



European Federation of Pharmaceutical  
Industries and Associations

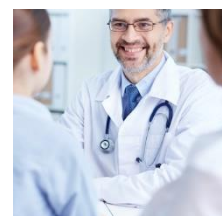
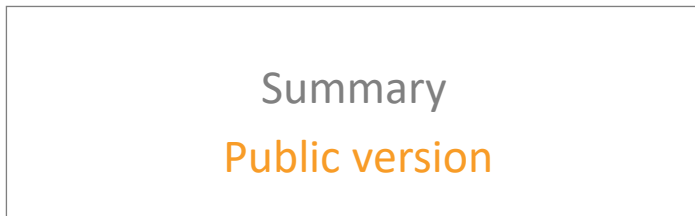
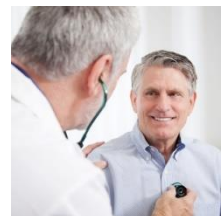


# Annual Regulatory GMP/GDP Inspection Survey 2024 Data

Author: MQEG Inspections topic team

Date: 10. June 2025

Version: 1





# EFPIA'S ANNUAL INSPECTION SURVEY

## Background and history

### \* History

- \* The annual inspection survey was initiated in 2003 by the research-based industry association EFPIA

### \* Scope

- \* Regulatory GMP/GDP inspections – all modes
- \* Inside and outside the own borders (domestic and foreign\*)
- \* Manufacturing sites and commercial affiliates worldwide
- \* Notified Bodies certifications for devices used in Medicinal Products

### \* Intent

- \* Monitor trends and new focus areas
- \* Promote reliance optimizing the use of inspection resources
- \* Materialise the benefits of PIC/S membership and MRAs

\* 'Foreign inspections' are undertaken outside of the inspectorate's country.

## INSPECTION SURVEY - DATA

### Outcome of the data<sup>\*1</sup>

*Back to physical presence and decreasing number of alternative modes*



#### At Affiliates

- Consistency in the numbers of inspections year to year - across all regions – mostly domestic
- 'For cause' inspections doubled from 2022 to 2023 and again 2023 to 2024

- Significant increase of inspections with follow up actions - no interrupted supply



#### At Manufacturing sites

- The total number of inspections increase, but the number of inspections per inspectorate decrease (more inspectorates inspecting).
- US, EU and Japan still perform the majority of foreign inspections<sup>\*3</sup>
- Other regions increase foreign inspections<sup>\*4</sup>
- Amongst PIC/S members there is less travel

<sup>\*1</sup> Provided by 27 global research-based pharmaceutical companies and two National Trade Associations

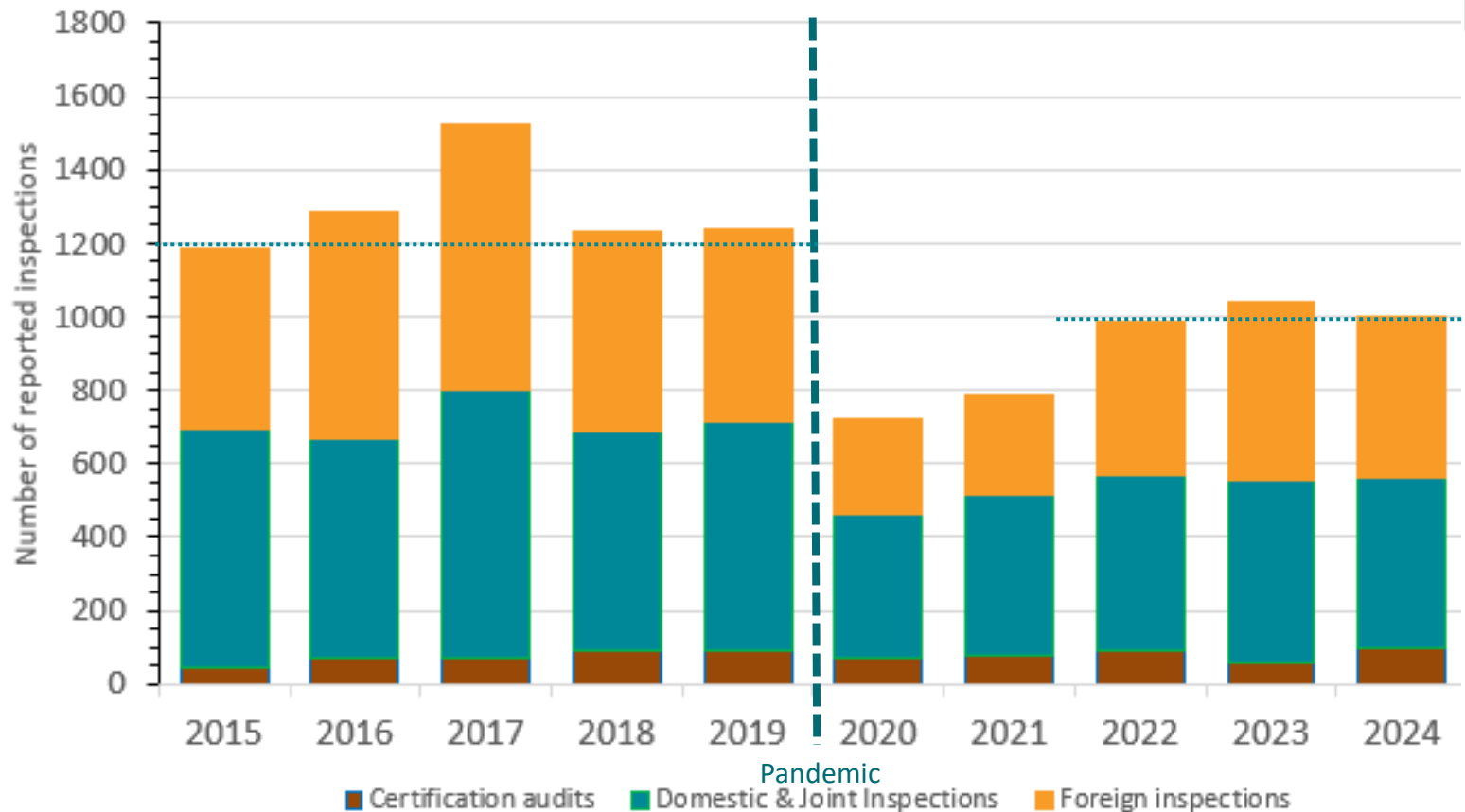
<sup>\*2</sup> Opportunities for a better risk-based approaches on inspections by Japan, Türkiye, Rep. of Korea, USA, Libya, Russia/EAEU and Brazil.

<sup>\*3</sup> US FDA 50% less in comparison to 2023 and before the pandemic

<sup>\*4</sup> e.g. Rep. of Korea, Chinese Taipei, and EAEU

## INSPECTION SURVEY – DATA - COMPARISON PRE-POST PANDEMIC

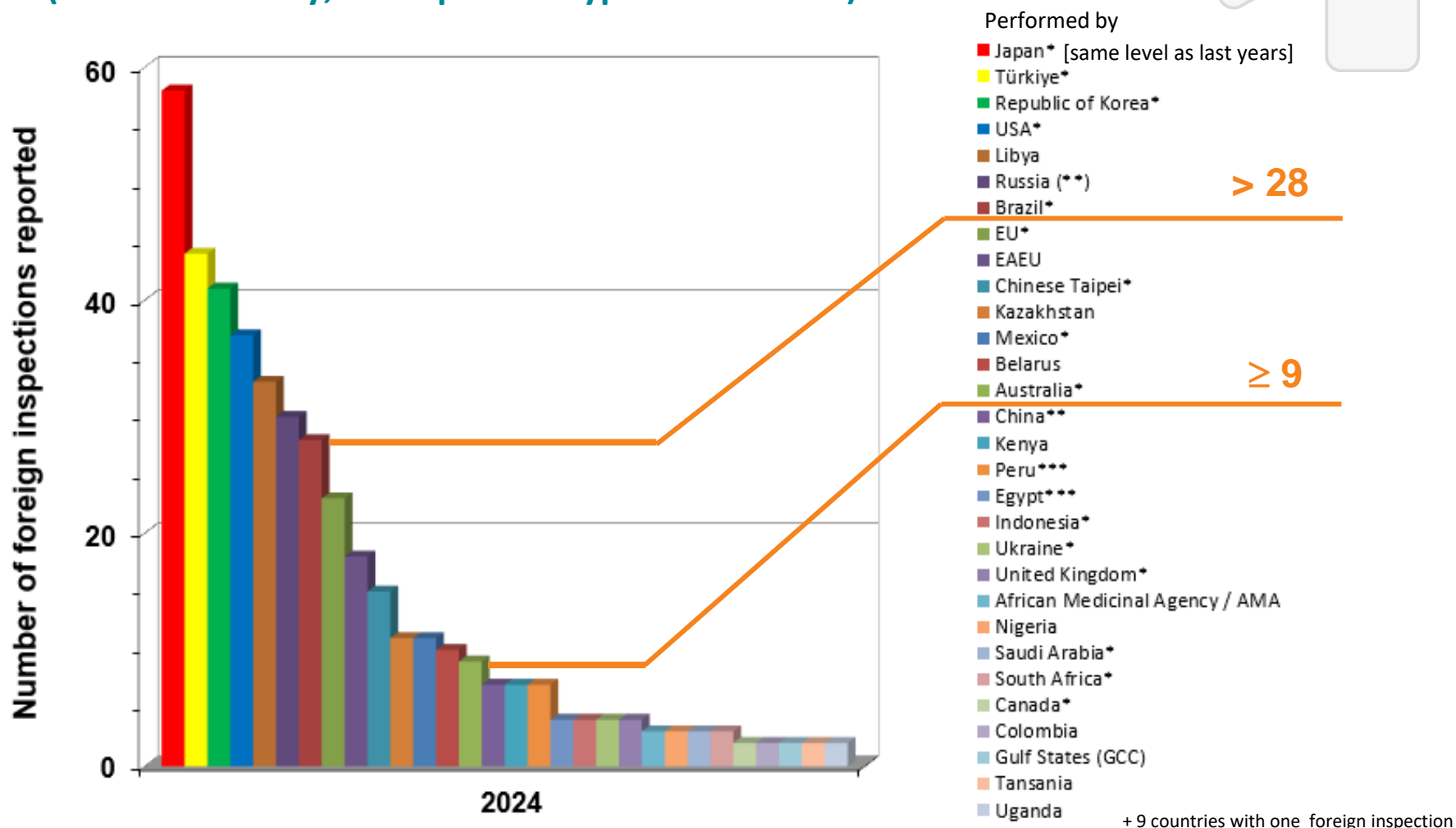
Had the pandemic a long-term positive impact on reliance?



\* Data indicate that the overall number of inspections has decreased by  $\approx 20\%$  post pandemic

# EFPIA'S ANNUAL INSPECTION SURVEY - DATA

## Number of foreign inspections at manufacturing sites (EU as one entity; all inspection types and modes)








\*Inspectorate is a PIC/S participating authority \*\*PIC/S Applicant \*\*\*PIC/S Pre-Applicant

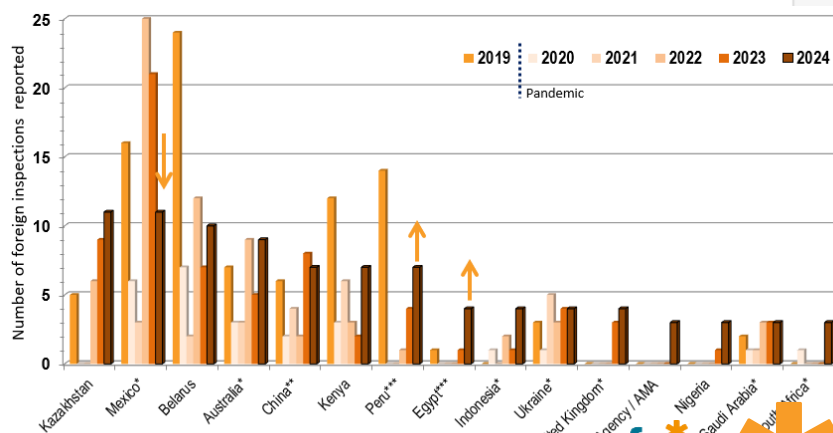
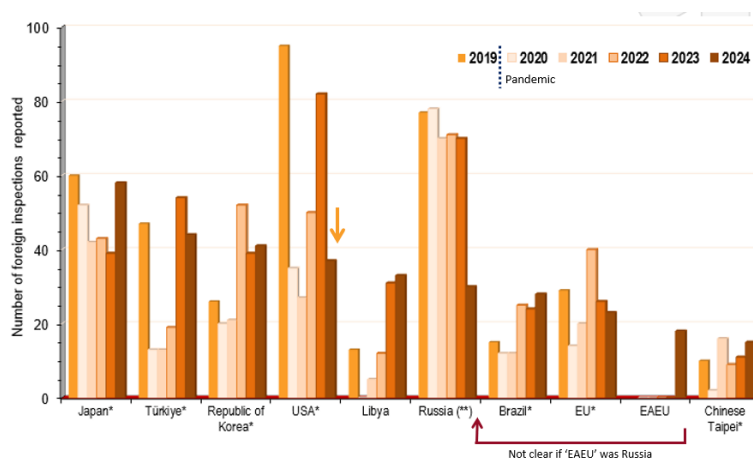
EFPIA ANNUAL INSPECTION SURVEY - 2024 DATA - PUBLIC VERSION

# EFPIA'S ANNUAL INSPECTION SURVEY - DATA

## What do the data tell us on foreign inspections?

*A varying picture*

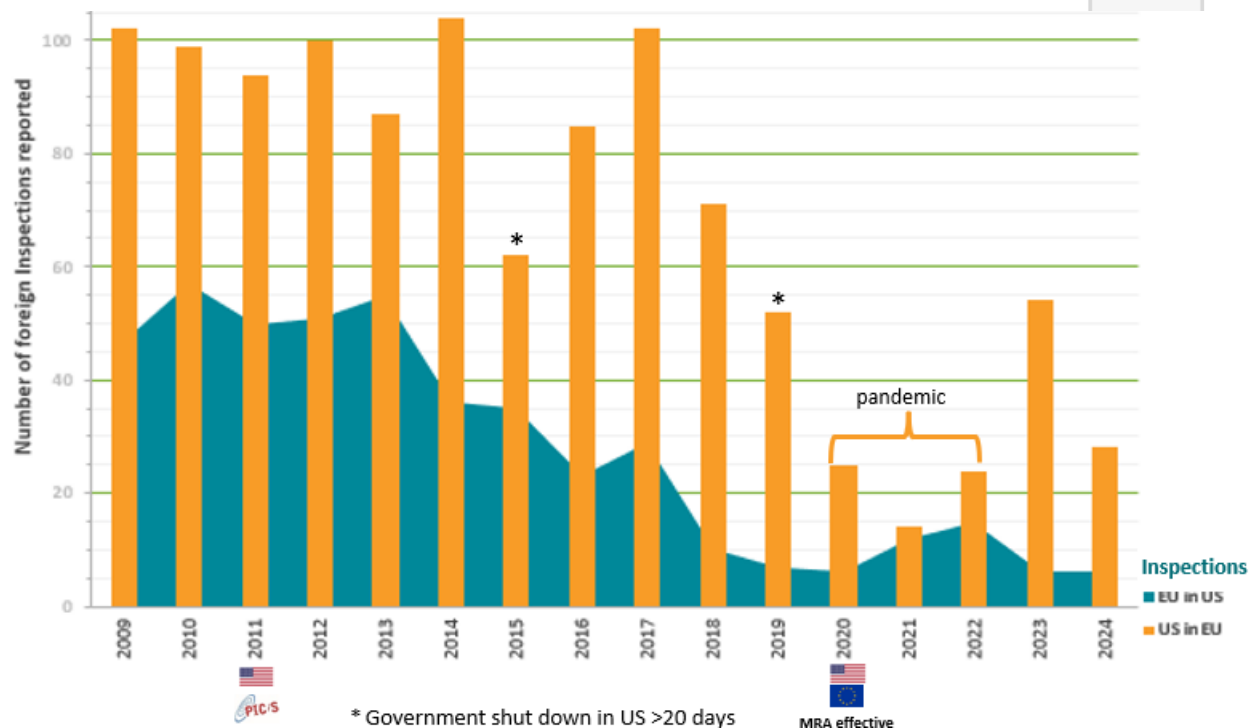
Tendency compared to last year		Inspectorates from
	Significant increase	None
	Increasing	Kenya, Peru
	Back to high rates before the pandemic, or even higher	Japan, Türkiye
	Stable at a high level	EU/EEA, South Korea, Brazil, Libya, Russia/EAEU*
	Decreasing (about -50%)	US, Mexico



# EFPIA'S ANNUAL INSPECTION SURVEY - DATA

## MRA EU - US

- \* Positive effect on implemented reliance as of the MRA
- \* Opportunities to further optimise:
  - \* To implement for both routine and preapproval inspections
  - \* To extend the scope e.g., Vaccines, plasma derived products, and ATMP



# Experience with Mutual Recognition Agreements (MRA)

### \* As trade agreements, MRAs confirm equivalence of legal frameworks

- \* Therefore, all MRA partners should allow recognising and acceptance of an inspection report performed by an EU/EEA inspectorate

### \* Operationalise MRAs

#### \* EU/US

- \* PAI inspection type by US are covered in the scope of EMA inspections

#### \* EU/Japan

- \* Highest number of inspections by Japan in the EU/EEA reported in the last 10 years (all modes\*)

- \* Document inspections by Japan (form 1&3) are covered by the MRA

*Note: GMP documents requested for submission are called 'inspections'*

\* Inspection modes e.g.,

- *Onsite/physical presence*: Inspectors are physically at a facility
- *Real time remote*: conducting the inspection using e-technologies (incl. document reviews)
- *Document review*: Inspectors evaluate using submitted documents only (e.g., available inspection reports, US- Form-4003)
- *Deferred*: Information about an inspection, which was deferred (e.g., unilateral reliance, MRA)



## EFPIA'S ANNUAL INSPECTION SURVEY - DATA

### Foreign inspections at manufacturing sites

#### Manufacturing

- \* **80% of foreign inspections are in EU/EEA, US and Switzerland; this demonstrates where research-based industry is manufacturing**
- \* EU/EEA (50%), US (27%), Switzerland (5%), China (4%), Singapore (3%), and Brazil (3%)
- \* For the EU/EEA it's mainly in Germany, France, Belgium, Denmark, Ireland, Italy
- \* Sites most exposed to multiple foreign inspections are in Germany (4) and Denmark (2)

#### Oversight

- \* **Number of foreign inspections at manufacturing sites post pandemic is slightly decreasing to the baseline before the pandemic**
- \* Individual sites receive more foreign inspections - higher than before the pandemic and highest ever

# EFPIA'S ANNUAL INSPECTION SURVEY - DATA

## Trends on inspection modes

**Physical presence**



Increasing, but not yet back to the level of before the pandemic

**Real time remote presence**



Trend of less year by year after the pandemic

**Document review**



Performed predominantly by Japan, also Brazil, Chinese Taipei, Kenya

**Reliance?**



Number of foreign inspections per inspectorate is trending slowly down

# EFPIA'S ANNUAL INSPECTION SURVEY - DATA

## Specific inspection matters

### API

- Inspections at API manufacturing sites are performed in the EU/EEA, US, Switzerland, Singapore, and Pakistan
- In the EU/EEA the focus is on Germany, Belgium, Ireland and Denmark

### GDP

- GDP inspections increased; more oversight
- More details are looked at

### ISO 13485 Certifications

- Performed mostly in EU/EEA (Denmark, Belgium, Germany, Finland), USA, Costa Rica, Australia

### Scheduled inspections

- 95% of total - result in more follow up actions than ever and more than if the inspection was unannounced
- About 20% more follow up actions are reported with scheduled inspections compared to unannounced inspections (both foreign and domestic)
- China and the US perform by far the most unannounced inspections (domestic)

### Annex 1

- Number of inspections at sterile manufacturing sites due to GMP Annex 1 implementation constant – no change

### Location of manufacturing sites

#### Globalisation

- \* **Trend towards globalisation of manufacturing till 2020; after the pandemic, the reported data on inspections demonstrate more sites are manufacturing for local / regional supply**
  - \* China, EU / EEA, Japan, US, Pakistan and Brazil are the countries with the most inspections by sites for local / regional supply
  - \* In EU /EEA Germany, Spain, Italy and Sweden are the countries with the most inspections with sites for local / regional supply reported in the last 9 years

#### Innovation

- \* **Locations of manufacturing facilities reporting PAI demonstrating where innovative products are manufactured – EU again number one – far leading**
  - \* MS where new, innovative products are manufactured include Denmark, then Germany, Belgium, Slovenia, Italy, Ireland, and France

## ANSWERS TO QUESTIONS

### Experience with expiring GMP certificates

**\* 67% companies asked their health authorities for renewal of an expired GMP/GDP Certificate which did not trigger an inspection.**

**\* What companies experienced**

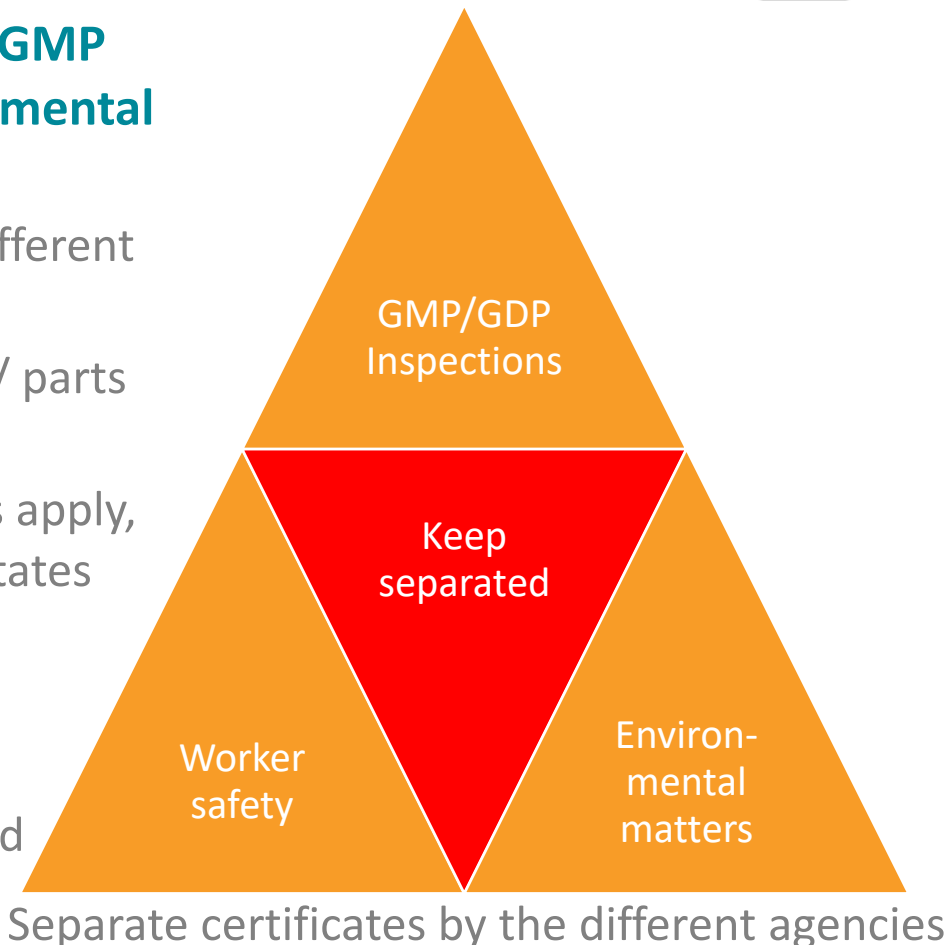
1. Reliance on other inspectorates e.g., Mexico, South Africa, Brazil, Colombia
2. The validity of their GMP certificate were extended to 5 years e.g., linked to license renewal, but for those that have already reach 5 years validity, an inspection was planned e.g., France
3. An inspection was performed and reliance not performed by e.g., Germany, Singapore, Turkey, Romania, Italy, Australia, United Kingdom (desktop assessment), Spain, Chinese Taipei
4. Inspections were performed before expiry date (also when not actively asked) by e.g., Health Canada; Croatia; Israel, Finland, Switzerland

## ANSWERS TO QUESTIONS

# Keep overseeing environmental and worker safety standards by other agencies responsible within the government

### \* The industry recommend keeping GMP inspections separate from environmental and worker safety inspections

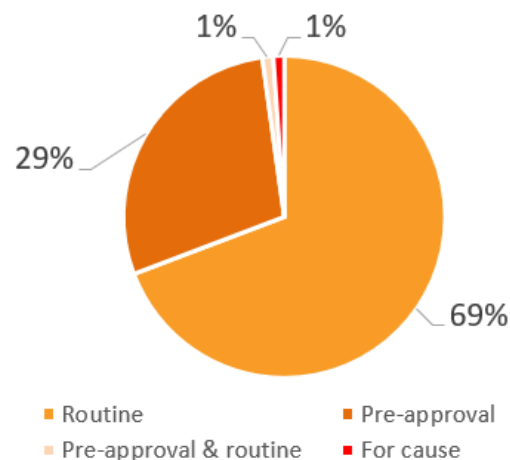
- \* Patients, environment, staff are different stakeholders
- \* Managed by different authorities / parts of the government
- \* Different legislation and standards apply, not harmonized across Member States
- \* Risk applicability of MRAs – even between EU Member States
- \* A potential combination will make GMP/GDP inspections complex and resource-intensive



## EFPIA'S ANNUAL INSPECTION SURVEY - DATA


### PIC/S Participating Authorities in a PIC/S member – no change, still high

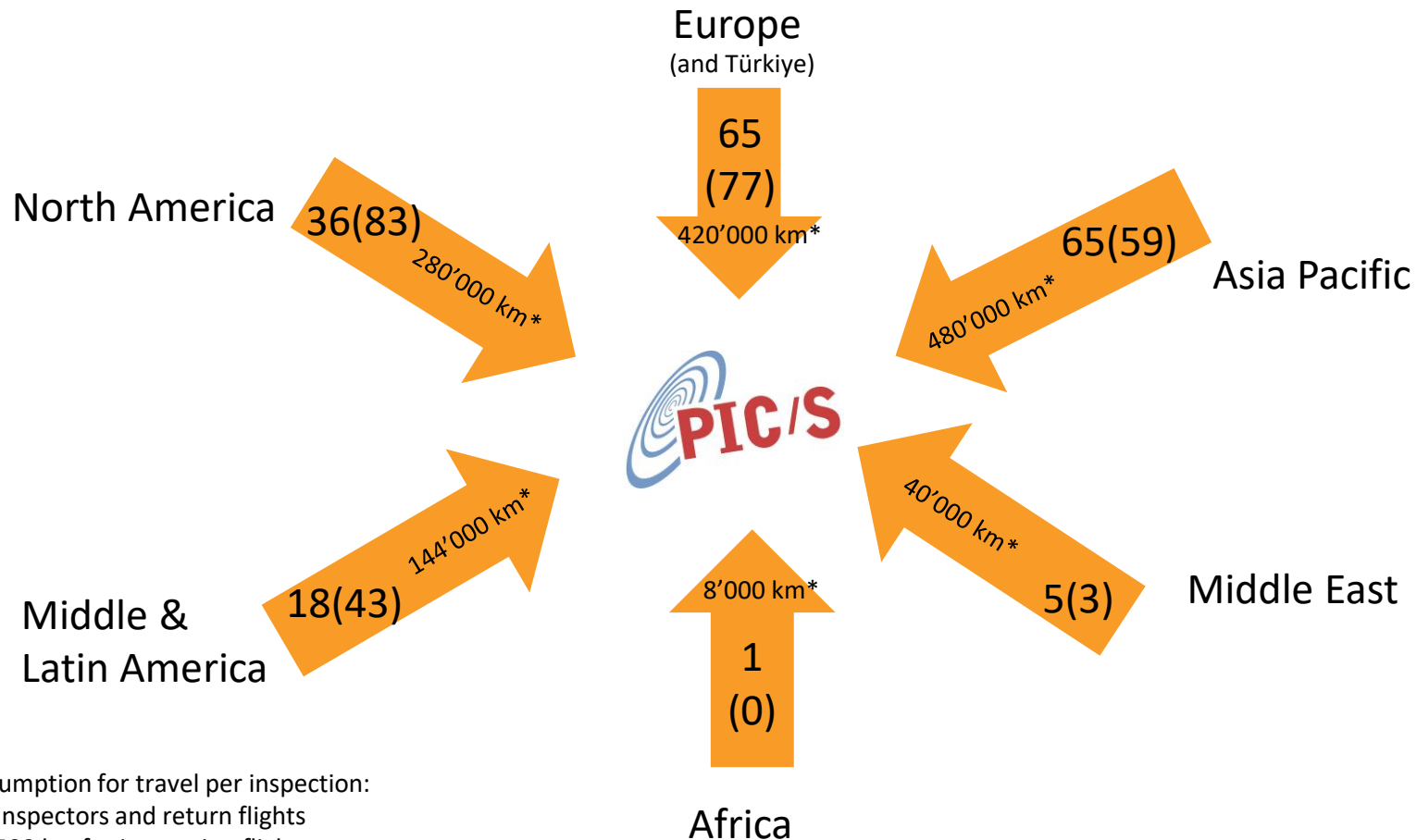
- \* With 62% of the reported over all foreign inspections where inspectorates and sites belong to PIC/S countries remains constant high (2023: 62%; 2022: 63%)
  - \* Japan, Türkiye, Republic of Korea, USA, Brazil and EU (Germany, Slovakia, Netherlands)
  - \* No shift in reasons for these inspections i.e., routine, PAI or 'for cause'
  - \* Reduced CO<sub>2</sub> footprint with less travel by inspectorates especially from US and Mexico
- \* The majority is for routine inspections (69%)
- \* Examples for applied well-informed reliance procedures are available and applied by e.g., Singapore (HAS)



## OPPORTUNITIES FOR PIC/S PARTICIPATING AUTHORITIES

### Reducing environmental footprint by reliance on PIC/S

  $\approx 1'400'000 \text{ km/y}^* \approx 21'000'000 \text{ kg CO}_2$   
( $1'900'000 \text{ km/y}^* \approx 26'000'000 \text{ kg CO}_2$ )



Assumption for travel per inspection:

- 2 inspectors and return flights
- 500 km for in a region flights
- 8'000 km for interregional flight

\*on average; 0.0658 kg CO<sub>2</sub> / flight km

Switzerland: Bundesamt für Zivilluftfahrt (BZL)

(2023 data)



## OPPORTUNITIES FOR INSPECTORATES - PIC/S TO FACILITATE?!

### Request: To use reliance mechanisms to adopt results of various inspection pilots

#### Legal basis

- Leverage and/or establish the legal framework to allow acceptance for official GMP documents from PIC/S participating authorities

#### Collaborate

- Continue harmonising inspection approaches
- Share experiences and best practices & seek feedback/advice from peer inspectorates\*<sup>1</sup>
- Establish an interoperable platform for e.g., inspection plans/scope, observations, outcomes
- Materialise pilots e.g., formalise agreements\*<sup>2</sup>, establish a collaboration tool/platform\*<sup>3</sup>

#### Training

- Support common understanding by training e.g., consistency of classification/rating and number/grouping of observations, risk ranking of the site along with one inspection per site
- Continue to enable confidence-building between inspectorates and for reviewers on GMPs including convergence of practice\*<sup>4</sup>

\*<sup>1</sup> This could be expanded with industry to better understand expectations. \*<sup>2</sup> e.g., Memorandums of Understanding (MoU)

\*<sup>3</sup> To manage time zone differences by e.g., review documents separately and share questions to the panel

\*<sup>4</sup> e.g., participation in PIC/S-ICMRA Joint inspection programs and trainings

## RELIANCE APPROACH - ANSWERS TO QUESTIONS

# A reflections on the positive outcome of the ICMRA Collaborative Hybrid Inspection Pilot (CHIP)

- \* **EFPIA member companies welcome the expansion of the pilot and flexibility adopting the inspection approach**

- \* There is opportunity to put all in common practice

- \* **Minimise increased efforts by using existing procedures e.g.,**

- \* Local inspectorate as lead and coordinating inspector

- \* Use other time zones for document inspection; use core inspection time for clarifications and interactions

- \* One inspection report with one set of agreed observations; co-inspectors/observers to reference as needed

**Note: Why companies did not apply in 2024 pilot - *responses received***

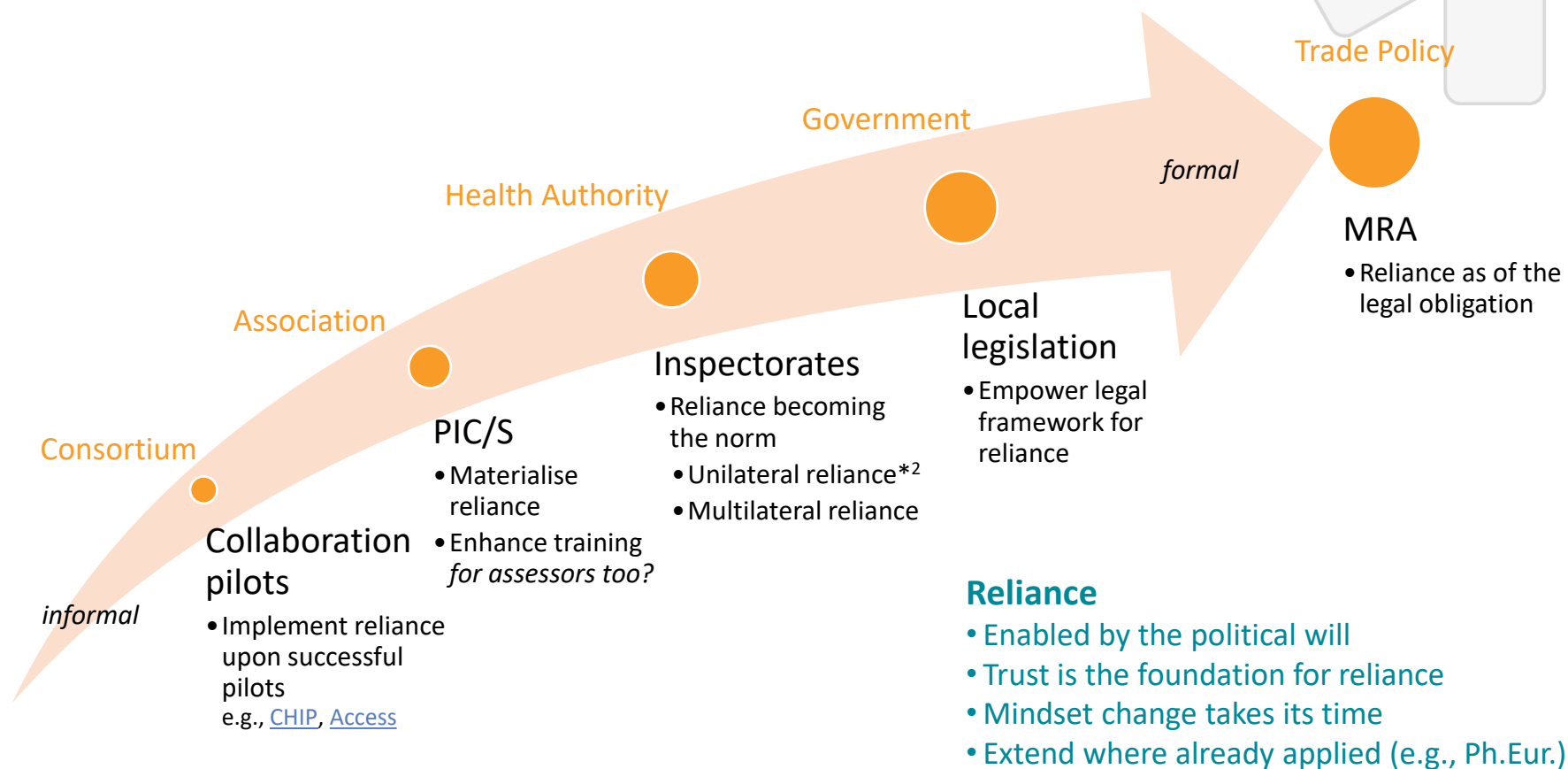
- \* Uncertainty about the return on investment

- \* Business priorities / resource allocation / management decisions

- \* Limited scope in the first round

# PATHWAYS EMPOWERING LEGAL FRAMEWORKS FOR RELIANCE

## Reliance is about insourcing knowledge - not outsourcing decision\*1



Think global, act local: Leverage existing knowledge to reduce inspections, length and scope

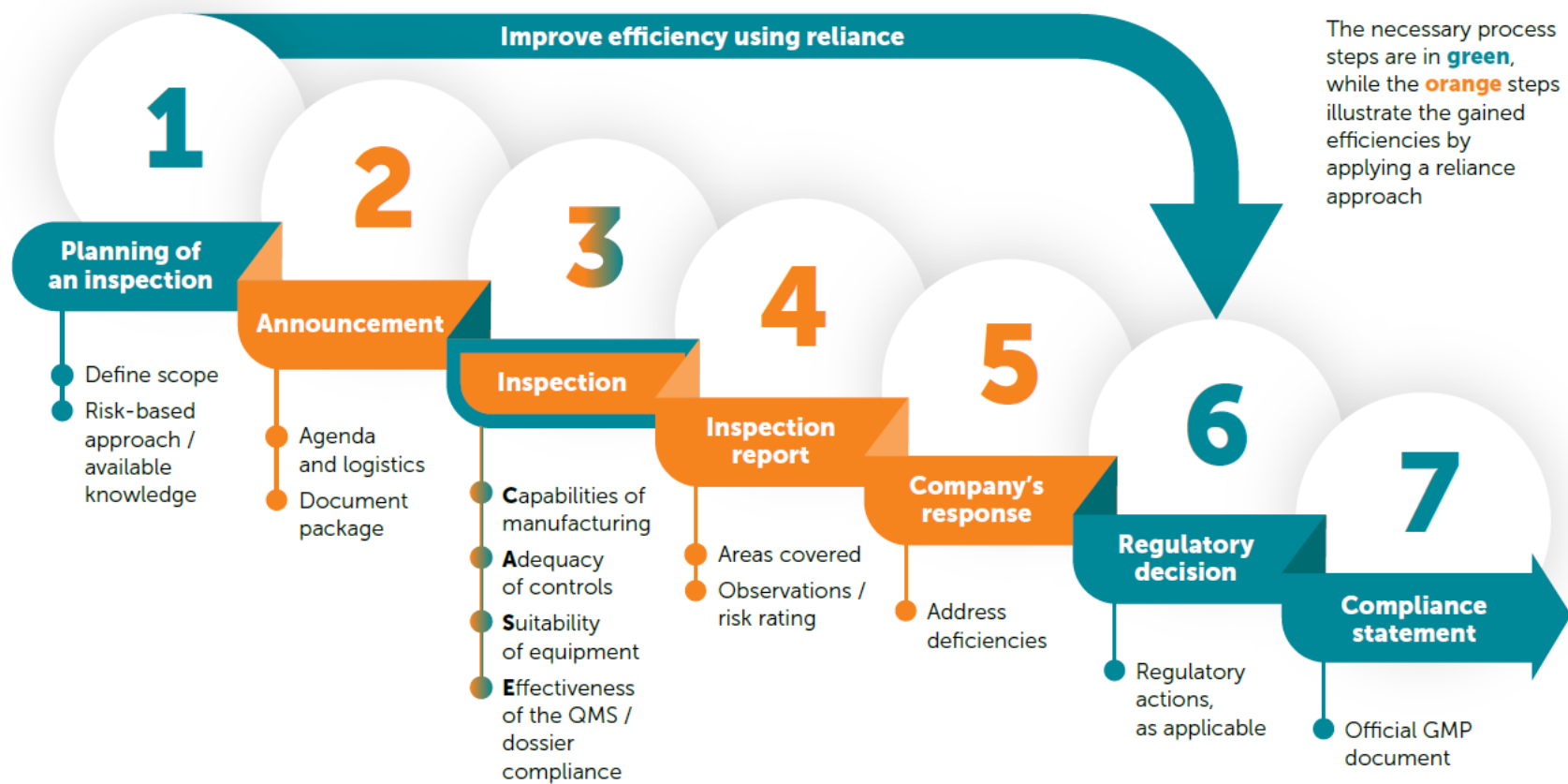
\*1 Citation from Regulatory harmonizations and convergence, 'Take 5' at DIA Europe 2025

\*2 'EFPIA welcomes EMA's unilateral reliance pilot enabling reliance on PIC/A member state inspections'

[EFPIA Position paper on Enhanced Good Manufacturing and Distribution Practices \(GMDP\) Inspection Efficiency](#) and [infographic](#)

# EFPIA INSPECTION INFOGRAPHIC

## Seven steps of any inspection process



[EFPIA inspection infographic, March 2024](#) uploaded on the [manufacturing webpage](#)

## FOR FURTHER READING



# Explaining reliance in the inspection landscape

- **Opportunities for Optimising the GMP Inspection Process post pandemic**, in publication based on 'Request for Optimising the GMP paper-based Inspection Process by Regulatory Authorities', EFPIA position paper, 26 June 2019.
- Alternative GMP/GDP Inspection **Practices in a Pandemic Situation** (COVID-19) and Beyond [EFPIA position paper](#), 28 May 2020.
- Proposals for Quality and GMDP aspects: **Regulatory response to Covid 19 crisis**, 30. Mar. 2022
- **Opportunities and Challenges with MRAs on GMP**, EFPIA Reflection Paper, 21. December 2022
- **Enhanced Good Manufacturing and Distribution Practices (GMDP) Inspection Efficiency**, [EFPIA position paper](#), 12. November 2024.
- **Inspection landscape: Good Manufacturing and Distribution Practices** [EFPIA infographic, March 2024](#)
- EFPIA: Annual Regulatory [GMP/GDP Inspection Survey's](#)



- **Considerations for effective regulatory reliance**, 21. June 2019
- **Convergence of Good Manufacturing Practice (GMP) standards and Related Inspections**, [IFPMA Position paper](#), v2, January 2020.
- **Points to Consider for Virtual GMP Inspections – an Industry perspective**, 5 Feb 2022, update in progress with Annexes on
  - 'best practices' and
  - 'IT considerations'
- Inspections [Infographic](#)
- Related: [import testing](#)



- Guidance on good practices for **desk assessment...** for medical products regulatory decisions, [WHO, TRS 1010 \(2018\), Annex 9](#).
- **Good reliance practices** in the regulation of medical products: high level principles and considerations, WHO, [TRS 1033](#), Annex 10, 2022, 237-267.
- International regulators recommend use of remote inspections as complementary tool beyond pandemic, EMA-News, [13. Dec 2022](#).
- Guidance related to GMP/GDP and PMF: **distant assessments**. [EMA/335293/2020](#), 15. Oct. 2020
- **Remote Interactive Evaluations** of Drug..., FDA, Guidance for Industry, FDA-2020-D-1136, April 22
- **Conducting Remote Regulatory Assessments**, Q&A, FDA [draft guidance for industry](#), July 22
- Joint Audit Programme for EEA GMP inspectorates - [JAP Procedure \(Rev.3\)](#)
- **Report on the review of regulatory flexibilities/agilities as implemented by National Regulatory Authorities during Covid-19 pandemic - December 2020**, [WHO & ICDRA](#), published November 2022
- **Reflections on the regulatory experience of remote approaches to GCP and GMP regulatory oversight during the COVID-19 Pandemic**. ICMRA, 26 November 2022. [Inspection pilot](#)
- ICMRA Collaborative Hybrid Inspection Pilot (CHIP), [Summary Report](#) March 5th, 2025.



- **EC-PIC/S Co-operation agreement** [EC Ares\(2022\)5237302-19/07/2022](#)
- **EC-PIC/S Working arrangement for the exchange of non-public information**, [EC Ares\(2022\)5725920-12/08/2022](#)
- **GMP-Inspection reliance**, [PIC/S guideline PI 048-1](#), 1 June 2018
- **Risk-based inspection planning**, [PIC/S guideline PI 037-1](#), 1 Jan. 2012
- **Classification of GMP Deficiencies**, [PIC/S guideline PI 040-1](#), 1 Jan. 2019.
- **Remote assessments**, [PIC/S guidance PI 056-1](#), 1. Jan 2025



- EMA, WHO, TGA, US-FDA, EDQM, Council of Europe, ANSM, EMA, HPRA AIFA, MHRA, **Report on the International Active Pharmaceutical Ingredient Inspection Programme 2011 – 2016**, March 2018, 1-13.
- H. Jin, N. Carr, H. Rothenfluh, TGA, **Medicines Regulations: Regulating Medicines manufacturers: Is an onsite inspection the only option?**, [WHO Drug Information](#), 31/2, 2017, 153-157.
- S. Rönninger, J. Berberich, V. Davoust, P. Kitz, A. Pfenninger, **Landscape of GMP/GDP inspections in research-based pharmaceutical industry**, [Part I: Data](#), *Pharm. Tech. Europe*, January, 2017, 6-10; [Part II: Considerations and Opportunities](#), *Pharm. Tech. Europe*, February, 2017, 5-9.
- S. Rönninger, P. Gough, V. Davoust, **Opportunities for Saving Resources in the Regulatory Inspection Process: MRA Example EU/US**, *Pharm. Tech. Japan*, 35, 2019, 15-25.
- A. Meshkovskij, S. Rönninger, **National GMP Inspection Practice for Biotech Pharmaceuticals: Communalities, Differences, Opportunities**, [CIS GMP News](#), 2018, 1, 26-31.
- S. Rönninger, A. Kurz, and F. Raya, **GMP/GDP Inspections: Challenges and Opportunities from COVID-19**, *Pharmaceutical Technology Europe*, 33 (11) 2022, 36-39; [print version](#); [full version](#)



## ACKNOWLEDGEMENTS

### Contributors to the EFPIA inspections survey 2024

- \* AbbVie
- \* Almiral
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- \* Bial
- \* Biogen
- \* Boehringer Ingelheim
- \* Bristol-Myers Squibb
- \* CSL Behring
- \* Daiichi Sankyo
- \* Eli Lilly and Company
- \* Grünenthal GmbH
- \* GlaxoSmithKline
- \* Johnson & Johnson

- \* Lundbeck
- \* Moderna
- \* Merck
- \* MSD
- \* Novartis
- \* Novo Nordisk
- \* Pfizer
- \* Roche
- \* Sanofi
- \* Servier
- \* UCB

#### National Trade Associations

- \* Apifarma (Portugal) Ophella\* Viatris\*
- \* LEEM (France)\*



European Federation of Pharmaceutical  
Industries and Associations



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# Reliance approaches

[EFPIA inspection infographic, March 2024](#) uploaded on the [manufacturing webpage](#)



# Well-informed reliance: How to confirm the GMP status

**The GMP Compliance evidence must be specific to which the application relates\***

**\* Companies may submit either to support the applications**










- a. A valid GMP certificate issued by any PIC/S authority with the product of interest stated.
- b. The GMP inspection report, with the product of interest included in the scope, together with the close-out letter (where applicable) for PIC/S authorities which do not issue GMP certificates
- c. Certificate of Pharmaceutical Product (CPP) issued by US FDA for the product of interest.
- d. Other evidence such as a manufacturing license issued by a PIC/S authority covering the product of interest and demonstrating that the site complies with GMP requirements.
- e. For APIs: A valid Active Pharmaceutical Ingredient (API) Registration Certificate covering the DS of interest listed on EudraGMDP.
- f. For applications supported by a valid Certificate of Suitability to the monographs of the European Pharmacopoeia (CEP) for the product of interest, the agency adopts a reliance approach to leverage the GMP compliance assessment under the EDQM Inspection Program for the sites specified in the CEP.

\* If the product of interest is not specified, a Written Confirmation for the product of interest from the PIC/S authority which issued the GMP certificate is to be supplemented

Based on Singapore authorities (HAS): Guidance on the Implementation of Good Manufacturing Practice (GMP) Evidence for Drug Substance (DS) Manufacturers, Aug 2024.

## FOR FURTHER READING

# Overview of ICMRA, ICH and PIC/S Pilots

Enabler	Efforts under way	
Harmonized regulatory requirements across regions	ICH Q GLs; <a href="#">Q12</a> , <a href="#">M4Q(R2)</a> , SPQS (expected start 2025)	
Comparable/convergent basis for making regulatory assessments; reports	<a href="#">ICMRA PQKM--PACMP and CHIP collaboration pilots</a> IPRP QWG & surveys	
Readily accessible and usable “reports” for reference by other regulators	<a href="#">ICH PQKM Task Force</a> <b>PIC/S</b> – more structured data in inspection reports	  
Assure <b>non-disclosure</b> of confidential trade secret information	<a href="#">ICMRA PQKM pilot design</a> <a href="#">ICH PQKM Task Force</a>	 
Regulators reviewing <b>same product, quality dossier, PAC-related submissions, etc.</b>	<a href="#">ICMRA PQKM WG on Identifiers to enable greater reliance</a>	
IT tool(s) to facilitate review and collaboration	<a href="#">Technological solution</a>	

ICMRA slide presented by Brendan Cuddy EMA @ DIA Europe 2025

## RELIANCE APPROACH – CHIP PILOT

# A reflection on the positive outcome of the ICMRA Collaborative Hybrid Inspection Pilot (CHIP)

- \* **EFPIA member companies welcome the flexibility adopting the inspection approach after each inspection**
- \* **Minimise increased efforts by using existing procedures**
  - \* Benefit for both industry and inspectors includes e.g., less travel, less time compared to overall time needed for several inspections and CAPAs
  - \* Consider using existing rules of engagement of the different inspectors according to approaches used in PIC/S revaluation or for the MRA procedure
- \* **Local inspector as lead and coordinating inspector**
  - \* Inter-inspector's communication using dedicated jet function
  - \* Recognise existing confidentiality agreements e.g., as of PIC/S membership or develop a template by ICMRA or PIC/S
- \* **One inspection report according to the national procedure with one set of agreed observations referencing to the reports by co-inspectors / observers**
  - \* Reports from the other inspectorates, reference/cite the core inspection report
    - \* Additional observation according to national laws, if necessary for compliance decision
    - \* Document own compliance decision according to national procedures
  - \* Lead inspector makes final decision on observation, ensuring observers are heard
    - \* Different opinions can always exist between different individuals / humans
    - \* Alignment is expected towards the compliance decision
- \* **Use core inspection time for clarifications and interactions**
  - \* Additional inspection time for document review recognising time differences

Basis: [ICMRA Collaborative Hybrid Inspection Pilot \(CHIP\) Summary Report March 5th, 2025](#).

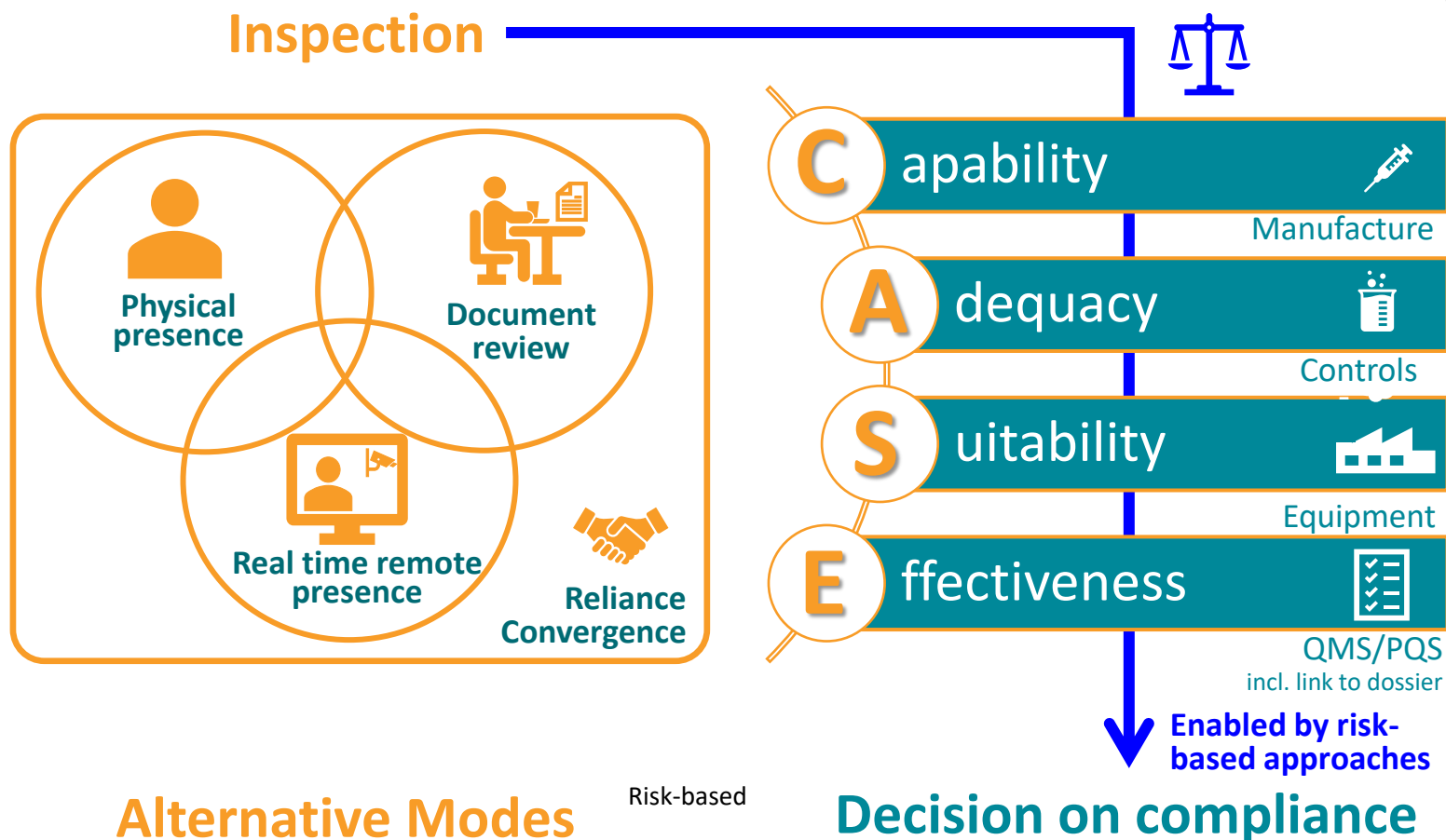
# Inspection modes



## KEEP IN MIND THE PURPOSE OF AN INSPECTION

### Is a site compliant?

No difference in inspection types (PAI\*, routine, surveillance, for cause)

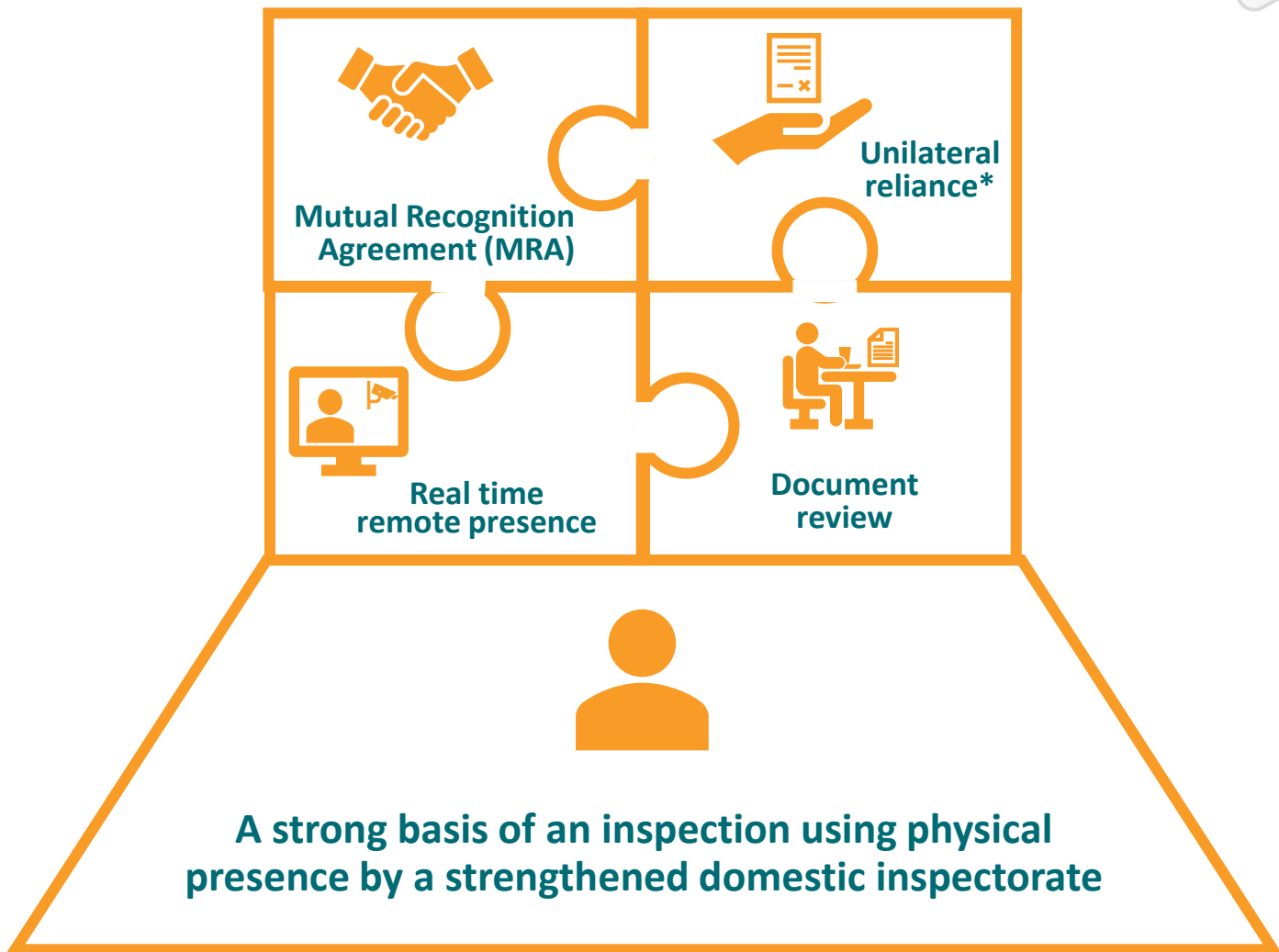


\* Experience: Pre-Approval Inspections (PAI) dedicate most of the time on inspecting the QMS/PQS and only briefly checking on the authenticity of submitted data and links to dossier.



# SCIENCE AND RISK-BASED INSPECTION APPROACH

## Collaboration, Reliance, Recognition

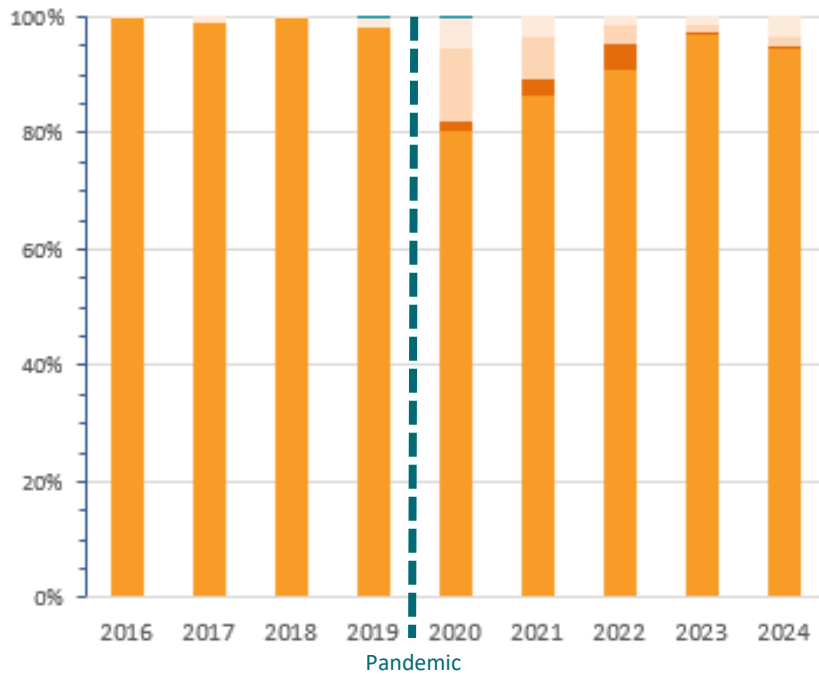


\*based on information from other stringent regulatory authorities

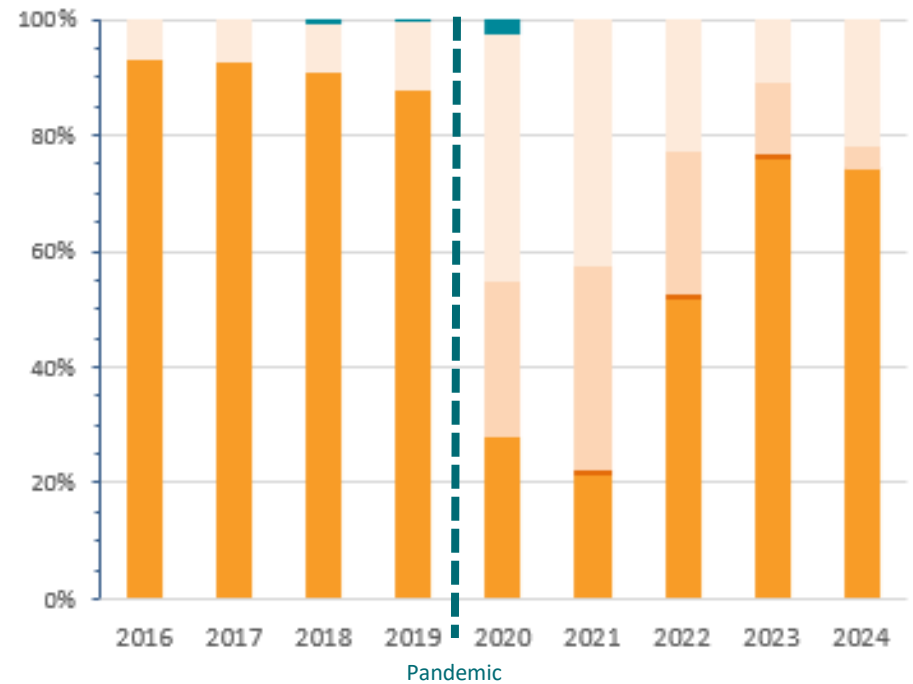
# ANNUAL EFPIA INSPECTION SURVEY - INSPECTION MODES

## Trending inspection modes

Inspection mode - domestic inspections



Inspection mode - foreign inspections



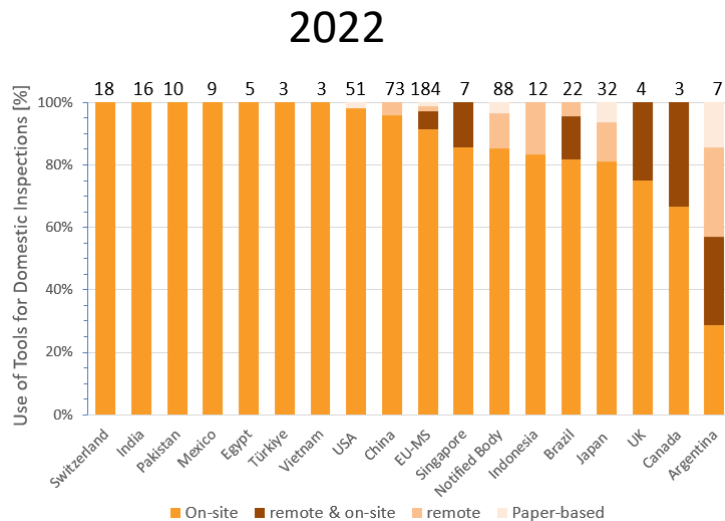
\* Physical presence is increasing but not yet back to the level of before the pandemic

\* The use of remote inspections is decreasing

- Physical presence
- Remote & on-site
- Remote
- Document
- Deferred

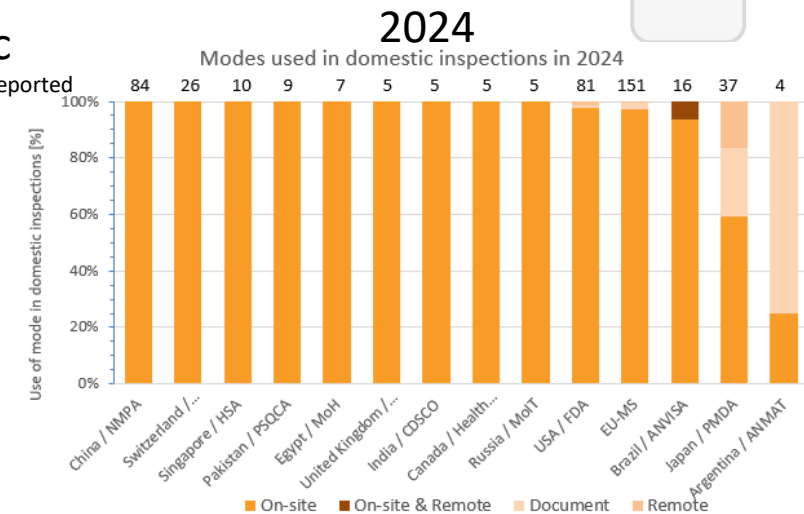
# INSPECTION MODES AT MANUFACTURING SITES

## Trending inspection modes pandemic to now



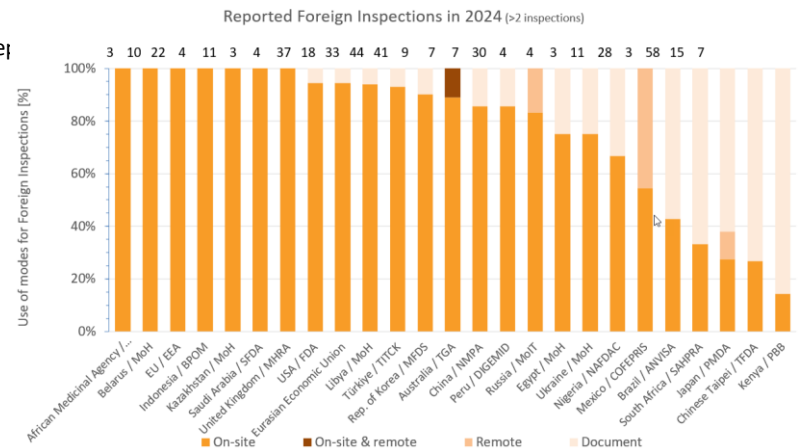
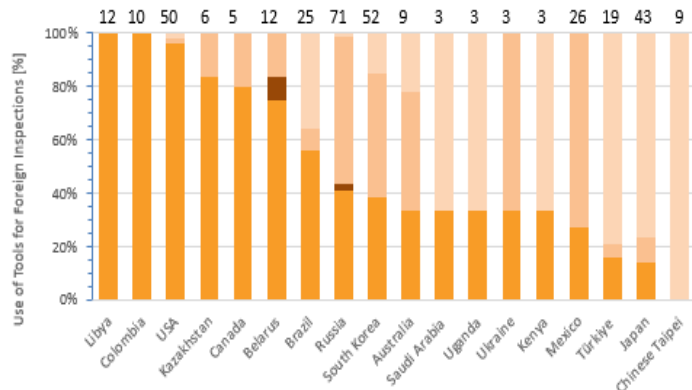
### Domestic

No of inspections reported



### Foreign

No of inspections reported





# Documents for inspection

## DOCUMENT INSPECTIONS

Information provided by the site can follow a commonly agreed standard for paper-based inspections

Check with survey results

<b>Site</b> 	<ul style="list-style-type: none"><li>• Site Master File (SMF)*</li></ul>	✓
<b>Product</b> 	<ul style="list-style-type: none"><li>• Annual Product Quality Review</li></ul>	✓
<b>Pharmaceutical Quality System</b> 	<ul style="list-style-type: none"><li>• Site Quality Manual</li></ul>	✓
<b>Additional information</b> 	<ul style="list-style-type: none"><li>• List of inspections / audits</li></ul>	✓



[Enhanced GMP/GDP Inspection Efficiency, EFPIA, Position Paper 19. May 2014.](#)



[Optimising the GMP paper-based Inspection Process EFPIA, Position Paper 26. June 2019.](#)

\*EXPLANATORY NOTES FOR PHARMACEUTICAL MANUFACTURERS ON THE PREPARATION OF A SITE MASTER FILE, PIC/S PE 008-4, Annex 1, January 2011

## DOCUMENT INSPECTIONS

# Survey results 2023 of standard document packages requested prior to an inspection – any mode

### \* Common documents requested in surveillance and pre-approval inspections

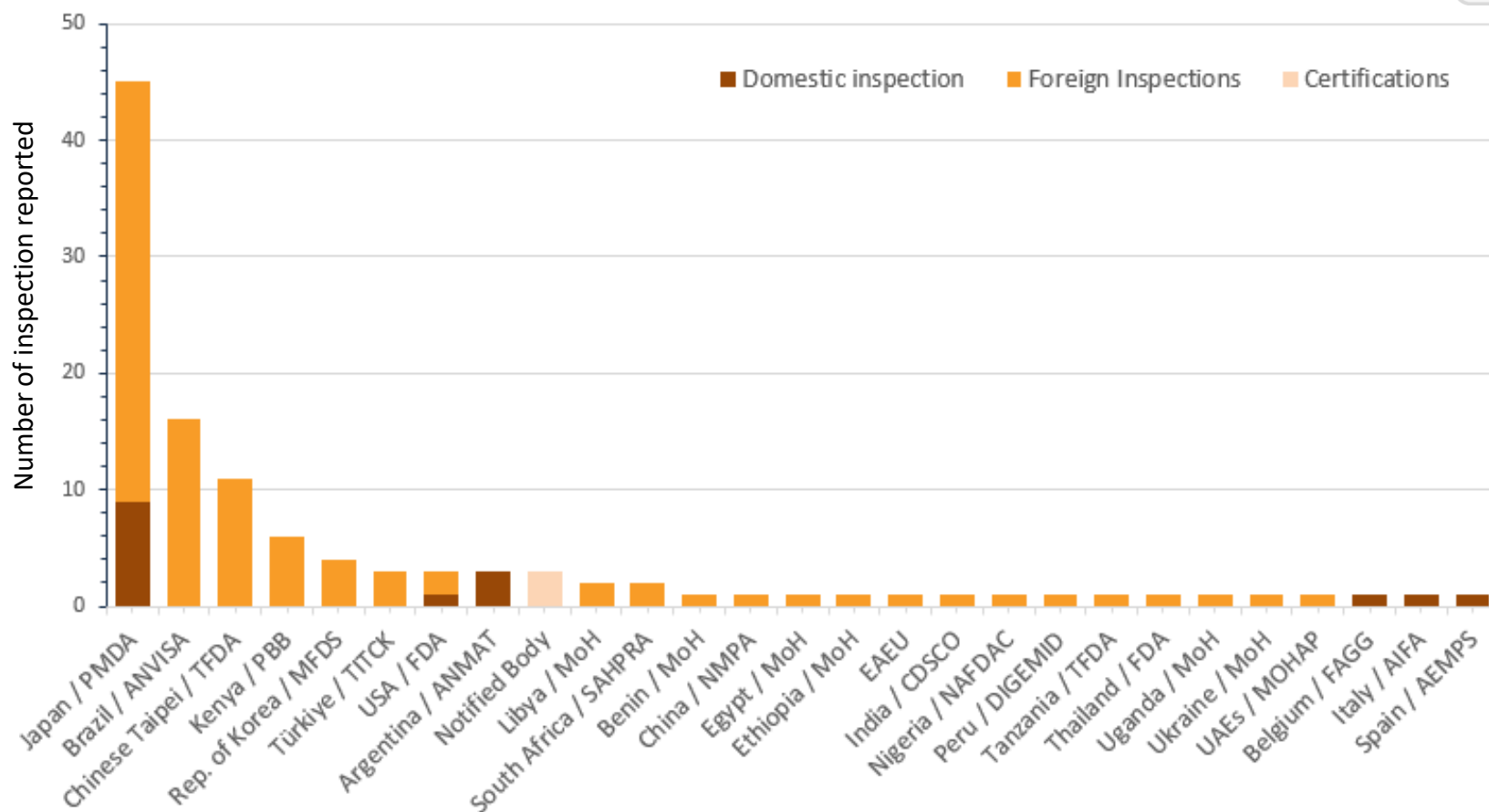
- \* Site Master File\*
- \* Annual Product Review\*
- \* Quality Manual\*
- \* Inspection History\*
- \* List of Deviations
- \* List of Major Changes
- \* List of Recalls
- \* Quality Agreements

### \* Additional documents usually requested in PAI

- \* Process Flow Diagrams
- \* Product Specifications
- \* Validation Documents
- \* List of countries where the product is approved
- \* List of Laboratory OOS results.

## DOCUMENT INSPECTIONS

### Inspectorates performing document inspections



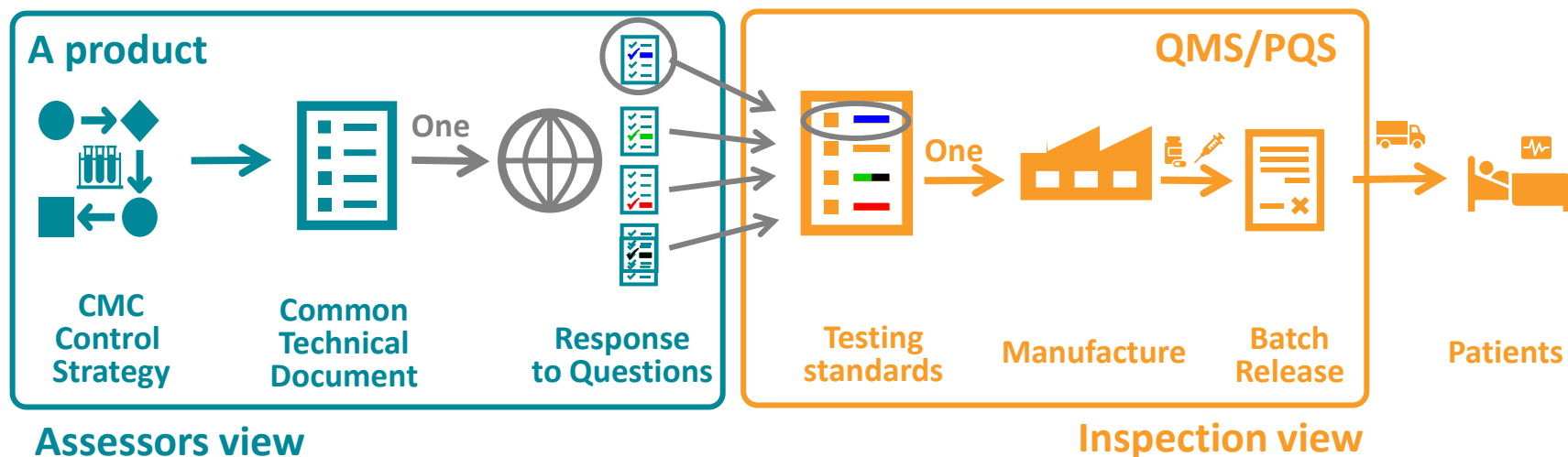


# Assessors in inspections

## ANSWERS TO QUESTIONS

### Roles and responsibilities of assessors (and inspectors)

- \* Assessors should get a training on what inspectors are doing
- \* Enhancement of GMP activities understanding by assessors through firsthand insights for improving filing reviews.
- \* Assessors should focus on their mandate i.e., scientific consistency of dossiers (i.e., not acting as inspectors) while inspectors emphasize GMP compliance
- \* Assessors could share areas that require verification with inspectors ahead of the inspection



Green: what assessors see, Orange: what inspectors see view; Gray companies' activities

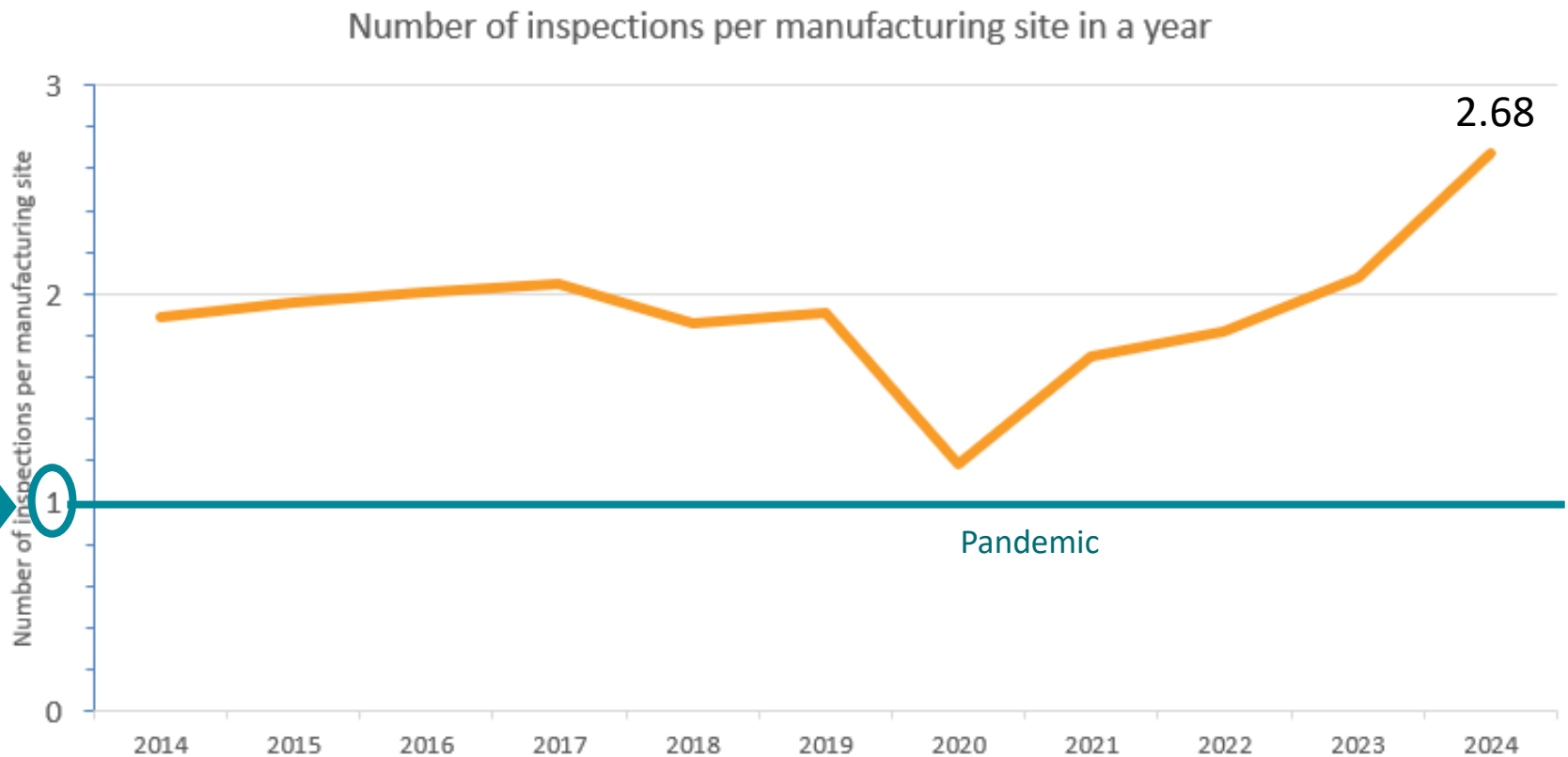
QMS/PQS: Quality Management System / Pharmaceutical Quality System



# General Data

## EFPIA'S ANNUAL INSPECTION SURVEY - DATA

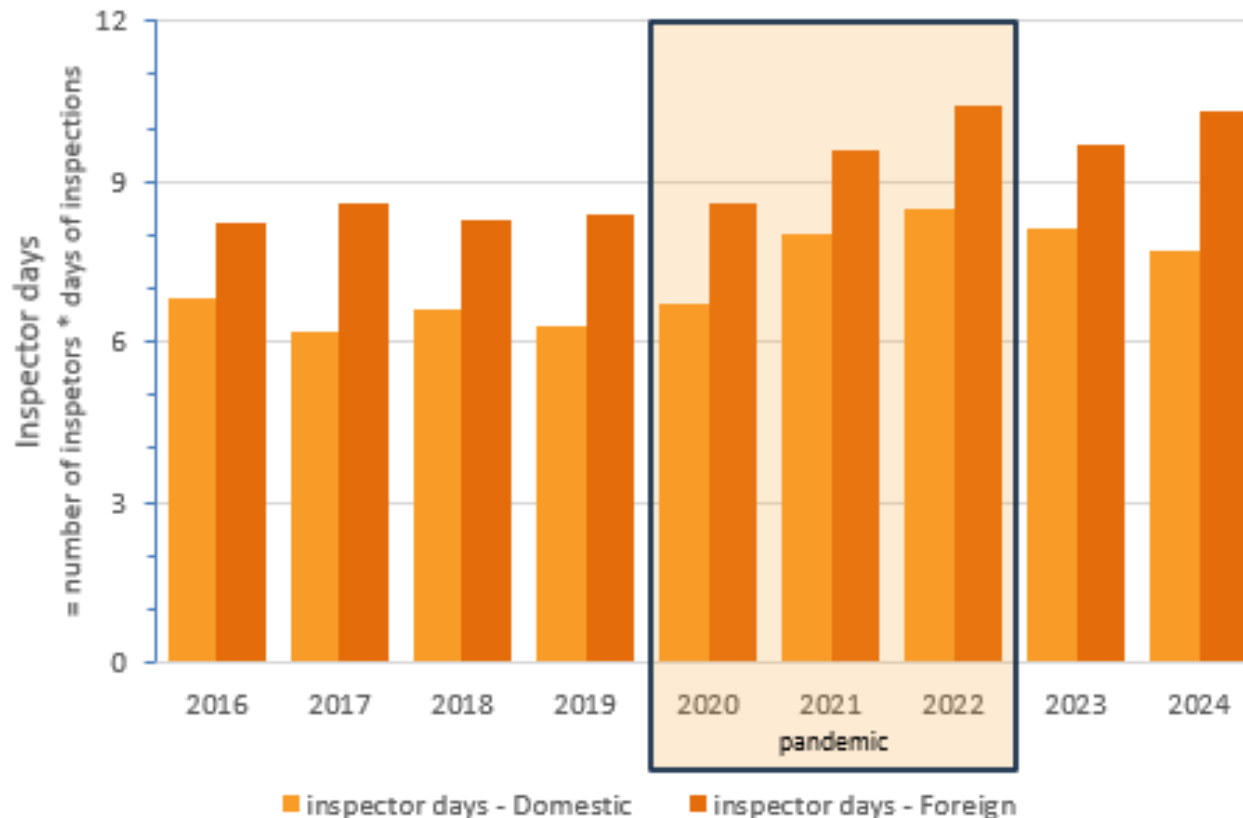
### The number of inspections at a manufacturing site





## EFPIA'S ANNUAL INSPECTION SURVEY – INSPECTOR DAYS

### Average of inspector days spend in domestic and foreign inspections (only onsite inspections)



- \* Domestic inspection have less inspector days than foreign inspections (not including travel!)
- \* Inspector days increased with the pandemic for both domestic and foreign inspections



# Inspections at Manufacturing Sites

# INSPECTIONS AT MANUFACTURING SITES

## Inspection matters

### Domestic inspections

- Physical presence is the almost exclusive inspection mode; the combination of physical and remote presence is rarely used

### Increasing trend towards more inspections at the same manufacturing site

- Back to the level before the pandemic

### Resources

- Inspector days used for domestic inspections: 7.7d and foreign inspections: 10.3d & travel

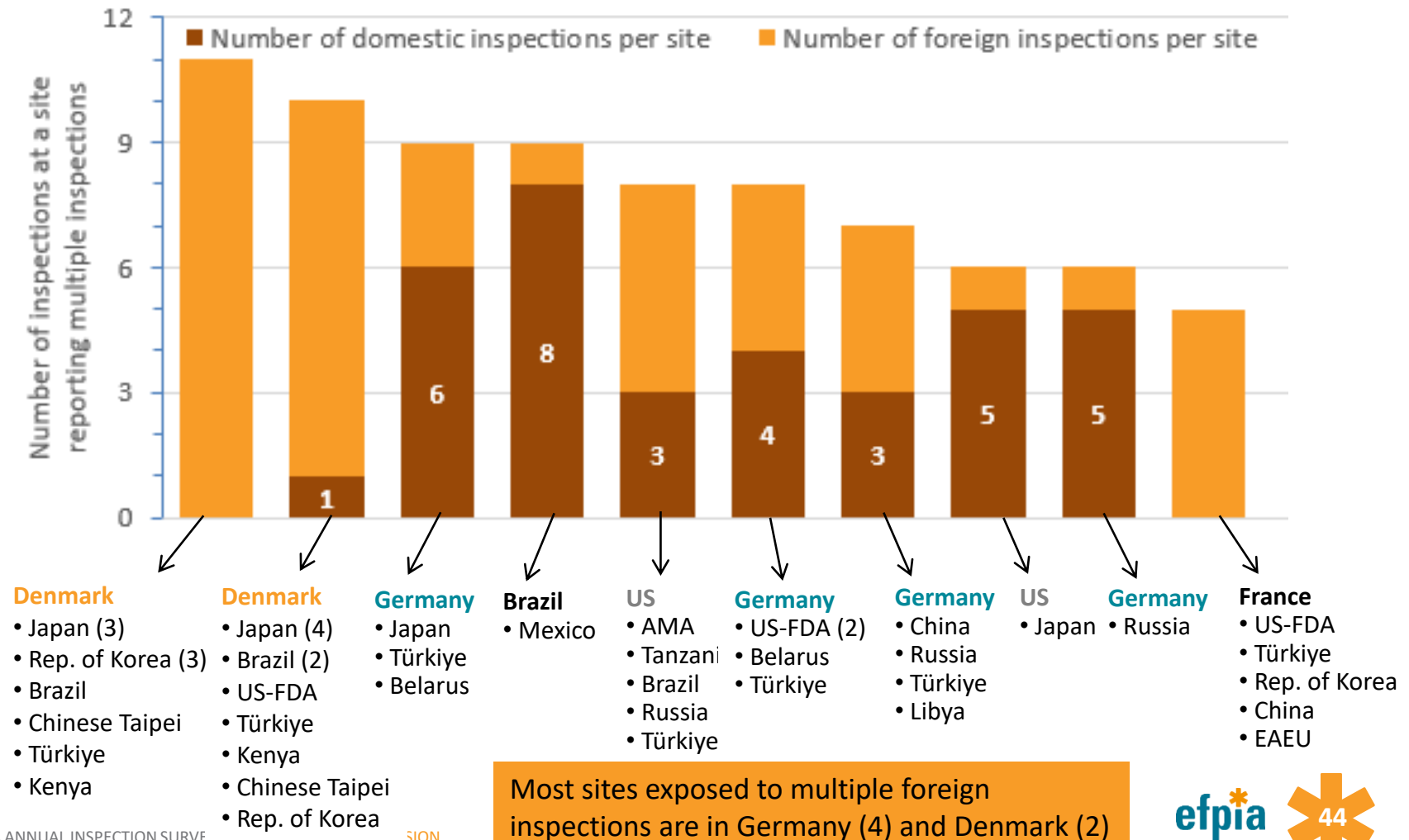
### Foreign and domestic inspectorates often focus on similar topics

- No effect on number of inspections at sterile manufacturing sites due to GMP Annex 1 implementation

## INSPECTIONS AT MANUFACTURING SITES

### Multiple inspections at one manufacturing site (6 and more)

Number of inspections per one site with foreign inspections

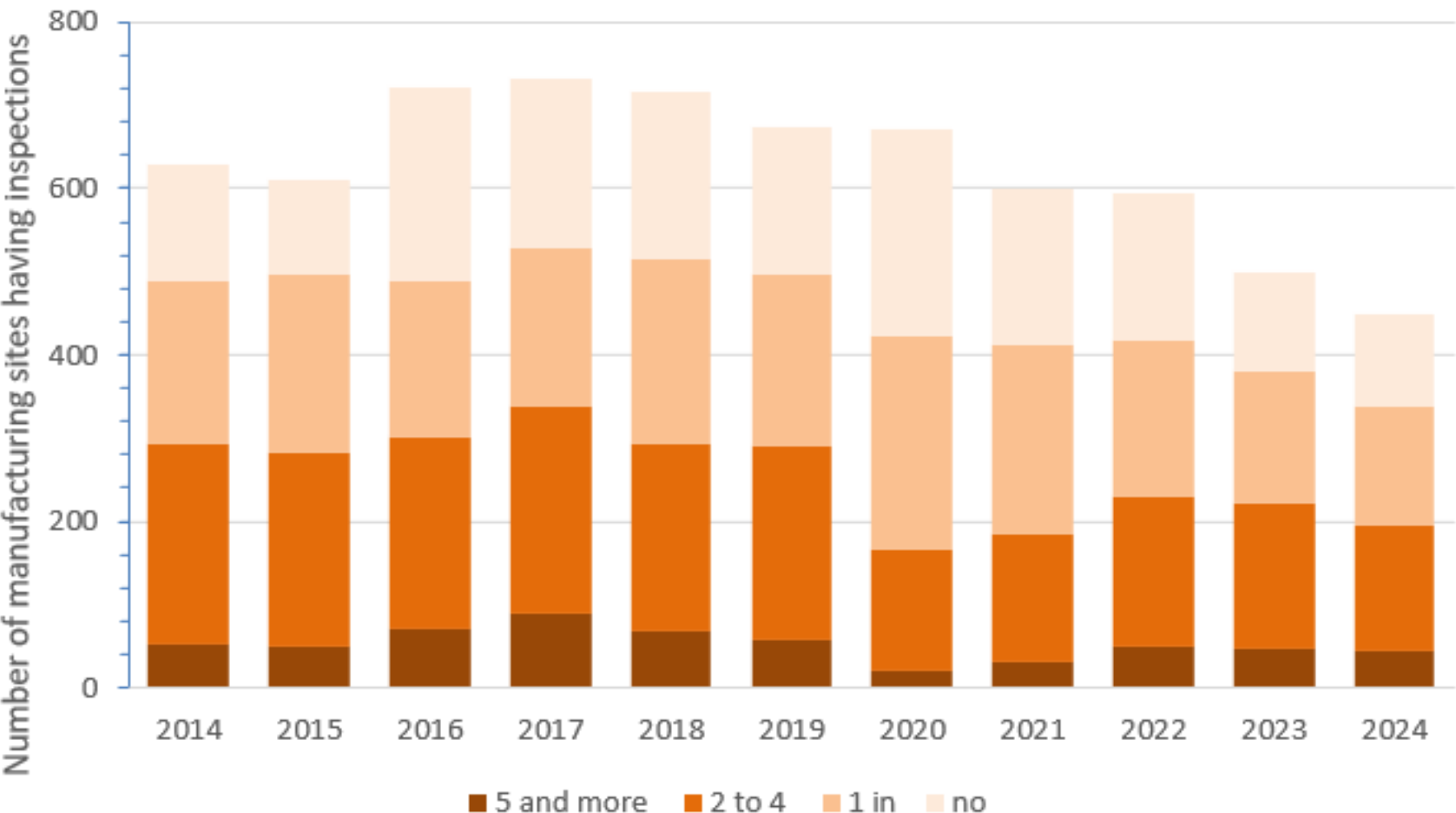




# INSPECTIONS AT MANUFACTURING SITES

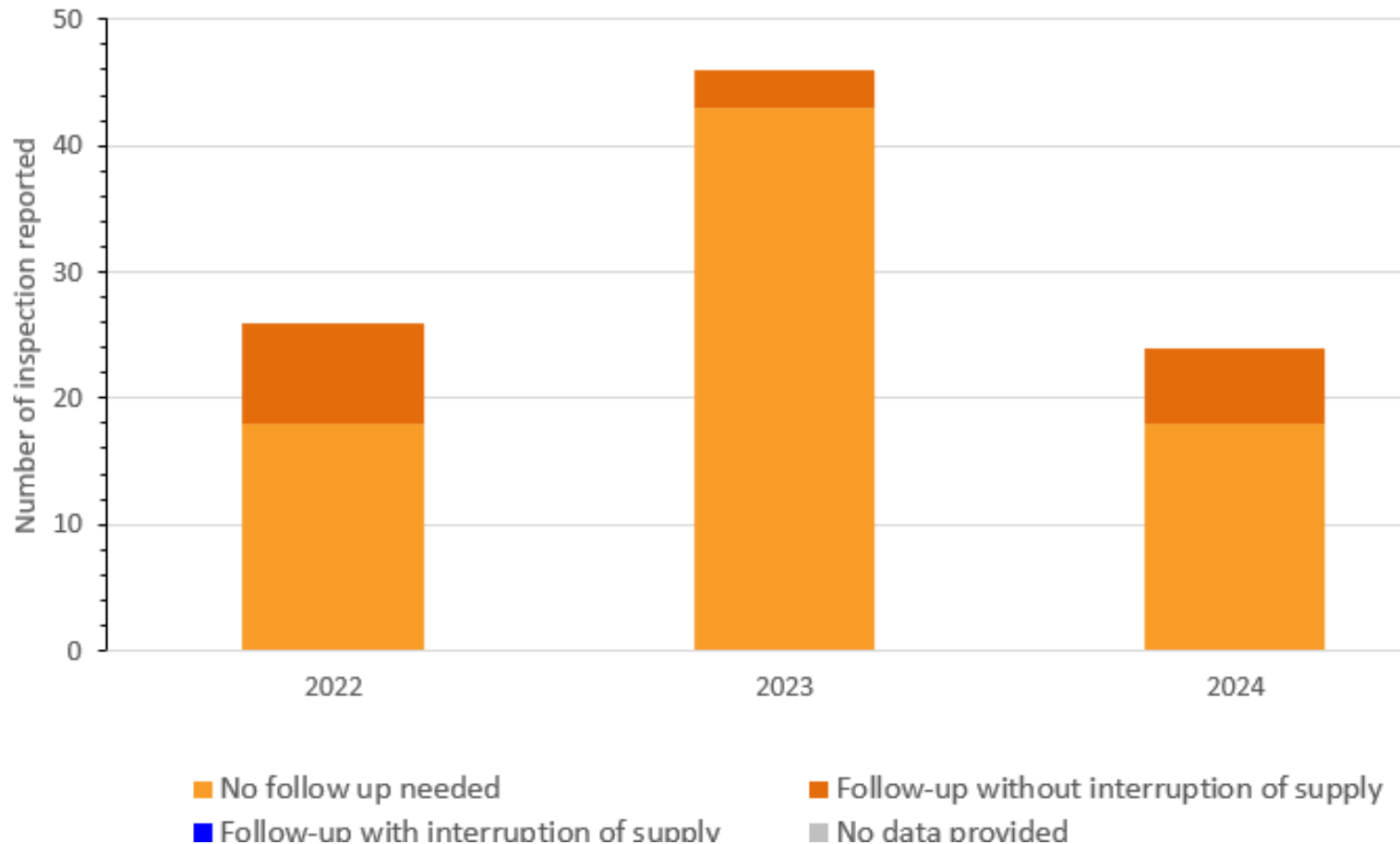
## Inspections at one manufacturing site

Number of sites having inspections



## INSPECTIONS AT MANUFACTURING SITES

For cause inspections do not result in interrupted supply

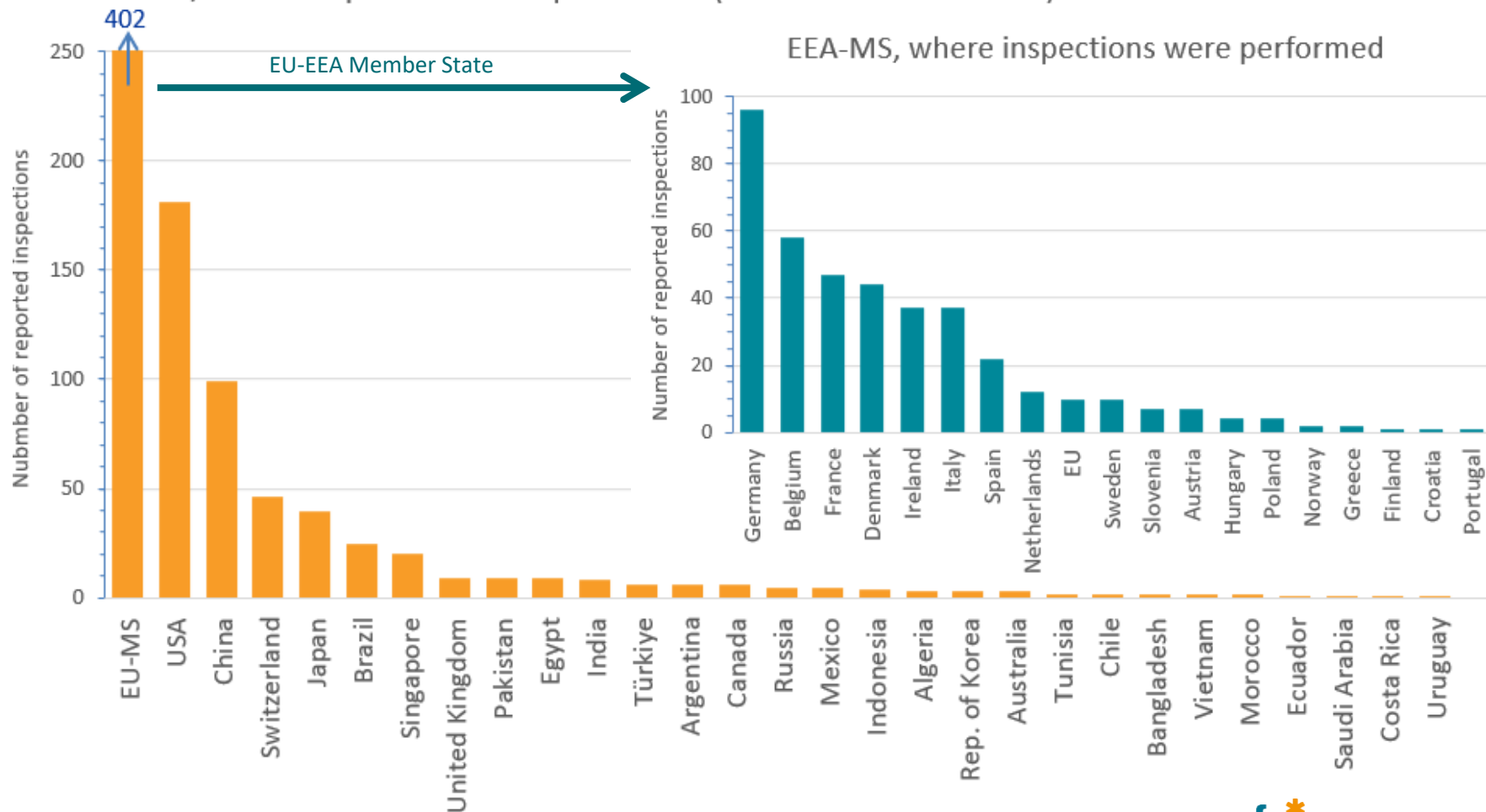


\* The number of 'for cause' inspections had a peak in 2023

## INSPECTIONS AT MANUFACTURING SITES

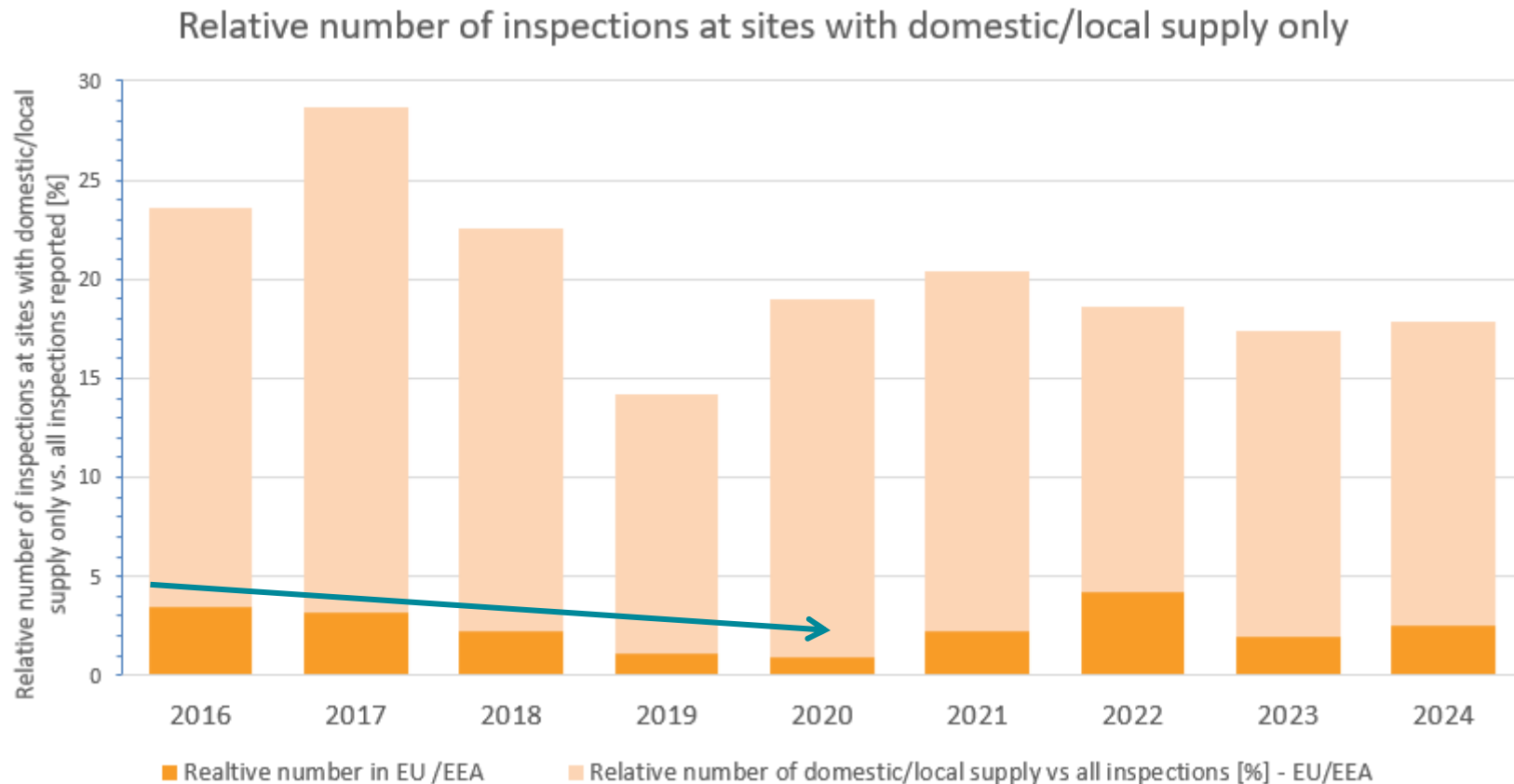
### Number of inspections (domestic and foreign) per country highlight's locations of manufacturing sites

Countries, where inspections were performed (Certifications excluded)



## INSPECTIONS AT MANUFACTURING SITES

### Inspections at sites with domestic/local supply only

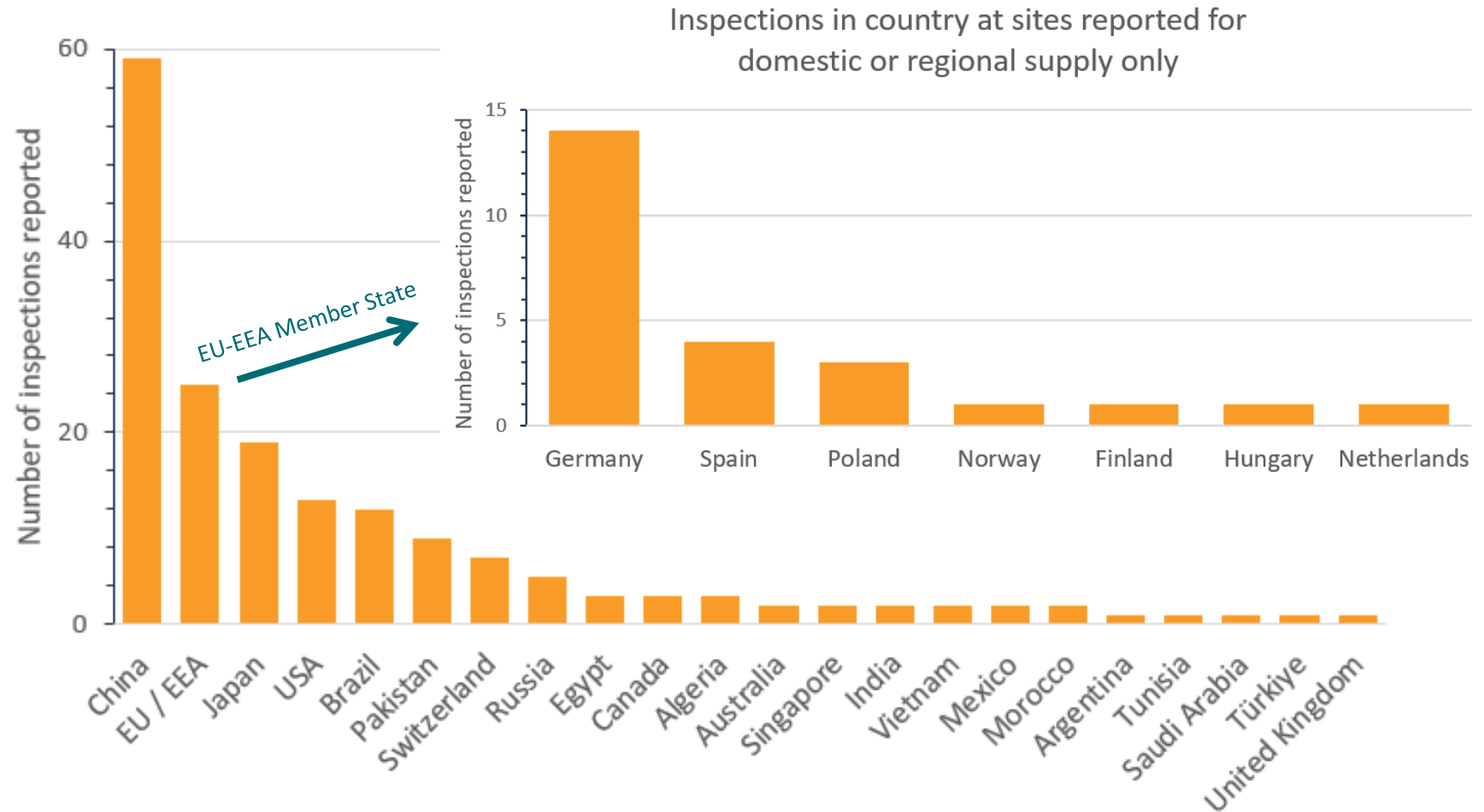


- \* The data show a trend towards globalisation of manufacturing until 2020 i.e., the pandemic. After that, more sites manufacturing for local / regional supply are reported to be inspected



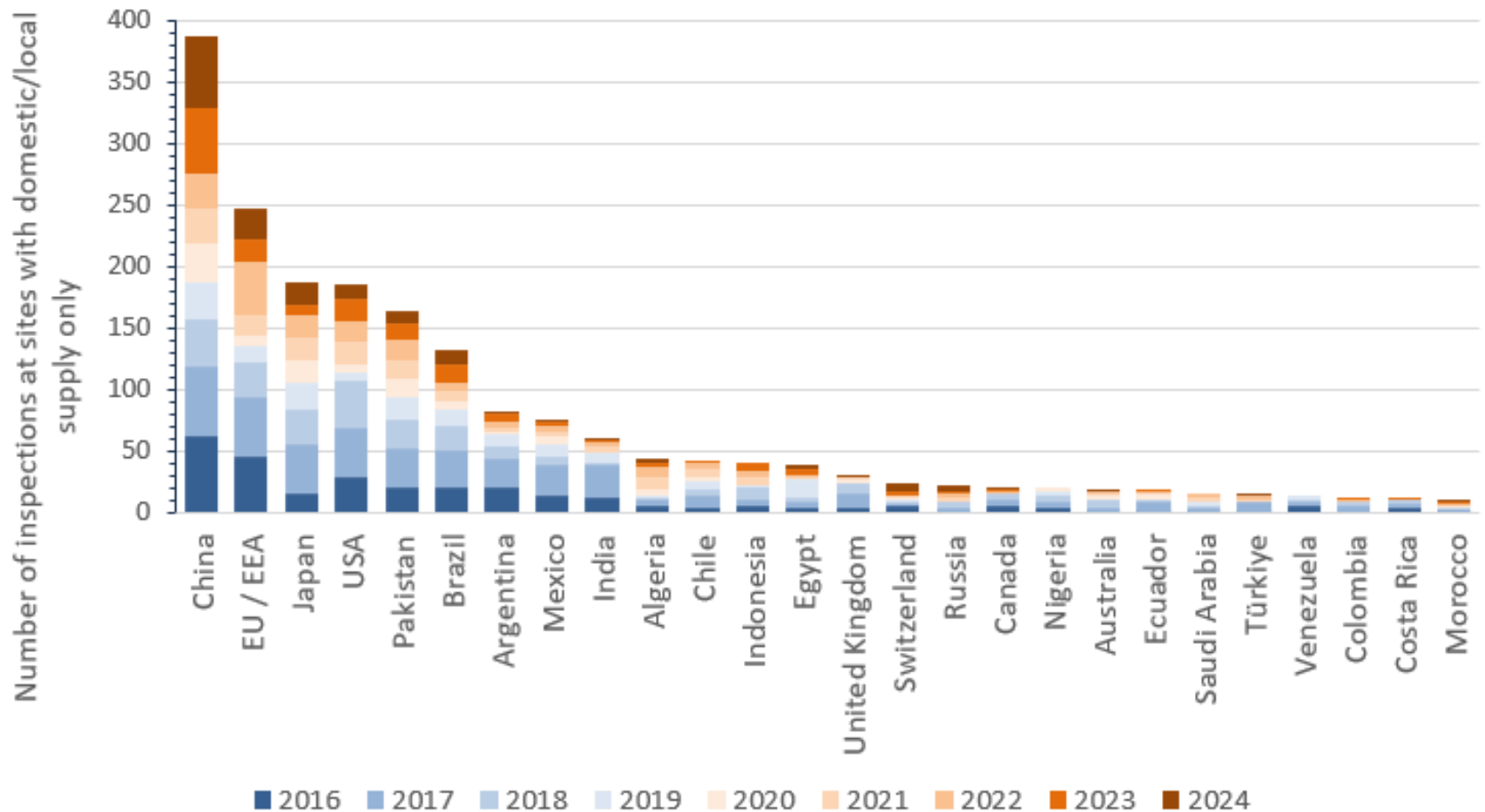
## INSPECTIONS AT MANUFACTURING SITES - SUPPLY

### Inspections in country at sites reported for domestic or regional supply only in 2024



## INSPECTIONS AT MANUFACTURING SITES - SUPPLY

Inspections in country at sites reported for domestic or regional supply only – several years history

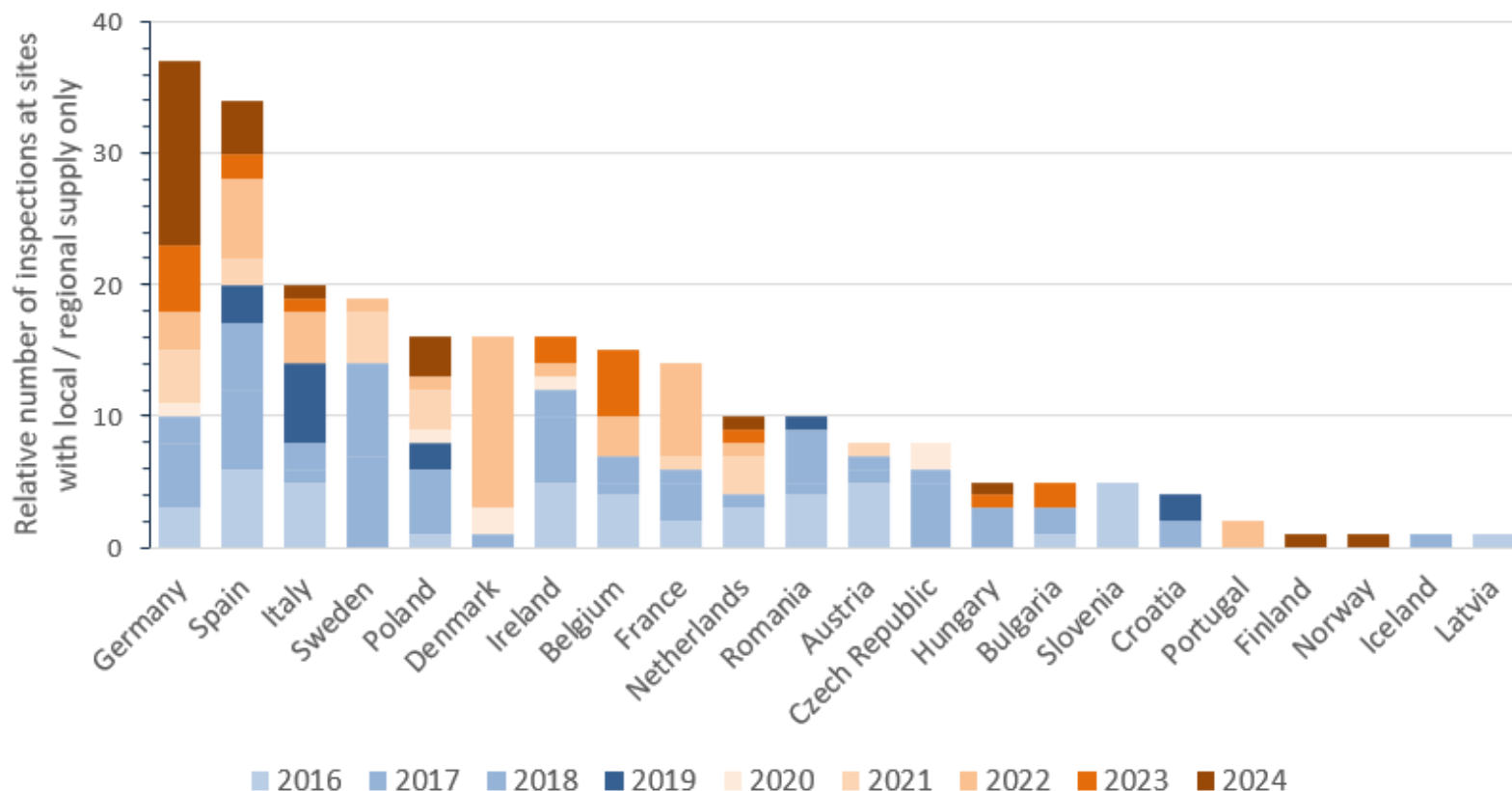


\* China, EU / EEA, Japan, US, Pakistan and Brazil are the countries with the most inspections by sites for local / regional supply

## INSPECTIONS AT MANUFACTURING SITES - SUPPLY

### Inspections in country at sites reported for domestic or regional supply only – several years history

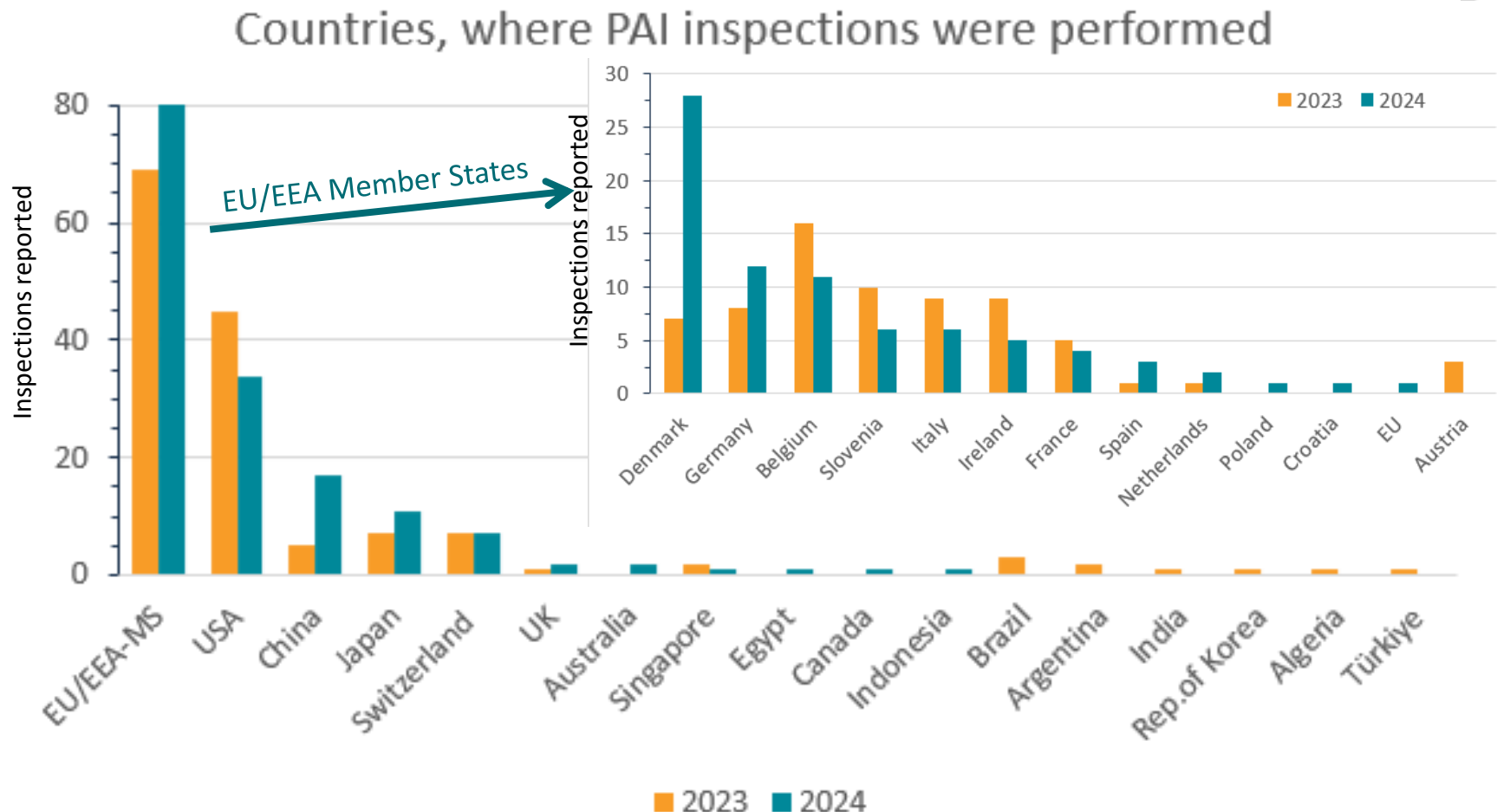
EU/EEA by country



\* Germany, Spain, Italy and Sweden are the countries with the most inspections with sites for local / regional supply in the EU/EEA reported in the last 9 years

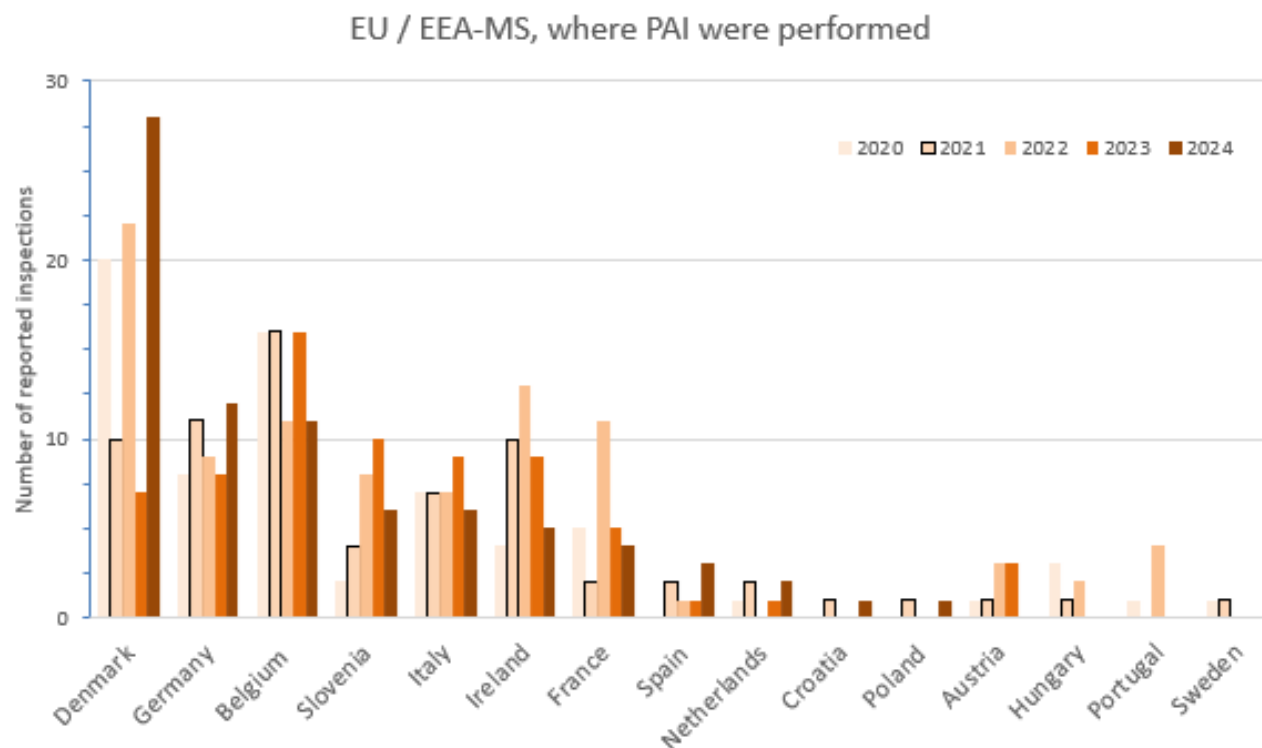
## INSPECTIONS AT MANUFACTURING SITES - PAI

Locations of manufacturing facilities reporting PAI demonstrating where innovative products are manufactured – EU again number one



## INSPECTIONS AT MANUFACTURING SITES - PAI

### EU/EEA competitiveness where new innovative products are manufactured



\* Member States where innovative products are manufactured include

- \* Denmark
- \* Germany
- \* Belgium
- \* Slovenia
- \* Italy
- \* Ireland
- \* France

## INSPECTIONS AT API MANUFACTURING SITES

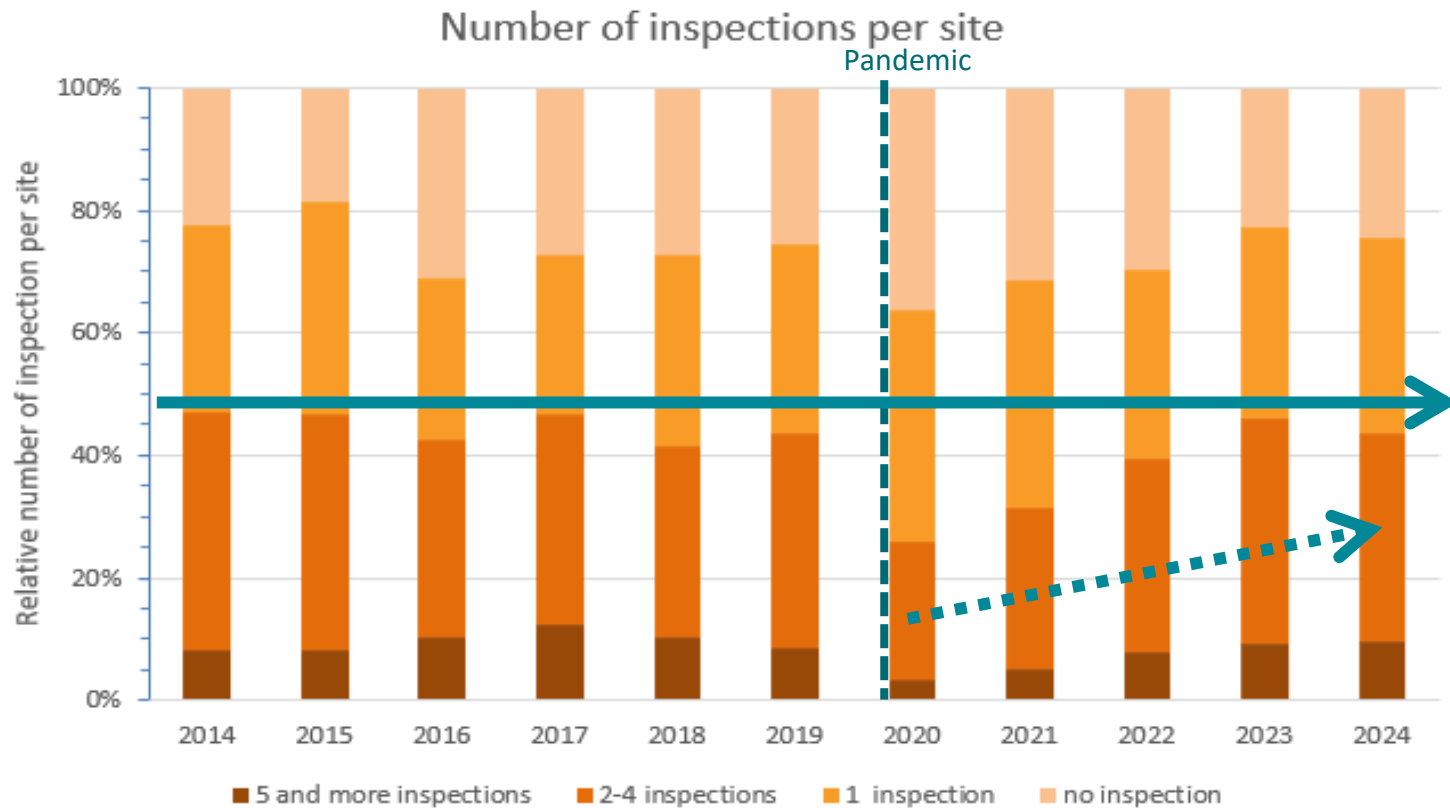
### Locations of inspected API manufacturing sites



Inspections at API manufacturing sites are performed in the EU/EEA, US, Switzerland,, Singapore, and Pakistan; in the EU/EEA in Germany, Belgium, Ireland and Denmark.

## INSPECTIONS AT MANUFACTURING SITES

### Number of inspections reported per site



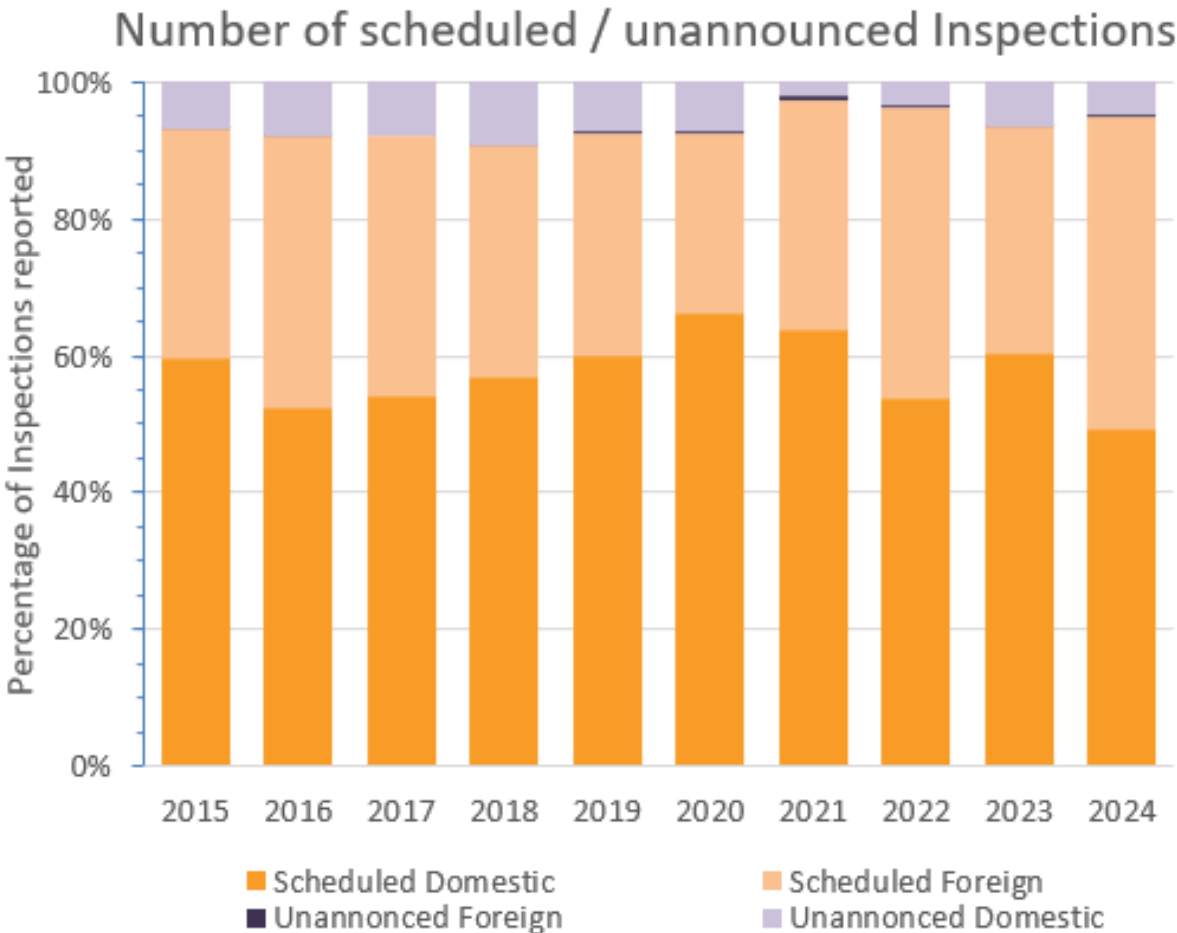
#### \* Data

- \* Increasing trend towards more inspections at the same manufacturing site
- \* Currently at the level of 2014-2019
- \* During the pandemic, the focus was to have more towards 1 inspection per site



# INSPECTIONS AT MANUFACTURING SITES

## Scheduled versus unannounced inspections



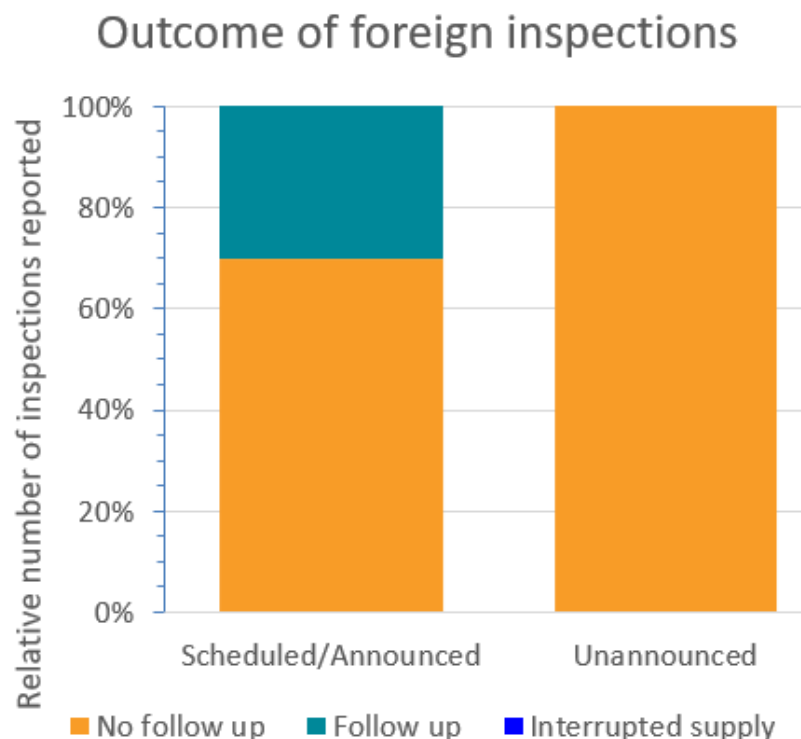
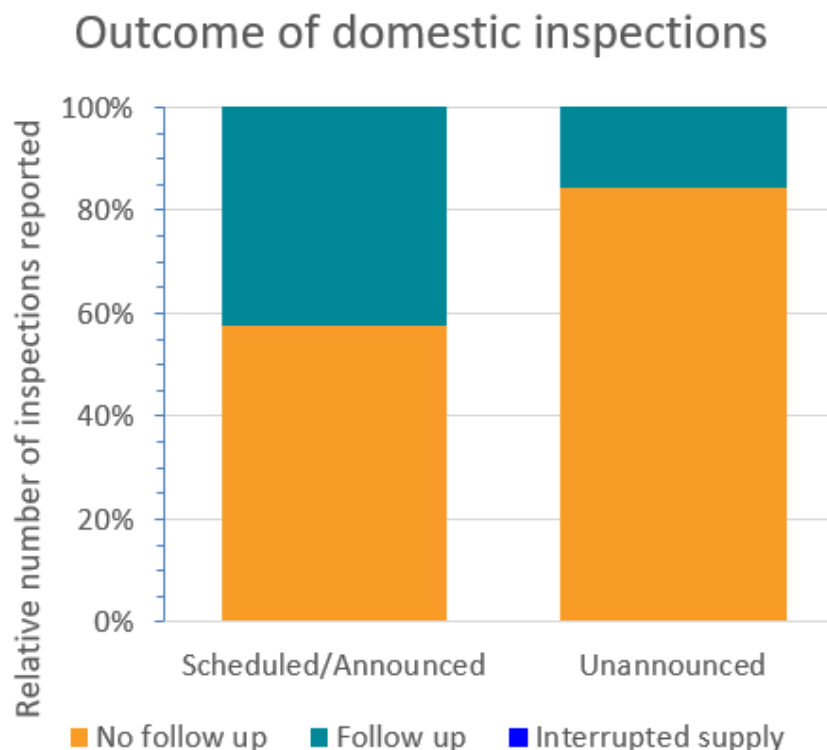
Inspectorate	Reported number of unannounced inspections in 2024
China / NMPA	21
USA / FDA	17
Notified Body	4
Japan / PMDA	2
Chile / ISP	2
Rep. of Korea / MFDS	1
Spain / AEMPS	1
Indonesia / BPOM	1
Brazil / ANVISA	1
Italy / AIFA	1

China and the US are reported to perform by far the most unannounced inspections (domestic)



## INSPECTIONS AT MANUFACTURING SITES

### Outcome of scheduled versus unannounced inspections



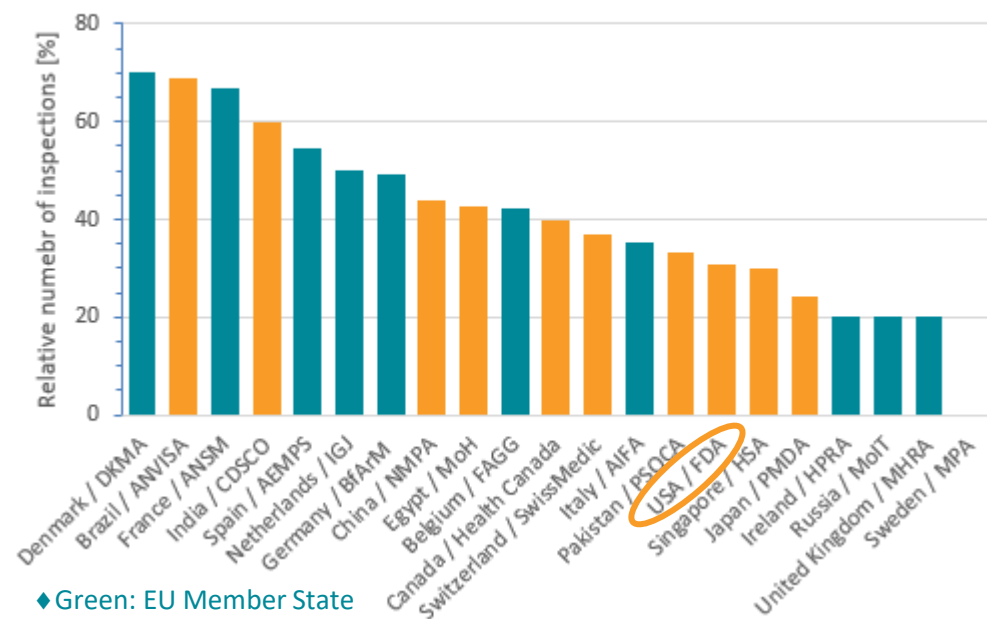
**\* About 20% more follow up actions are reported with scheduled inspections compared to unannounced inspections (both foreign and domestic)**

Note: Non of the inspections ended with interrupted supply

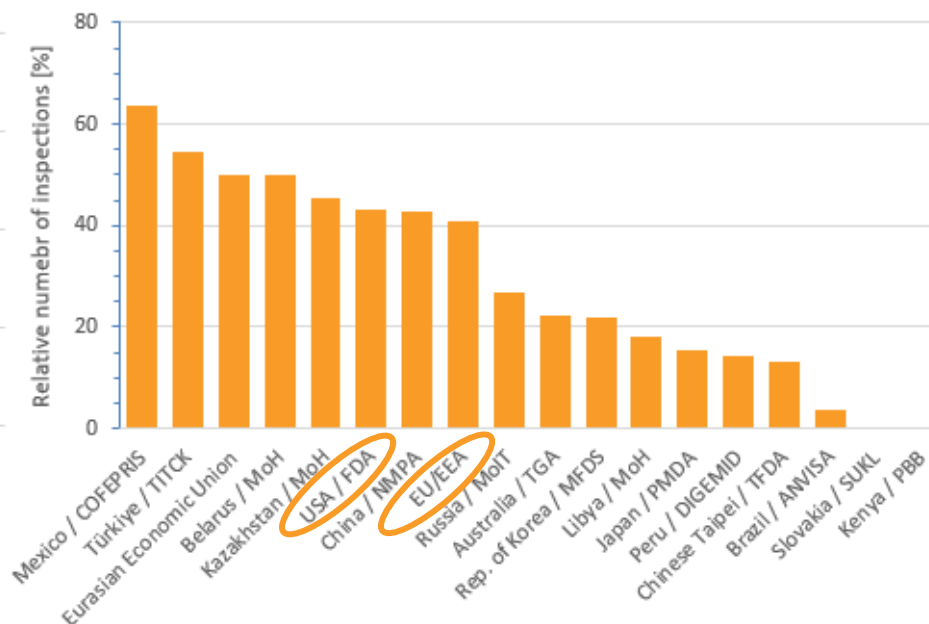
## INSPECTIONS AT MANUFACTURING SITES

### Rate of inspections with follow-up actions

Rate of domestic inspections with follow up  
(5 or more inspections reported)



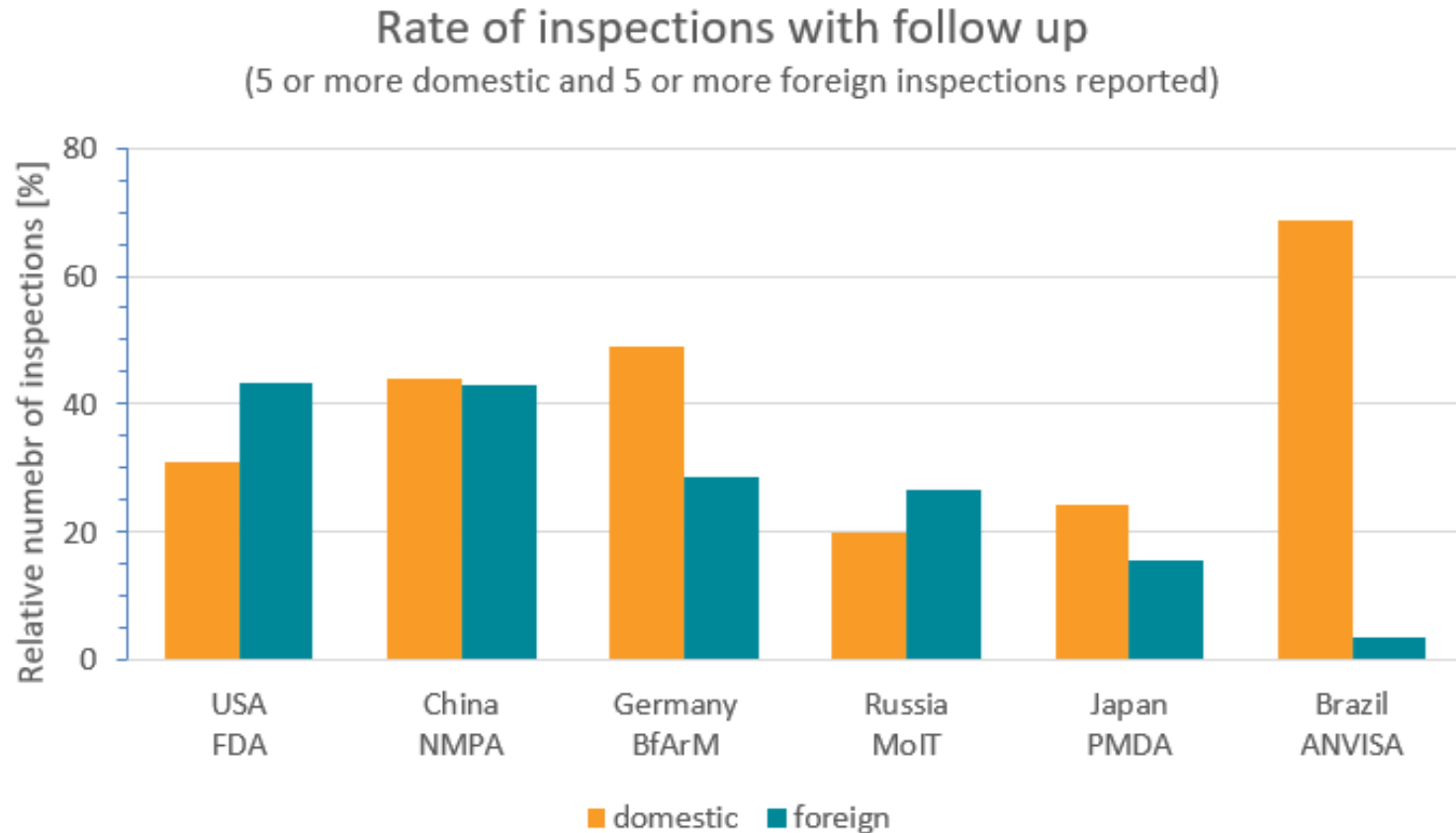
Rate of foreign inspections with follow up  
(5 or more inspections reported)



- ✱ For most inspectorates domestic inspections have more follow up action than foreign inspections – but not e.g., US-FDA
- ✱ The order of countries is different on follow up actions reported to be addressed in domestic versus foreign sites – different behaviours?

## INSPECTIONS AT MANUFACTURING SITES

### Rate of inspections with follow-up actions



**\* Even if FDA is doing announced foreign inspection companies report to have more inspections with follow up in 3<sup>rd</sup> countries than for sites in the US**

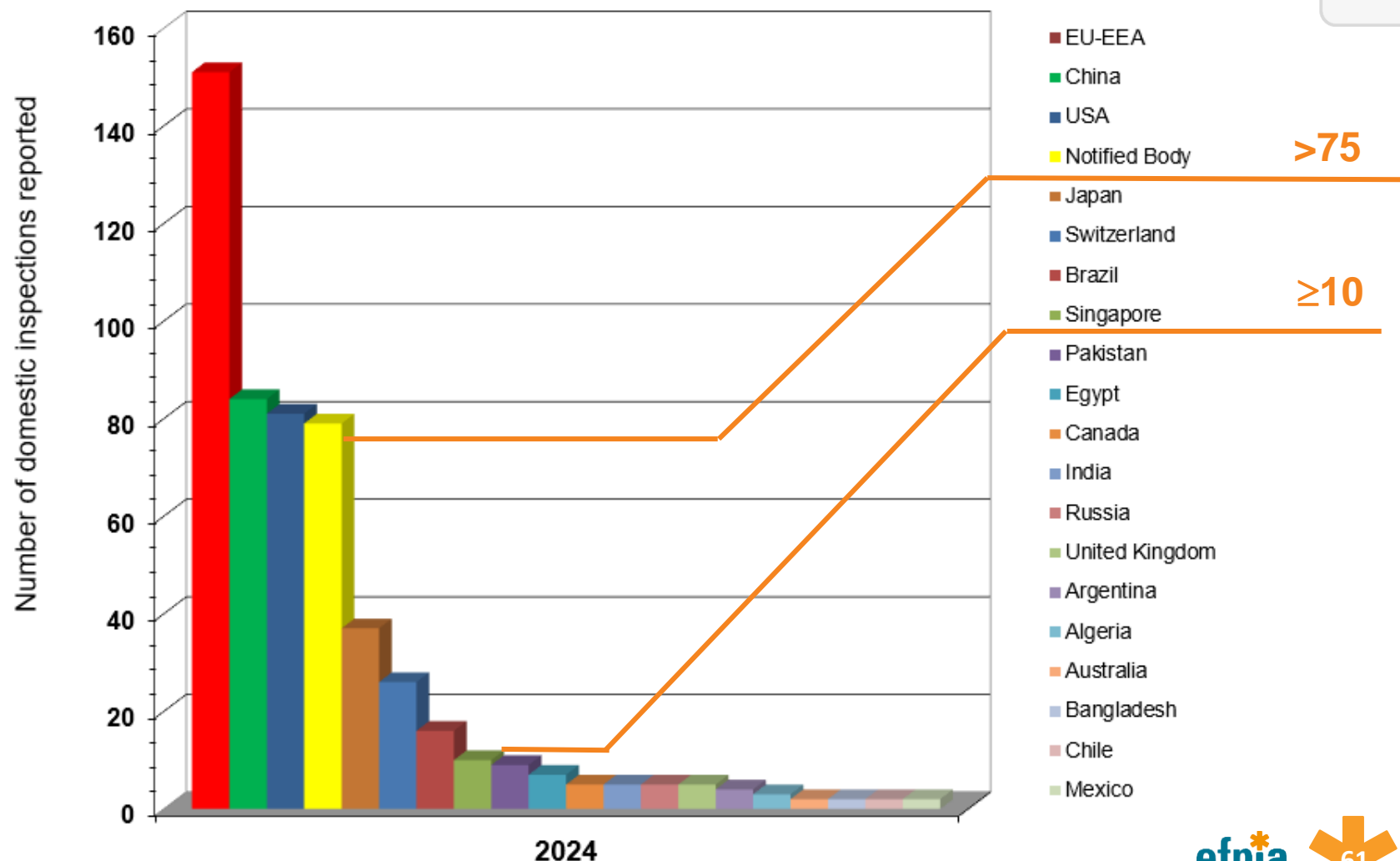


# Domestic Inspection Activity

## DOMESTIC INSPECTIONS AT MANUFACTURING SITES

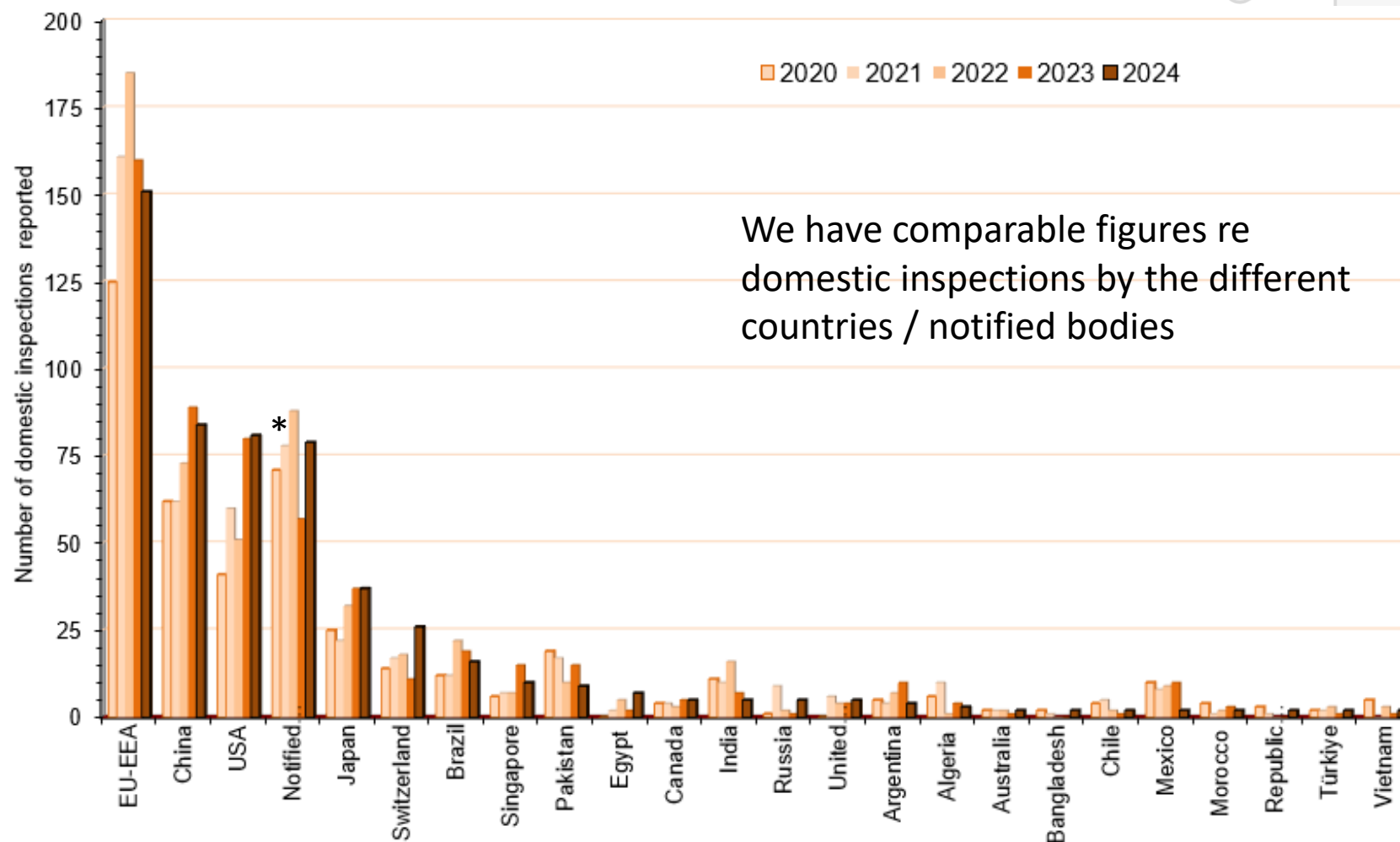
### Number of domestic inspections

ordered by country (>1 inspections; EU/EEA as one entity; all modes)



## DOMESTIC INSPECTIONS AT MANUFACTURING SITES

### Number of reported domestic inspections



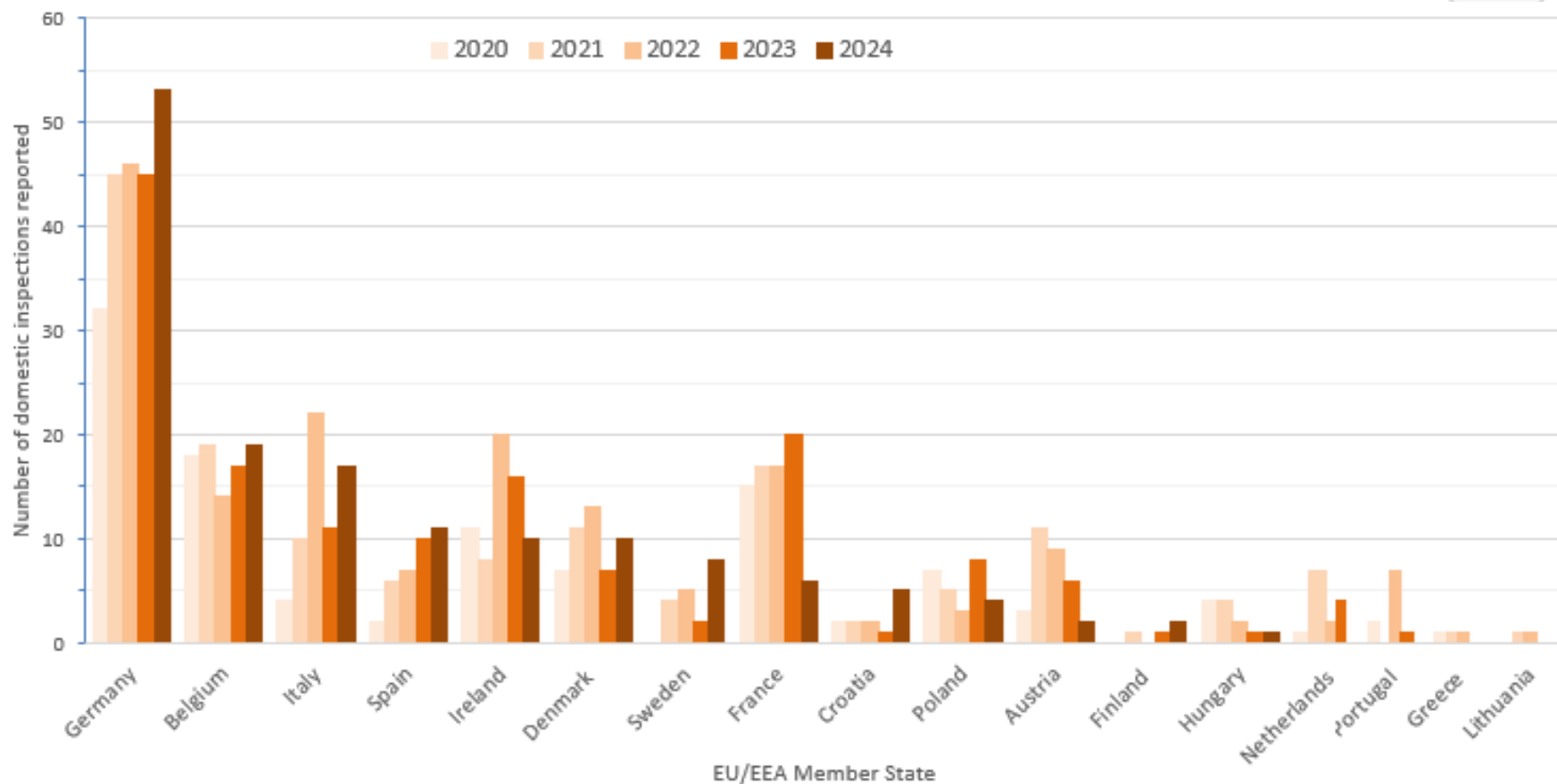
Only listed if more than 2 domestic inspections reported

Note: Notified Bodies doing certifications for devices included in Medicinal Products

EFPIA ANNUAL INSPECTION SURVEY - 2024 DATA - PUBLIC VERSION

## DOMESTIC INSPECTIONS AT MANUFACTURING SITES

### Number of reported domestic inspections by authorities in EU/EEA Member States

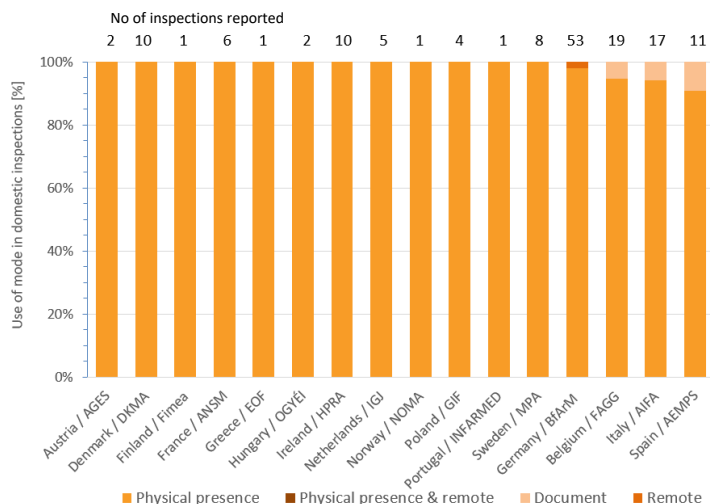


# DOMESTIC INSPECTIONS AT MANUFACTURING SITES

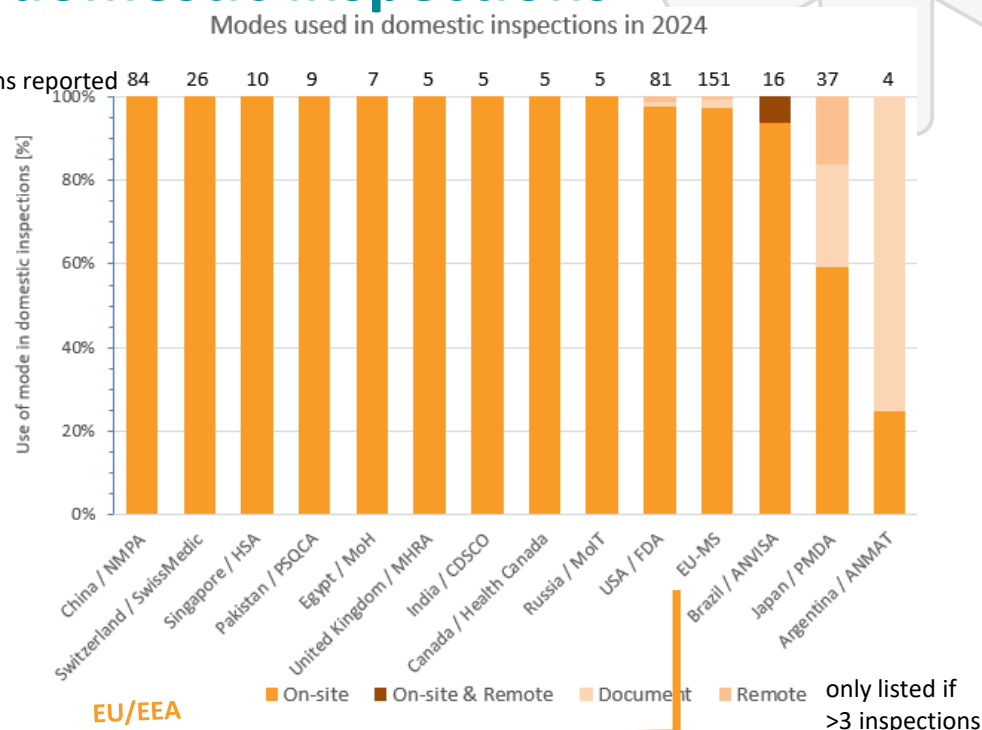
## Inspection modes used in domestic inspections

### \* Domestic inspections

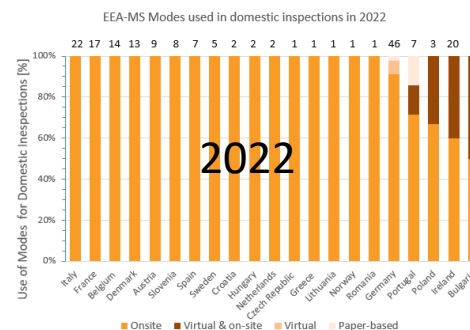
- \* Physical presence is the almost exclusive inspection mode
- \* The combination of physical presence and remote presence is rarely used



only listed if  
>2 inspection



EU/EEA



Significant less use of the  
remote inspection mode in  
comparison to 2022

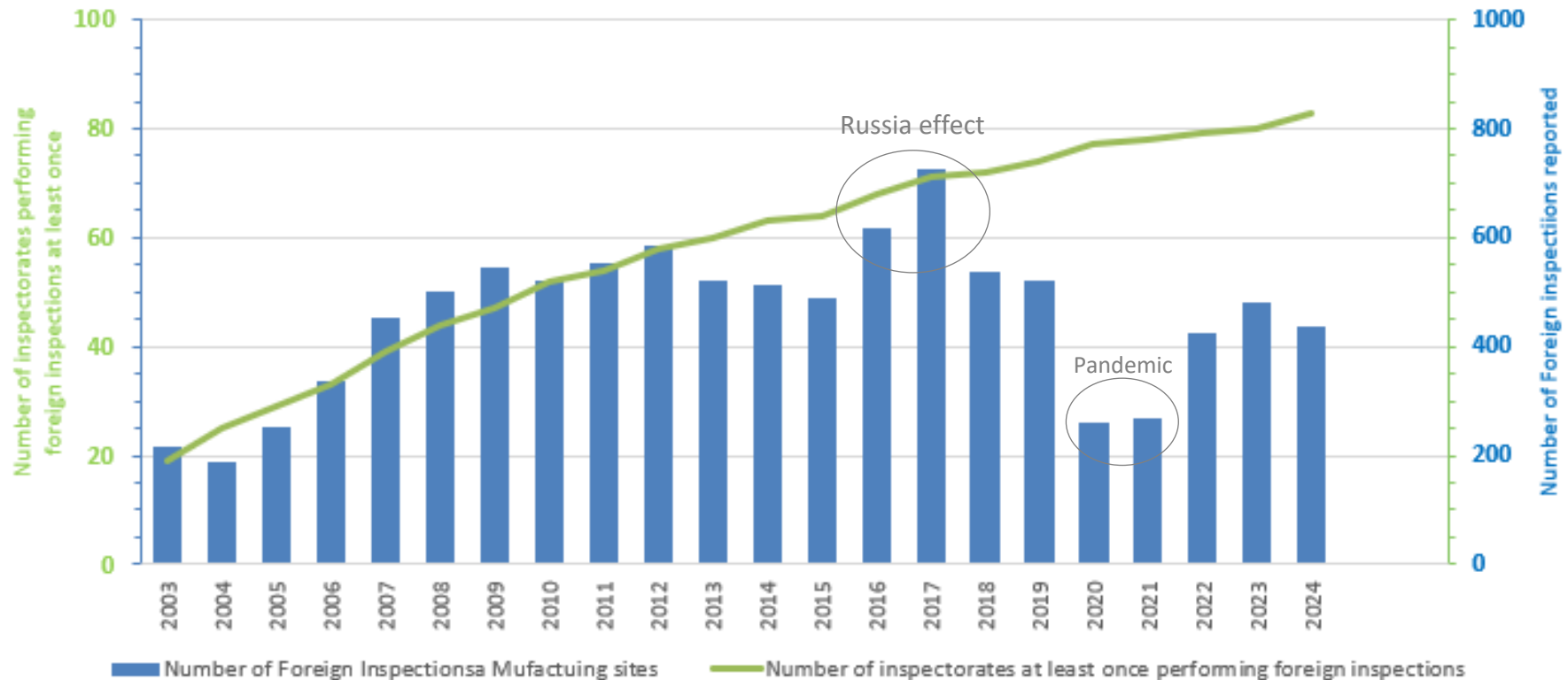




# Foreign Inspection Activity

## FOREIGN INSPECTIONS AT MANUFACTURING SITES

Foreign inspection reported and corresponding inspectorates performing inspections at least once

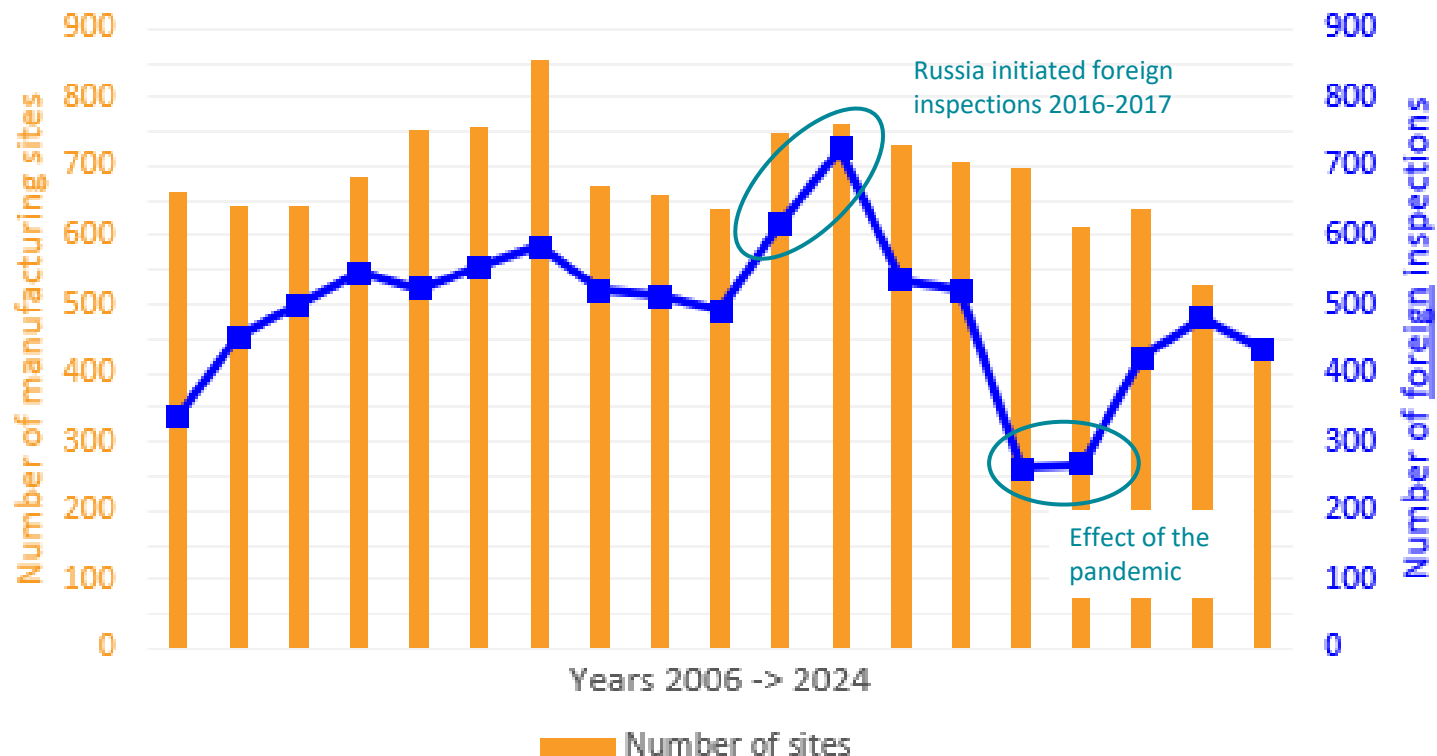


✳ Despite the total number of inspectorates performing foreign inspections continue to increase, the number of foreign inspections tends to stay flat

## FOREIGN INSPECTIONS AT MANUFACTURING SITES

### Number of foreign inspections at manufacturing sites

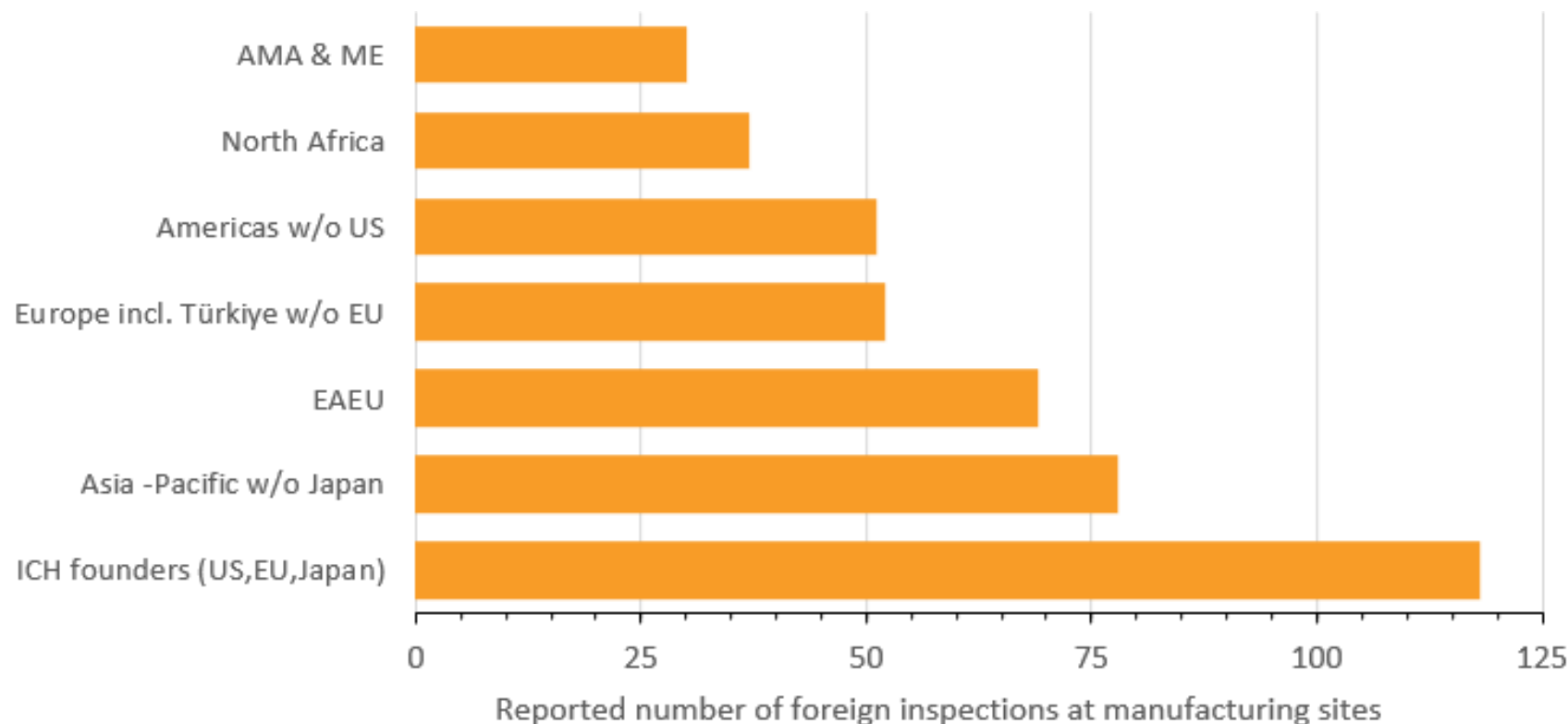
Evolution of number of manufacturing sites versus number of foreign inspections



**\* Number of foreign inspections at manufacturing sites post pandemic is back to the baseline before the pandemic, perhaps slightly decreasing**

## INSPECTION SURVEY - 2024 DATA

### Number of foreign inspections at manufacturing sites by region of the inspectorate

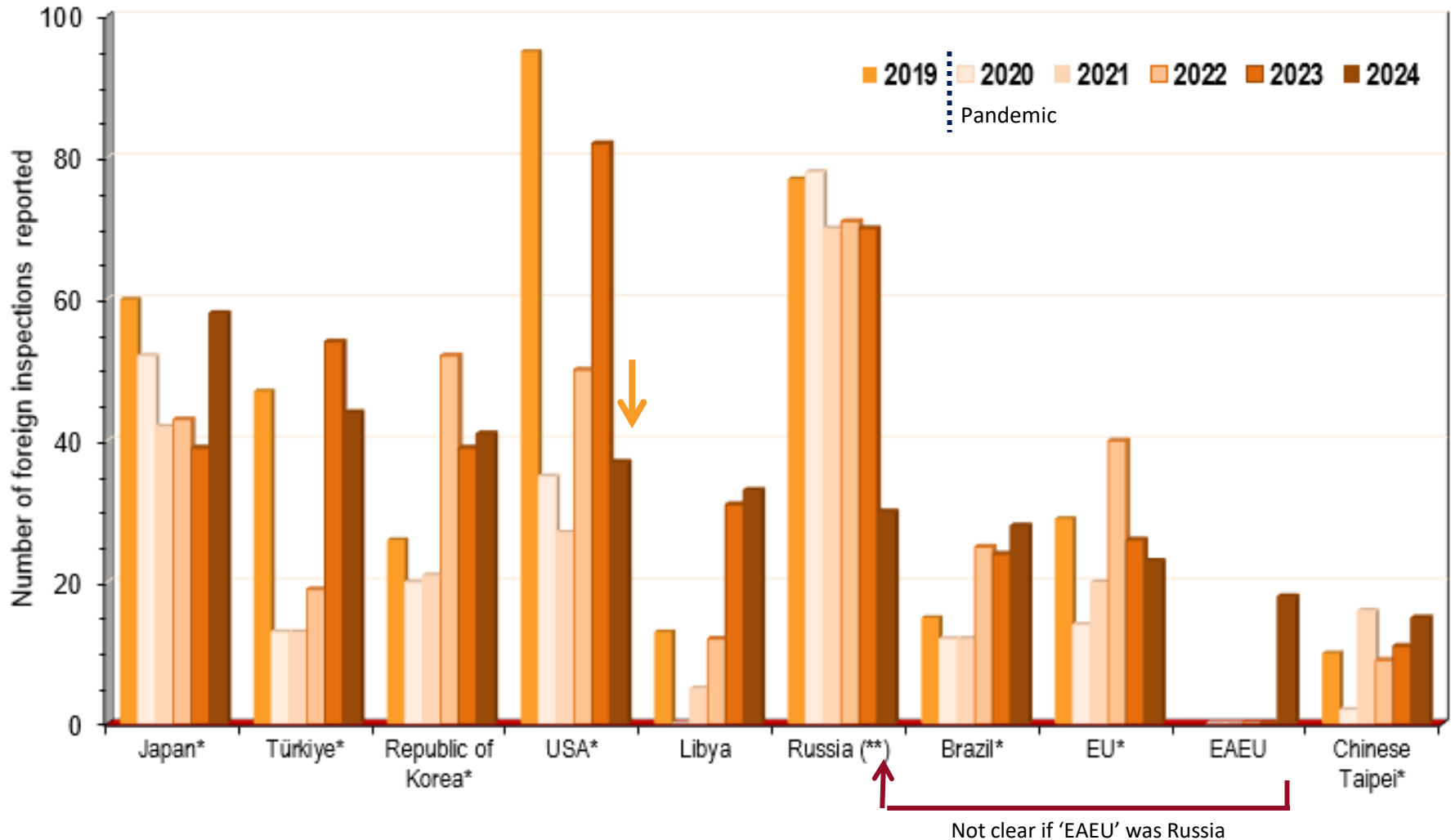


\* mostly driven by Rep. of Korea and Chinese Taipei

AMA & ME; African Medicinal Agency & Middle East, EAEU: Eurasians Economic Union

## FOREIGN INSPECTIONS AT MANUFACTURING SITES 2024

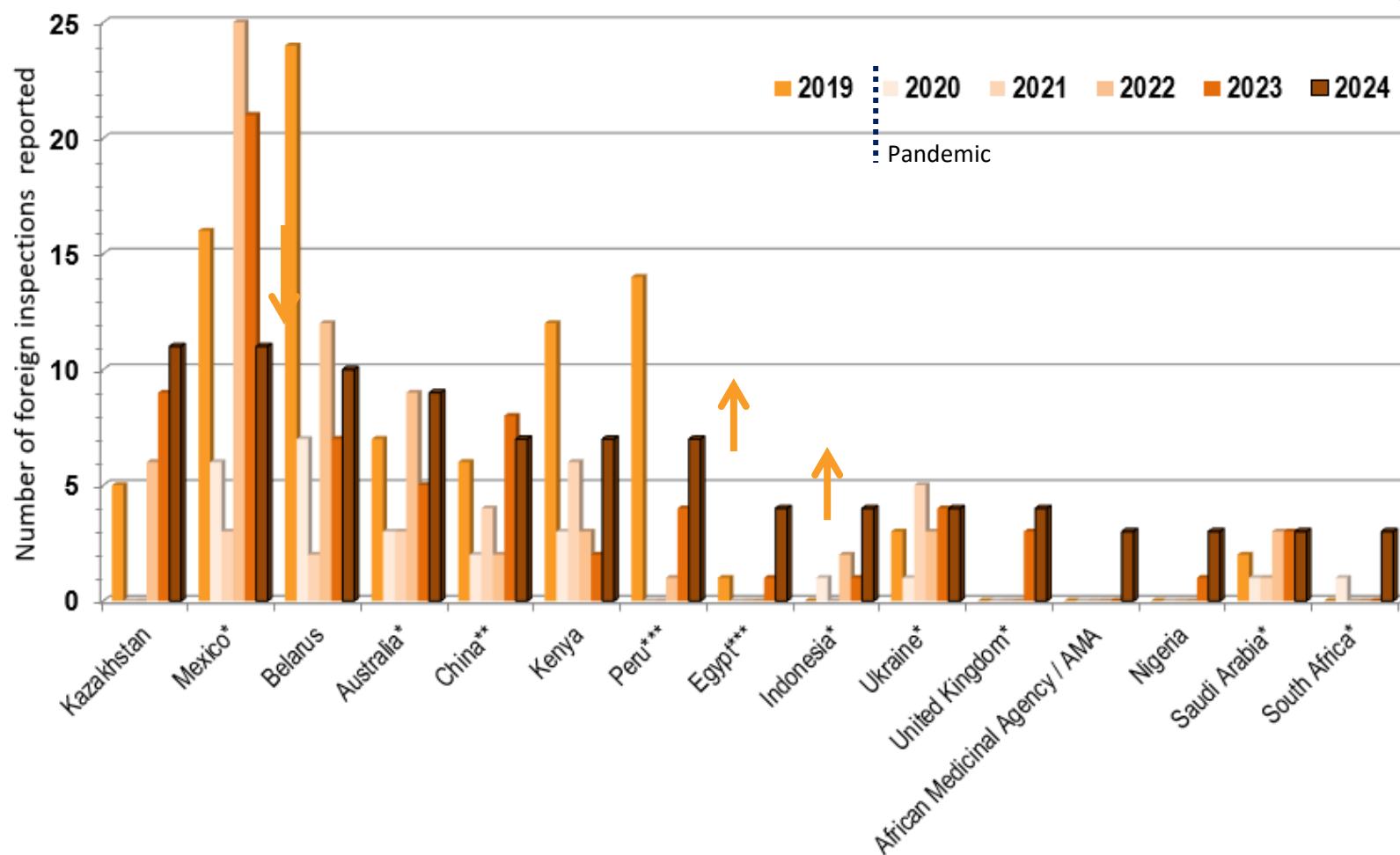
### Number of foreign inspections by country 1/2



\*Inspectorate is a PIC/S member \*\*PIC/S applicant

## FOREIGN INSPECTIONS AT MANUFACTURING SITES 2024

### Number of foreign inspections by country 2/2



\*Inspectorate is a PIC/S member \*\*PIC/S Applicant \*\*\*PIC/S pre-Applicant

# FOREIGN INSPECTIONS AT MANUFACTURING SITES

## Countries performing foreign inspections

\* 82 jurisdictions have performed foreign inspections from 2003 to 2024

\* 38 jurisdictions performed foreign inspections in 2024

Albania	Ethiopia	Mexico*	Switzerland*
<b>African Medicinal Agency<sup>a</sup></b>	EU/EEA <sup>b</sup>	Nepal	Syria
Argentina*	Ghana	New Zealand	Tanzania
Armenia	Gulf States (GCC)	Nigeria	Thailand
Australia*	<b>Guinea<sup>a</sup></b>	Oman	Tukmenistan
Belarus	Honduras	Padua Neu Guinea	Tunisia
<b>Benin<sup>a</sup></b>	Hong Kong China	Pakistan	Türkiye*
Bosnia Herzegovina	Iceland	Panama	Uganda
Botswana	India	Peru***	Ukraine*
Brazil*	Indonesia*	Republic of Korea*	United Arab Emirates
Burundi	Iran*	Russia(**)	United Kingdom*
Cambodia <sup>1</sup>	Iraq	Rwanda	USA*
Canada*	Israel	Saudi Arabia*	Venezuela
Chile***	Ivory Coast	Sierra Leone	Vietnam
China**	Japan*	Singapore*	WHO
Chinese Taipei*	Jordan	South Africa*	Yemen
Colombia	Kazakhstan	Sri Lanka	Zimbabwe
Congo	Kenya	Sudan	
Costa Rica	Lebanese		
EAEU	Libya		
Ecuador	Malawi		
EDQM	Malaysia*		
Egypt***	Malta		

References:

**a new in 2024**

b EU/EEA countries as one inspectorate only

Orange: foreign inspection in 2024

Light blue: active in previous years; no reports in 2024

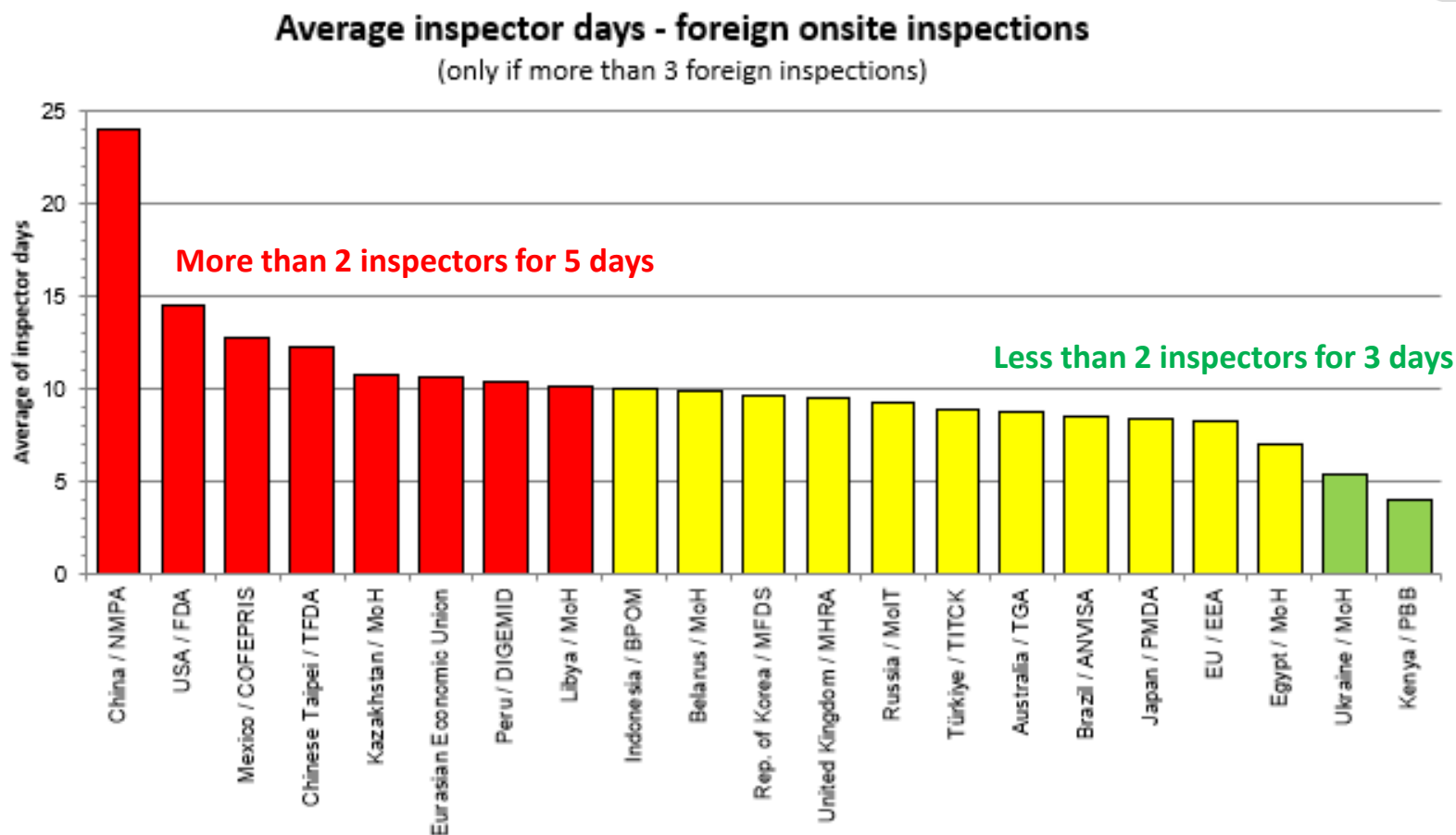
Green: no foreign inspection for the last 5 years

\*Inspectorate is a PIC/S member \*\*PIC/S applicant

\*\*\*PIC/S pre-applicant

## FOREIGN INSPECTIONS AT MANUFACTURING SITES

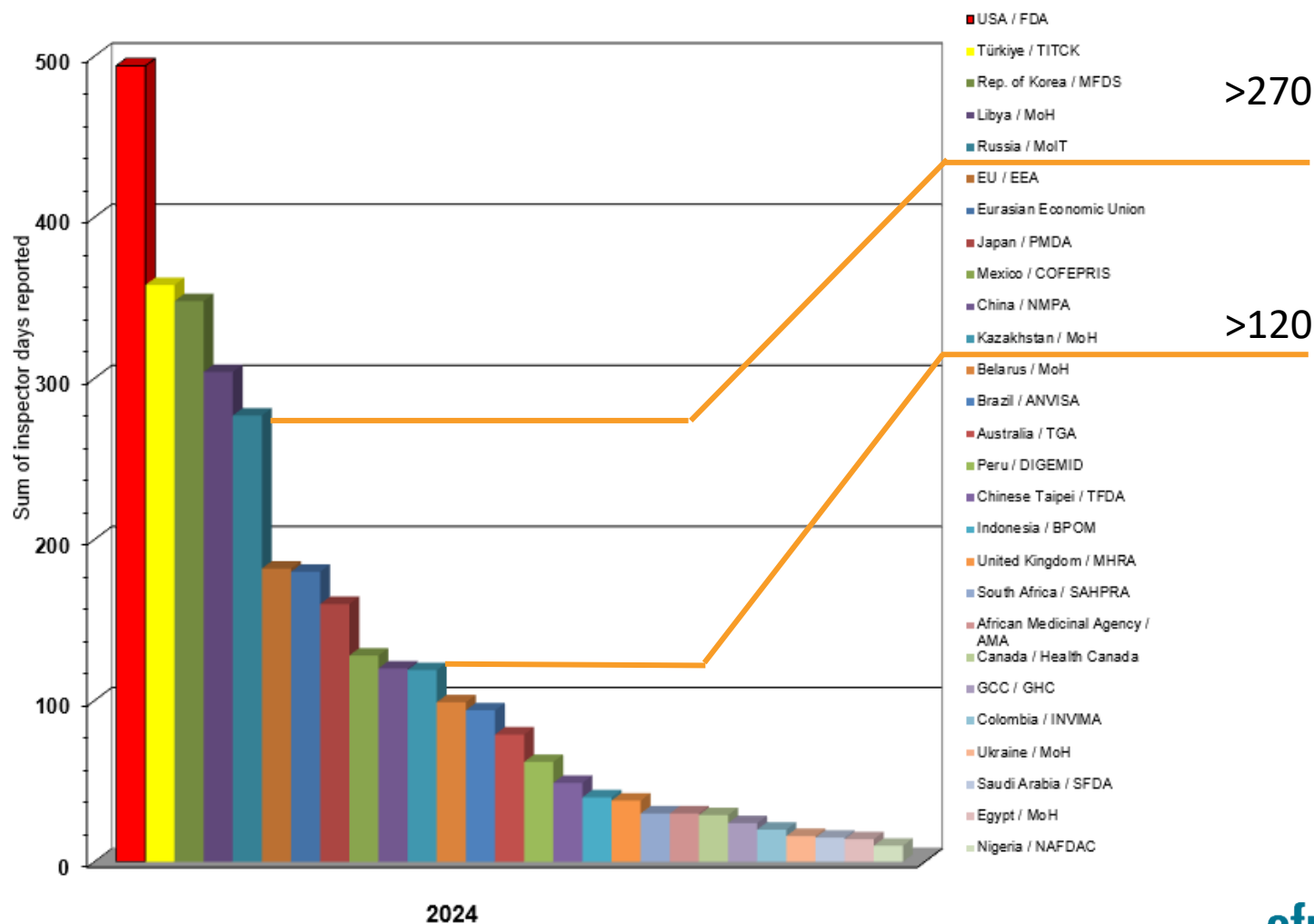
### Average inspector days for foreign inspections at a manufacturing site (onsite only)





## FOREIGN INSPECTIONS AT MANUFACTURING SITES

### Inspector days spent on foreign inspections at manufacturing sites (onsite only)



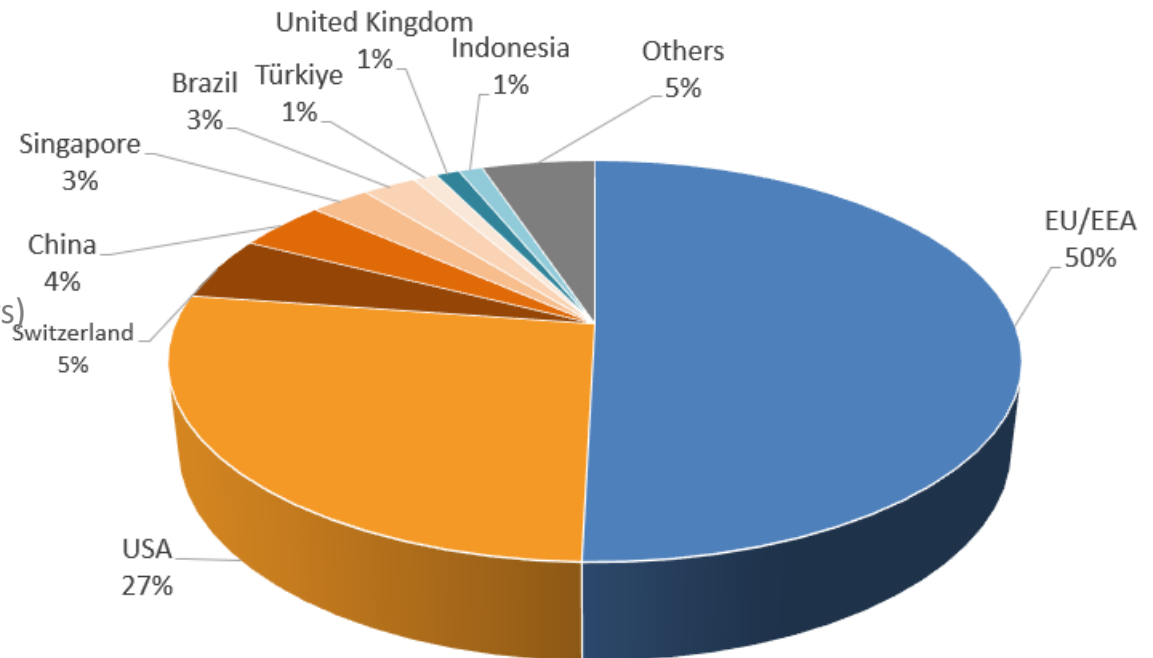
## FOREIGN INSPECTIONS AT MANUFACTURING SITES

### Locations of manufacturing facilities hosting foreign inspections

✱ The location, where conducting foreign inspections, demonstrate that research-based manufacturers are mainly based in

- ✱ EU
- ✱ US
- ✱ Switzerland
- ✱ China
- ✱ Singapore

(no change from previous years)

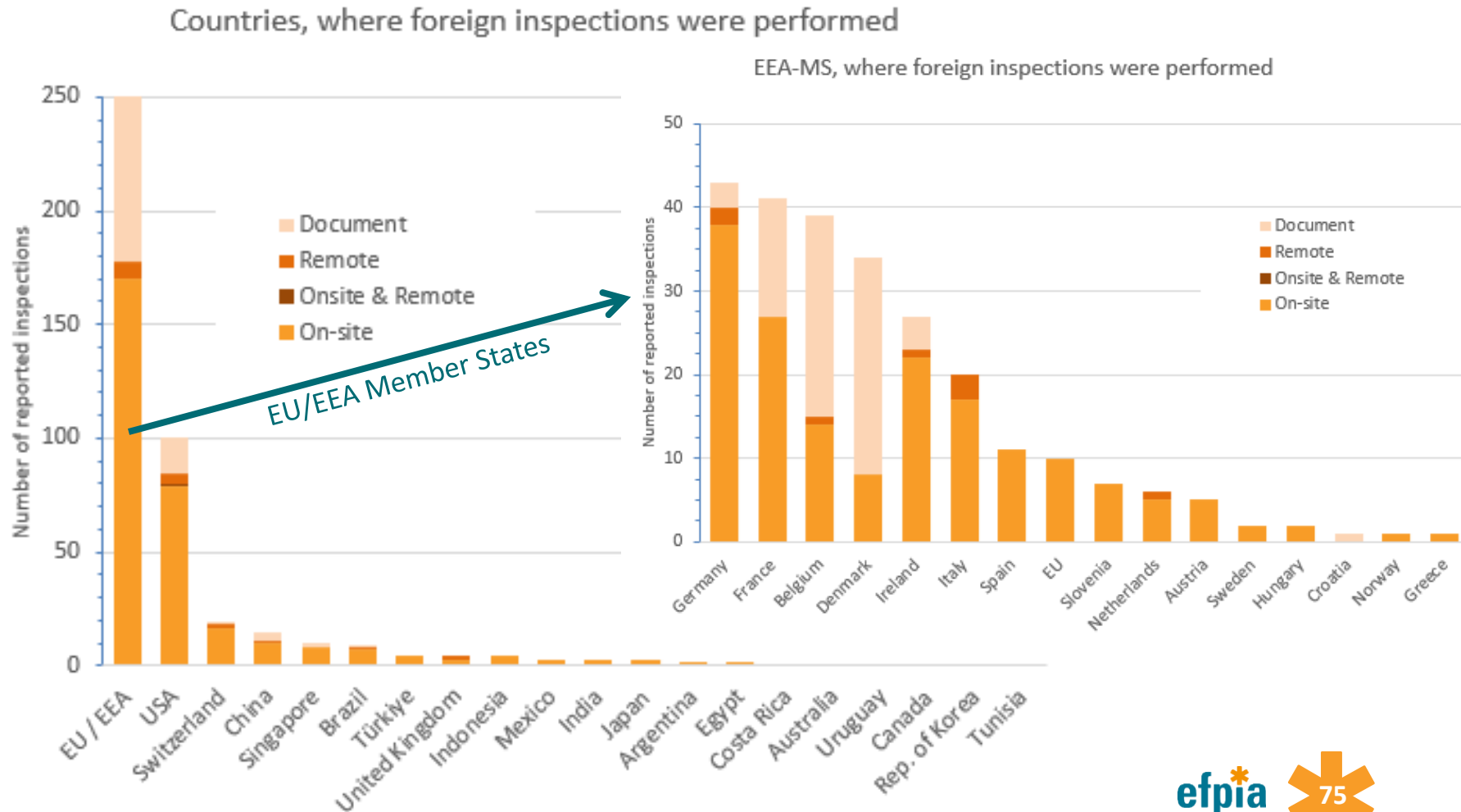


+ 11 other countries with 3 or less inspections

About 80% of the foreign inspections are conducted in EU/EEA, US and Switzerland

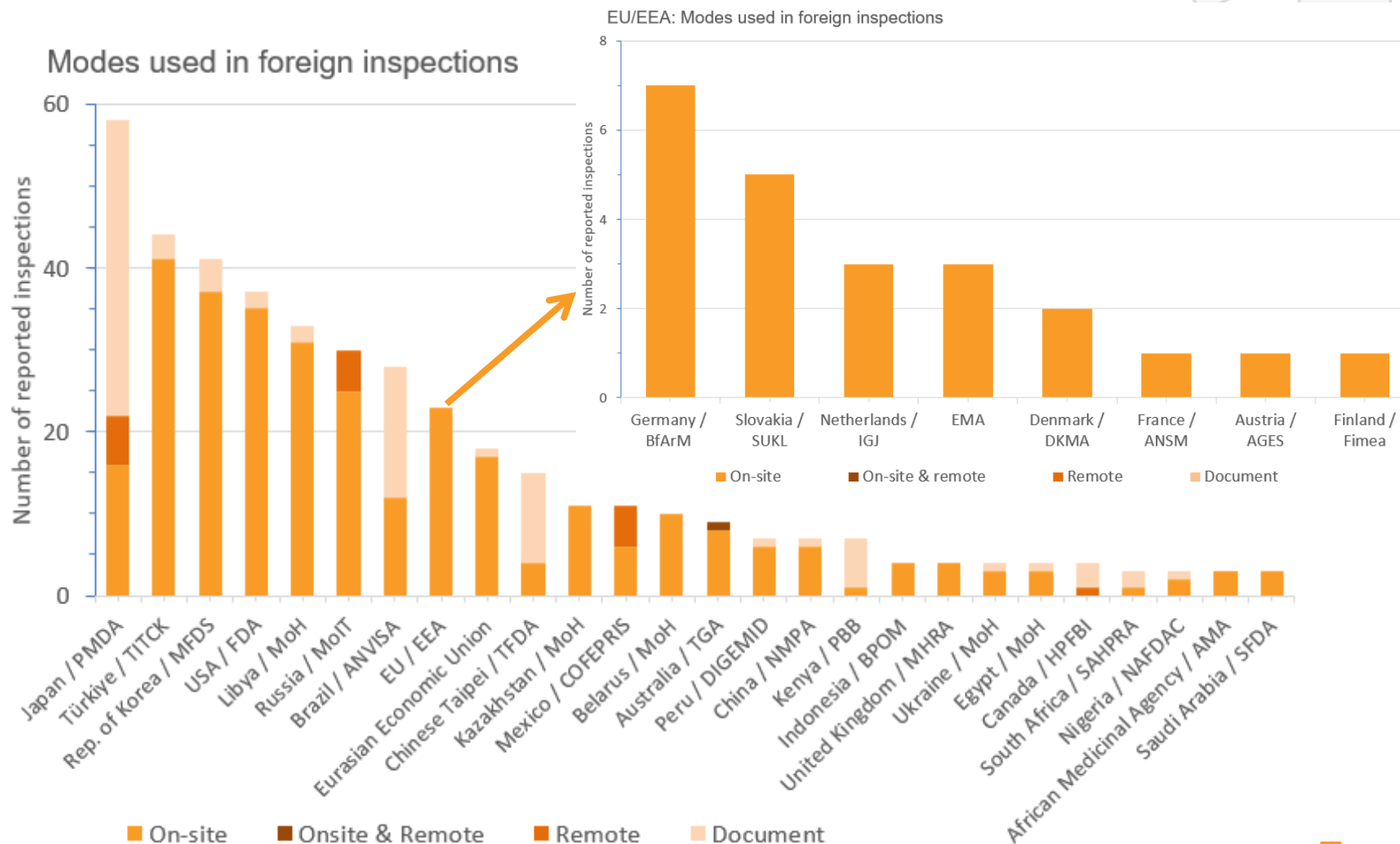
## FOREIGN INSPECTIONS AT MANUFACTURING SITES

### Locations of Manufacturing Sites Hosting Foreign Inspections

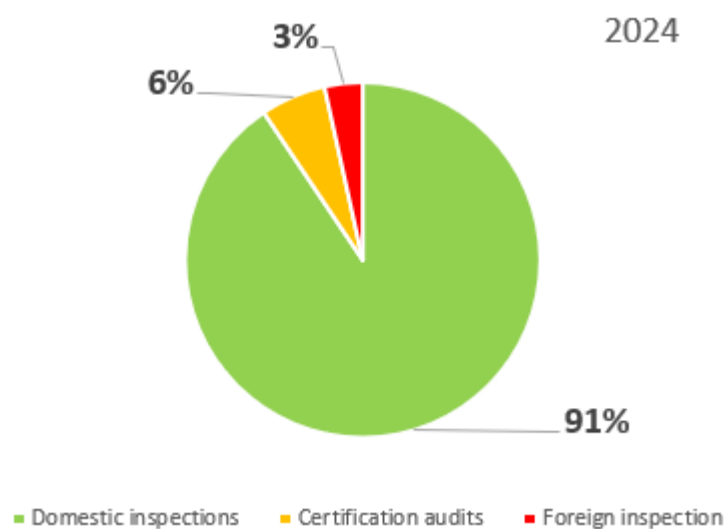


## FOREIGN INSPECTIONS AT MANUFACTURING SITES

### Modes used by inspectorates in foreign inspections

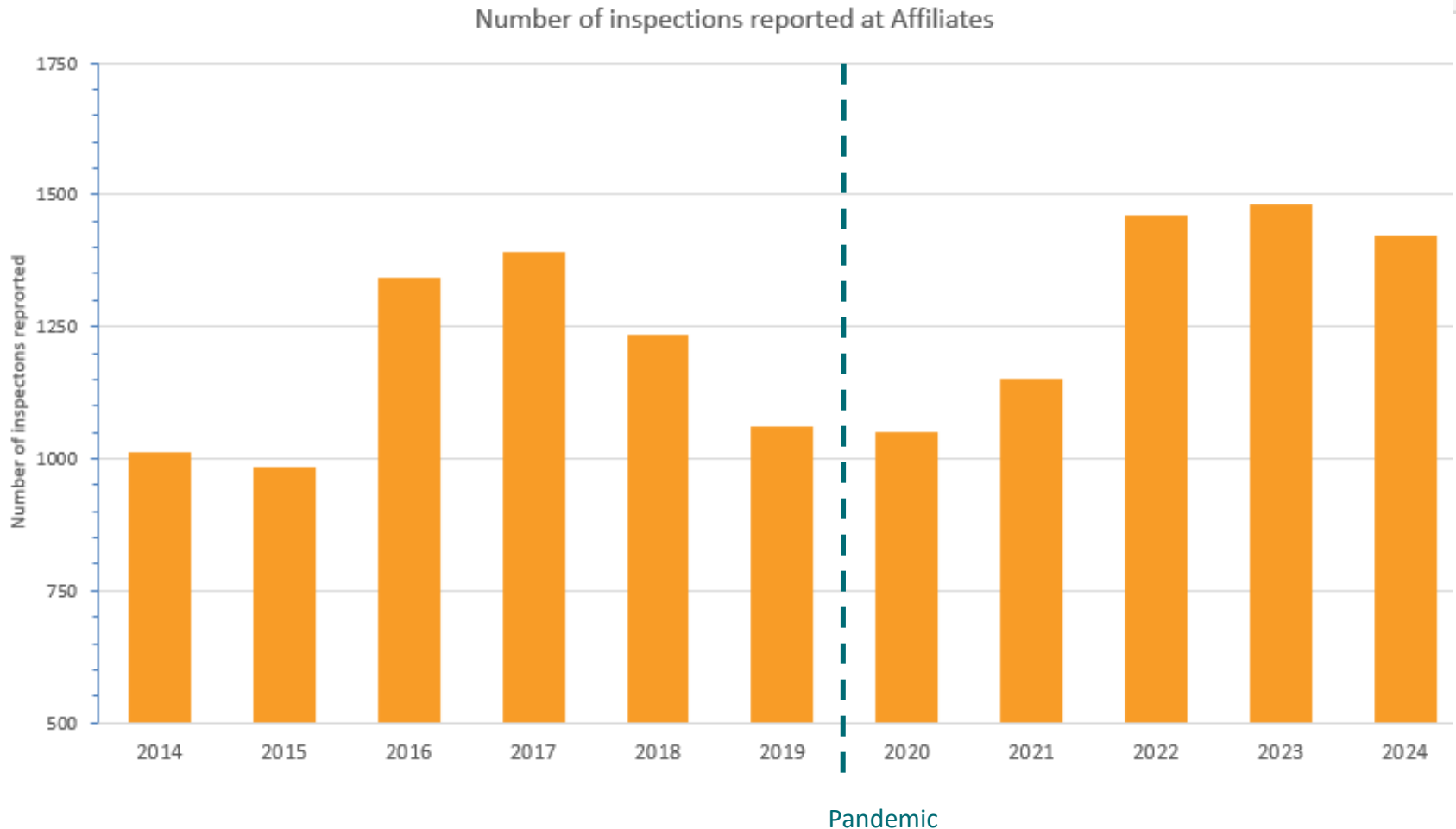


# Inspections at Affiliates



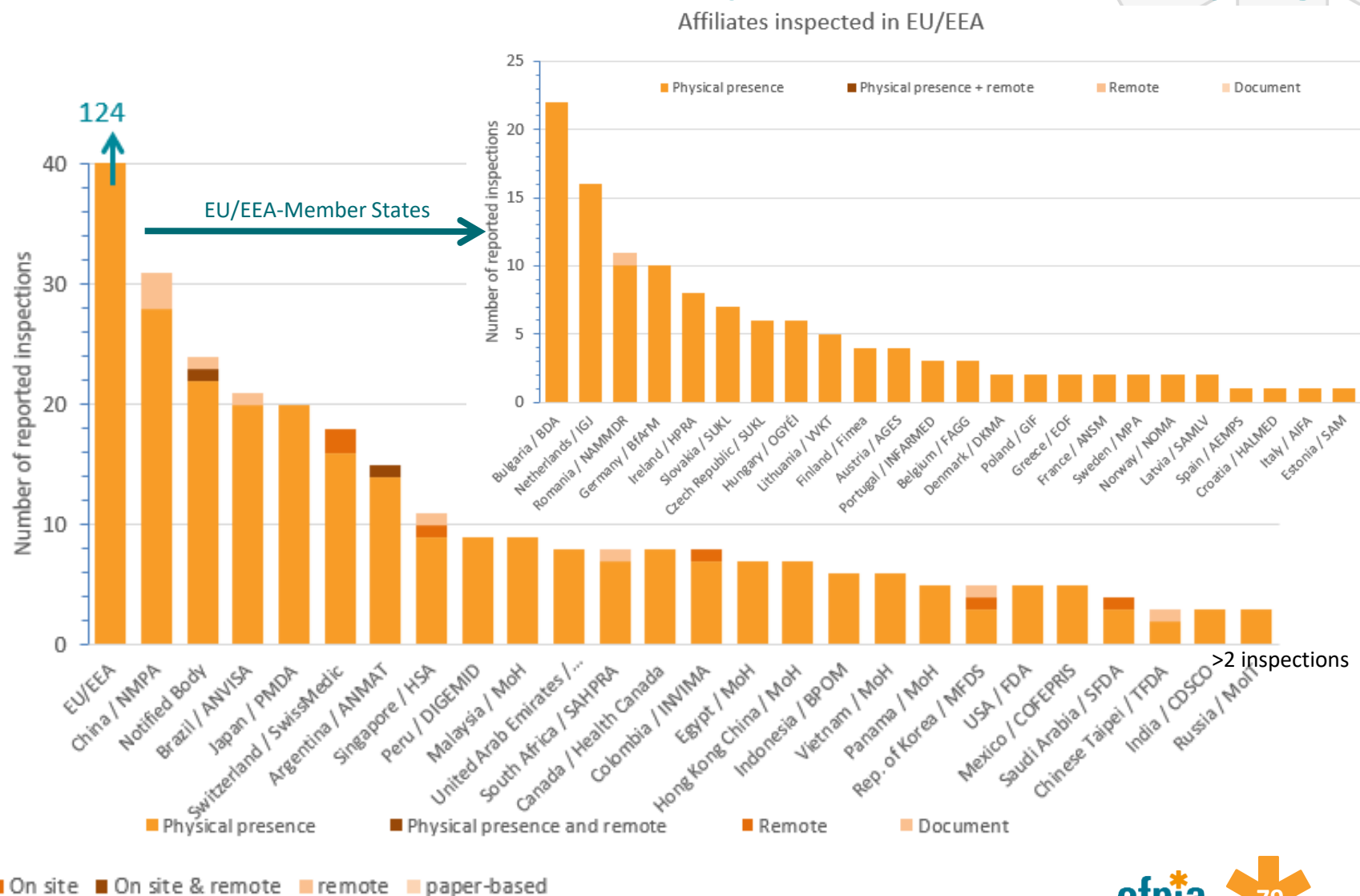
## INSPECTIONS AT AFFILIATES

### Constant level of inspections at affiliates with very limited influence by the pandemic



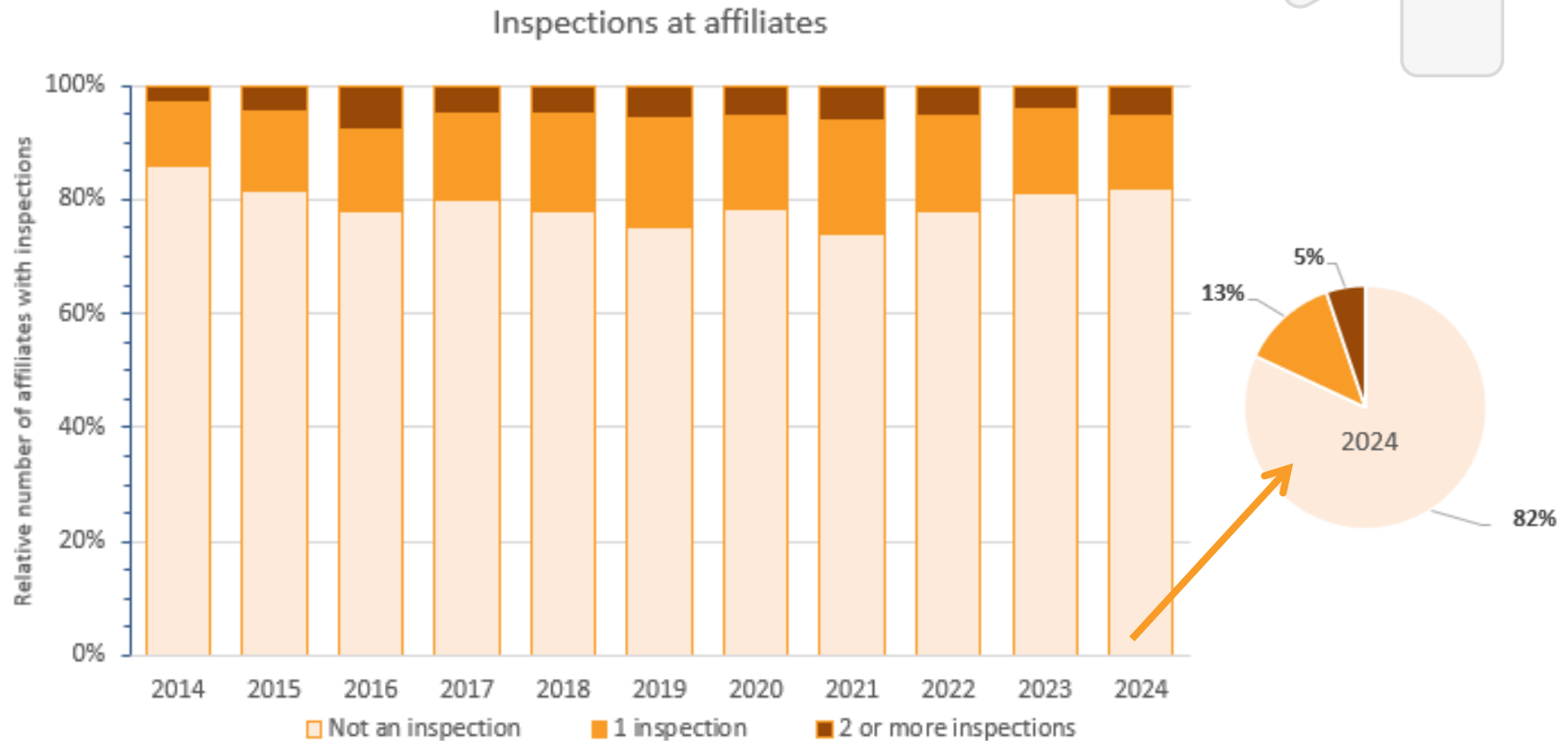
## INSPECTIONS AT AFFILIATES

# Local affiliates have received inspections - no trend by region



## INSPECTIONS AT AFFILIATES

### Number of affiliates inspected



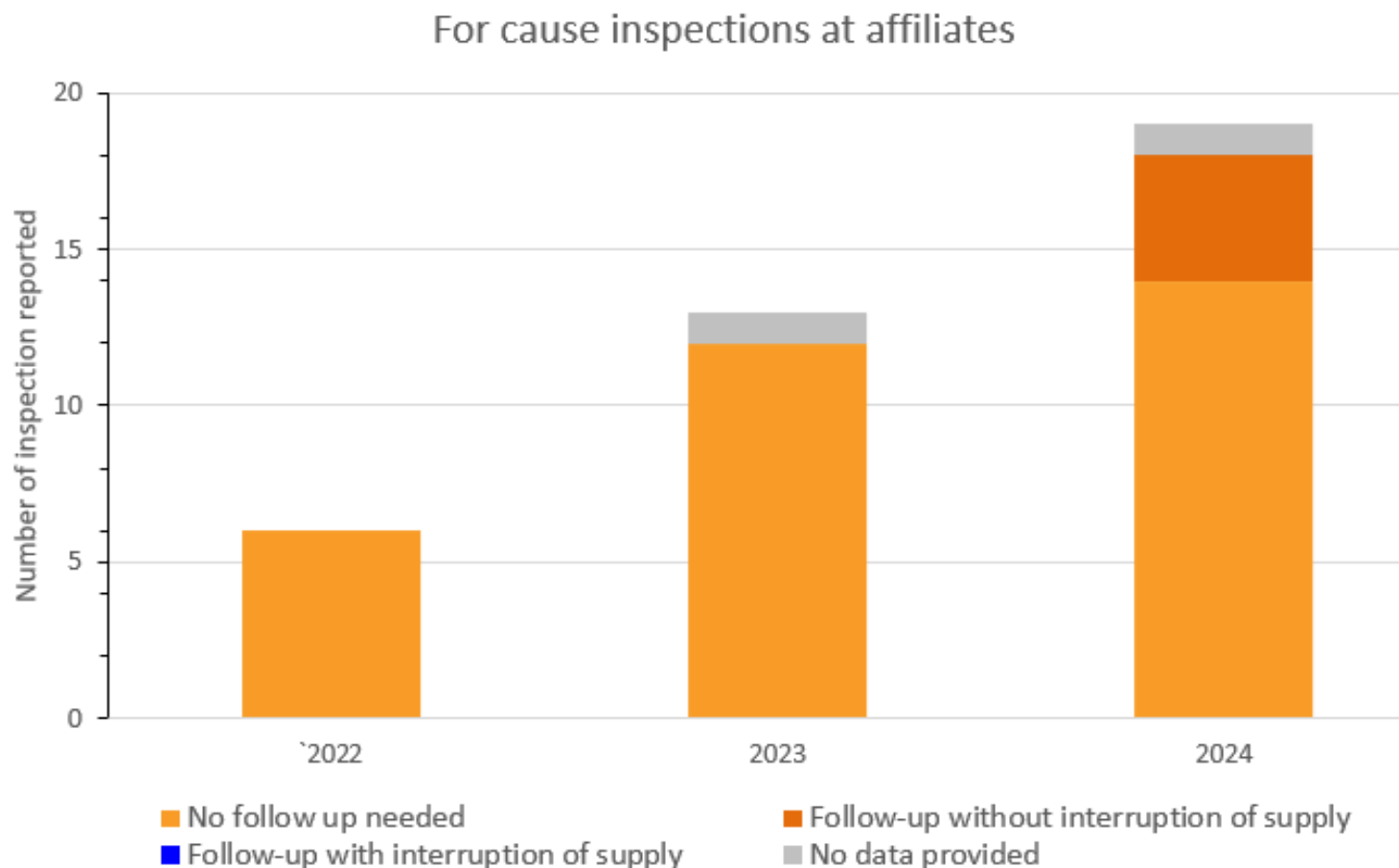
#### \* Facts

- \* Number of oversight constant
- \* 80% without inspections – assumption: inspections every 5 years?



## INSPECTIONS AT AFFILIATES

### For cause inspections do not result in interrupted supply



**\* The number nearly doubled 2022 to 2023 and again to 2024**

# Specific Evaluations

## SPECIFIC EVALUATIONS



# PIC/S

### LEVERAGE TOOLS e.g.,

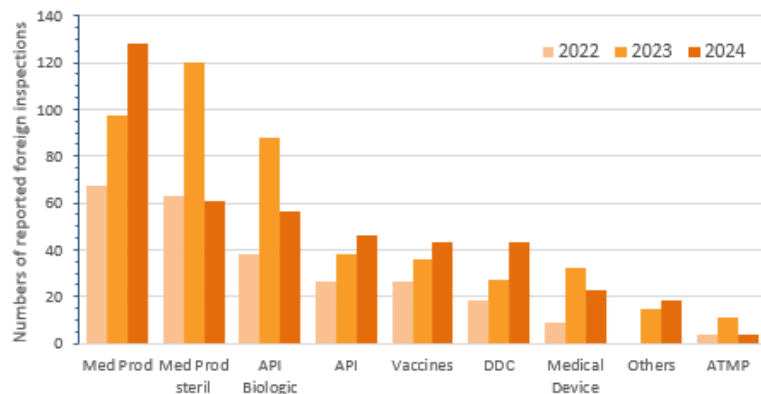
- **Risk-based inspection planning,**  
PIC/S guideline PI 037-1, 1 January 2012
- **GMP-Inspection reliance,**  
PIC/S guideline PI 048-1, 01 June 2018

## SPECIFIC EVALUATIONS – PIC/S

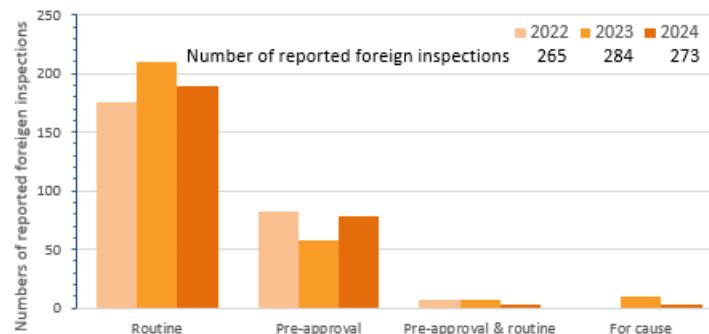
# PIC/S Participating Authorities

1'976  
inspector days used  
(2'500 days in 2023)

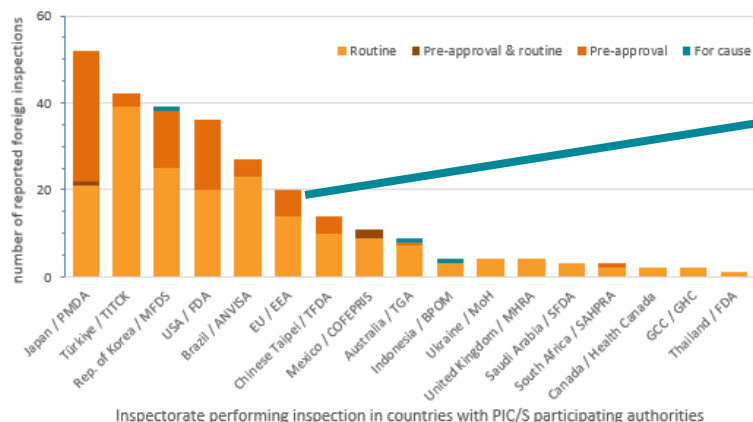
PIC/S participating authority in a PIC/S member country



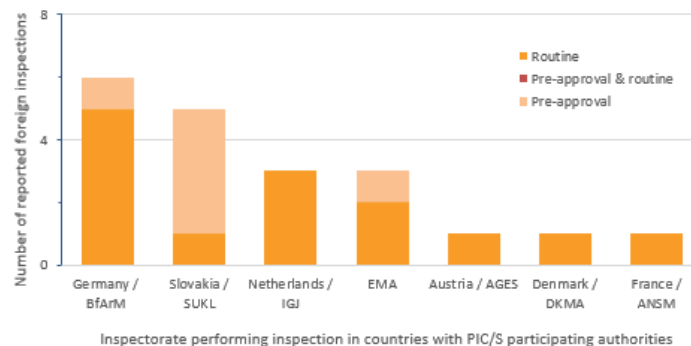
PIC/S participating authority in a PIC/S member country



Foreign inspection between PIC/S participating authorities



Foreign inspection from EU/EEA authorities in PIC/S countries



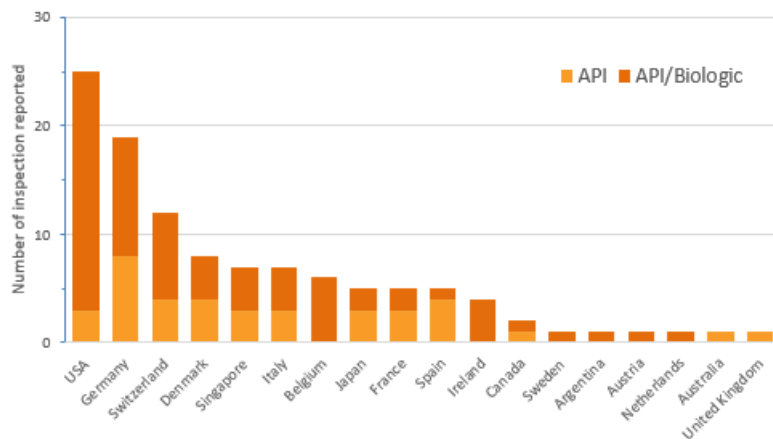
\* 272/434 (2024: 62%; 2023: 62%; 2022: 63%) of the reported foreign inspections at manufacturing sites are amongst the PIC/S participating authorities

## SPECIFIC EVALUATIONS – PIC/S

# API inspections among PIC/S members

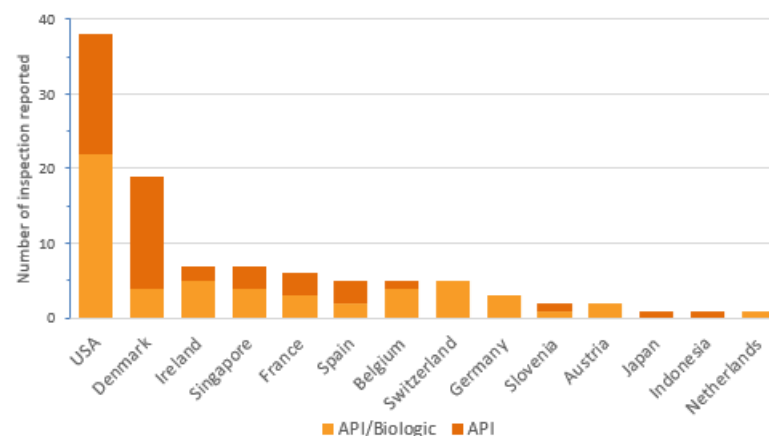
## Domestic oversight by inspectorates

PIC/S member inspectorate performing domestic API inspections

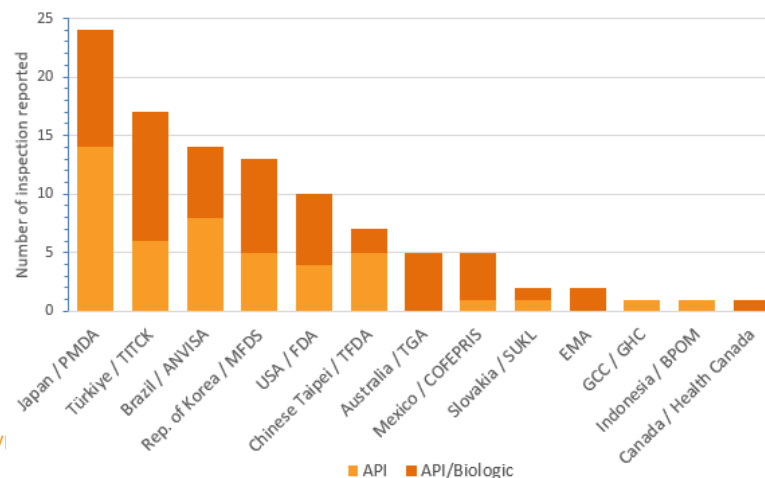


## Sites receiving foreign inspections

Site in countries with a PIC/S participating authority receiving inspections from another PIC/S member participating authority

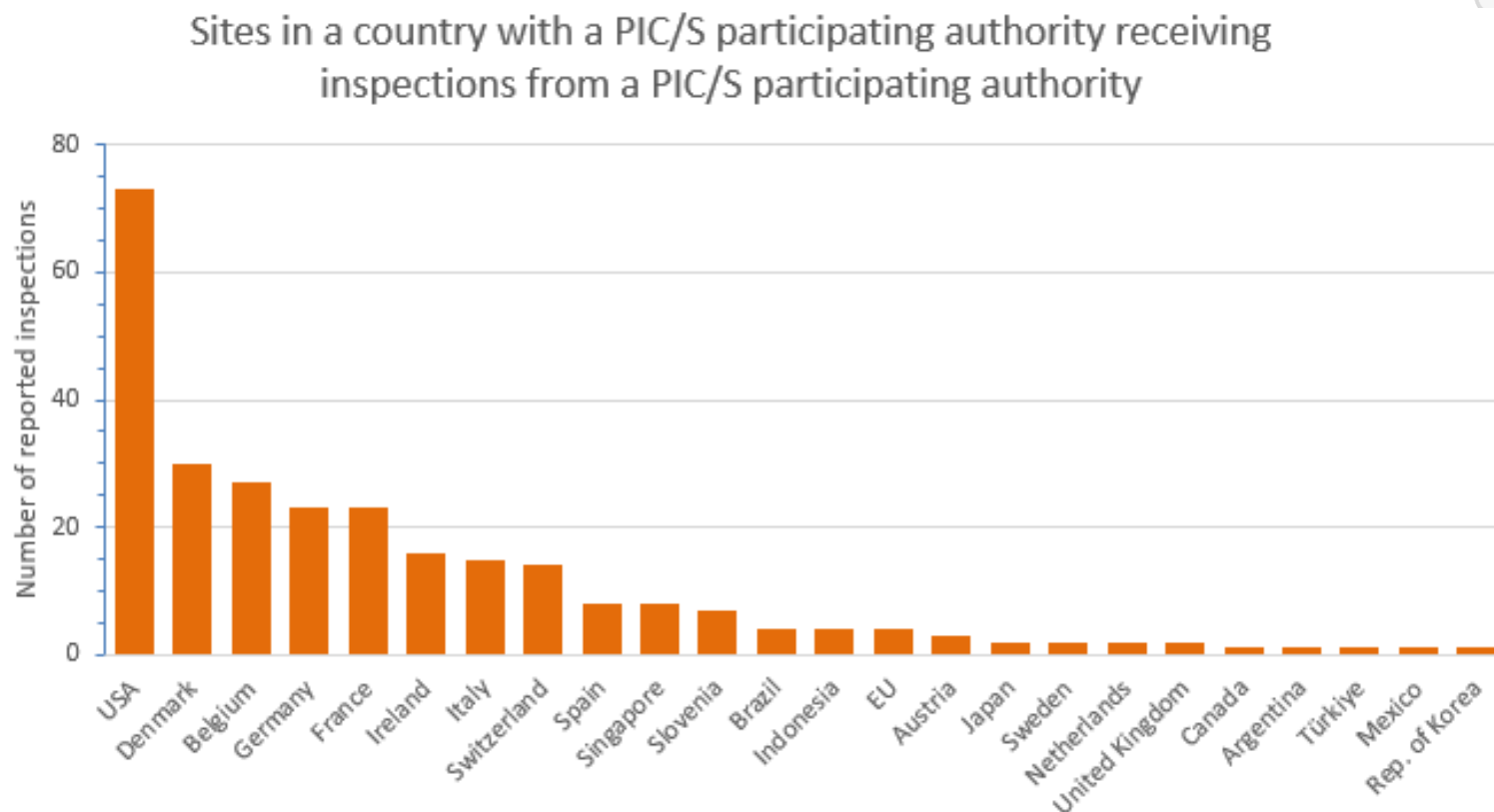


PIC/S inspectorate inspecting in countries with a PIC/S participating authority



## SPECIFIC EVALUATIONS – PIC/S

### Sites in a country with a PIC/S participating authority receiving inspections from a PIC/S participating authority



**\* Countries receiving most often the inspections from PIC/S participation authorities are US, Denmark, Belgium, Germany, France**



## SPECIFIC EVALUATIONS – PIC/S

### Applying reliance?!

**PIC/S inspectorates reported to be domestic active, but no foreign inspections reported**

- \* Argentina / ANMAT
- \* Belgium / FAGG
- \* Greece / EOF
- \* Hungary / OGYÉI
- \* Ireland / HPRA
- \* Italy / AIFA
- \* Norway / NOMA
- \* Poland / GIF
- \* Portugal / INFARMED
- \* Singapore / HSA
- \* Spain / AEMPS
- \* Sweden / MPA
- \* Switzerland / SwissMedic

Note:

This represents the data from our survey. We understand PIC/S is planning to issue further information on PIC/S efforts in the field of reliance soon.

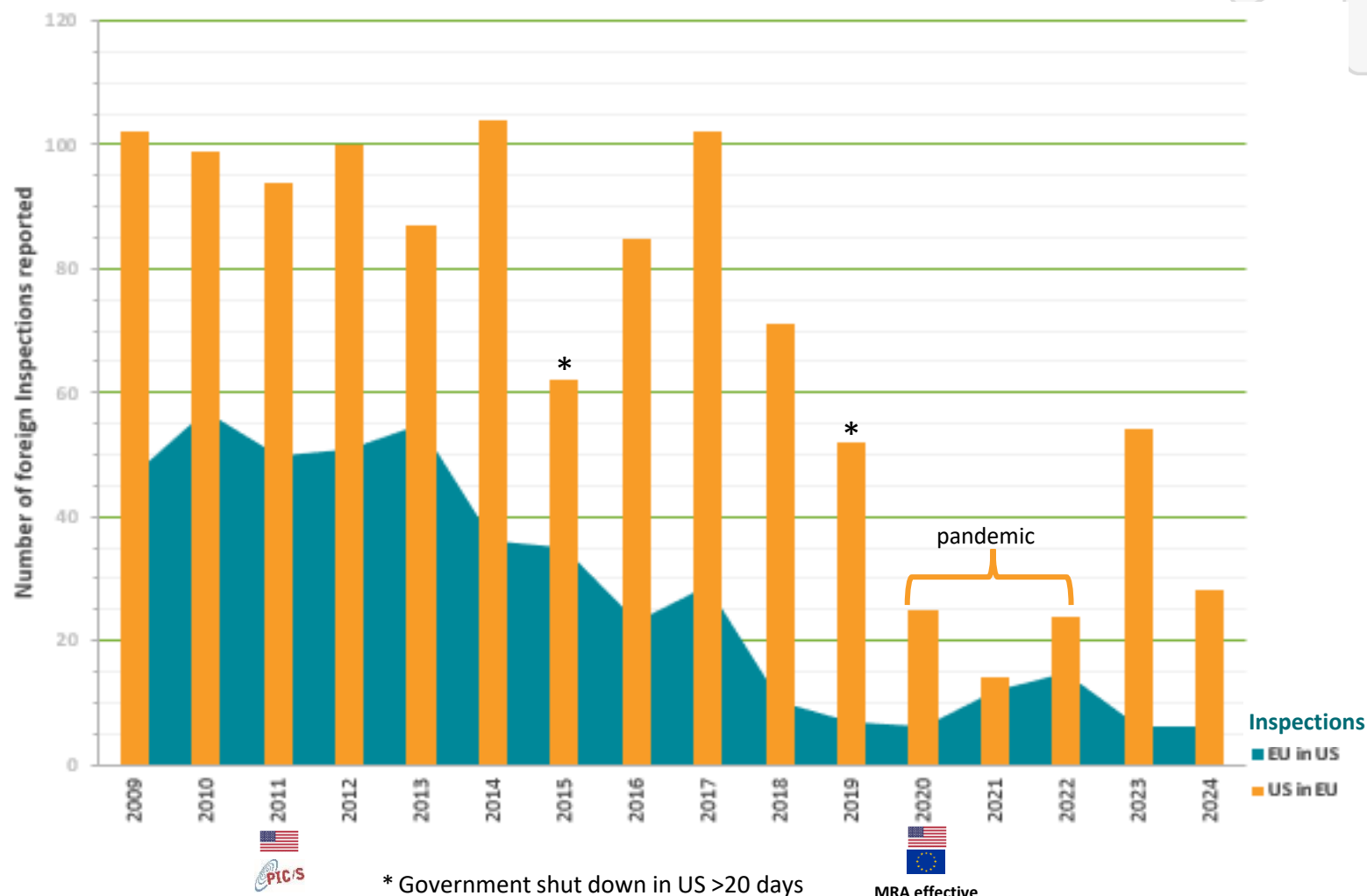
# MRA EU - US





## ANNUAL EFPIA INSPECTION SURVEY – MRA US/EU

Full EU / US MRA implementation could leverage further benefits

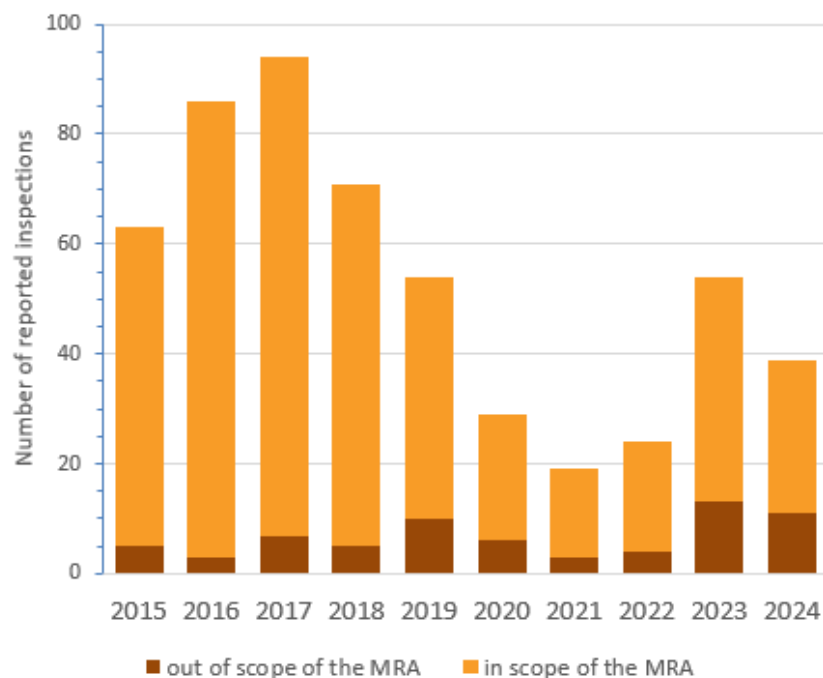




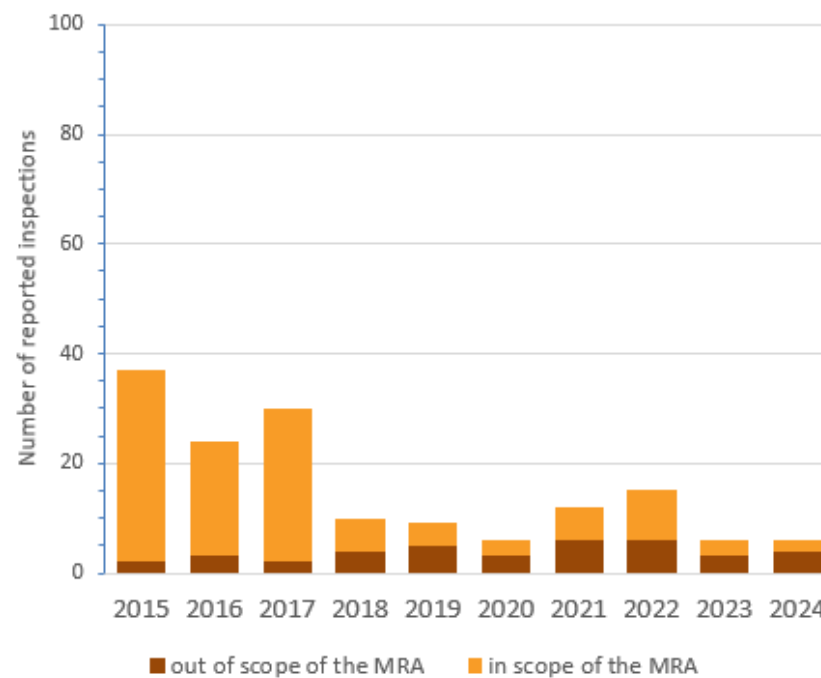
# ANNUAL EFPIA INSPECTION SURVEY – MRA US/EU

## Inspections in each other territory as of scope

Inspections by US-FDA in EU/EEA

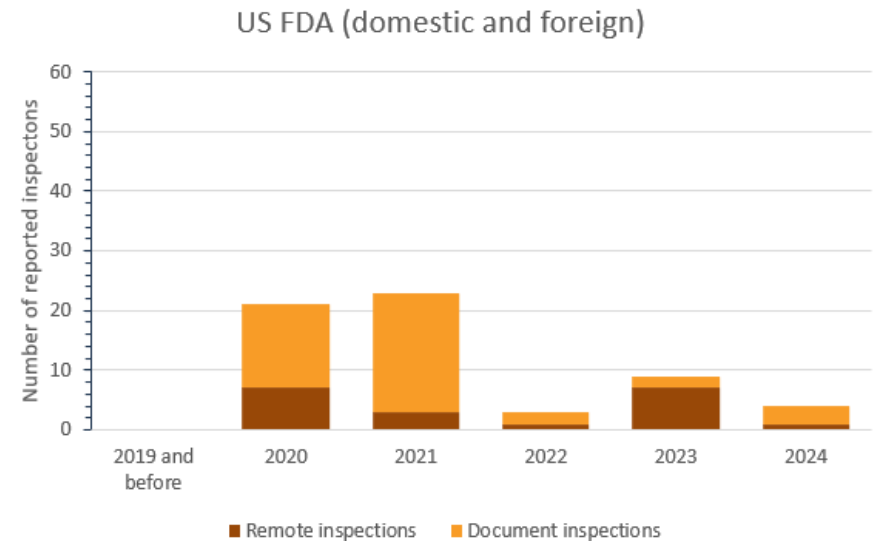
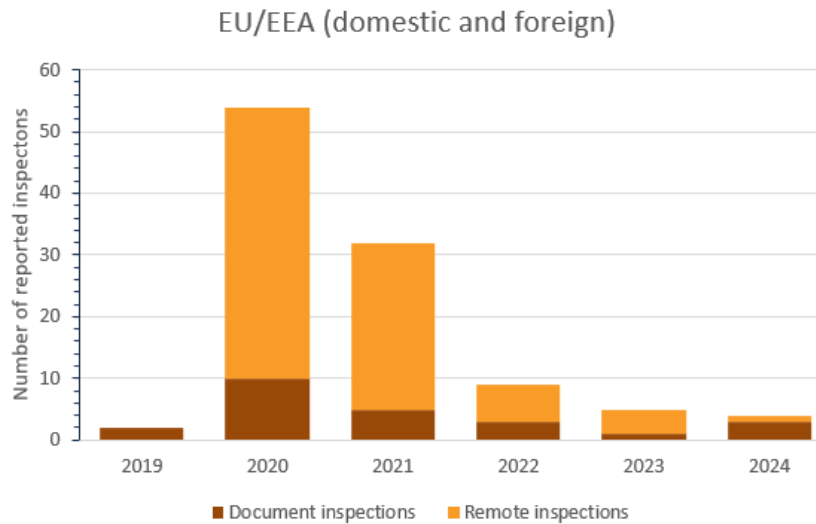


Inspections by EU/EEA inspectorate in US



## INSPECTION ACTIVITY – EU/EEA AND US

### Remote (evaluations) and document inspections

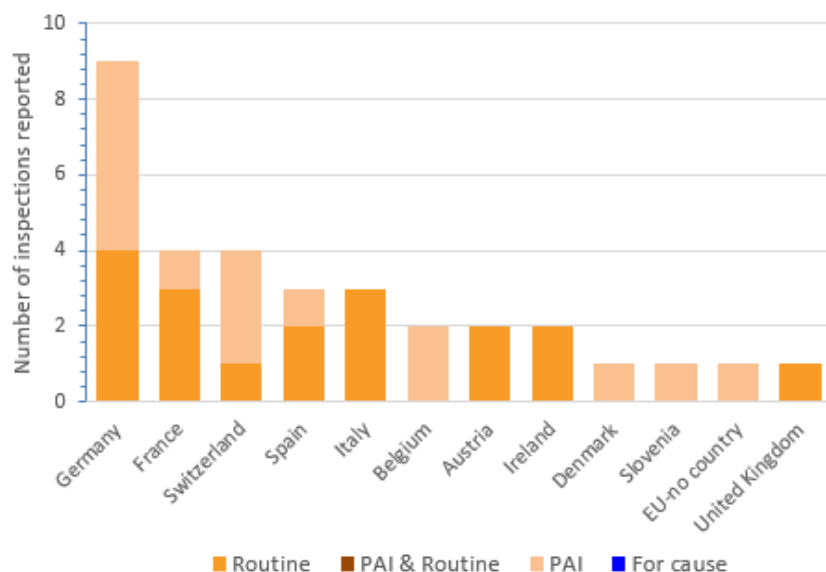


- \* EU/EEA: Trend of less remote inspections year by year after the pandemic
- \* US: No trend but slightly decreasing

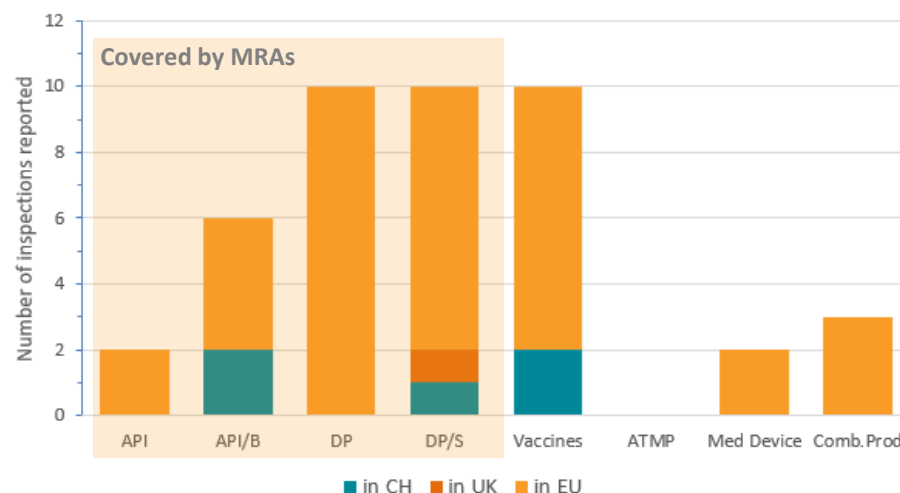
## ANNUAL EFPIA INSPECTION SURVEY – MRAs OF US

# Full MRA implementation could leverage further benefits

Inspections by US FDA in an MRA country  
EU/EEA, CH, UK



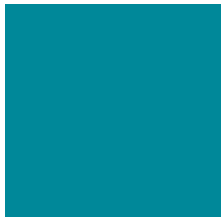
Inspections from US in MRA countries by product type



✱ 11 out of 28 inspections from the US in EU had been reported to be for vaccines, combination products or ATMP



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