US-EU Mutual Recognition Agreement

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MUTUAL RECOGNITION AGREEMENT: BACKGROUND AND BENEFITS

Mutual Recognition Agreement

Timeline	Activity
1998	Agreement on Mutual Recognition between the European Community and the United States of America (1998 US/EU MRA)
2012	Enacted the Food and Drug Administration Safety and Innovation Act (FDASIA)
2014	US-EU launched the Mutual Reliance Initiative
2017	US-EU agree on the terms of the amended Pharmaceutical Annex to the 1998 US/EU MRA

Benefits

- Greater efficiency
- Reduce duplication
- Reallocate resources to facilities of highest risk

Pathway to Mutual Recognition Agreement

- Exchanged and analyzed ideas
- Observed EU internal audits
- Developed assessment process
- Negotiated agreement

In the beginning…

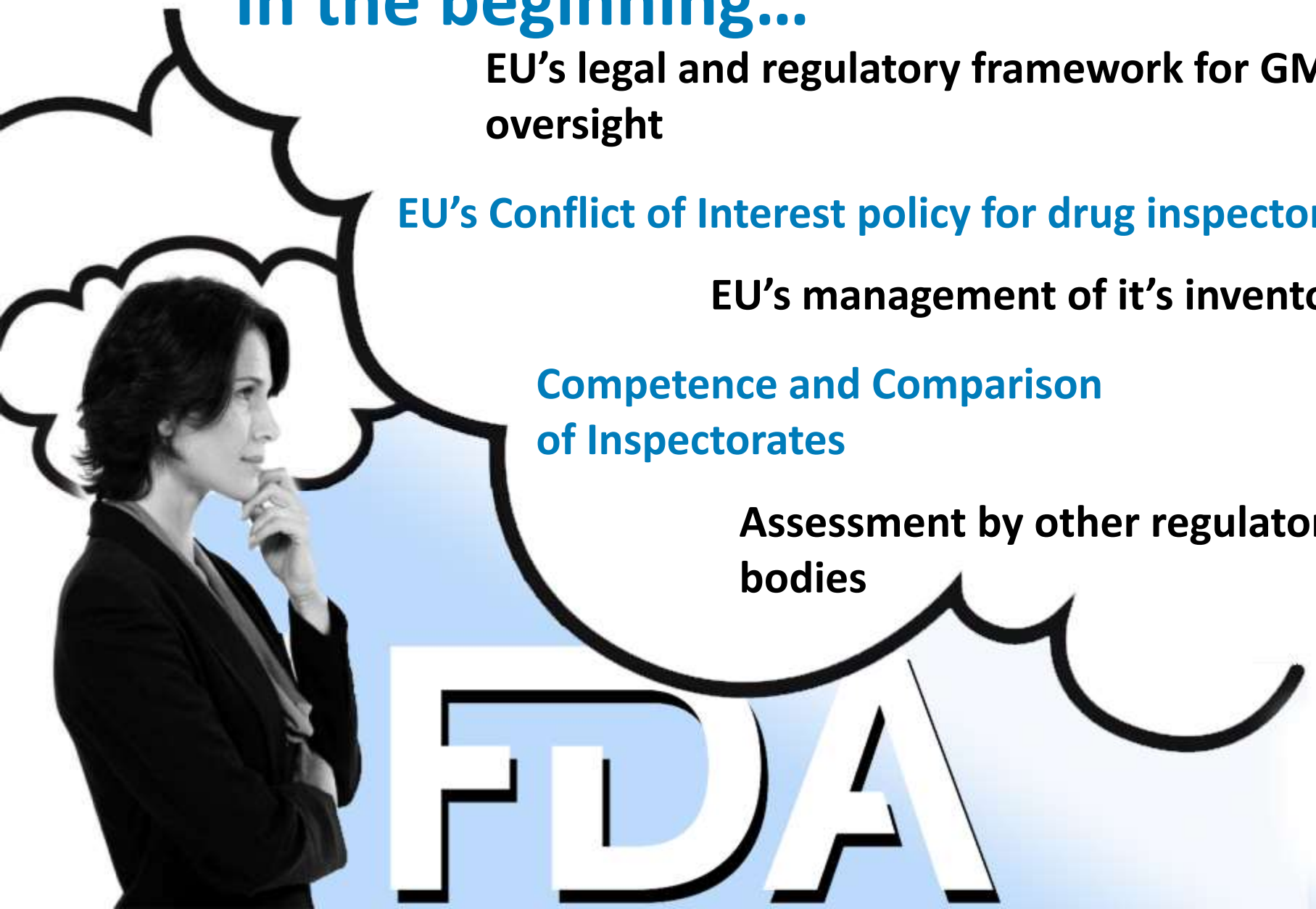
EU's legal and regulatory framework for GMP oversight

EU's Conflict of Interest policy for drug inspectors

EU's management of it's inventory

Competence and Comparison of Inspectorates

Assessment by other regulatory bodies



In the beginning…

Competence of FDA Investigators

Consistency across FDA district offices

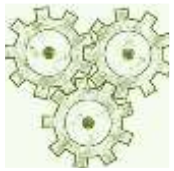
Current roles and responsibilities within FDA

Need for unredacted inspection reports

Joint Audit Programme (JAP)

Purpose

- Ensure consistency of GMP standards and a harmonized approach throughout Europe Union



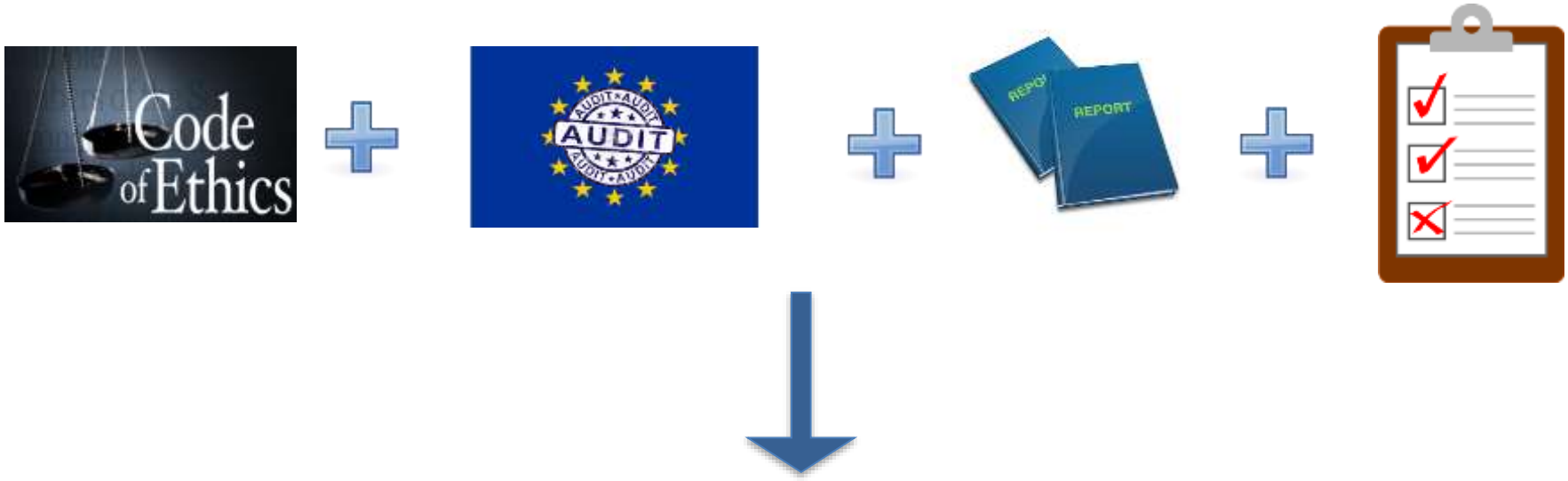
Process

- EU auditors from two different EU countries go into a third EU country

Tools

- PIC/S Evaluation Guide
- EU auditor's inspectional expertise and experience

Capability Assessments



U.S. FOOD & DRUG ADMINISTRATION

The Mutual Recognition Agreement

As of July 11, 2019 FDA may now officially rely upon drug manufacturing inspection reports from regulatory authorities in the following 28 European Union countries*:

***Limitations:** The capability determinations apply to routine surveillance inspections. In the future the following product and inspection types may be included in the coverage of the agreement, pending further consideration: Vaccines for human use; Plasma derived pharmaceuticals; Investigational products (clinical trial material); and, Veterinary products. Excluded from the MRA scope are human blood, human plasma, human tissues and organs and veterinary immunologicals.

** Slovakia – only for inspections of chemically synthesized active pharmaceutical ingredients intended for use in drug products for human oral administration and manufactured in a dedicated, single product facility. *** Malta - capability excludes sterile or aseptically processed drugs and biological products; and non-sterile, highly potent drug products.

2017 AMENDED PHARMACEUTICAL ANNEX TO THE 1998 US/EU MRA

2017 Revision to Pharmaceutical Annex to the 1998 U.S./EU MRA

Decision No 1/2017

of the Joint Committee established under Article 14 of the Agreement on Mutual Recognition between the European Community and the United States of America, amending the Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs)

THE JOINT COMMITTEE,

Having regard to the Agreement on Mutual Recognition between the European Community and the United States of America (the "Agreement") done in 1998, and in particular its Article 14 and Article 21; and

Whereas the Joint Committee is to take a decision to amend the Sectoral Annex on GMPs pursuant to Article 21(2) of the Agreement;

HAS DECIDED AS FOLLOWS:

1. Attachment A to this Decision is the United States – European Union Amended Sectoral Annex for Pharmaceutical Good Manufacturing Practices ("Amended Sectoral Annex") which amends the Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs) done in 1998 and replaces it with a consolidated version.

2. Attachment A has been agreed by the Parties.

This Decision, done in duplicate, shall be signed by representatives of the Joint Committee who, pursuant to Article 21(2) of the Agreement are authorized to act on behalf of the Parties for purposes of amending the Annexes. This Decision shall be effective from the date of the later of these signatures.

On behalf of the United States of America	On behalf of the European Union
Signed in Washington DC, on January 19, 2017	Signed in Brussels, on March 1st 2017

Scope

- Includes a vast majority of drugs
- Certain products will be reevaluated in the future, such as vaccines, veterinary products, and pre-approval inspections
- Surveillance inspections of human drug facilities located within the US and EU

What Products are Currently Under the MRA?

- Marketed finished pharmaceuticals for human use, including
  - Medical gasses
  - Radiopharmaceuticals (not PET)
  - Herbal products (regulated as drugs)
  - Homeopathics
- In process materials
- APIs
- Marketed biological products
  - Allergenic products
  - Therapeutic biotech-derived biologics (well characterized recombinant products)

Are Any Products Excluded from the MRA?

- Human blood and plasma
- Human tissues and organs
- Veterinary immunologicals

Future Scope Considerations

- Veterinary products
  - Decision by December 2019

- Vaccines and plasma derived pharmaceuticals
  - Decision by July 2022

CURRENT STATE

Why is FDA inspecting in MRA capable countries?

The EU and FDA will always reserve the right to conduct their own inspection, if necessary.

Situations where FDA might conduct its own inspections include:

- Products are outside of the MRA scope
- Conduct of specific manufacturing types were not part of the capability assessment
- Inspection is application/product-specific
- EU's inspection information is outside the MRA Reference Date
- EU is unable to conduct the inspection within FDA's timeline request
- For-cause inspections

Impact of MRA on FDA's Inspections

(Nov 1, 2017 through June 1, 2019)

	# of Inspections
EU inspections conducted on behalf of FDA	54
FDA inspections conducted on behalf of EU	12
FDA inspections in EU deferred	106

A New World for Pharmaceutical Inspections

The Mutual Recognition Agreement

http://www.fda.gov/MRA

Questions? FDA-MRA@fda.hhs.gov