Panel thoughts and reflections

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Committee on Stronger Food
And Drug Regulatory Systems Abroad

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Examples of Countries that use FRPs

Primary FRP (Expedited regulatory pathways for medicines targeting unmet medical need): Accelerated approval/Assessment, Priority review, Breakthrough therapy, CM authorisation, MA under Exceptional Circumstances, Prime, Sakigake, etc.

Secondary FRP (Reliance pathways to facilitate regulatory decisions): Used by NRAs or regional regulatory initiatives (RRIs) wherein their decisions can be expedited by the ***reliance*** *on or* ***recognition*** *of prior reviews. (*Verification or Abridged reviews, “Pro-forma” registration, WHO PQP/Collaborative Registration process, etc)

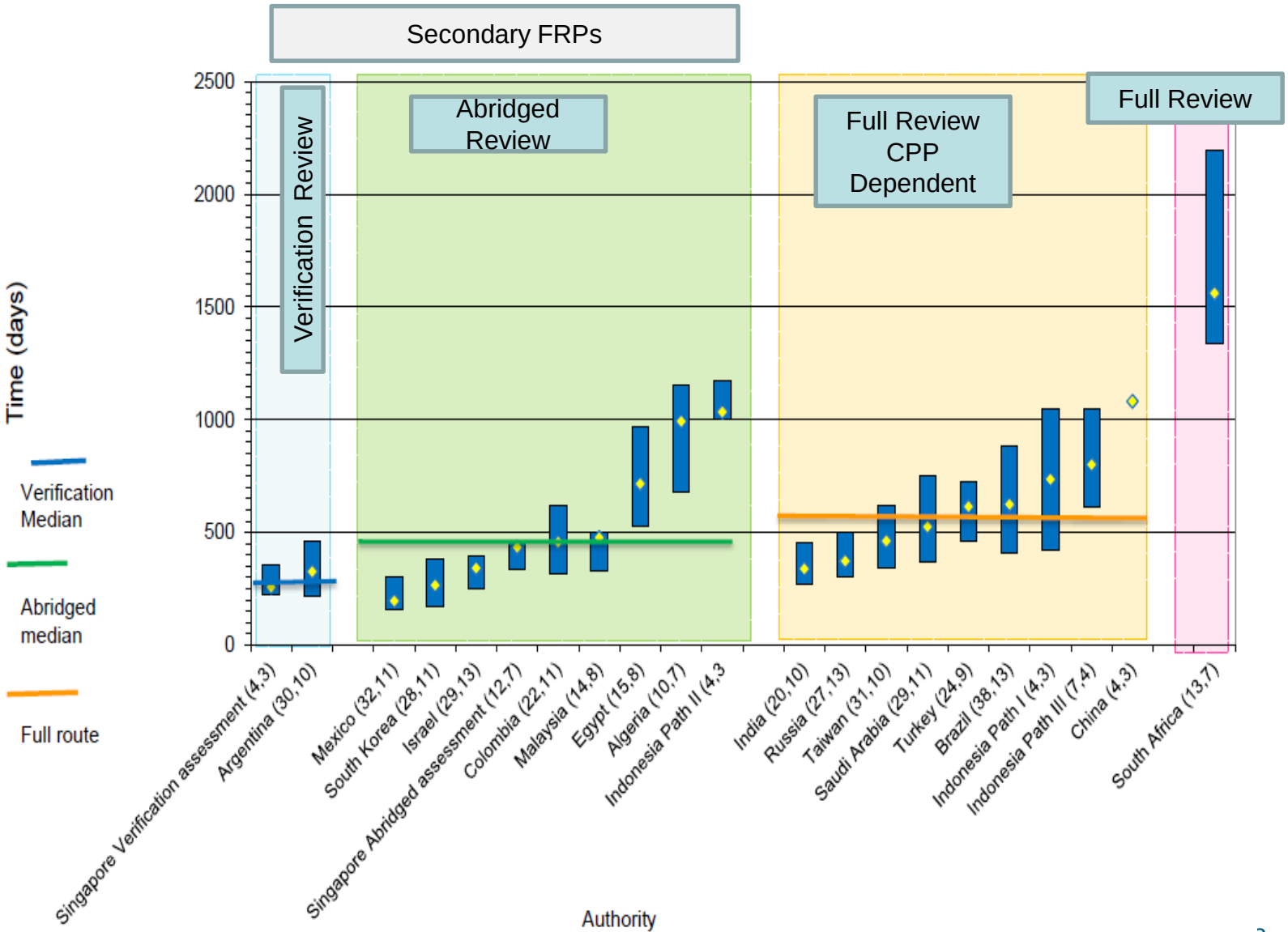
Regional Regulatory Initiatives: Zazibona (SADC); EAC (East Africa); WAHO (West Africa); CRS (Carribean); PAHO (Latin America); APEC (Asia Pacific); GCC (Middle East)

Regulatory approval times for NASs approved 2015- 2016 by *type of review*

Data supplied by companies on NAS approved 2015-2016

Box= 25-75 percentile

Diamond = Median



Regional Regulatory Initiatives Use Different Approaches

Product Typically has a Prior Authorisation (Reference Agency, PQ, Etc)
(or may be a first review in some instances)

Worksharing
Zazibona

- Country A (Lead)
- Country B (support)
- Country C (support)

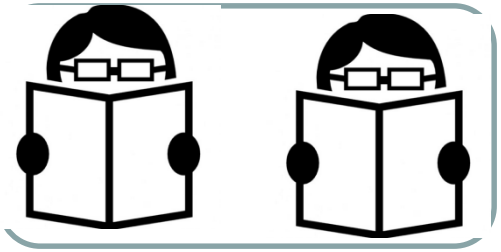
Individual Country Acceptance

Joint Assessments
ACSS, EAC, ASEAN

- Country A (speciality)
- Country B (speciality)
- Country C (speciality)

Individual Country Acceptance

Centralised
CRS-CARPHA, WHO-PQ, EMA

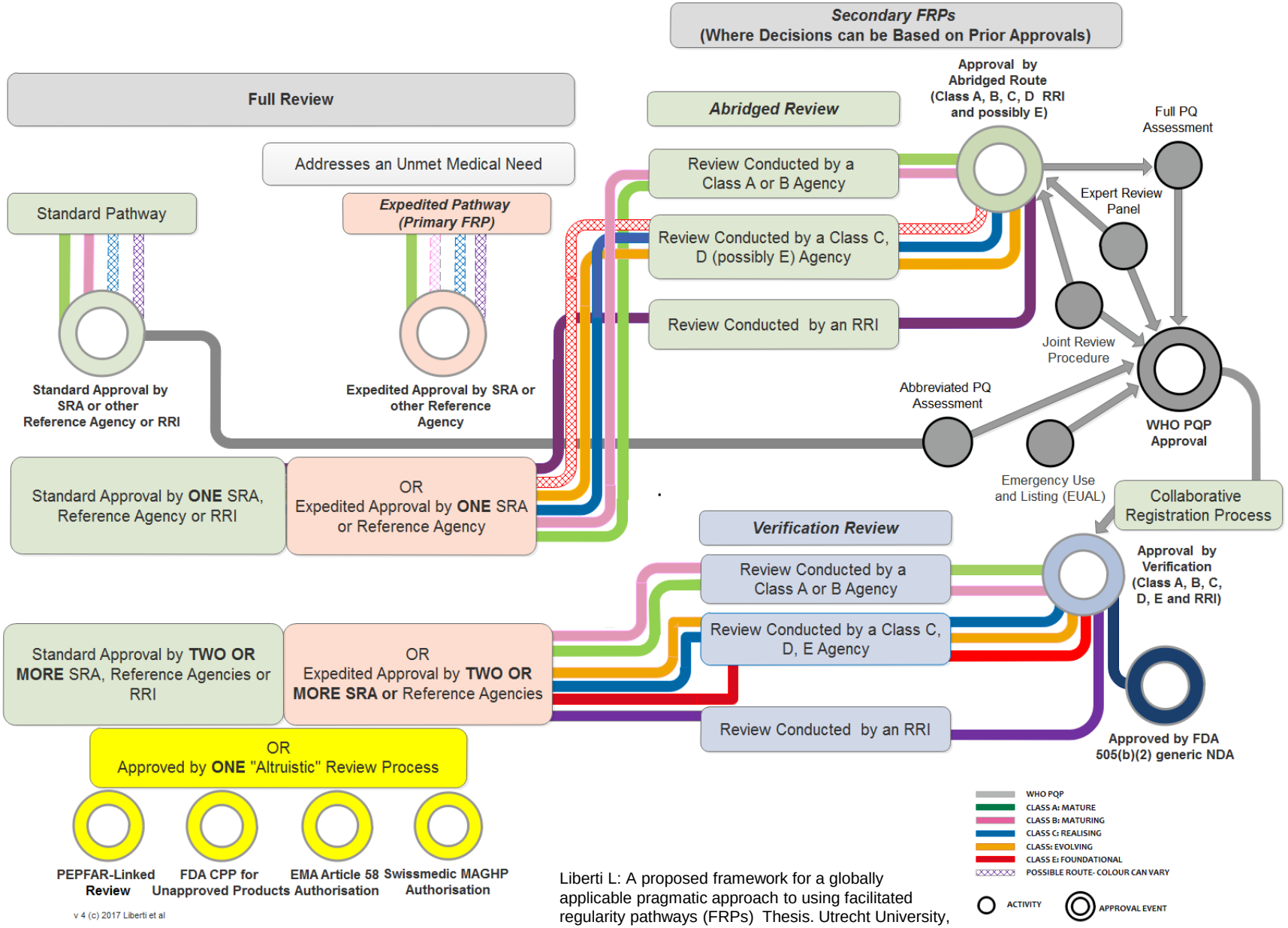


Central Review

Individual Country Acceptance

Each is Fit-For-Purpose

Step 4 Metro Map: An integrated Framework for the use of Primary and Secondary FRPs



Liberti L: A proposed framework for a globally applicable pragmatic approach to using facilitated regularity pathways (FRPs) Thesis. Utrecht University, 2017

Benefits

- Efficient use of staff and advisors
- Focus on added-value activities
- Applicable to NMEs and generics
- Alignment/convergence with international standards
- Reduce burden of duplication for sponsors; improved process predictability

- May also help reduce backlog of
  - Post-authorisation commitments
  - Labelling changes and variations

Challenges

- Assessor reluctance to rely on prior decisions
  - **Trust:** How much should the regulatory authority rely on the reference authority; what detailed information is needed from the reference authority?
  - **Assessment:** what are the areas the reviewers should evaluate specifically and in what depth?
  - **Will:** How to enable the reviewers to see that such approaches do not diminish the review quality or level of scrutiny for local decision making
- Unrealistic expectations from industry regarding very **short timelines**
- Post approval systems needed in place to manage pharmacovigilance and changes

Challenges

- Use may be limited by the legal framework of the agency
- “One size does not fit all”
- Inadequate dossier submissions and screening, leading to avoidable queries/delays
- Difficulty obtaining (un-redacted) assessment reports and CPPs
- Differing skill levels across participating countries
- **no *mutually recognised framework* for reliance assessments**

Solutions

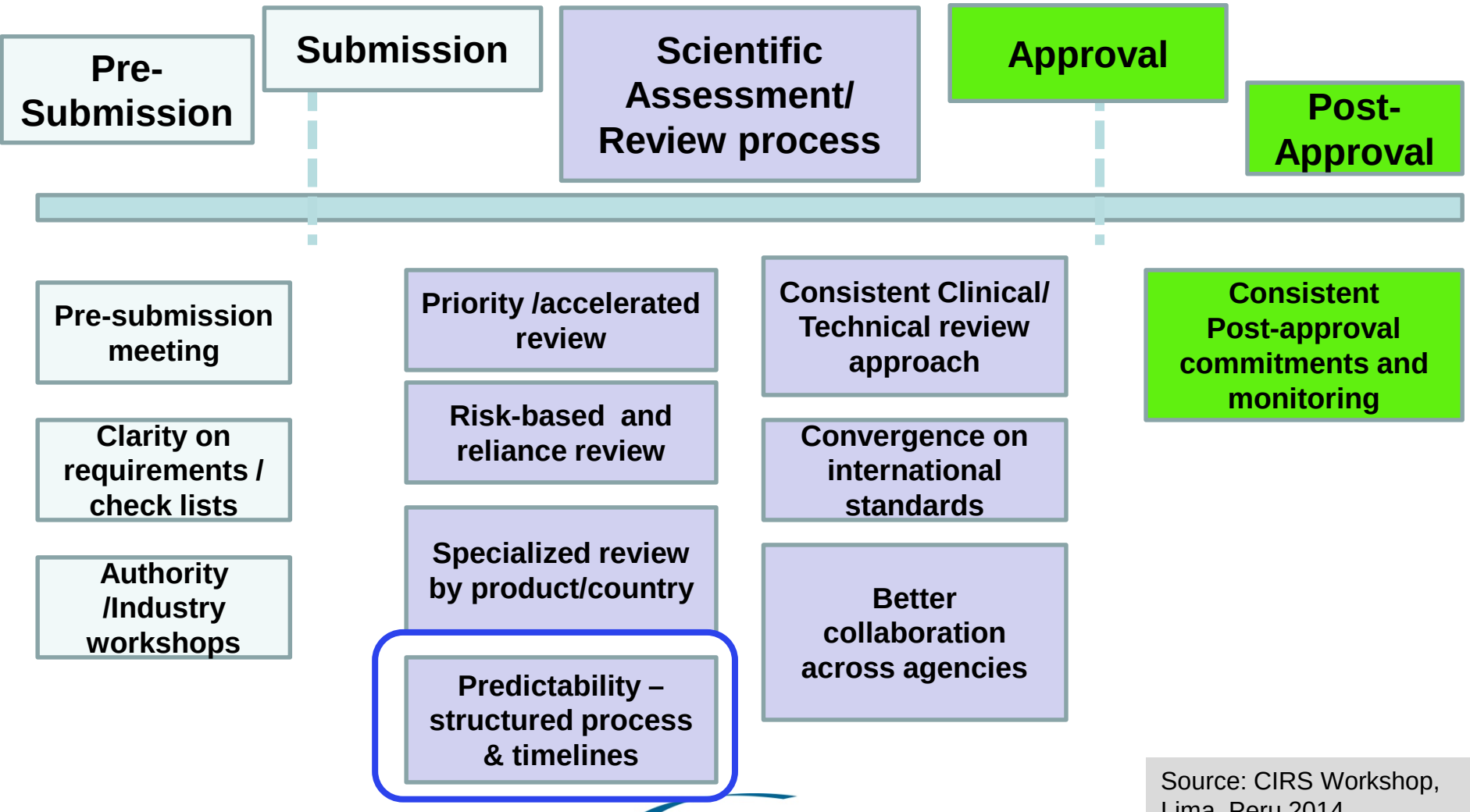
- Regulators' activities should be 'added-value" and "Fit-for Purpose"
- Reviewers need to refine their processes based on regulatory science
- Regulatory authority convergence toward global standards

- Industry should align on format of data, presentation, and the level of detail
- Discuss industry experiences with regulatory authorities to improve processes

- Training for both industry and regulatory authorities
- Transparency facilitated by access to assessment reports and exploring digital solutions

- Develop a Good Reliance Practice Guidance

An Ideal Medicine Regulatory Pathway



Source: CIRS Workshop, Lima, Peru 2014

CIRS Centre for Innovation in Regulatory Science

Good Regulatory Practices- The Cornerstone of Trust

Good Regulatory Practices

Good Registration Management

Review Authorities	*Good Review Practices (GRevP)*	*Good Submission Practices (GSubP)*	*Applicants*

Good Reliance Practices → **TRUST in DECISION MAKING PROCESSES**

Australia: TGA COR approach (Jan 2018)

List of countries and jurisdictions determined to be comparable overseas regulators (CORs)

COR-A (120

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Comparable Overseas Reports (COR-A) pathway - First registration decision

2 November 2018

Cabozantinib (CABOMETYX) is the first medicine to be registered on the Australian Register of Therapeutic Goods (ARTG) via the TGA's new COR-A pathway, which came into effect in January 2018.

The application relates to an extension of the available indications to include first line treatment of adults with poor or intermediate risk of advanced renal cell carcinoma (RCC). The extension of indication was registered on the ARTG on 1 November 2018 following approval by EMA on 8 May 2018.

Category: Prescription medicines
URL: https://www.tga.gov.au/node/872103

United Kingdom	Medicines and Healthcare products Regulatory Agency (MHRA)
United States	Food and Drug Administration (FDA)
Jurisdictions	
European Union	European Medicines Agency (EMA) - centralised and decentralised processes

on 1 COR report

The Reliance "Trust" Commitment

'Before I say "Yes" I'd like to carry out a risk assessment'

Building Trust for Effective Collaborations

PRINCIPLES OF GOOD SUBMISSION
(from GSubP Guideline)

1. *Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile*
2. *Compliance to Up-to-date Regulatory Requirements*
3. *Well-Structured Submission Dossier with Appropriate Cross-references*
4. *Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data*
5. *Effective and Efficient Communications*

PRINCIPLES OF A GOOD REVIEW
(from GRevP Guideline)

1. *Balanced*
2. *Considers context*
3. *Evidence-based*
4. *Identifies signals*
5. *Investigates and solves problems*
6. *Makes linkages*
7. *Thorough*
8. *Utilizes critical analyses*
9. *Well-documented*
10. *Well-managed*

I Sasaki: APAC RA-EWG / JPMA
Nov 2016