Maximizing the Impact of Regional Regulatory Initiatives: An analysis of process characteristics from the FRPath® database

Lawrence Liberti, Mario Alanis, Bakani Ncube (The FRPath Project)
Angelika Joos (MSD Europe, Inc.)

Background

Regional Regulatory Initiatives (RRIs) have emerged as an approach to streamline regulatory processes and reduce duplicative efforts in pharmaceutical product approvals; however, the heterogeneity of the pathways used by these initiatives often poses challenges for stakeholders seeking to optimize their use. For example, RRIs may use reliance, priority or other facilitated regulatory pathways (FRPs) to meet their needs but the diversity in these pathways can result in confusion and underutilization. This study aimed to compare process characteristics of various RRI pathways using data from the FRPath® database in order to identify best practices that could be recommended for the optimized development and use of RRI pathways.

Methods

Data were extracted from the FRPath database (www.frpath.org) a project of the nonprofit Erudee Foundation (www.erudee.org) by the authors. This resource represents a comprehensive, curated database of globally identified regulatory pathways designed to simplify and accelerate the assessment process, thereby accelerating the availability of medicines in their respective jurisdictions. The data included in the profiles for each RRI pathway were derived from public documents (agency websites and the pathway descriptors noted therein, white papers, professional journals, press releases etc) and in some cases were enhanced with input by the regulators or local specialists.

Key process characteristics, including types of products eligible, target time for review, mechanism of uptake by member states, and participating regulatory agencies in each initiative, among others, were assessed by the authors using descriptive statistics. A global approach was taken, with RRIs from anywhere in the world being included in the assessments. It was expected that some RRIs would have more than one FRP.

Limitations of the Analysis

The lack of details in the public domain that fully describe the characteristics of the pathways available in the assessed RRIs, together with limited descriptions of the procedures for using these pathways were obstacles to developing a fully comparative analysis.

Observations

Twelve RRI pathways were identified. Their characteristics are described herein.

Table 1: Comparison of Foundational Characteristics

Name of initiative	Date of Pathway Enactment	Participating Countries	Scope of Products	Product should address an unmet medical need
ASEAN harmonized requirements for drug registration (SIAHR)- Full JA	Info not found	Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, Vietnam	New Chemical Entities (NCEs), Biotechnological Products (Biotech), Major and Minor Variations, and Generics	Yes
ASEAN Expedited Joint Assessment Procedure	Info not found	Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, Vietnam	Products approved by reference NRAs or WHO	Yes
CARPHA Verification Review of Medicines and Vaccines	Info not found	Belize, Guyana, Haiti, Jamaica, Suriname, and Trinidad and Tobago plus other territories, countries	All Pharmaceutical Products	Yes
CARPHA Verification Review for Biotherapeutic Product Applications	Info not found	Belize, Haiti, Guyana, Jamaica, Suriname, Trinidad and Tobago	Biologics/vaccines, Biosimilars	Yes
The Central American Mechanism for the Joint Evaluation of Medicines	1-Aug-20	Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama, with the support of the Pan American Health Organization (PAHO)	Chemical synthesis medicines which are not required to show bioequivalence in any of the Central American countries Including NCEs and generics)	No
EAC Medicines Regulatory Harmonization Program	30-Mar-12	Kenya, Tanzania, Uganda, Rwanda, Burundi, South Sudan	All pharmaceutical products	Negotiable
EEU Mutual Recognition Procedure	6-May-17	Armenia, Belarus, Kazakhstan, Kirghizstan, Russia	All products	Negotiable
EEU Decentralized Procedure	12-Feb-16	Armenia, Belarus, Kazakhstan, Kirghizstan, Russia	All products	Negotiable
GHC Central Registration	Info not found	United Arab Emirates, Bahrain, Saudi Arabia, Oman, Qatar, Kuwait, Yemen	All pharmaceutical Products (Any Medicine Manufactured on Pharmaceutical Basis)	Yes
IGAD Joint Assessment Procedure	Info not found	Djibouti, Eritrea*, Ethiopia, Kenya, Somalia, South Sudan, Sudan and Uganda. *Eritrea apparently suspended activity.	All pharmaceutical Products, NME's (small molecules), Generics, PQ Generics, Biologics/vaccines, Biosimilars	Negotiable
West African Health Organization (WAHO) Regional Joint Assessment Procedure for Medicine Registration and Marketing Authorization of Medicinal Products	20-Jul-17	Benin, Burkina Faso, Cabo Verde, Cote d'Ivoire, The Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, Togo	Medicinal products	Yes
ZAZIBONA Collaborative Medicines Registration Process	1-Jan-15	Zambia, Zimbabwe, Botswana, Namibia, South Africa, Tanzania, Malawi, DRC, Mozambique and Malawi (active countries) as well as Eswatini, Angola, Seychelles and Madagascar (non-active)	Essential medicines, excluding WHO PQ'ed products going through WHO CRP	Yes

Figure 1. Target Time Ranges for RRI Pathways (Time range, N)

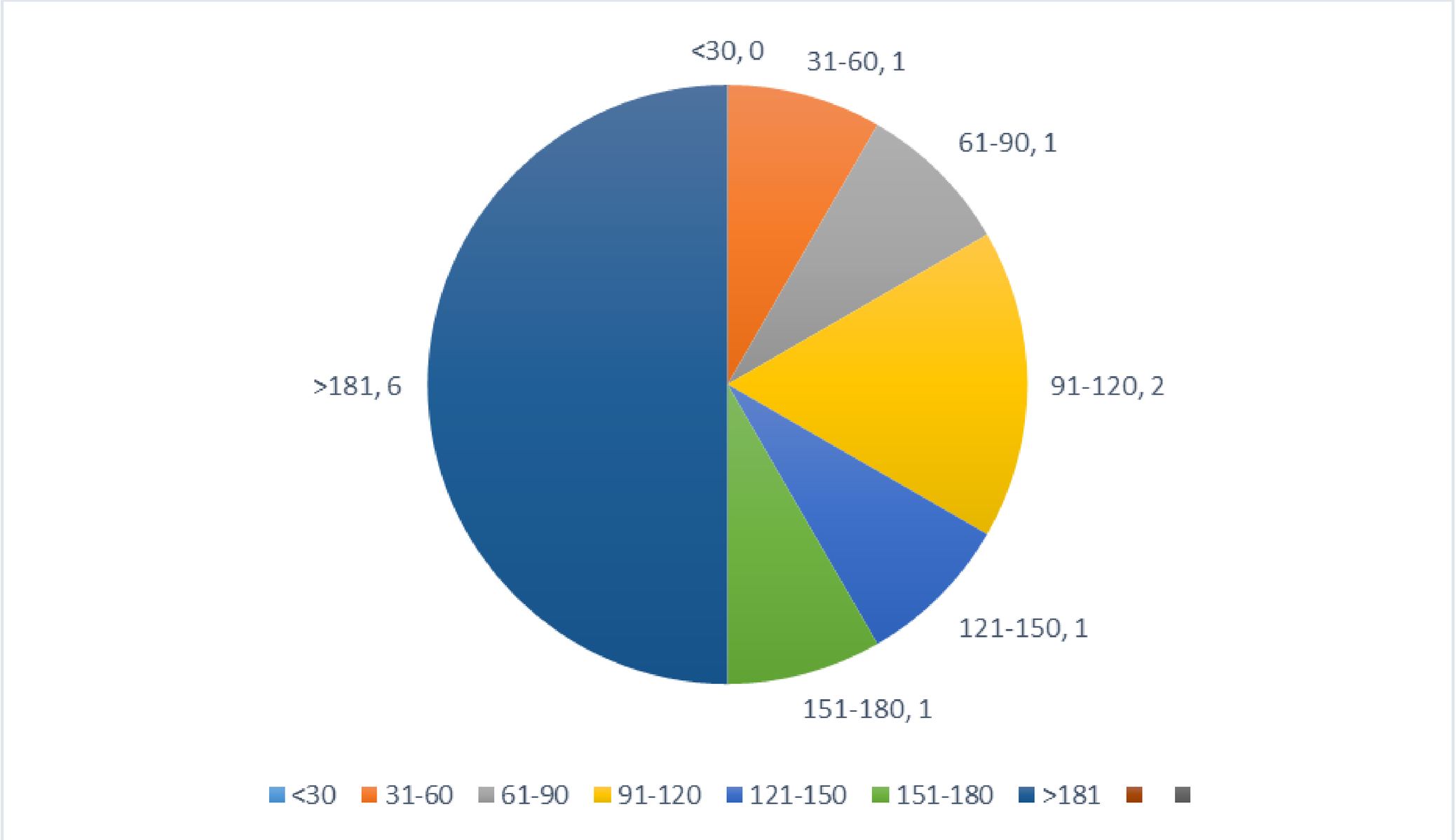
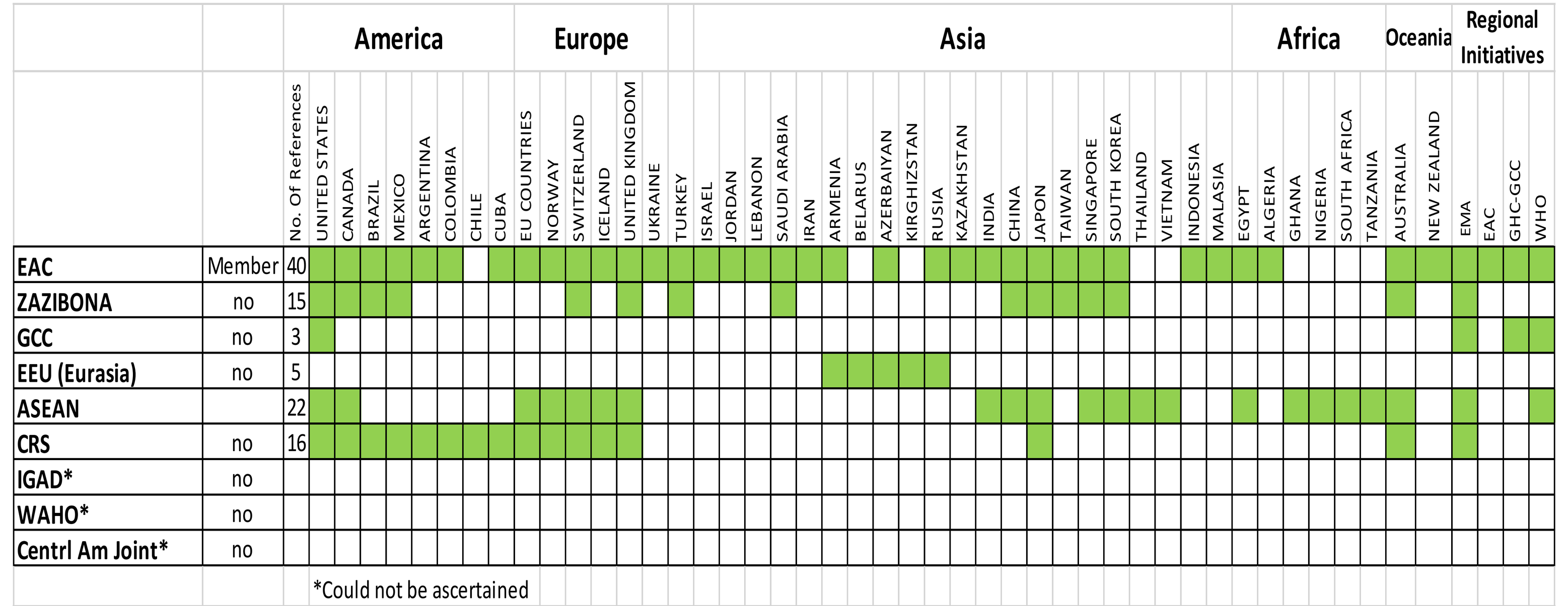


Table 2. Who Relies on Who?



Opportunities for Optimizing the Use of Reliance by RRIs

Future research could further explore the impact of process characteristics on the effectiveness of these initiatives and on their return on investment. Based on our observations we find an opportunity for:

- Agencies to increase transparency regarding their RRI pathway processes and characteristics.
- The consideration of the "Best Practices" identified through our analyses.
- Further agency and user real-world input into the FRPath® profiles.
- The sharing of sponsor experiences with each RRI and their pathways, so as to collaboratively identify best practices, opportunities for optimization and a better understanding of the Return on Investment for their use.

Figure 2. Assessment Approaches Used by RRIs

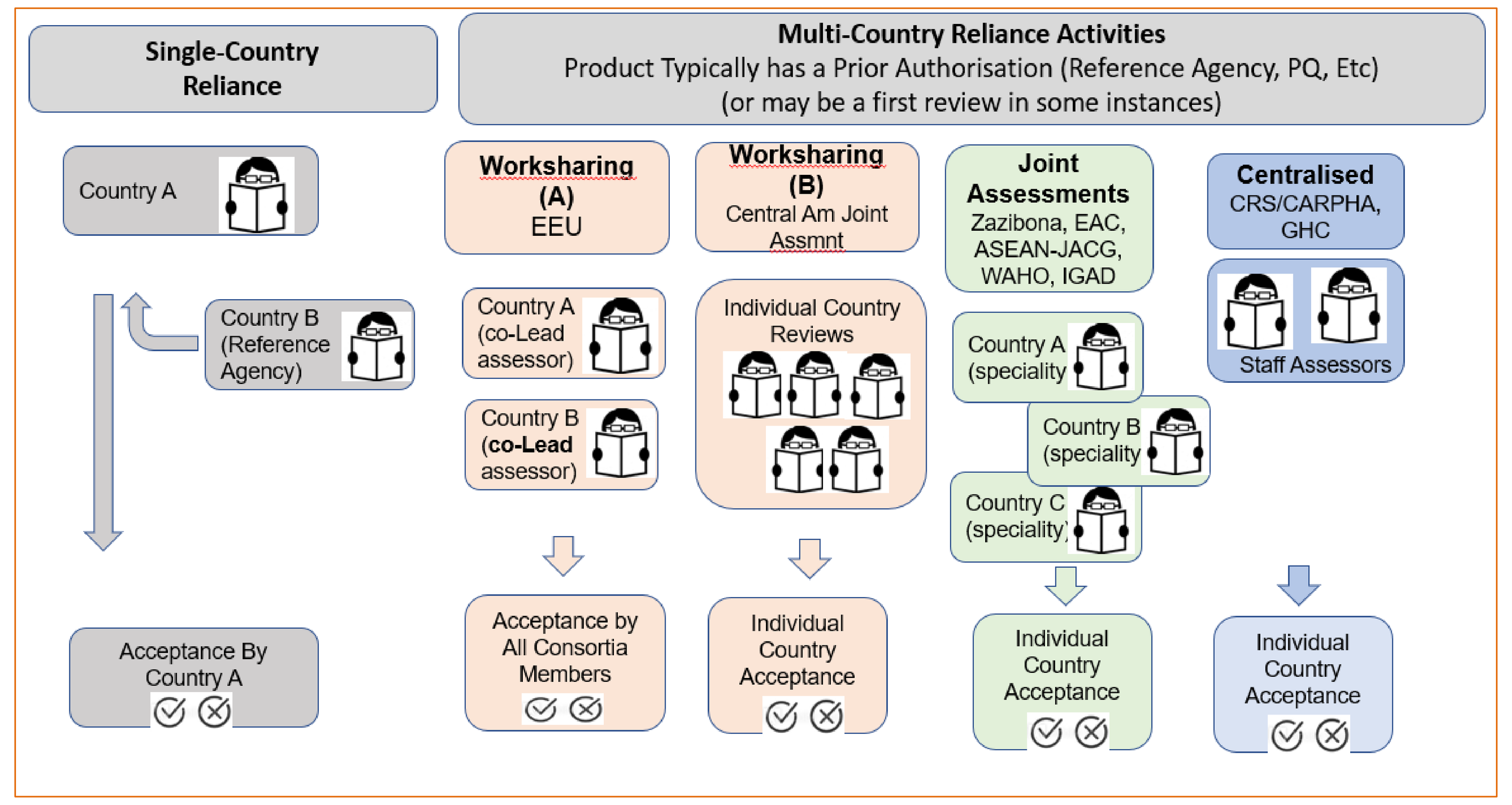


Table 3 . Our Recommendations for Reliance "Best Practices" for RRIs

Common Practices Observed Across 199 FRPs described in the FRPath® database	Our "Best Practices" Recommended for Regional Regulatory Initiatives (RRIs)	Is the Recommended "Best Practice" in use by RRIs?
Target timeline of 91 to >180 days	Target timeline (agency time) of 90 days or less	2 of 12
Transparent instructions not available	Transparent guidelines/SOPs on website	11 of 12
Require legalized CPP at time of submission	eCPP/alternate submitted AFTER submission/before approval	4 of 12
Questions sent at specified times during assessment	Questions sent at specified times during assessment	5 of 12
Not used for innovator products	Use for innovators	4 of 12
Cumbersome Reference Agency list	Accept any WLA	1 of 12
More than three Reference Decisions needed	Use one Reference Agency decision	3 of 12

Observations

Our analyses revealed significant differences in the process characteristics of the initiatives studied. For example, target agency review times ranged from less than 60 days (ASEAN) to more than 180 days (EAC, EEU, Zazibona) illustrating the diversity in these pathways. Such heterogeneity contributes to uncertainty with regard to timing and outcomes, which can be a deterrent to their use.

Our study provides important insights into the process characteristics of RRIs highlighting areas of strengths and weaknesses. These findings can inform stakeholders seeking to optimize the use of these initiatives by identifying key features that could be leveraged for maximum impact.

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