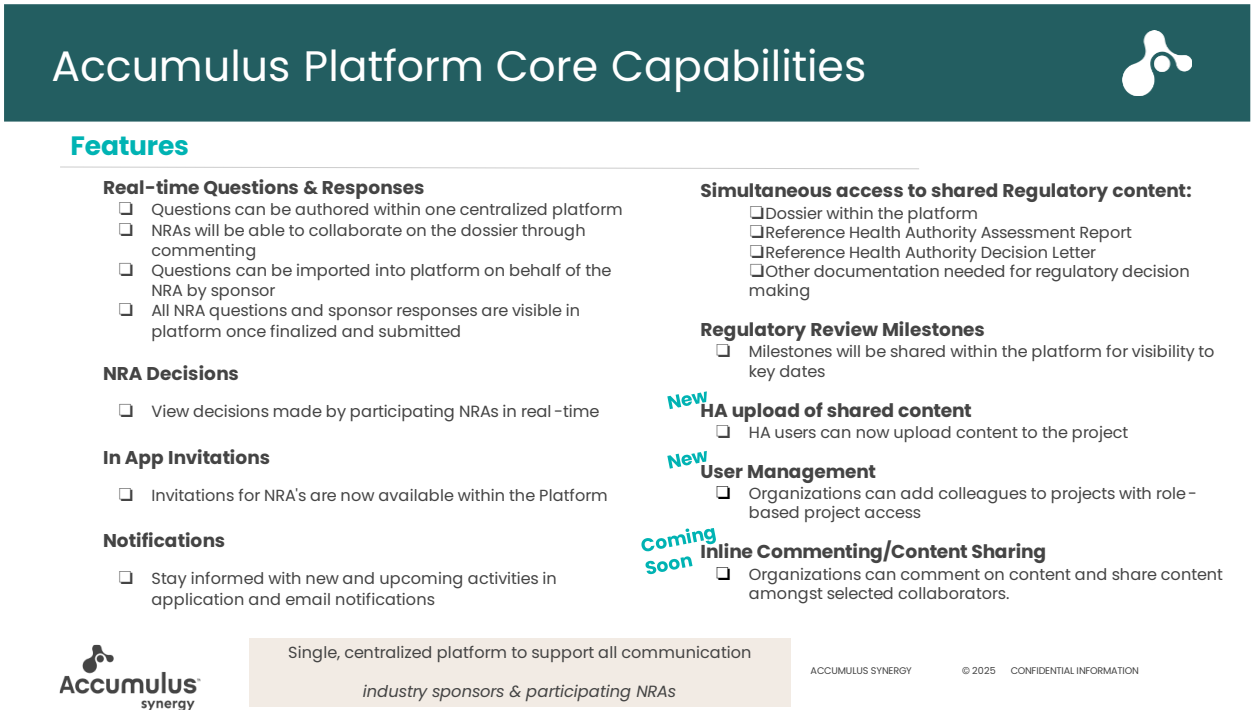
Use of digital/cloud-based sharing – What are the principles and how could this aid agencies as they look to increase efficiency and effectiveness?

Dominique Lagrave, Senior Vice President, Innovation, Accumulus Synergy

Accumulus is a non-profit organisation and technology developer, focusing on its efforts to engage with regulatory agencies globally and develop a platform to facilitate regulatory collaboration and information exchange. Accumulus engages with various stakeholders, including regulators, trade associations, non-governmental organisations and technical partners, to drive the adoption of cloud technology and enhance collaboration.

Key features and capabilities

Accumulus developed its platform from the ground up, prioritising security and scalability. The platform is cloud-based, requiring no installations, and supports real-time information sharing across multiple regulatory agencies. Key features of the platform include real-time question and response tracking, decision tracking, large-scale invitation processes, notifications, dossier exchange, milestone tracking, and more recently, collaborative content upload and review (see below). The platform can aid collaboration across the drug development lifecycle, including joint scientific advice, joint assessment and joint CMC review.



Implementation and impact

Since January 2024, the Accumulus platform has supported seven projects covering a range of topics, including CMC post-approval change, clinical line extension and collaborative protocol review. The platform has over 230 active accounts from regulatory agencies in 52 countries, demonstrating its growing adoption and impact.

The first project involved providing a major CMC change relying on unredacted EMA assessments simultaneously with 48 countries. 87% of the countries approved the change within seven months, reducing the global approval timeline from an average of 2.5 years to under 6.5 months (nearly 80% reduction). In addition, 70% of the agencies granted approvals without questions. When asked for feedback on the platform, the agencies highlighted the

benefits of being able to observe and learn from each other's questions and responses. They also found the interface accessible and easy to use, requiring minimal training.

Next steps

Accumulus plans to continue expanding its platform's capabilities and reach, including supporting joint protocol design and enabling agencies to become fully self-sufficient within the platform. Accumulus has also partnered with the Coalition for Epidemic Preparedness Innovations (CEPI) on a project to build a global regulatory preparedness framework that leverages Accumulus' platform for real-time collaboration and providing information equity across countries. A pilot with seven regulatory agencies is exploring joint assessment of CMC for a platform technology, aiming to identify best practices to support vaccine developers in public health emergencies.

Summary

The Accumulus platform is enhancing regulatory collaboration, information exchange, predictability and transparency. It also has a role in regulatory strengthening and capacity building by allowing agencies to learn from one another. By engaging with a wide range of stakeholders and continuously improving its technology, Accumulus aims to streamline regulatory processes, improve access to medicines, and ultimately benefit patients worldwide.

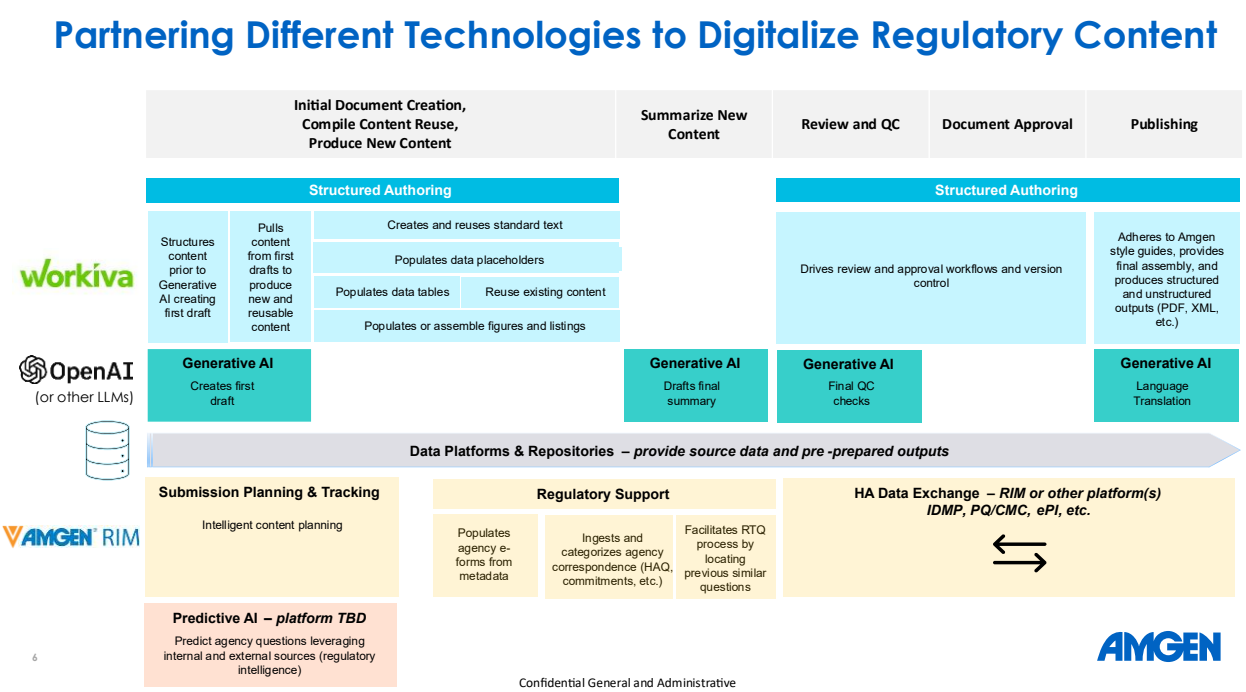
Innovative digital regulatory transformation

Michael Abernathy, Digital Regulatory Innovation Lead, Amgen, USA

There are several key challenges within the healthcare system that underscore the need for improved data management and technology integration to enhance patient outcomes. While patients struggle to find information due to outdated systems, companies often fail to structure and standardise data, complicating data mining and assessment. Furthermore, the process of authoring, submitting, reviewing, and assessing regulatory filings is staggered and prolonged, delaying access to medicines.

Automating regulatory filings for CMC

Amgen has integrated different technologies to digitalise regulatory content and automate the generation of regulatory filings (see below). For example, for CMC, a common taxonomy was created and mapped to CMC data, allowing internal company systems to be connected and automation workflows implemented. The first automated regulatory CMC filing was submitted to the Accumulus platform using Workiva, a financial software adapted for regulatory purposes. AI was utilised to write summaries and identify nonconformances, demonstrating the potential for technology to streamline regulatory processes. The automated system allows for flexible filing outputs in various formats, catering to both mature and less mature health authorities.



Accumulus pilot

The Accumulus platform enables multiple health authorities to have simultaneous access to the same regulatory filing, promoting transparency and collaboration. Amgen is piloting the platform with a post-approval submission and has provided unredacted information from the EMA reference assessment to over 20 relying agencies. There is great potential for such technology to reduce timelines and enhance productivity, which could help to eliminate drug shortages and provide funding for innovation.

Summary

By leveraging digital technologies, document generation has been accelerated from weeks/months to hours. Although real-time data exchange is not yet fully realised, progress is being made towards this goal through the Accumulus platform. The overarching aim should be to replace the staggered submission wave model with a single simultaneous global submission. By utilising available technologies, regulators can enhance their position within the global healthcare ecosystem and better serve patients.

Use of cloud-based sharing: Challenges and opportunities

Suraiya Suliman, Manager: PEM Post-registration, South African Health Products Regulatory Authority (SAHPRA)

Many regulatory authorities face significant backlogs and inconsistent timelines for approval, which hinder access to medicines. Ensuring that products remain available on the market throughout their lifecycle is crucial. There is a growing interest in maintaining product availability post-approval.

Collaborative efforts on post-approval changes

Several collaborative projects and pilots are being conducted on post-approval changes (PACs). For example, the International Coalition of Medicines Regulatory Authorities (ICMRA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), International Pharmaceutical Regulators Programme (IPRP), and Pharmaceutical Inspection Co-operation Scheme (PIC/S) are aligning efforts to support a global regulatory Pharmaceutical Quality Knowledge Management (PQKM) capability for CMC-related PAC submissions, products and facilities. The IPRP Working Group also engages in discussions on PACs, classifications and harmonisation of submission requirements. Differences in risk classifications, terminology and submission types among regulatory authorities pose significant barriers to harmonisation.

Opportunities and challenges with cloud-based submissions

There are several opportunities and challenges associated with a single cloud-based submission being made simultaneously to multiple agencies (see below), such as with the Accumulus system.

Opportunities	Challenges
Accelerated review timelines - due to increased efficiency	Submissions stored outside the regulatory system – convincing assessors of the sameness of data can be challenging
Assurance of sameness - as agencies receive the same dossier	Regional and country-specific requirements - differences in scientific requirements for PACs can extend timelines due to additional questions.
Visibility of other regulatory authorities' communications e.g. Q&A – Prevents duplication and provides learning opportunities	Individual country queues may prevent timely handling of applications
Enable reliance and work sharing opportunities	

Summary

Innovative solutions are needed to overcome regulatory barriers and improve efficiency in regulatory processes. While cloud-based submissions offer significant opportunities, addressing the challenges associated with external data storage, regional requirements and resource allocation is crucial for successful implementation.

Regulation meets innovation: Leveraging AI for health product safety

Christelna Reynecke, Chief Operations Officer, South African Health Products Regulatory Authority (SAHPRA)

Why use AI in medicine regulation?

Regulatory authorities face numerous challenges due to external environmental changes, such as the introduction of new health technologies and the increasing number of product applications and clinical trials. The global regulatory environment is becoming more complex, necessitating greater efficiency.

By automating routine tasks, artificial intelligence (AI) can help to reduce bottlenecks and delays, leading to faster and more accurate assessments. Example use cases include benefit-risk stratification; assisted structured assessment (extracting key information and summarising review sections for the technical reviewers); completing a pre-screening activity on submissions to ensure they comply with the regulations, guidelines and technical specifications; comparison of the Prescribing Information/Patient Information Leaflet for generic products against comparators; and document classification. Automation also provides opportunities for continuous improvement and training for assessors. In addition, AI can be used to interrogate large complex datasets, providing deeper insights that enhance regulatory decision making.

SAHPRA's AI strategy and tools

SAHPRA's AI strategy aligns with WHO guidance and follows the national blueprint set out by the South African Department of Information and Digital Communications. The strategy focuses on enhancing regulatory capabilities while ensuring ethical standards and compliance with data privacy laws.

SAHPRA has developed two prototypes for AI-based tools:

- **Risk assessment tool:** Applies predefined rules to determine the risk associated with generic products based on product and manufacturing attributes, improving consistency and classification speed. This risk and triage process usually takes 1-2 hours to complete manually but only 3-8 minutes with the tool.
- **GMP screening tool:** Checks technical compliance and produces draft review reports, enhancing efficiency in the review process (reducing timelines from 3 weeks to 40 minutes).

Current AI tools in development include a technical screening tool for compliance checks of submitted dossiers as well as a bio-availability/bio-equivalence review assistant AI algorithm. Further use cases that are being explored as part of the greater SAHPRA AI strategic plan include a clinical trials submission review assistant; using AI in pharmacovigilance adverse events triaging; creating an AI-assisted evaluator training simulation to assess and train technical reviewers; exploring the use of AI to draft public assessment reports based on reviewer evaluation reports; and supporting the Substandard and Falsified Medicines National Action Plan team by identifying sales and advertisements of health products on unauthorised channels e.g. using social media scrapers.

Enhancing collaboration through AI

AI improves the ability of regulatory agencies to collaborate with counterparts at regional, continental and global levels by enhancing efficiency and data sharing across borders. It can strengthen the capacity of regulators across Africa by providing tools and skills necessary for effective product evaluation, helping to support the goals of the African Medicines Agency. It would be a positive step for Heads of Agencies to start considering what policies and legislative changes might be needed to further enhance collaboration, and what type of regulatory landscape and vision should be jointly created in terms of a new way of working across Africa with regards to data sharing.

Key considerations and challenges

While AI offers many benefits, it also presents challenges such as ensuring data quality, addressing cybersecurity risks, managing staff resistance to change, and securing funding for development and maintenance. Well-developed strategies and governance are essential for successful AI implementation. SAHPRA is establishing an AI oversight committee to ensure ethical, transparent, and high-standard regulatory practices. The agency's AI tools are designed with data privacy in mind, complying with national and international standards.

Summary

AI will revolutionise health product regulation by improving efficiency, enhancing decision making and enabling cross-border collaboration. SAHPRA is committed to leveraging AI to improve public health outcomes and ensure that regulatory practices are aligned with global best practices. As AI continues to evolve, it is crucial to innovate and collaborate to fully realise its potential in transforming regulatory practices.

AI in Collaborative Regulatory Models

Content:

- **Regional & Continental Collaboration:**
- AI helps strengthen collaboration by automating tasks and creating a shared regulatory data environment.
- **African Medicines Agency (AMA)**: AI's role in enabling cross-border regulatory alignment and capacity building .
- **Global Models:**
- AI can facilitate streamlined regulatory processes, including work-sharing and reliance pathways between agencies.

List of attendees

Affiliations are stated as they were at the time of the meeting.

Regulatory agencies		
Constance Chisha	Senior Registration Officer Human Medicines	**Medicines Regulatory Authority, Zambia**
Zodumo Fikeni	Portfolio Coordinator – New Medicines	**South African Health Products Regulatory Authority**
Zibuyile Hadebe	Portfolio Coordinator	**South African Health Products Regulatory Authority**
Dr Star Khoza	Clinical Evaluator	**South African Health Products Regulatory Authority**
Lillian Kwinika	HR Manager	**South African Health Products Regulatory Authority**
Jeremiah Manyangu	Drugs Registration Officer	**Tanzania Medicines & Medical Devices Authority**
Ntombi Mthembu	Manager, HPA Renewals	**South African Health Products Regulatory Authority**
Karin Naidoo	Portfolio Coordinator	**South African Health Products Regulatory Authority**
Duduzile Ntoko	Quality Manager	**South African Health Products Regulatory Authority**
Mercy Acquaye Owusu-Asante	Head, Manufacturing Facilities Department	**Food and Drugs Authority, Ghana**
Raphael Sanches Pereira	Health and Regulation Expert	**ANVISA, Brazil**
Dr Azuana Ramli	Director	**National Pharmaceutical Regulatory Agency, Malaysia**
Richard Rukwata	Director General	**Medicines Control Authority, Zimbabwe**
Dr Boitumelo (Tumi) Semete	Chief Executive Officer	**South African Health Products Regulatory Authority**
Dr Supriya Sharma	Chief Medical Adviser	**Health Canada**
Joseph Ofosu Siaw	Acting Director, Business Development and International Partnership	**Food and Drug Administration, Ghana**
Mamotho Sindane	Manager, Risk and Internal Audit	**South African Health Products Regulatory Authority**
Itumeleng Skhosana	Manager, Strategic Business Planning and Performance Monitoring	**South African Health Products Regulatory Authority**
Pratibha Sobrun	Senior Manager, Health Products Authorisation	**South African Health Products Regulatory Authority**
Suraiya Suliman	Manager: PEM Post-registration	**South African Health Products Regulatory Authority**
Prof Steffen Thirstrup	Chief Medical Officer	**European Medicines Agency**
Dr Eveline Trachsel	Head of Medicinal Products Approval and Vigilance, Member of the Management Board	**Swissmedic**
Michael Wiseman	Assistant Secretary, Department of Health and Aged Care	**Therapeutic Goods Administration, Australia**
Ghada Zaki	Senior Regulatory and Pricing Associate	**Egyptian Drug Authority**

Pharmaceutical companies		
Michael Abernathy	Executive Director, Global Regulatory Affairs/Digital Regulatory Innovation Lead	**Amgen, USA**
Veronica Baffa	CARE Therapeutic Area Head, GRA	**Chiesi, Italy**
Ginny Beakes-Read	VP and Head, Global Regulatory Policy	**Johnson & Johnson, USA**
Eric Chauke	Regulatory Affairs Head/ Responsible Pharmacist	**Bayer, South Africa**
Dr Dorah Diale	Head of Regulatory Affairs	**Roche, South Africa**
Bunmi Femi-Oyekan	Senior Director / Accord Access Regulatory	**Pfizer, Nigeria**
Graeme James	Head of Regulatory Zone Africa and Global Health Unit	**Sanofi-Aventis, South Africa**
Maipelo Machailo	Africa Cluster Regulatory Lead	**GlaxoSmithKline, South Africa**
Nora Masoga	Assistant Director, Regulatory Affairs SSA	**MSD, South Africa**
Nevena Miletic	Regulatory Policy and Science Chapter Leader	**F. Hoffmann-La Roche, Switzerland**
John Mwangi	Regulatory Policy Science Lead	**Bayer, Kenya**
Puvi Naidoo	Regulatory Lead, SSA Cluster	**Pfizer, South Africa**
Gina Partridge	Regulatory and Quality Director – SASSA Alliance	**Eli Lilly and Company, South Africa**
Shamima Rashid	Responsible Pharmacist / RA Compliance Lead	**Astellas, South Africa**
Niraz Reddy	Regulatory Director Performance Emerging Markets	**GlaxoSmithKline, South Africa**
Dr Natalia Shunmugan	Senior Director, Global Regulatory Intelligence and Policy	**Ultragenyx, USA**
Githa Singh	Regulatory Affairs Director	**AbbVie, South Africa**
Portia Tabile	Head of Regulatory Affairs & Responsible Pharmacist	**Takeda, South Africa**
Nola Tewabe	Director, Regulatory Policy	**Amgen, UK**
Amira Younes	Director, Global Regulatory Policy, Europe, Middle East and Africa	**MSD, United Arab Emirates**
Academic and non-profit organisations		
Chimwemwe Chamdimba	Head of the African Medicines Regulatory Harmonisation	**African Union Development Agency (AUDA-NEPAD)**
Lorraine Danks	Senior Program Officer	**Gates Foundation, South Africa**
Prof Hans-Georg Eichler	Consulting Physician	**Association of Austrian Social Insurances**
Dominique Lagrave	Senior Vice President, Innovation	**Accumulus Synergy, USA**
Dr Stephanie Leigh	Director – WITS Pharmacy Regulatory Science Hub (PRSH) and Head of Division: WITS Pharmacy Practice	**WITS University, South Africa**
Dr Murray Lumpkin	Lead for Global Regulatory Systems Initiatives	**Gates Foundation, USA**
Dr David Mukanga	Deputy Director Africa Regulatory Systems	**Gates Foundation, Kenya**
Dr Nancy Ngum	Public Health Officer	**AUDA-NEPAD**
Francisco Nogueira	Chief Executive Officer	**Accumulus Synergy, USA**

Dr Tariro Sithole	Technical Officer – Health Products Regulation	**World Health Organization, Ethiopia**
Prof John Skerritt	Enterprise Professor in Health Research and Chair, Scientific Advisory Council, CIRS	**University of Melbourne, Australia**
Maxine Turner	Academic	**WITS University, South Africa**
Centre for Innovation in Regulatory Science (CIRS)		
Dr Magda Bujar	Associate Director, Regulatory Programme and Strategic Partnerships	**CIRS**
Gill Hepton	Administrator	**CIRS**
Adem Kermad	Senior Research Analyst	**CIRS**
Juan Lara	Senior Research Analyst	**CIRS**
Dr Neil McAuslane	Scientific Director	**CIRS**
Anna Somuyiwa	Head	**CIRS**
Prof Stuart Walker	Founder and Senior Adviser	**CIRS**

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The Centre for Innovation in Regulatory Science is a neutral, independent UK-based subsidiary of Clarivate plc. Its mission is to maintain a leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and health technology assessment (HTA) policies and processes. CIRS provides an international forum for industry, regulators, HTA bodies and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy. It is governed and operated by Clarivate for the sole support of its members' activities. The organisation has its own dedicated management and advisory boards, and its funding is derived from membership dues, related activities, and grants.

Workshop organised by

Dr Magda Bujar, Associate Director, Regulatory Programme and Strategic Parterships, CIRS

Dr Neil McAuslane, Scientific Director, CIRS

Prof Stuart Walker, Senior Advisor and Founder, CIRS

Anna Somuyiwa, Head, CIRS

Report prepared by

Dr Jenny Sharpe, Communications Manager, CIRS

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Keep in touch

Centre for Innovation in Regulatory Science (CIRS)

70 St Mary Axe, London EC3A 8BE, UK

Email: cirs@cirsci.org

Website: www.cirsci.org