Reliance and Work-Smart regulation

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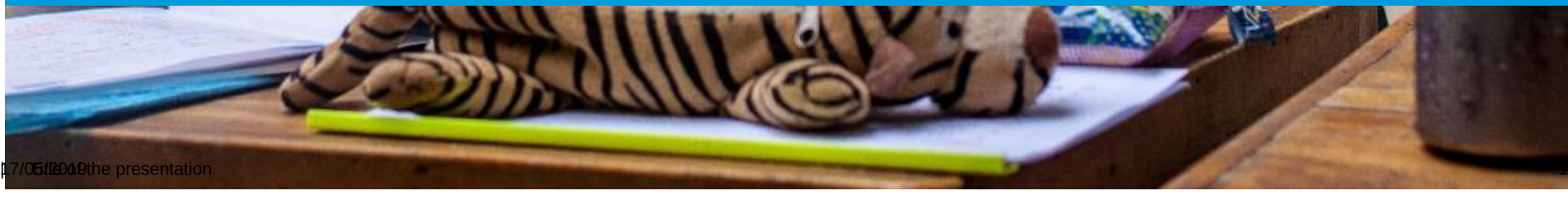
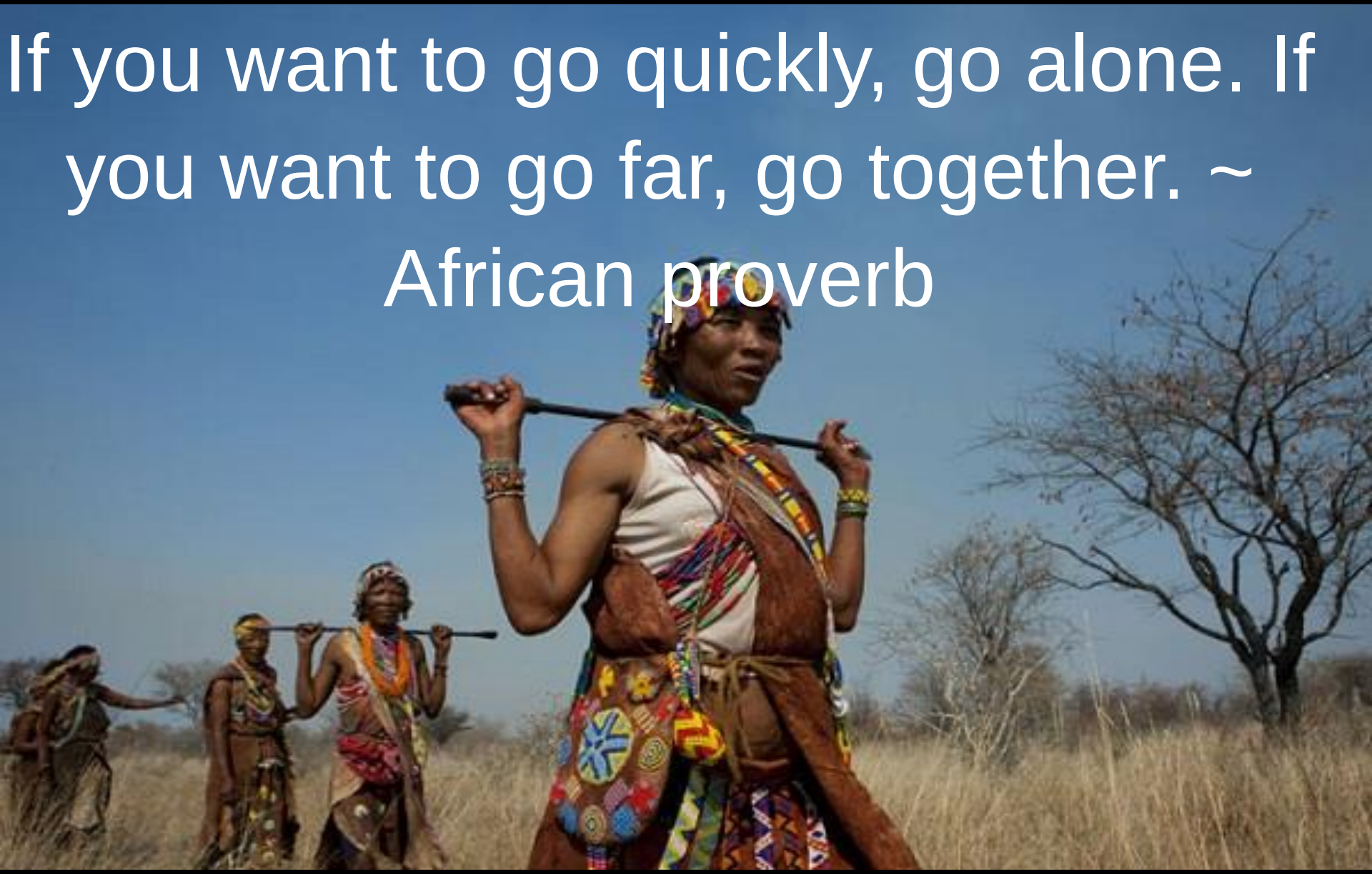
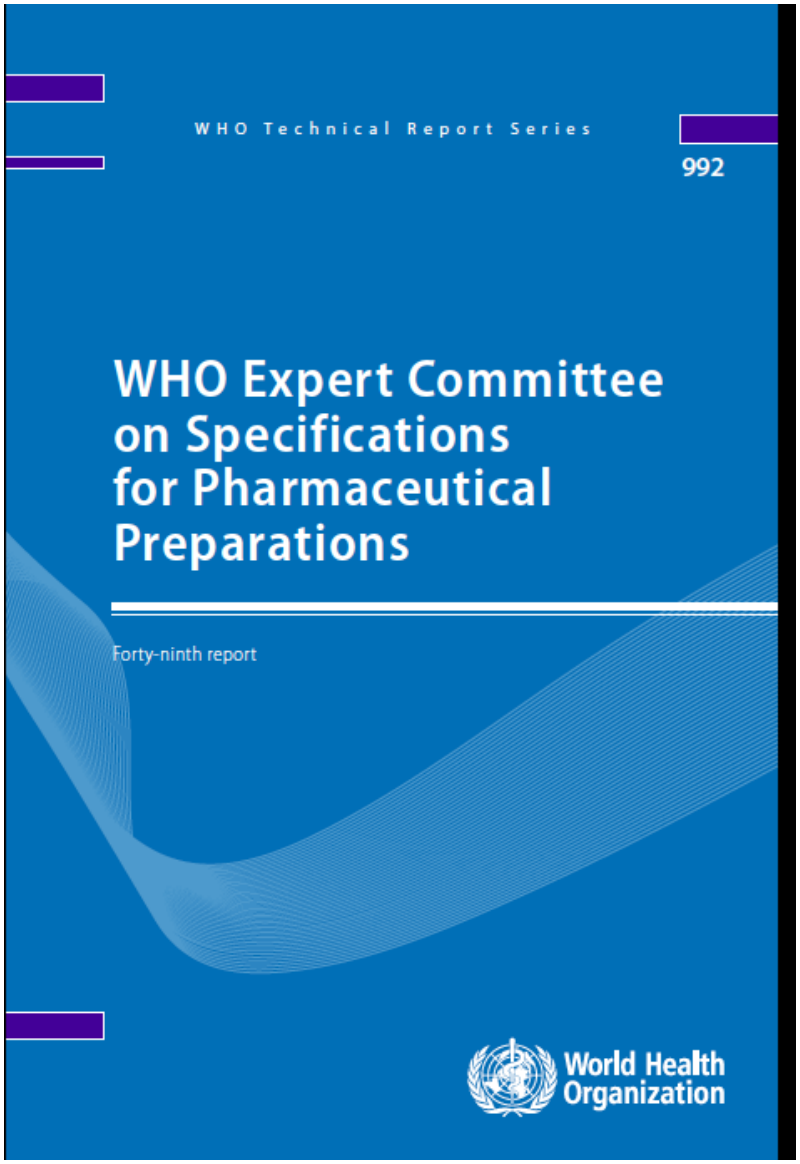



If you want to go quickly, go alone. If you want to go far, go together. ~ African proverb

All pharmaceutical products, including multisource products, should be used in a country **only after approval** by the national or regional authority. Regulatory authorities should require the documentation of a multisource pharmaceutical product to meet the following:

- GMP;
- Quality requirements; and
- Pharmaceutical product interchangeability



WHA Resolutions: WHA 67.20 (2014); WHA 67.21 (2014); WHA63.12 (2010)

IDEAL SITUATION

Robust Registration Systems

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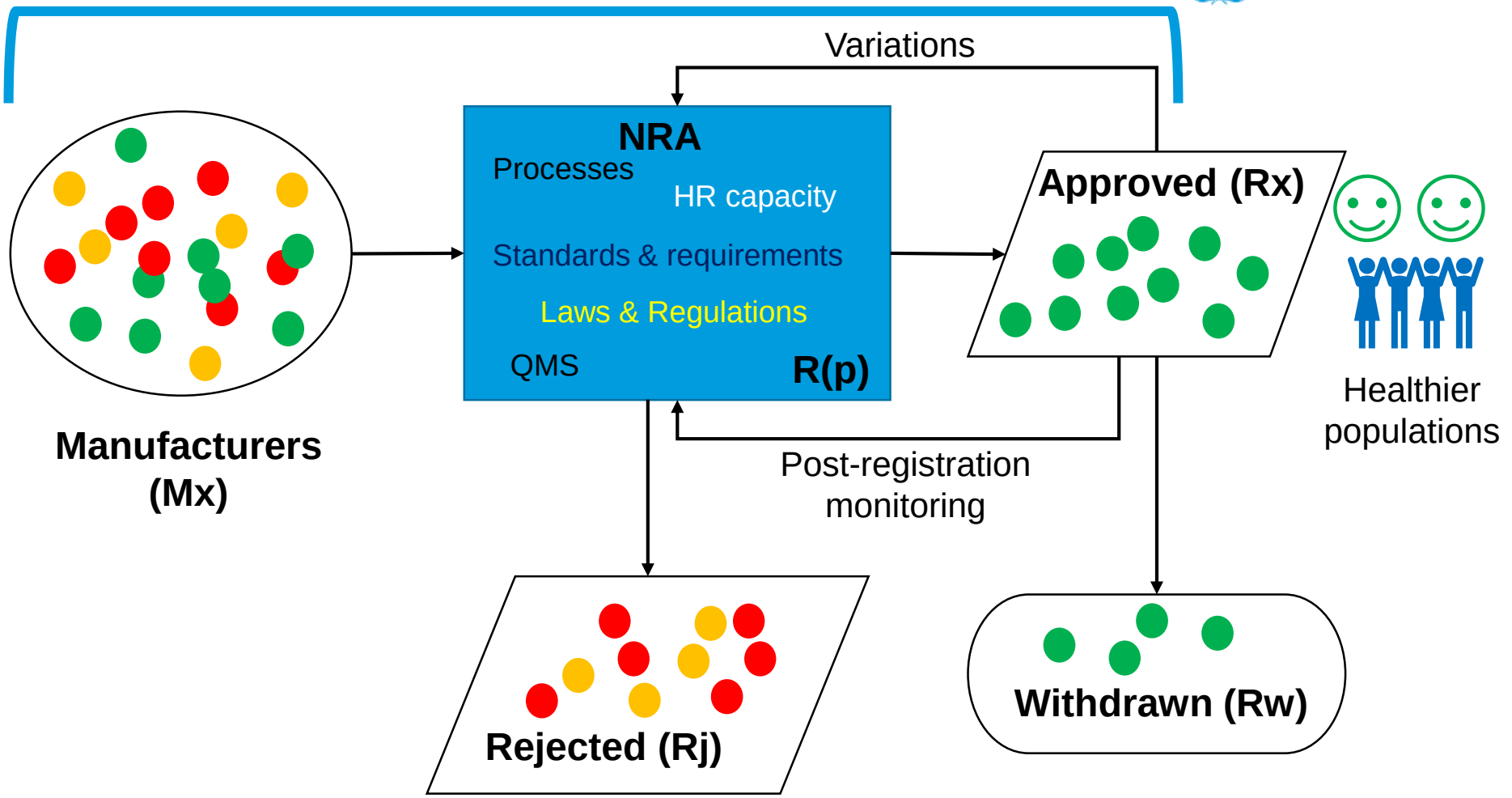
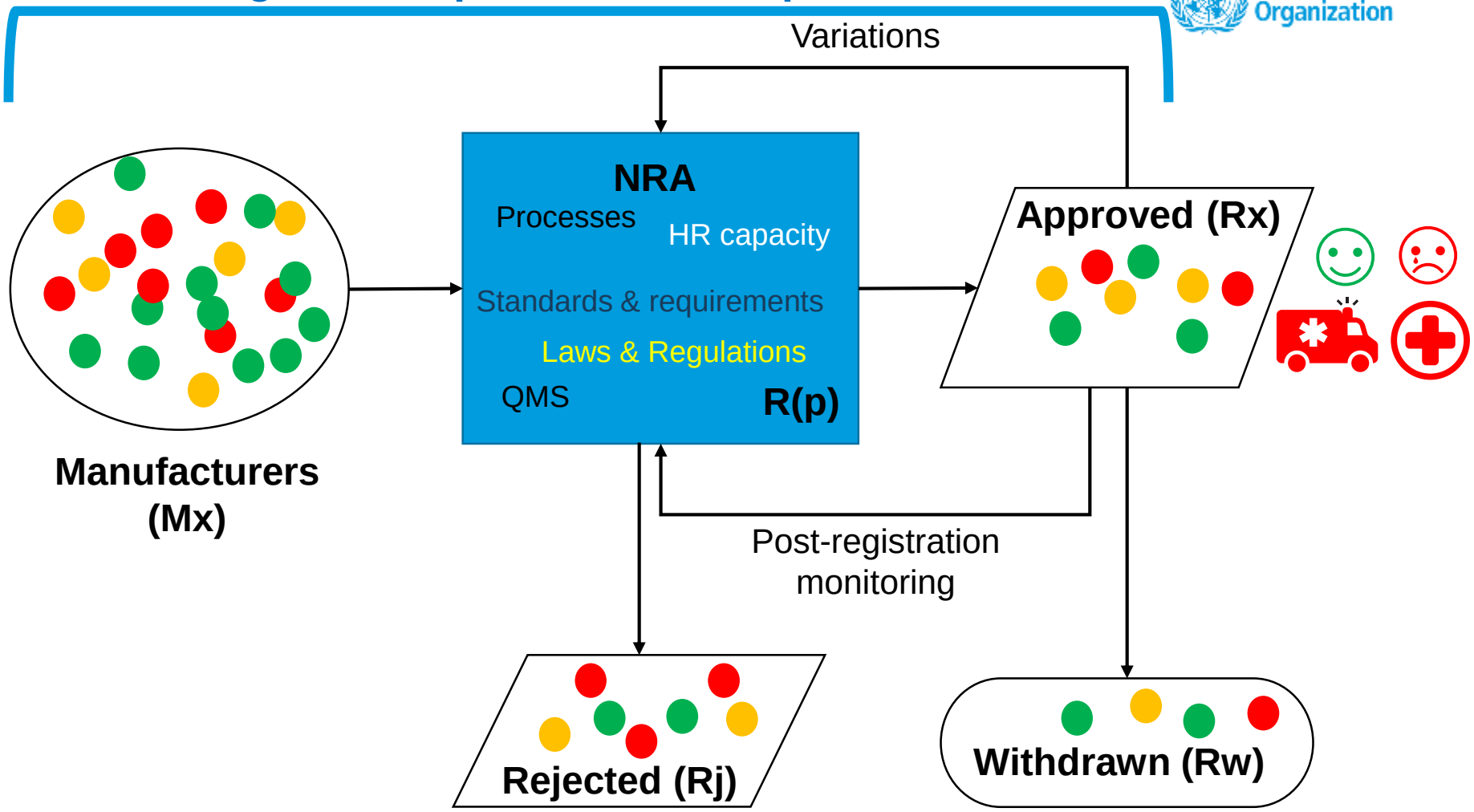


Medicines Regulation Process Flow

REALITY

Registration processes not optimized

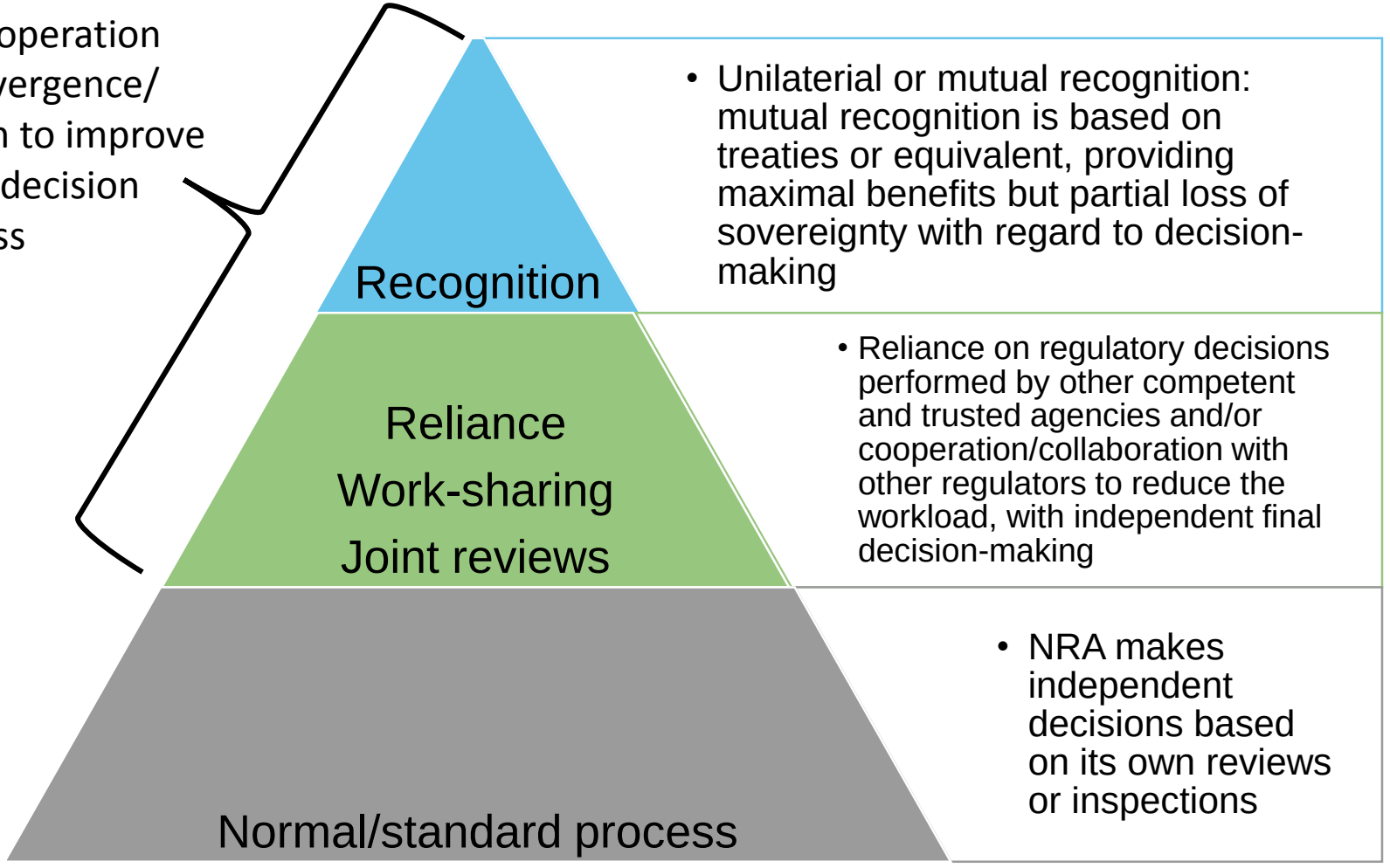
World Health Organization



Medicines Regulation Process Flow

Regulatory decision making

Regulatory cooperation based on convergence/ harmonization to improve the quality of decision making process

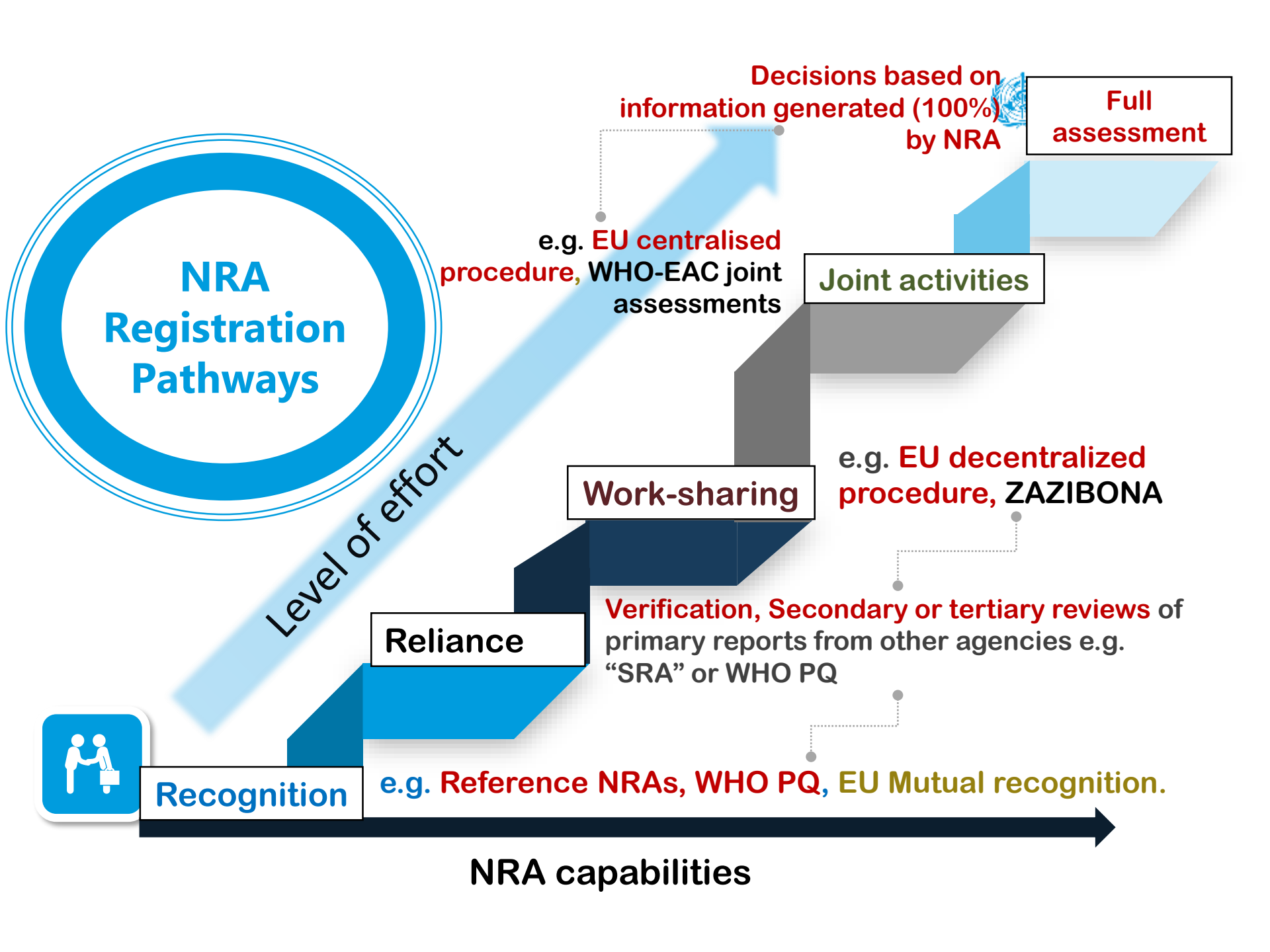


WHA resolution 67.20 (2014)

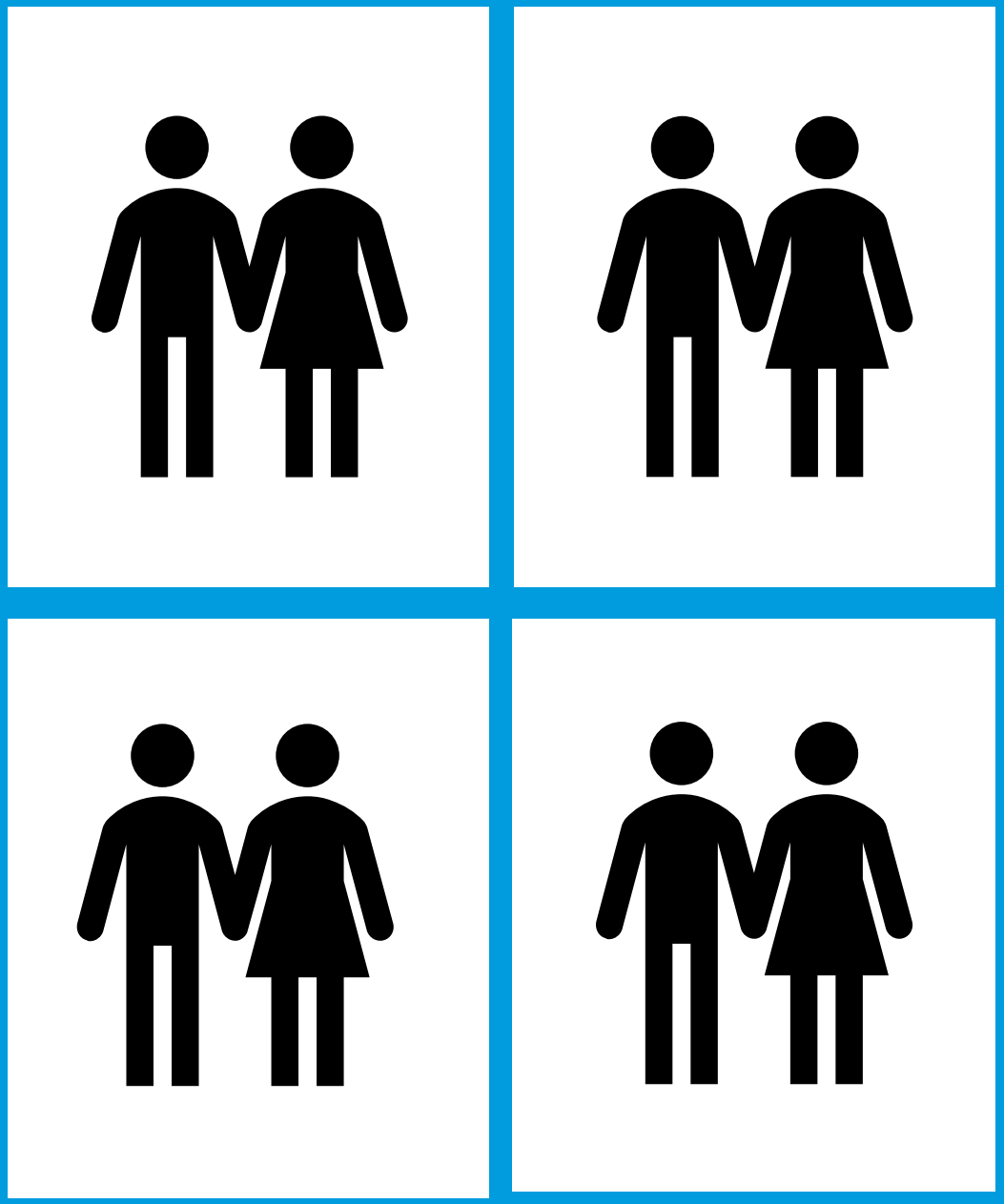
Defining Reliance and Recognition

- **Reliance**: act whereby a regulatory authority in one jurisdiction may take into account/give significant weight to work performed by another regulator or other trusted institution in reaching its own decision.

- **Recognition:** the routine acceptance of the regulatory decision of another regulator or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B.


NRA Registration Pathways
Level of effort
Decisions based on information generated (100%) by NRA
Full assessment
e.g. EU centralised procedure, WHO-EAC joint assessments
Joint activities
Work-sharing
e.g. EU decentralized procedure, ZAZIBONA
Reliance
Verification, Secondary or tertiary reviews of primary reports from other agencies e.g. "SRA" or WHO PQ
Recognition
e.g. Reference NRAs, WHO PQ, EU Mutual recognition.
NRA capabilities

of children globally are immunized with WHO prequalified vaccines through the GAVI alliance



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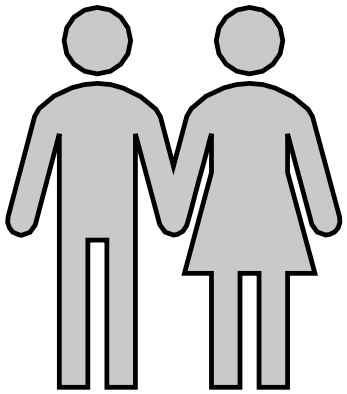
PEOPLE ON ANTIRETROVIRAL THERAPY ACROSS THE GLOBE ARE TREATED WITH WHO PREQUALIFIED GENERIC MEDICINES




How do WE get the quality assured product to these patients faster, and more efficient?
How do WE ensure continued supply of quality assured products post-registration?

Facilitated pathways to "transfer" regulatory information & knowledge

World Health Organization

PRINCIPLES

- **Sharing information** (assessment, inspection and testing results) that serve as basis for national decisions – avoiding duplication.
- **Voluntary participation** – reference authorities, participating authorities and manufacturers/sponsors

WHO collaborative procedure

Vaccines: 2004
Medicines: Started in 2012
Diagnostics: Pilot 2019
Vector control: Pilot 2020

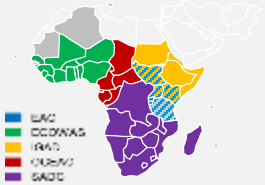
**CRP-lite

"SRA" collaborative procedure

Initiated in 2015
European Medicines Agency (EMA)
Medicines and Healthcare Products Regulatory Agency (MHRA)
20 African NRAs

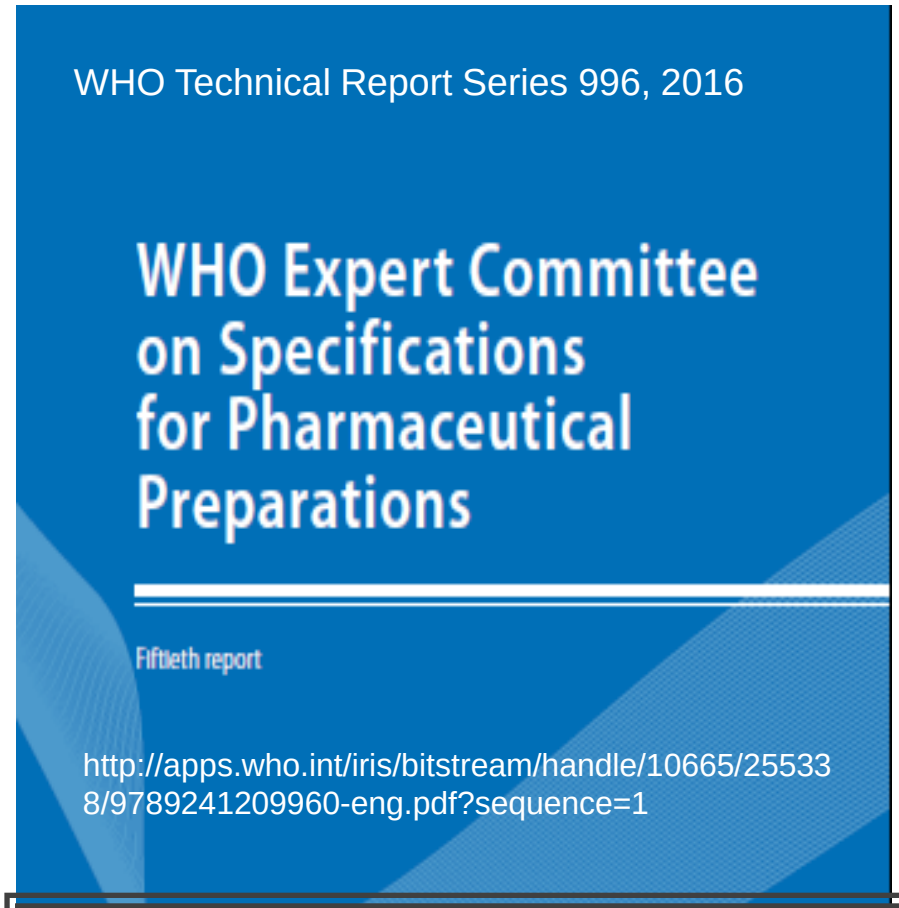
Regional networks

African Medicines Regulatory Harmonization Project (AMRH)



ASEAN SIAHR Project

Caribbean Public Health Agency
CARPHA



Annex 8

Collaborative procedure between the World Health Organization (WHO) Prequalification Team and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines

Published guidelines

WHO Technical Report Series 1010, 2018

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Fifty-second report

http://apps.who.int/iris/bitstream/handle/10665/272452/9789241210195-eng.pdf?ua=1

World Health Organization

Annex 11

Collaborative procedure in the assessment and accelerated national registration of pharmaceutical products and vaccines approved by stringent regulatory authorities

Published guidelines

WHO Technical Report Series 1010, 2018

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Fifty-second report

http://apps.who.int/iris/bitstream/handle/10665/272452/9789241210195-eng.pdf?ua=1

Annex 9

Guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions

Published guidelines

Concept of collaborative registrations (Reliance)

To support the national registrations, regulators can benefit from already organized scientific assessments and inspections, if

- Having access to regulatory expertise from trusted party (complete assessment and inspection reports)
- Having the same product
- Having same essential technical data
- Understanding validity of B/R for local environment**
- National legislation and sovereignty are not affected
- Respect confidentiality of commercially sensitive information
- Manage properly regulatory follow-up

Recall the regulator's dilemma...

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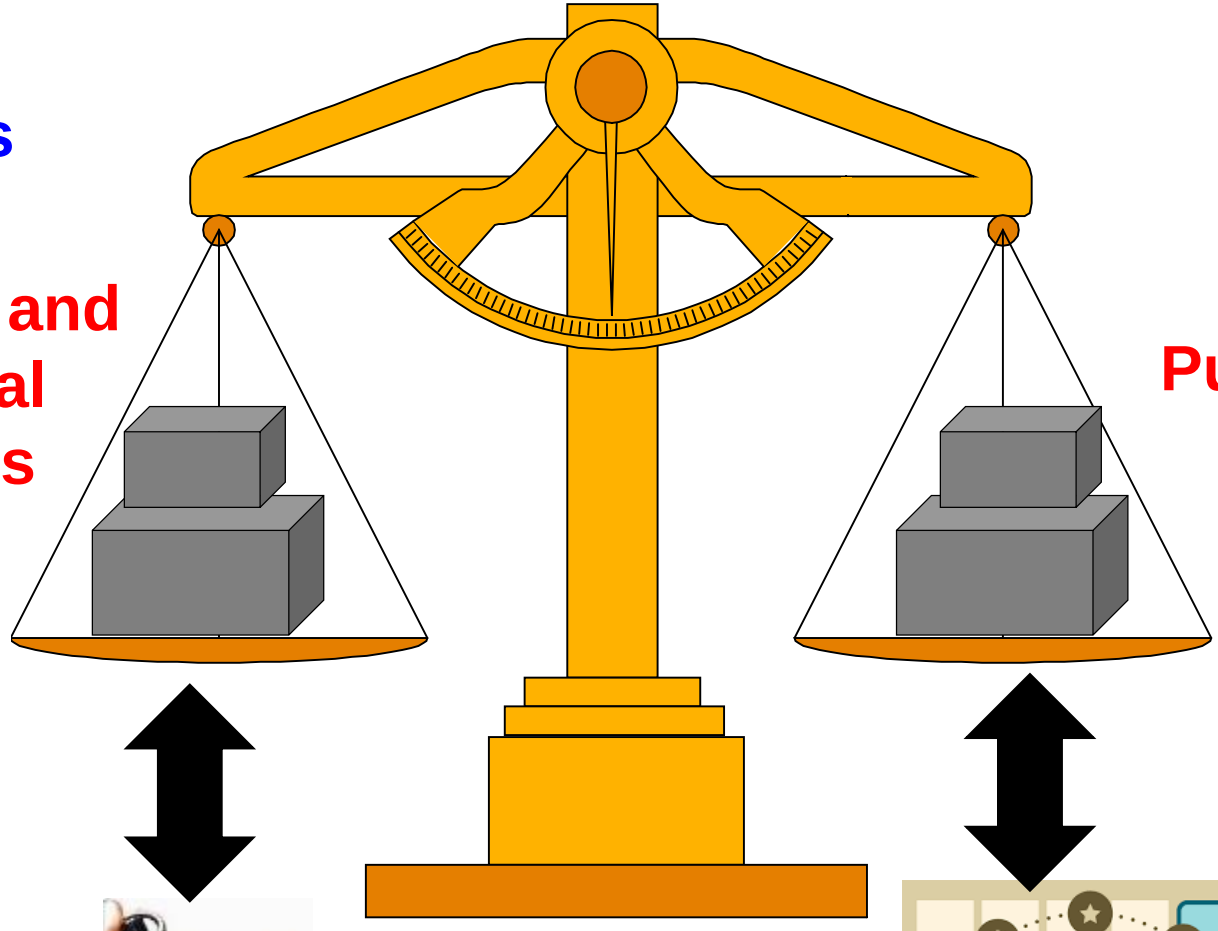
Access

Economic and industrial interests

Market Control

Public health



IDEAL SITUATION - WITH FACILITATED PATHWAYS

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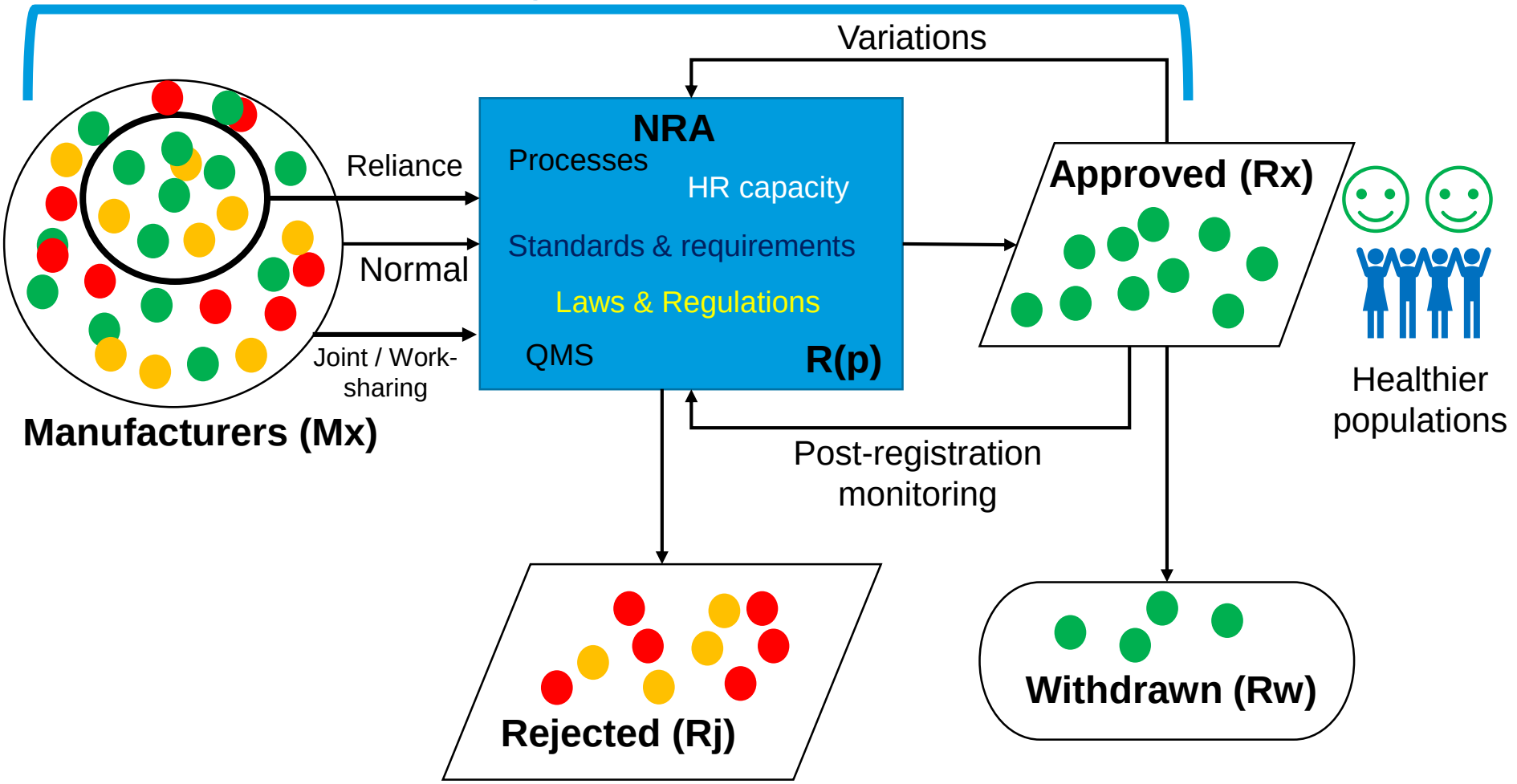
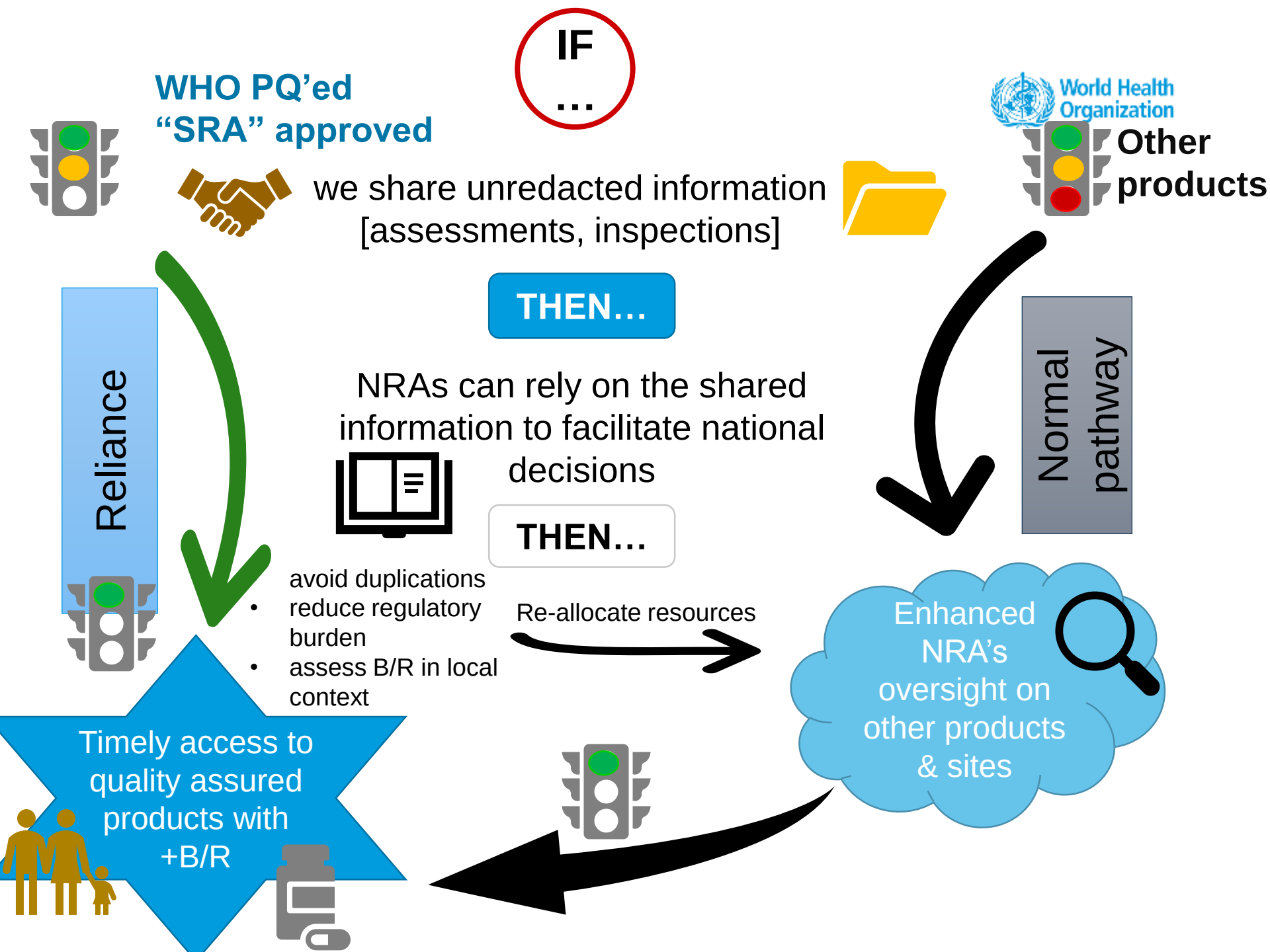
Streamlined Registration processes



Medicines Regulation Process Flow


IF
…
WHO PQ'ed
"SRA" approved
World Health Organization
Other products
we share unredacted information
[assessments, inspections]
THEN…
Reliance
Normal pathway
NRAs can rely on the shared information to facilitate national decisions
THEN…
avoid duplications
reduce regulatory burden
assess B/R in local context
Re-allocate resources
Enhanced NRA's oversight on other products & sites
Timely access to quality assured products with +B/R

Shared regulatory approach

A modern regulator

harmonization
cooperation
efficient
work-sharing
reliance
recognition
joint
risk-management
effective
outcome-oriented
collaboration

World Health Organization

Access to safe, effective, good quality and affordable essential medicines & health technologies

(1) Time to approval; (2) incidence of SSFFCs, (3) # of certified suppliers per essential medicine, (4) compliance rate to GMP & GxP standards, (5) # of reported ADRs per 100,000 population

(a) # of submitted & approved products , (b) # of approved facilities, (c) # of submitted & approved clinical trials, (d) % of samples tested, (e) # of ADRs/product related reports

(a) # of products reviewed & approved, (b) # of facilities inspected & approved based on reliance (recognition of decisions by others), work-sharing, & centralised procedures, (c) # of reviewed multi-country trials, (d) utilisation of certified QC labs

National level

- Review & approval of clinical trials
- Registration of medicines
- Licensing & inspection (local)
- Vigilance
- Import & export control
- Medicine information (incl. advertising & promotion
- PMS (incl. access to OMCL for Testing Services)
- Vaccine lot release

Collaboration

- Access to Laboratory Testing Services (OMCL)
- Review of dossiers
- Review of multi-country clinical trials
- GxPs inspection (external)
- Vigilance (regional alert system)
- Regional integrated system for controlling imports & exports
- Medicine information (incl. advertising & promotion

Policy & legal framework, human resources, financial resources, political support / will, infrastructure and equipment

Source: L Gwaza & G.N. Mahlangu (2015). Business Plan for the African Medicines Agency

Laboratory Testing Services

- WHO National Control Laboratory Network for Biologicals 2017
- Use of WHO PQ'ed laboratories for testing of pharmaceuticals

Lessons learnt with respect to facilitated pathways – for NRAs

World Health Organization

Barriers to reliance

1. Legislative prohibitions ???
2. Backlog in reviews (use of FIFO)
3. Lack of tools for recognition, reliance or work sharing (one approach for all applications)
4. Change management

Key enablers for reliance

1. Enabling laws
2. Risk based approach to registration and Inspections
3. Guidelines
4. Procedures to guide staff
5. Staff awareness on reliance approaches
6. Communication (internal and external)

“At a time in which medical product manufacturing is truly a global enterprise, there is much to be gained by partnering with regulatory counterparts to reduce duplicative efforts and maximize global resources while realizing the greatest bang for our collective inspectional buck. By partnering with these countries we can create greater efficiencies and better fulfil our public health goals, relying on the expertise of our colleagues and refocusing our resources on inspections in higher risk countries.” FDA Commissioner Scott Gottlieb, M.D. October 31, 2017.

This is the Regulator's Dilemma!!...

"The need to maintain such a delicate balance by applying ***appropriate standards*** *that are* ***scientifically justified*** *and* ***risk proportionate*** *to* ***protect public health*** *while ensuring economic and industrial interests are not hindered".*

The Future …..

Individual NRAs with specific jurisdictions

transition

Regulatory Networks

"A cord of three strands will not be broken"