EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Mutual Recognition Agreements and Reliance in the Regulation of Medicines

EU perspective

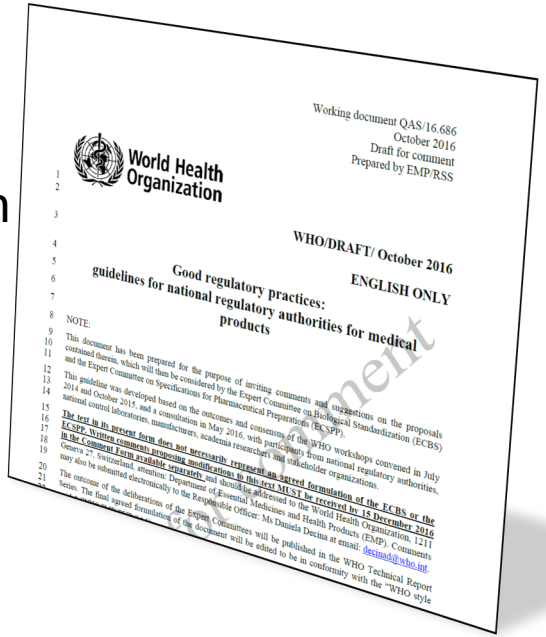
The National Academy of Sciences, Engineering and Medicine - 10 July 2019

Dr Agnes Saint Raymond, International Affairs Division, EMA
Brendan Cuddy, Manufacturing Quality and Supply Chain Integrity, EMA

Disclaimer

Reliance: a working definition

WHO Good Regulatory Practice guideline definition of reliance



Working document QAS/16.686
October 2016
Draft for comment
Prepared by EMP/RSS

World Health Organization

WHO/DRAFT/ October 2016

ENGLISH ONLY

Good regulatory practices: guidelines for national regulatory authorities for medical products

NOTE:

This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Committee on Biological Standardization (ECBS) and the Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP).

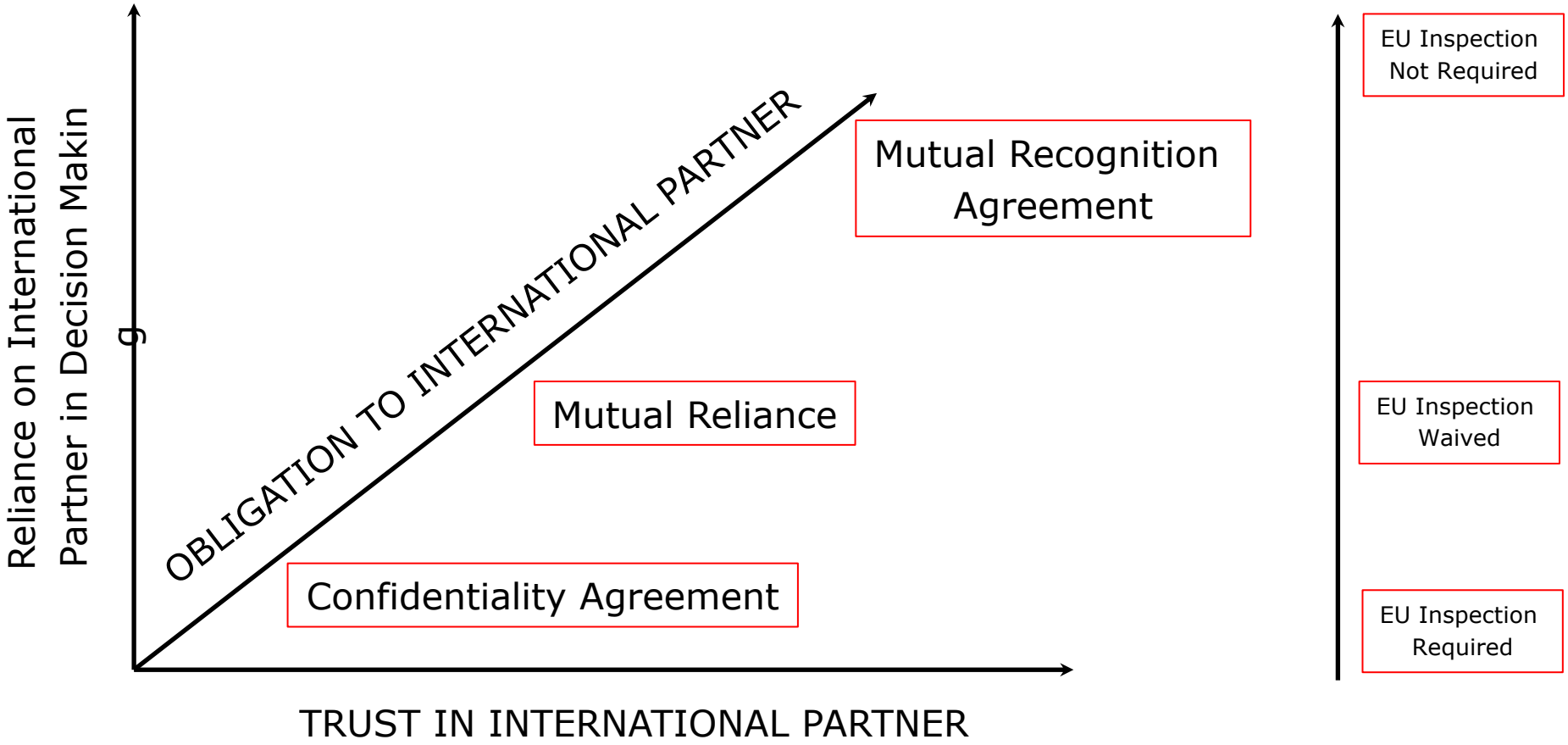
This guideline was developed based on the outcomes and consensus of the WHO workshops convened in July 2014 and October 2015, and a consultation in May 2016, with participants from national regulatory authorities, national control laboratories, manufacturers, academia researchers and stakeholder organizations.

The text in its present form does not necessarily represent an agreed formulation of the ECBS or the ECSPP. Written comments proposing modifications to this text MUST be received by 15 December 2016 in the Comment Form available separately and should be addressed to the World Health Organization, 1211 Geneva 27, Switzerland, attention: Department of Essential Medicines and Health Products (EMP). Comments may also be submitted electronically to the Responsible Officer: Ms Daniela Decina at email: decinad@who.int.

The outcome of the deliberations of the Expert Committees will be published in the WHO Technical Report Series. The final agreed formulation of the document will be edited to be in conformity with the "WHO style

- ✓ **Take account (part or full) of assessment done by others**
- ✓ **Retain responsibility for decision**

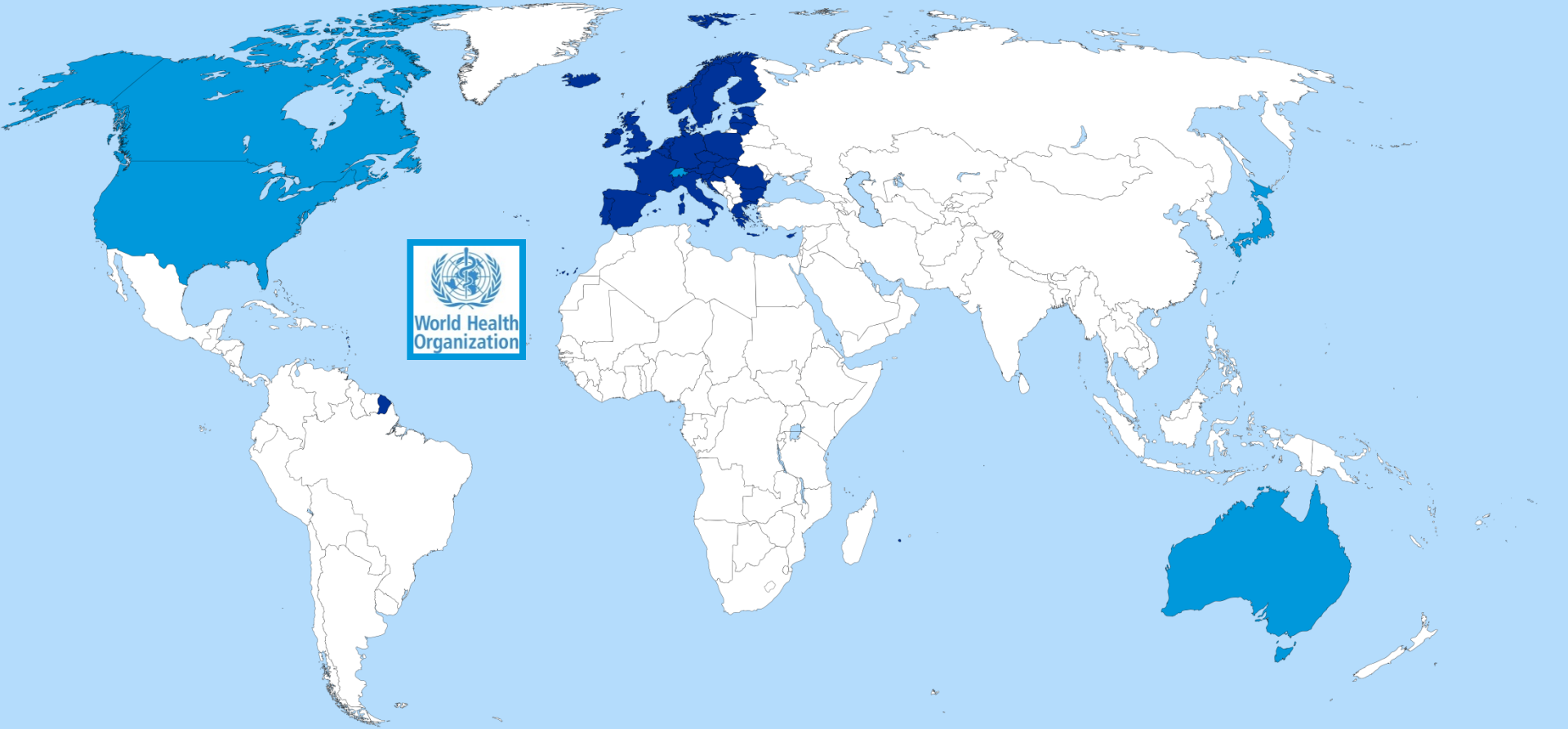
http://www.who.int/medicines/areas/quality_safety/quality_assurance/GoodRegulatory_PracticesPublicConsult.pdf?ua=1


Reliance on International Partner in Decision Making
OBLIGATION TO INTERNATIONAL PARTNER
Mutual Recognition Agreement
Mutual Reliance
Confidentiality Agreement
TRUST IN INTERNATIONAL PARTNER
EU Inspection Not Required
EU Inspection Waived
EU Inspection Required

2019	EU	FDA	AU	NZ	CH	JP	CAN	SG	other
EU		CA CC **(MRA)**	CA MRA	CA MRA	CA MRA	CA MRA	CA MRA		EDQM IL
FDA			CA	CA	CA	CA	CA	CA	CA (many) EDQM
AU				CA MRA			CA MRA	CA MRA	(PIC/S)
NZ									
CH							CA	CA	
JP									
CAN								CA	
SG									(PIC/S)
other									

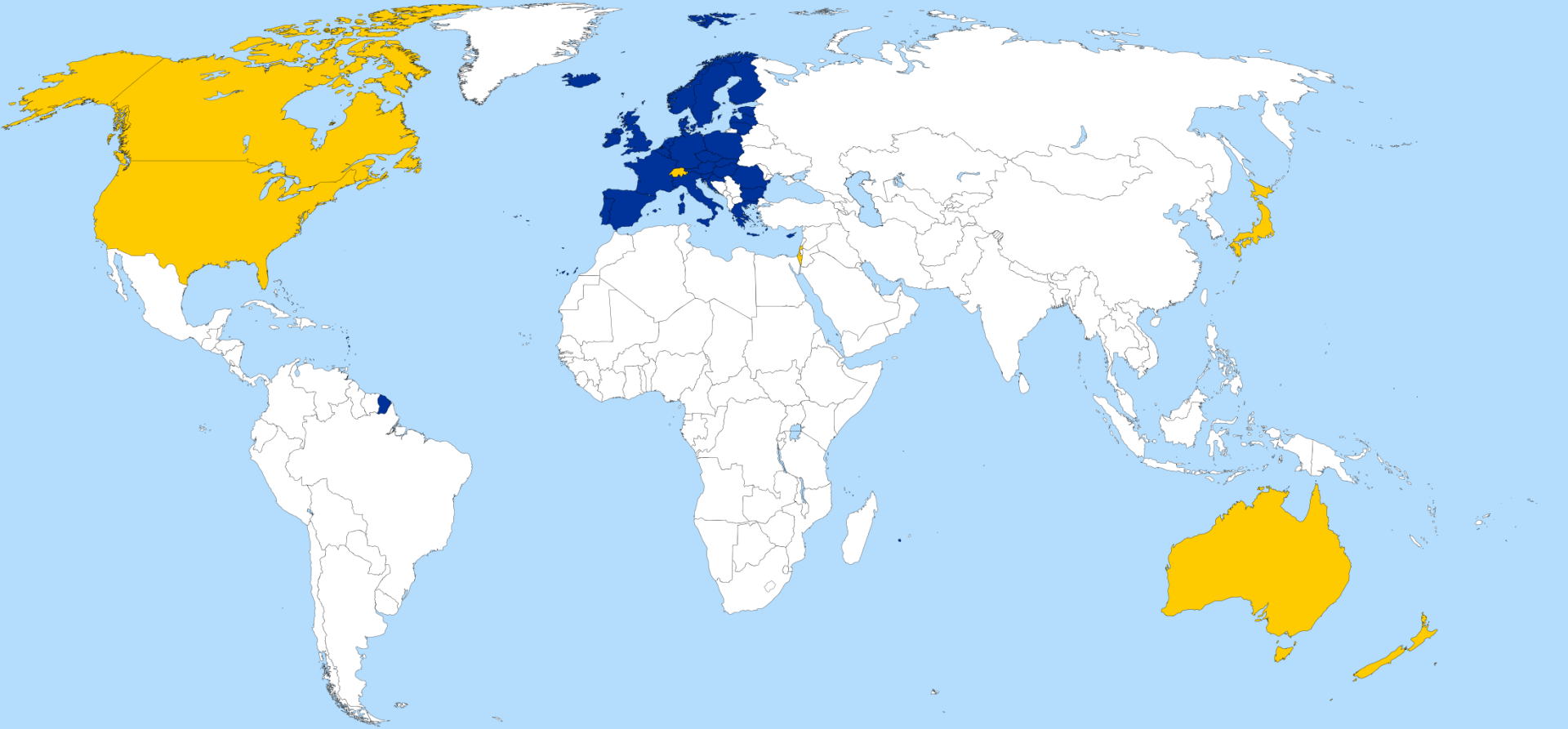
Confidentiality agreement partners

EUROPEAN MEDICINES AGENCY



Mutual recognition agreement and ACAA* partners

EUROPEAN MEDICINES AGENCY



*ACAA: Agreement on Conformity Assessment and Acceptance of Industrial Products (Israel only)

GMP Information Exchange in MRA's

Type of Instrument for Information Exchange	Exchanged Between	Message
Batch Certificate [BATCH]	Manufacturer in MRA and EU Importer	Batch meets spec / MA compliant / GMP compliant.
Inspection Report [IR]	MRA Partner Authority and EU Authority	Site was inspected and complies GMP / details on products and facility
GMP Certificate [GMP]	MRA Partner Authority and EU Authority	Site was inspected and complies GMP / details on products / limited facility info.
Rapid Alert [RA]	MRA Partner Authority and EU Authority	Recalls of defective medicines from territory

Comparison Between MRA's

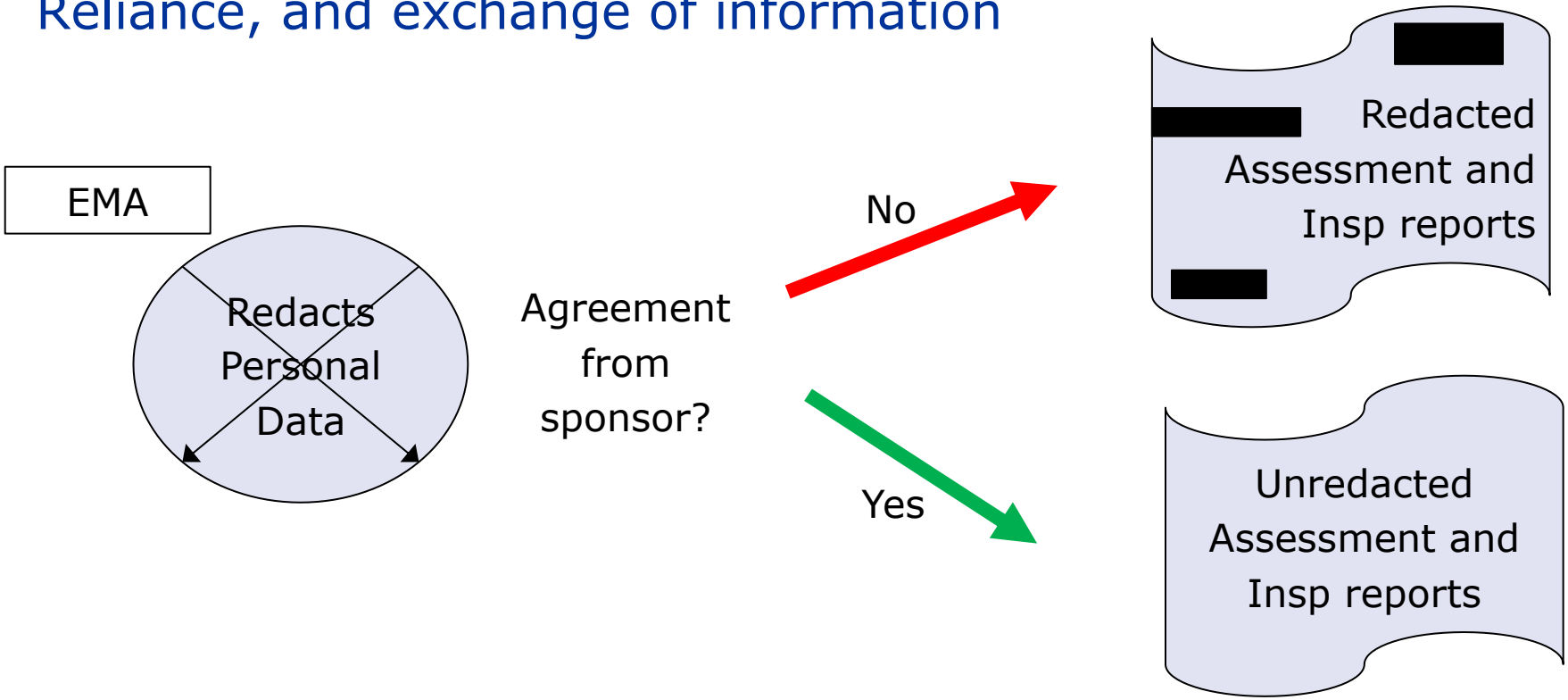
MRA	BATCH	GMP	RA	IR
EU-AUS	YES	YES	YES	NO
EU-NZ	YES	YES	YES	NO
EU-CH	YES	YES	YES	NO
EU-CAN	YES	YES	YES	NO
EU-JAPAN	YES	YES	YES	NO
EU-ISRAEL	YES	YES	YES	NO
EU-US	YES (Pending)	NO	YES	YES

- All MRAs except of US MRA are based on GMP certificates;
- Inspection reports are normally only provided upon reason request.
- Since the FDA does not issue GMP certificates the MRA uses the term "official GMP documents"
- Includes GMP non-compliance statement issued by authorities of the EU, and notice of observations, untitled letters, warning letters, and import alerts issued by the FDA.

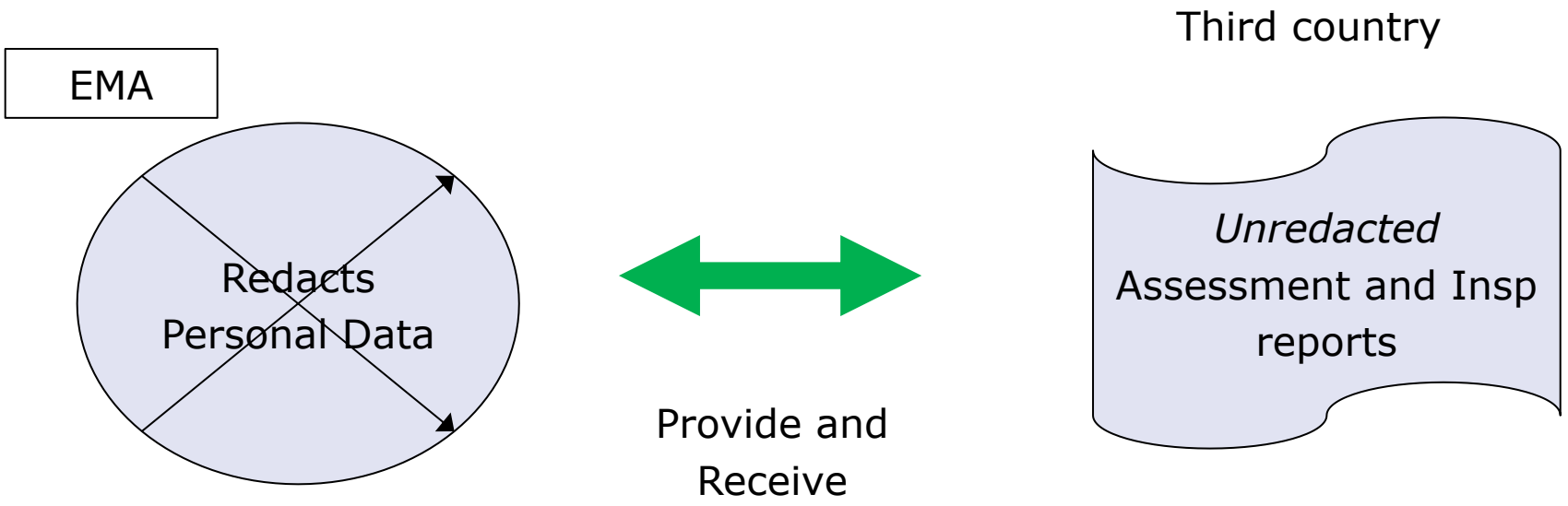
Databases and other Information Exchanges

- All EU MRA partners have full access to the EUDRAGMDP database and are informed about NCS, MIAs, EU GMP Certs. etc. in this way; in addition CH, JP, IL, AU are already entering or intend to enter data in EudraGMDP too.
- EU authorities have access to similar FDA database under US MRA.
- Further the EU uses the following FDA documents: the 90-day facility classification decisional letter and CPPs and inspection reports.
- Changes in legislation and guidance (EU communicates these normally through sharing of GMDP IWG minutes and other documents with the MRA partners).
- CH, AU, CA, IL share with the EU Member States also MRA annual reports containing updates on such topics as: legislation, regulatory requirements, GMP standards, inspection procedures, non-compliance management procedures, alert procedures, access to laboratories, QMS, internal and external audits. EU/EEA shares its annual reports with these authorities too.

Reliance, and exchange of information



Reliance, and exchange of information **with** Confidentiality Arrangement



Other ways of working
Clusters

Regular meetings between EMA, FDA (and other countries) on defined topics or therapeutic areas

Interactions often product-specific, contribute to harmonization

Currently 30 such platforms:

Advanced therapy medicinal products, biosimilars, blood products, non-clinical oncology, oncology-haematology medicinal products, orphan medicinal products, paediatric medicinal products, patient engagement, pharmacogenomics, pharmacometrics / Modelling and simulation, pharmacovigilance, rare diseases, vaccines, veterinary medicinal products

Other ways of working
GMP Inspections

Regular meetings between EMA, FDA (and other countries) on Inspections and Availability of Medicines (shortages/supply disruptions).

- Inspection of 3rd country API Manufacturers.
- Inspection of 3rd country FP Manufacturers (Pilot).
- Quadrilateral Teleconference on Shortages of Medicinal Products.
- Regular GMDP IWG meetings (4 per year).

Other ways of working
GMP Inspections

- Joint inspections or observed inspections between MRA partners further increase knowledge of and trust in the other partners.
- There are the regular JAP and MRA audits to support continued improvement process and knowledge in the other partners.

,

GMP Inspection programmes

- To increase mutual confidence between the regulators in the field of GMP inspections
- To achieve a better use of resources through better communication, coordination and collaboration on sites of common interest
- To facilitate risk based inspection planning
- To collect feedback

March 2018

Report on the International Active Pharmaceutical Ingredient Inspection Programme 2011 – 2016

1. Executive summary

The purpose of the International Active Pharmaceutical Ingredient Inspection Programme is to create a framework for greater international collaboration and information sharing on Good Manufacturing Practice (GMP) inspections of Active Pharmaceutical Ingredient (API) manufacturers worldwide. This framework supports a better distribution of inspection capacity, allowing more sites to be monitored to increase the GMP oversight, and a reduction of unnecessary duplication by avoiding inspections of the same product or sites carried out by more than one participating authority within a similar time period.

The International API Inspection Programme has been operating since 2008, first as a pilot in late 2008 to late 2010, and as a full programme since January 2011. At the close of the pilot, a final report detailing the activities, accomplishments, challenges and path forward was issued. It was agreed that a formal assessment of the programme should occur, and to revise terms of reference if need be.

Since then, the programme has continued and has grown in both membership and sites of

https://www.ema.europa.eu/en/documents/report/report-international-active-pharmaceutical-ingredient-inspection-programme-2011-2016_en.pdf

Thank you for your attention

Further information

European Medicines Agency
Spark Building Orlyplein 24 1043 DP Amsterdam, Netherlands
Telephone +31 887816000

Send a question via our website
www.ema.europa.eu/contact

Follow us on **@EMA_News**