European Federation of Pharmaceutical Industries and Associations

Annual Regulatory GMP/GDP Inspection Survey 2024 Data

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Summary

Public version

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.

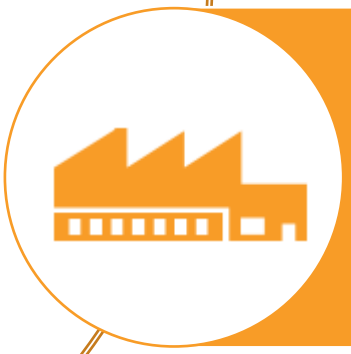
Outcome of the data*1

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



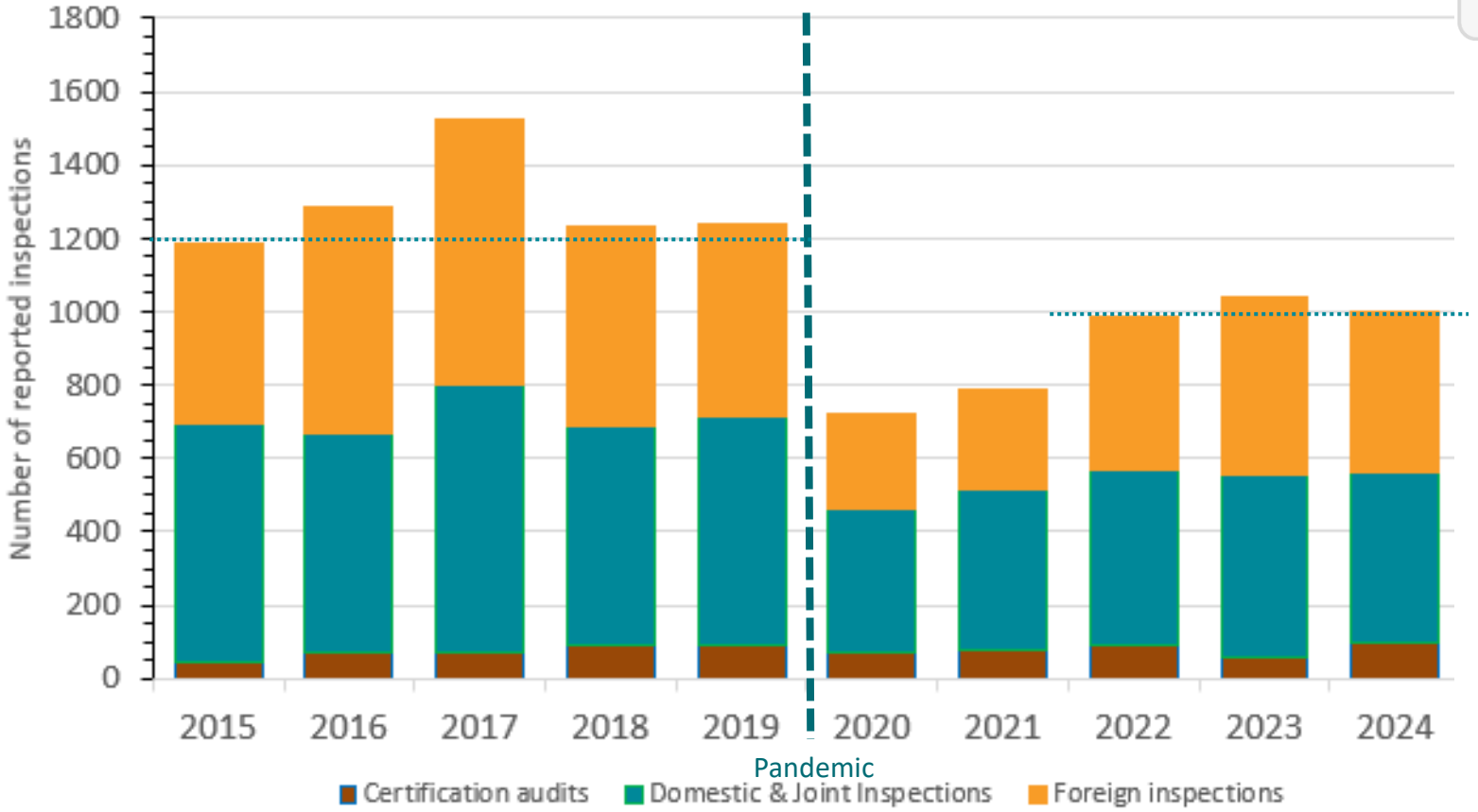
At Manufacturing sites

- 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*3
- Other regions increase foreign inspections*4
- Amongst PIC/S members there is less travel

*1 Provided by 27 global research-based pharmaceutical companies and two National Trade Associations
*2 Opportunities for a better risk-based approaches on inspections by Japan, Türkiye, Rep. of Korea, USA, Libya, Russia/EAEU and Brazil.
*3 US FDA 50% less in comparison to 2023 and before the pandemic
*4 e.g. Rep. of Korea, Chinese Taipei, and EAEU

For cause inspection is an inspection, which is triggered by a concern (e.g. complaint, recall, suspected violation of regulation, fraud)

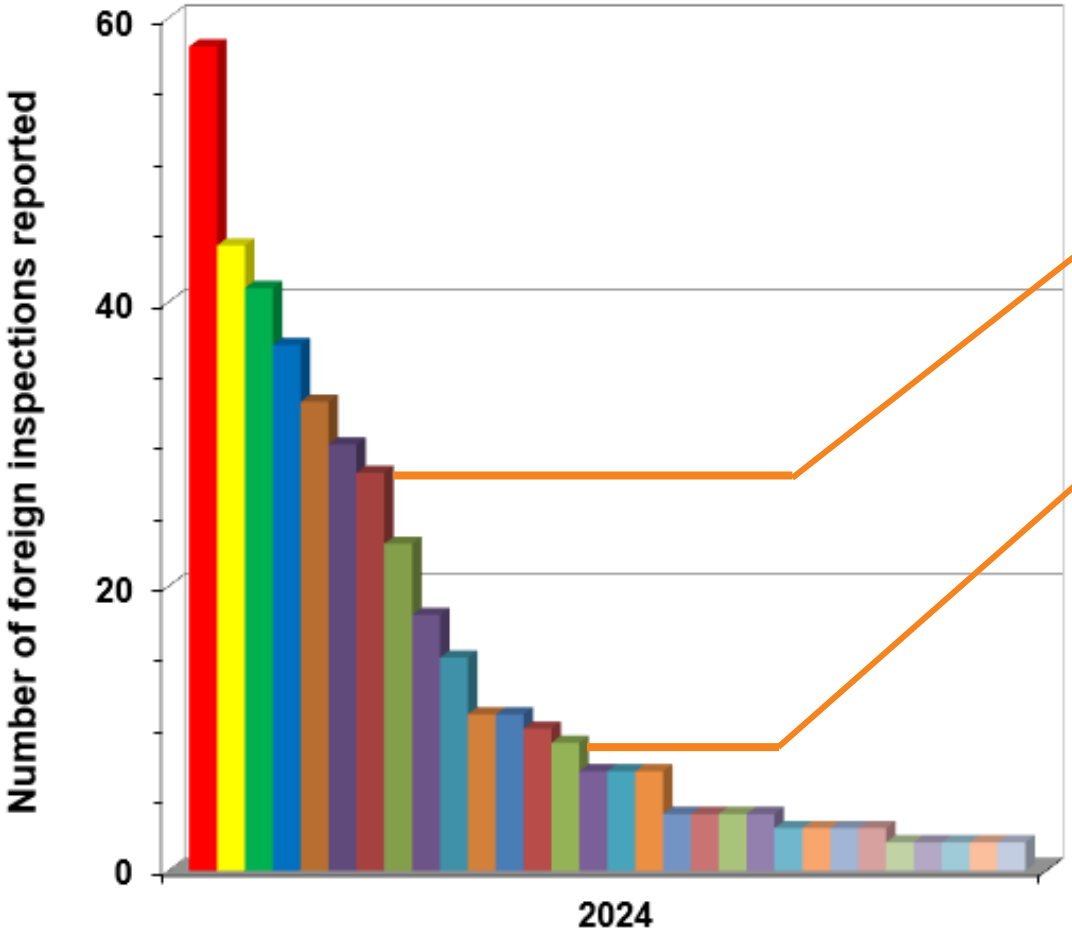
Had the pandemic a long-term positive impact on reliance?



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

Number of foreign inspections at manufacturing sites

(EU as one entity; all inspection types and modes)



Performed by

- Japan* [same level as last years]
- Türkiye*
- Republic of Korea*
- USA*
- Libya
- Russia (**)
- Brazil*
- EU*
- EAEU
- Chinese Taipei*
- Kazakhstan
- Mexico*
- Belarus
- Australia*
- China**
- Kenya
- Peru***
- Egypt***
- Indonesia*
- Ukraine*
- United Kingdom*
- African Medicinal Agency / AMA
- Nigeria
- Saudi Arabia*
- South Africa*
- Canada*
- Colombia
- Gulf States (GCC)
- Tansania
- Uganda

> 28

≥ 9

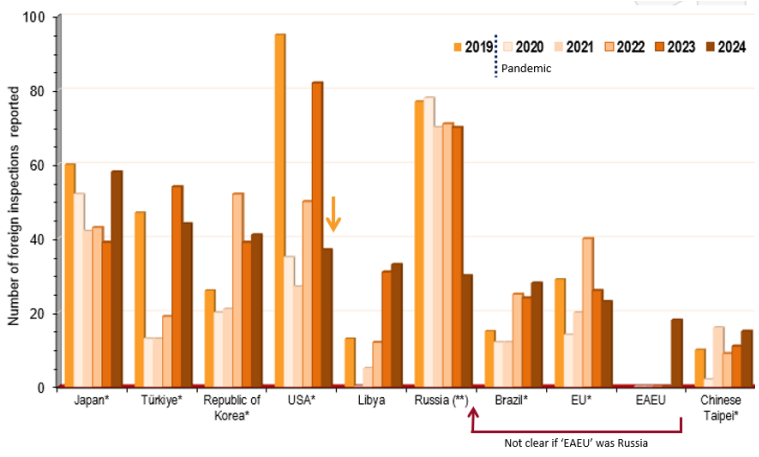
+ 9 countries with one foreign inspection

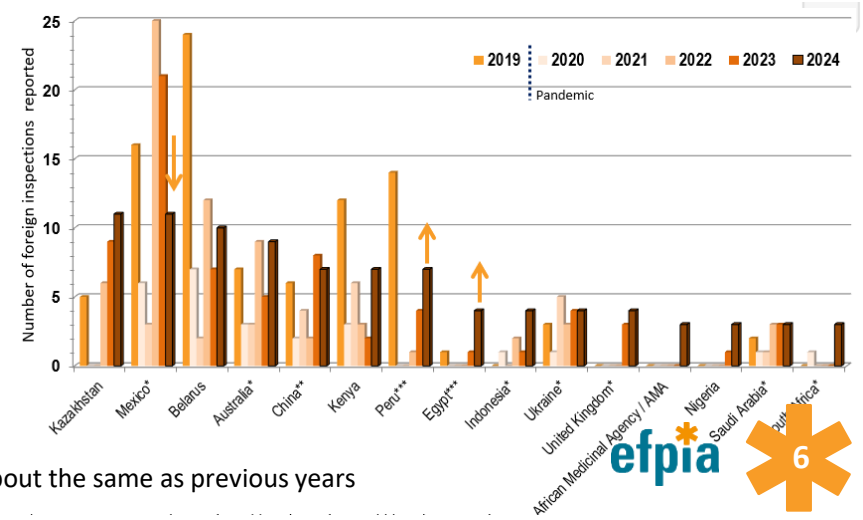
*Inspectorate is a PIC/S participating authority **PIC/S Applicant ***PIC/S Pre-Applicant

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

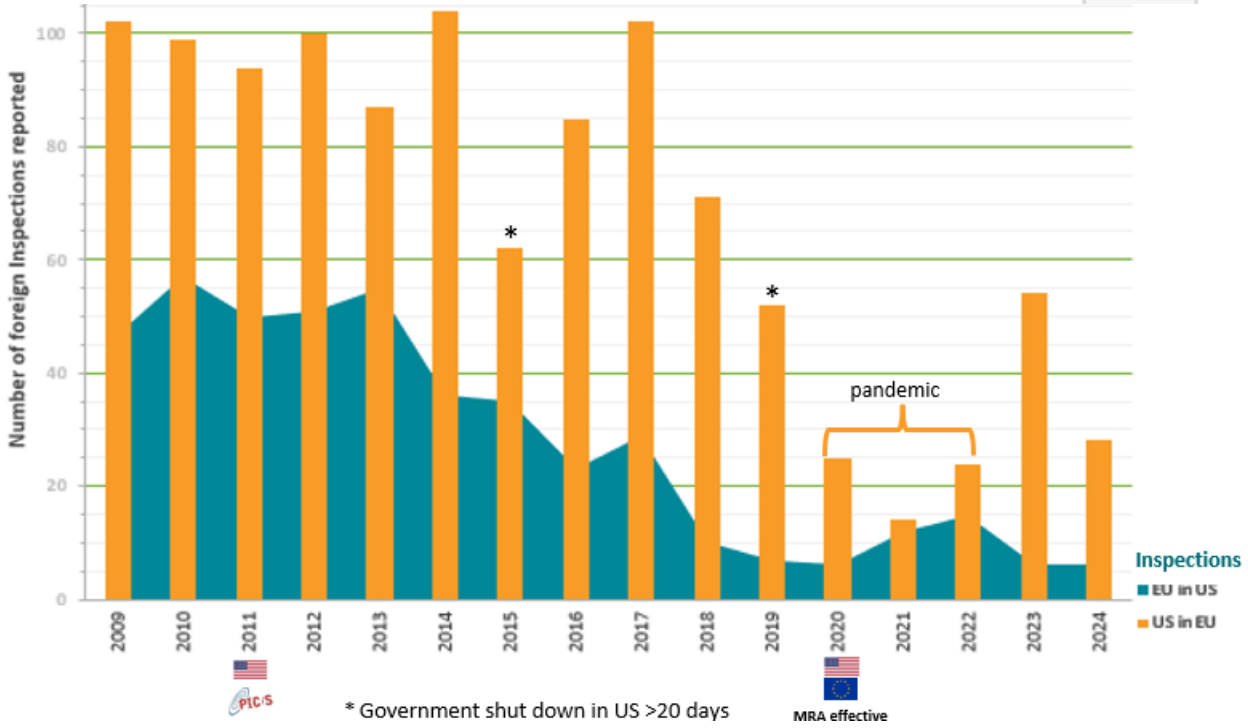




*Russia + EAEU is about the same as previous years

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)

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

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

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

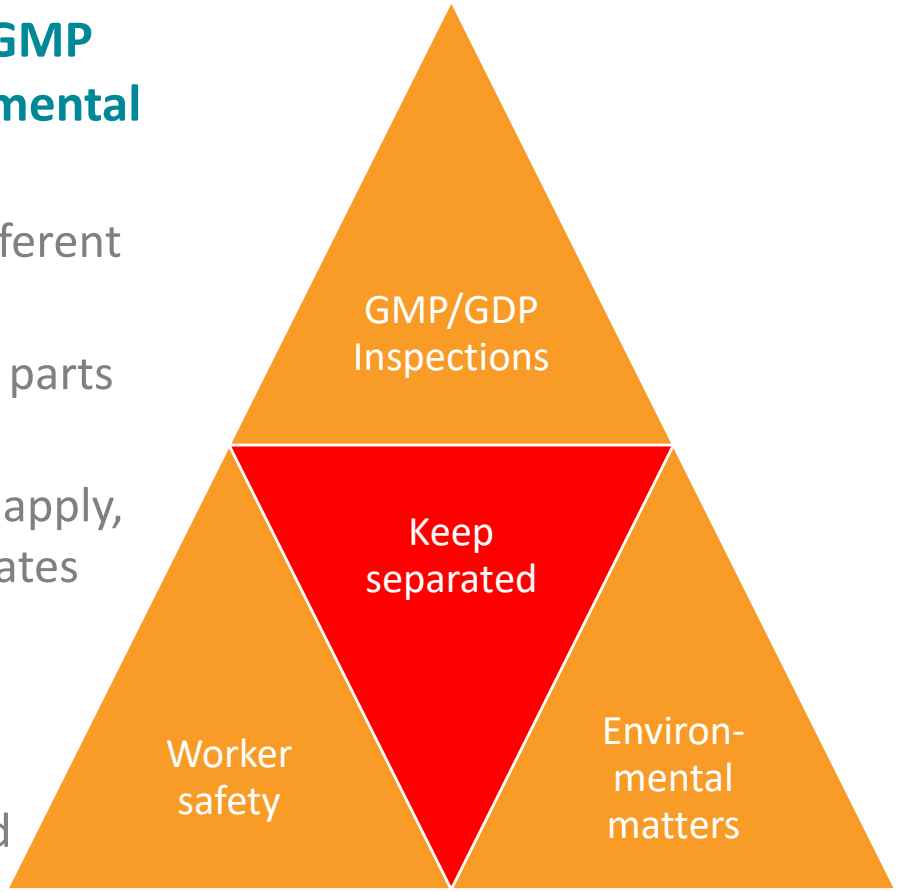
- **Locations of manufacturing facilities reporting PAI demonstrating where innovative products are manufactured – EU again number one – far leading**
  - MS where new, innovative products are manufactured include Denmark, then Germany, Belgium, Slovenia, Italy, Ireland, and France

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

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

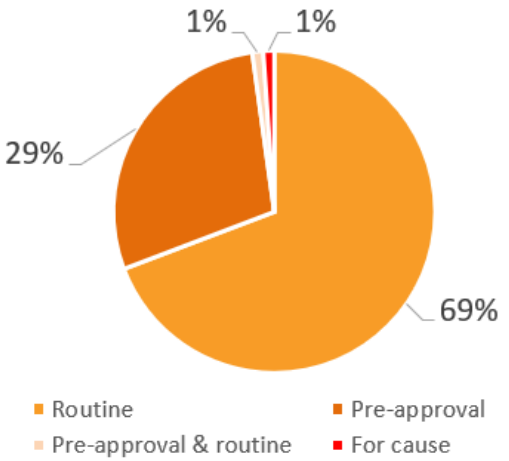
- **The industry recommend keeping GMP inspections separate from environmental and worker safety inspections**
  - Patients, environment, staff are different stakeholders
  - Managed by different authorities / parts of the government
  - Different legislation and standards apply, not harmonized across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



Separate certificates by the different agencies

PIC/S Participating Authorities in a country, where the inspectorate is also a PIC/S participating authority – no change, still high

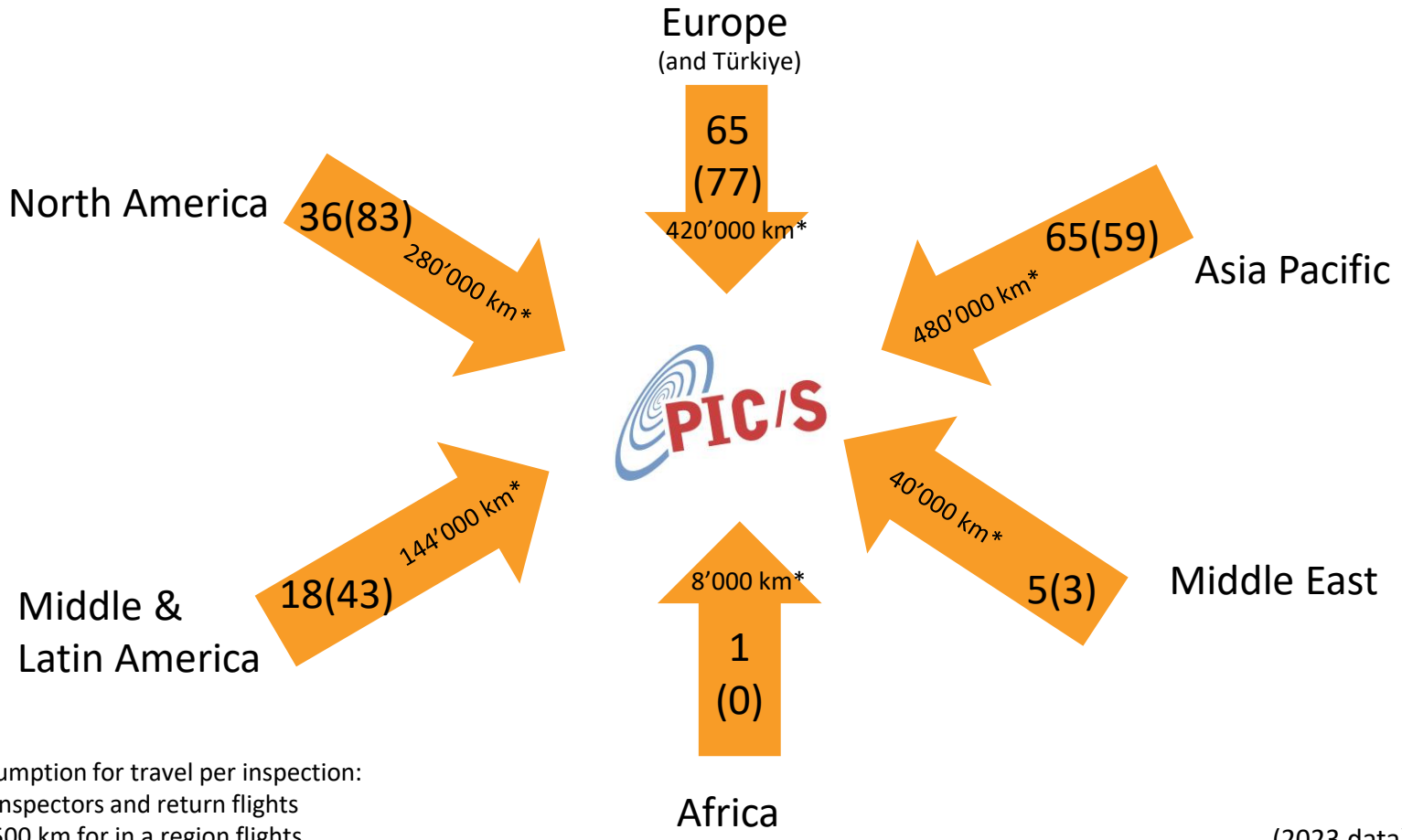
- **With 62% of the reported over all foreign inspections where inspectorates and sites belong to PIC/S countries remains constant high (2023: 62%; 2022: 63%)**
  - Japan, Türkiye, Republic of Korea, USA, Brazil and EU (Germany, Slovakia, Netherlands)
  - No shift in reasons for these inspections i.e., routine, PAI or 'for cause'
  - Reduced CO_2 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)**



Reducing environmental footprint by reliance on PIC/S

≈ 1’400’000 km/y* ≈ 21’000’000 kg CO_2

(1’900’000 km/y* ≈ 26’000’000 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_2 / flight km

Switzerland: Bundesamt für Zivilluftfahrt (BZL)

(2023 data)

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*1
- Establish an interoperable platform for e.g., inspection plans/scope, observations, outcomes
- Materialise pilots e.g., formalise agreements*2, establish a collaboration tool/platform*3

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*4

*1 This could be expanded with industry to better understand expectations. *2 e.g., Memorandums of Understanding (MoU)
*3 To manage time zone differences by e.g., review documents separately and share questions to the panel
*4 e.g., participation in PIC/S-ICMRA Joint inspection programs and trainings

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

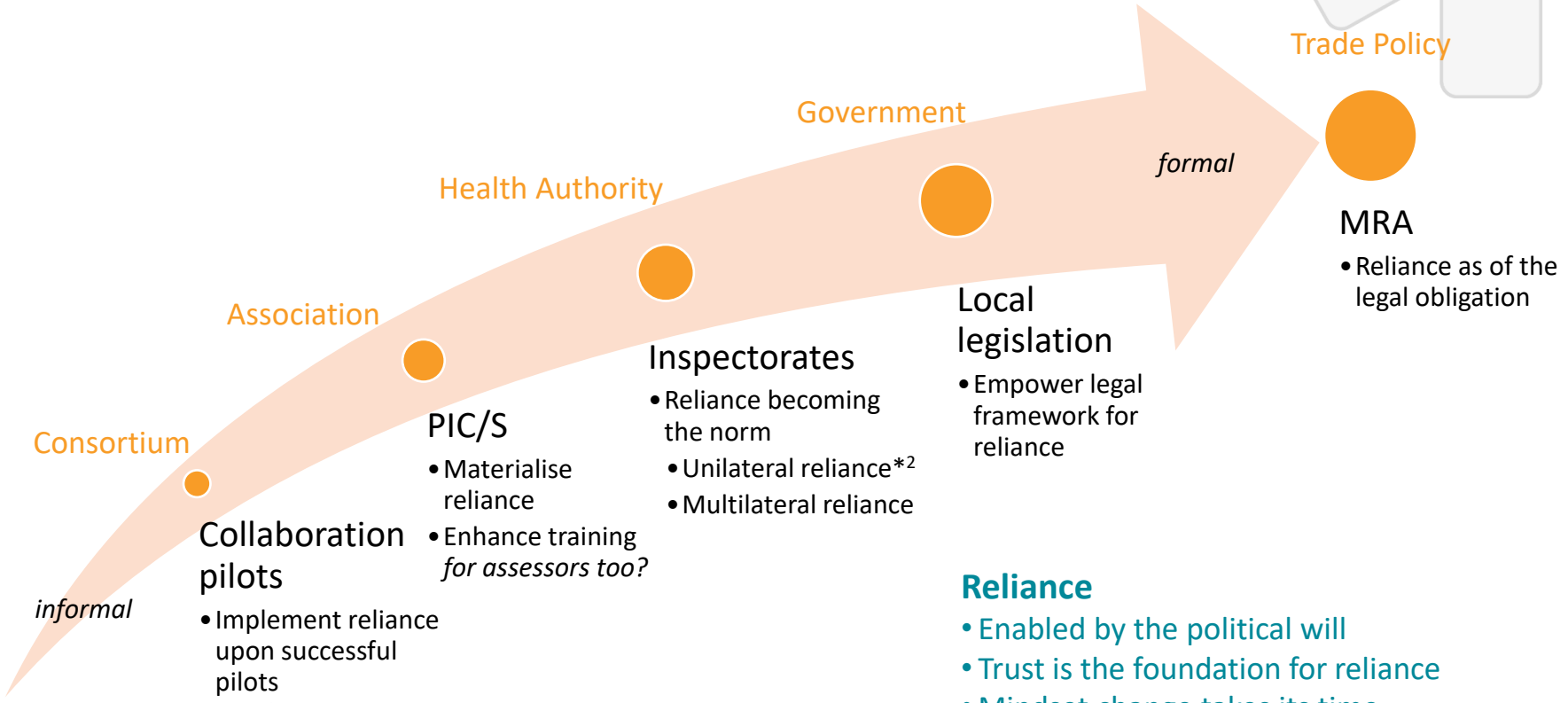
- **EFPIA member companies welcome the expansion of the pilot and flexibility adopting the inspection approach**
  - There is opportunity to put all in common practice
- **Minimise increased efforts by using existing procedures e.g.,**
  - Local inspectorate as lead and coordinating inspector
  - Use 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



Reliance

- Enabled by the political will
- Trust is the foundation for reliance
- Mindset change takes its time
- Extend where already applied (e.g., Ph.Eur.)

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

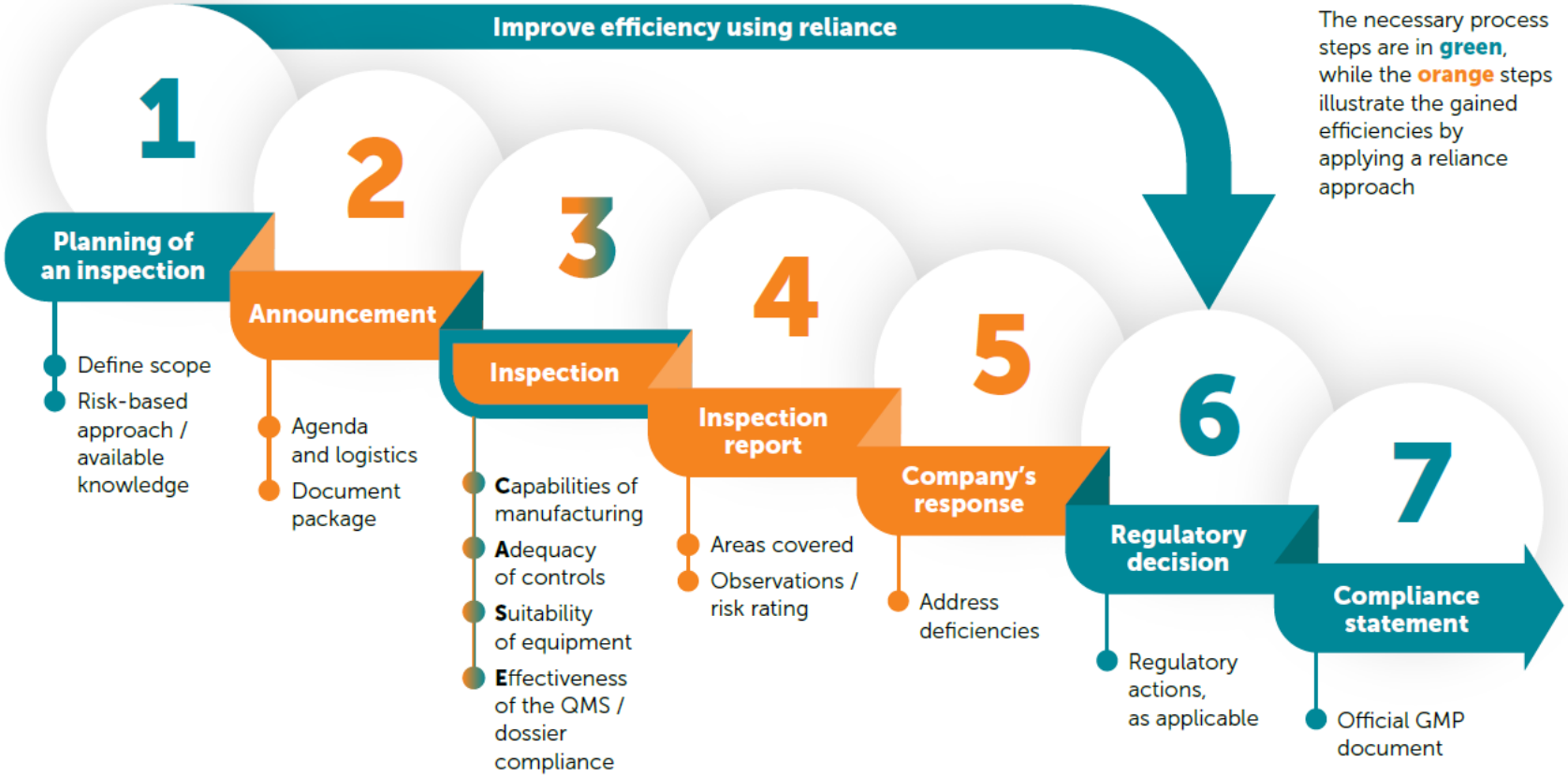
*1 Citation from Regulatory harmonizations and convergence, 'Take 5' at DIA Europe 2025

*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

- 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.

- **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

- **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 or Europe, ANSM, DMA, 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

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Contributors to the EFPIA inspections survey 2024

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- 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)*

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

ICMRA slide presented by Brendan Cuddy EMA @ DIA Europe 2025

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.

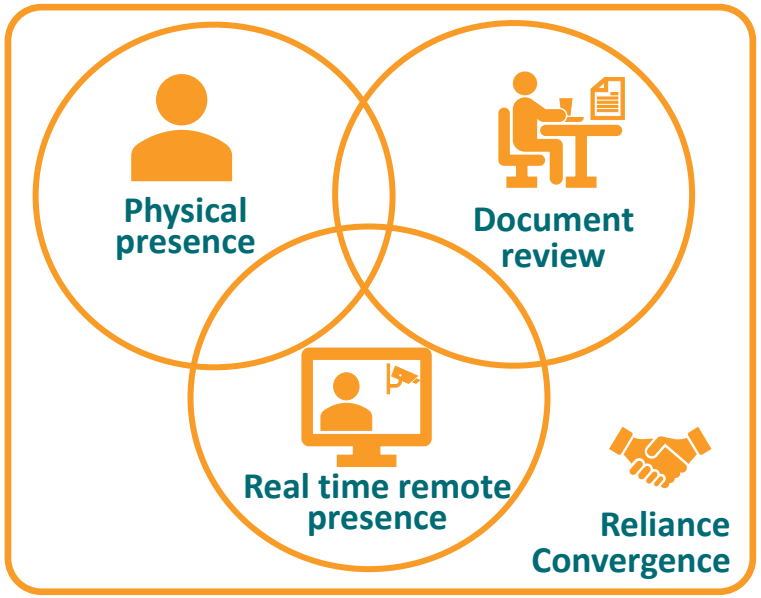
Inspection modes

KEEP IN MIND THE PURPOSE OF AN INSPECTION

Is a site compliant?

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

Inspection



C apability
Manufacture

A dequacy
Controls

S uitability
Equipment

E ffectiveness
QMS/PQS
incl. link to dossier

Enabled by risk-based approaches

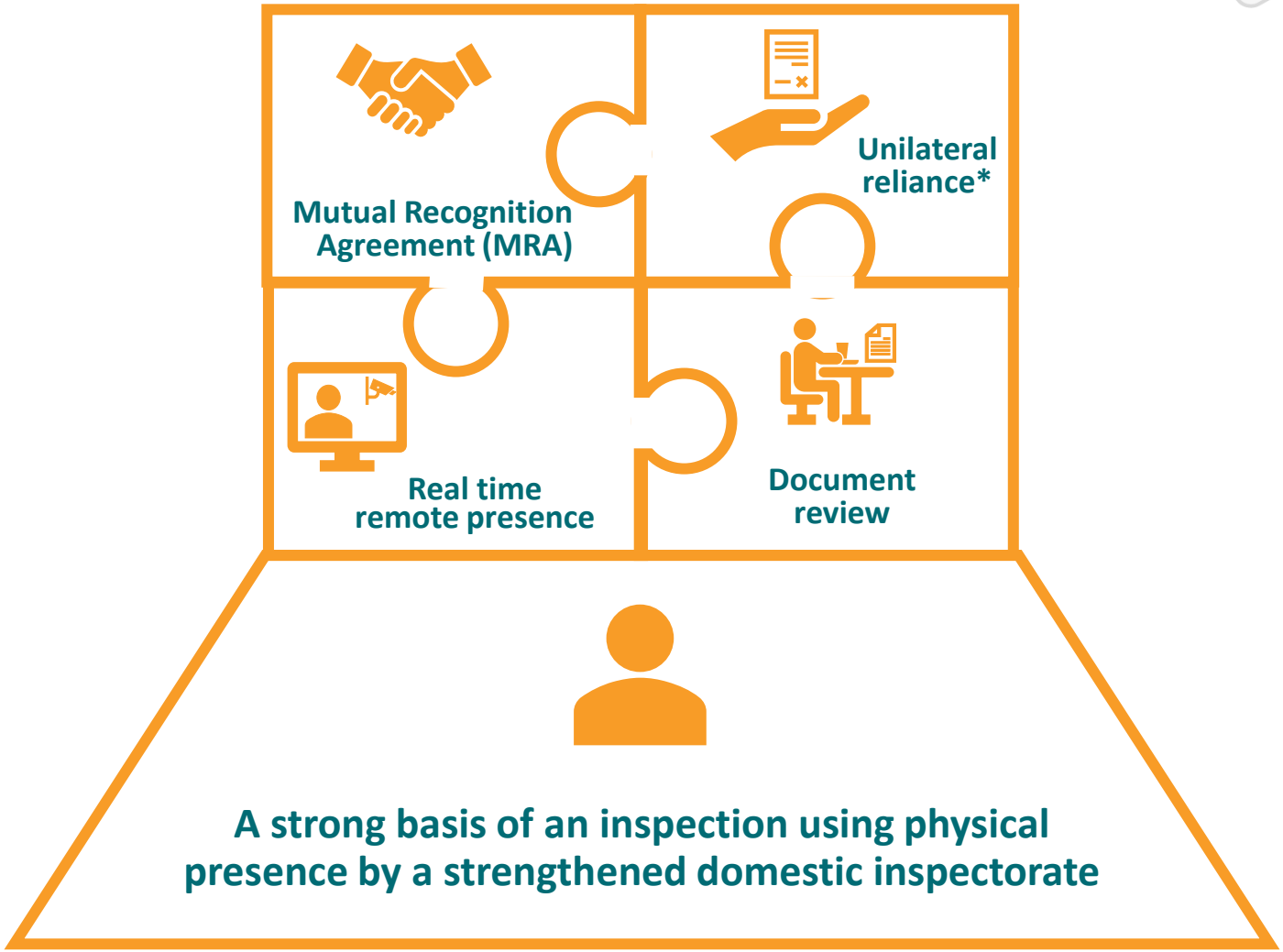
Alternative Modes

Risk-based

Decision on compliance

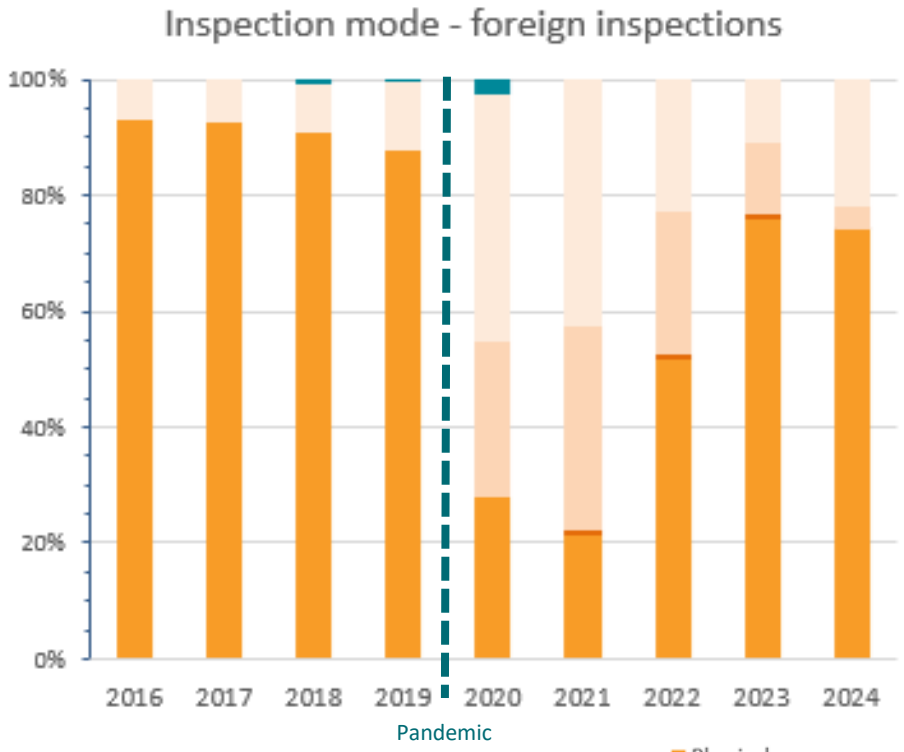
* Experience: Pre-Approval Inspections (PAI) dedicate most of the time on inspecting the QMS/PQS and only briefly checking on the authenticity of submitted data and links to dossier.

Collaboration, Reliance, Recognition



*based on information from other stringent regulatory authorities

Trending inspection modes

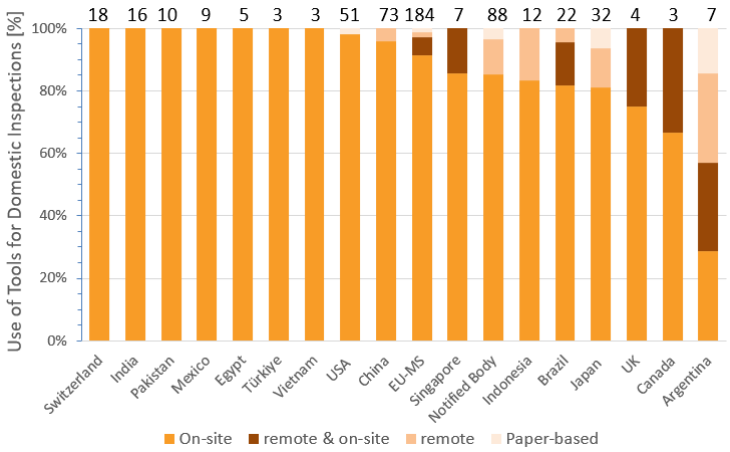


- Physical presence is increasing but not yet back to the level of before the pandemic
- The use of remote inspections is decreasing

INSPECTION MODES AT MANUFACTURING SITES

Trending inspection modes pandemic to now

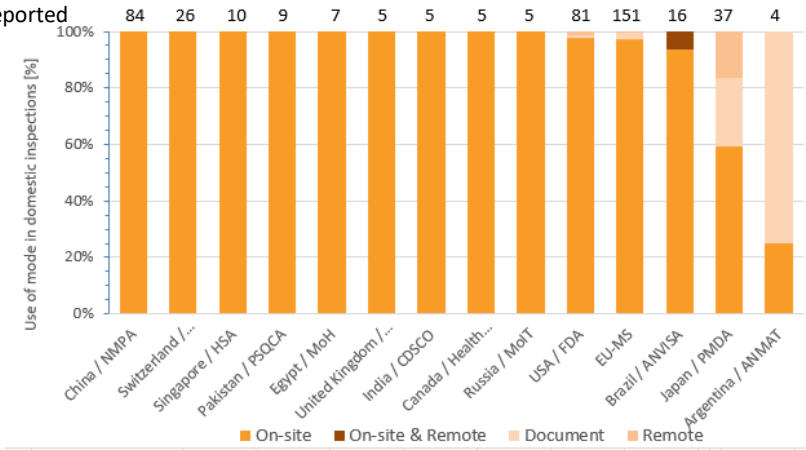
2022

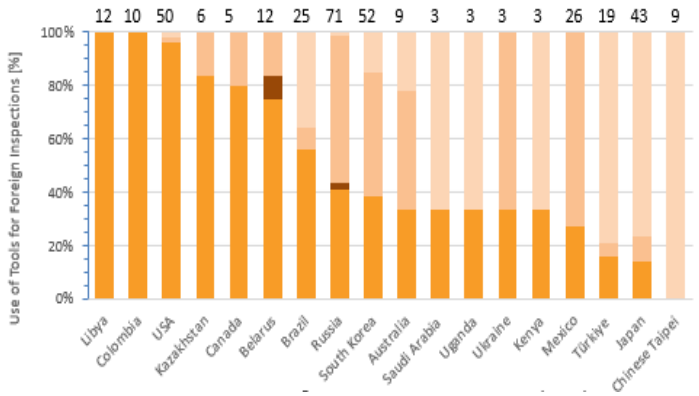


Domestic

No of inspections reported

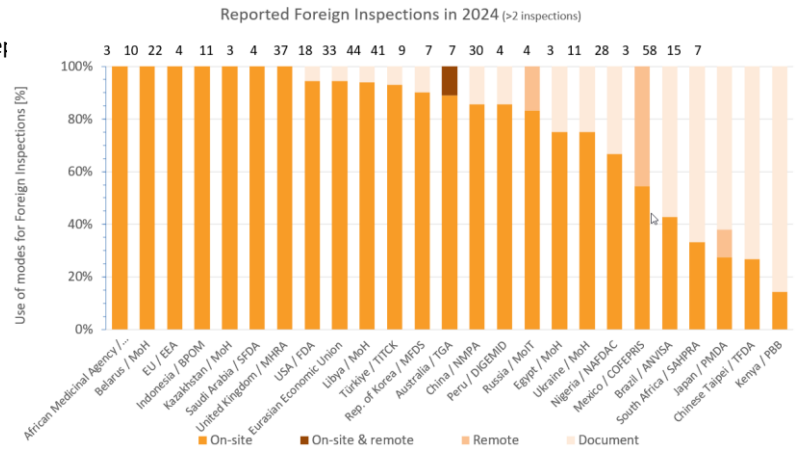
2024





Foreign

No of inspections rep



The 2022 graphic show only inspectorates performing three and more inspections
The 2024 graphic show only inspectorates performing four an more inspections

Documents for inspection

DOCUMENT INSPECTIONS

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

Check with survey results

Site	• Site Master File (SMF)*	✓
Product	• Annual Product Quality Review	✓
Pharmaceutical Quality System	• Site Quality Manual	✓
Additional information	• List of inspections / audits	✓

Adobe Acrobat Document

Enhanced GMP/GDP Inspection Efficiency, EFPIA, Position Paper 19. May 2014.

Adobe Acrobat Document

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

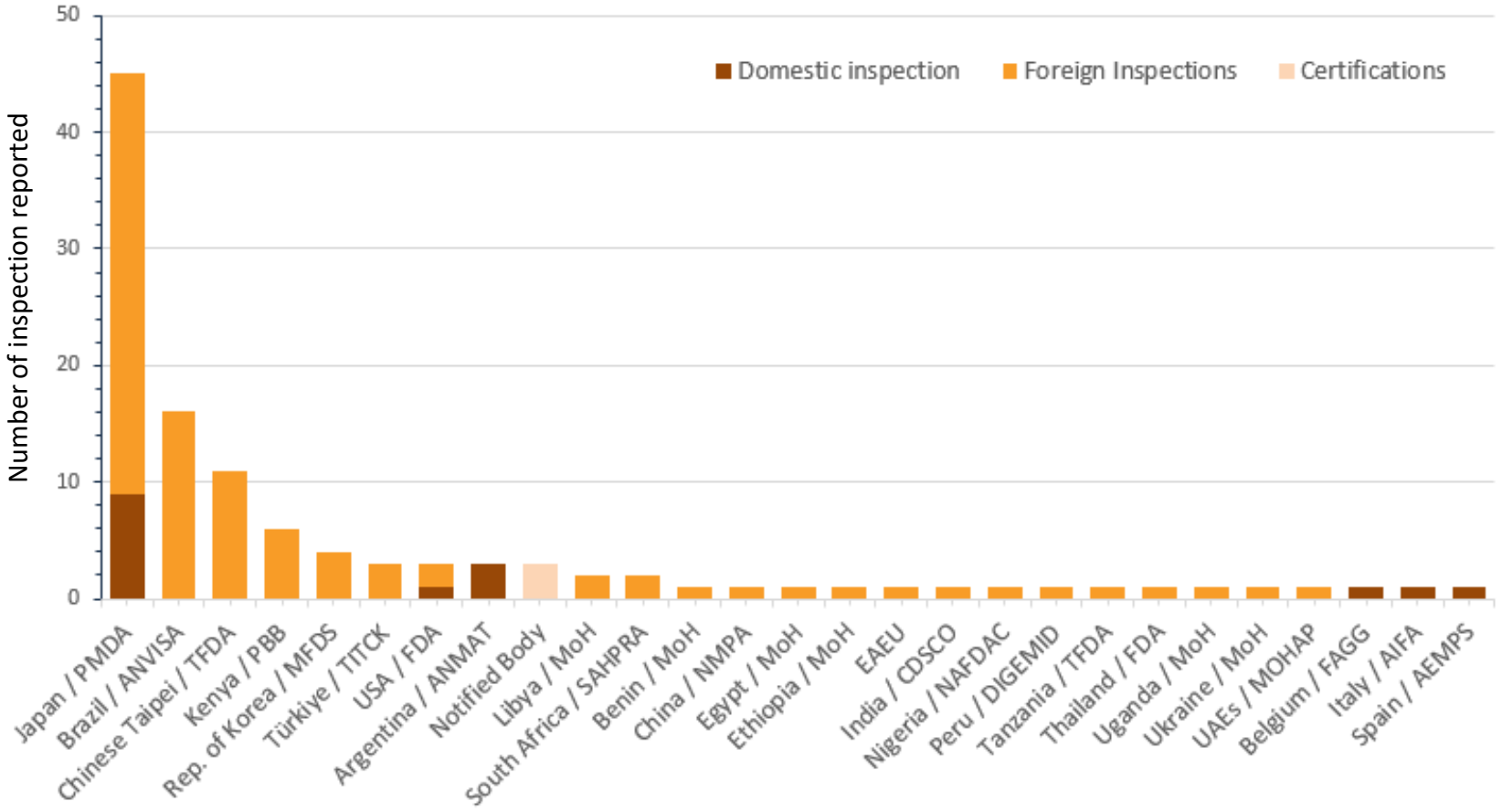
Survey results 2023 of standard document packages requested prior to an inspection – any mode

- **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.

*Recommended as of the EFPIA 2014 position paper

DOCUMENT INSPECTIONS

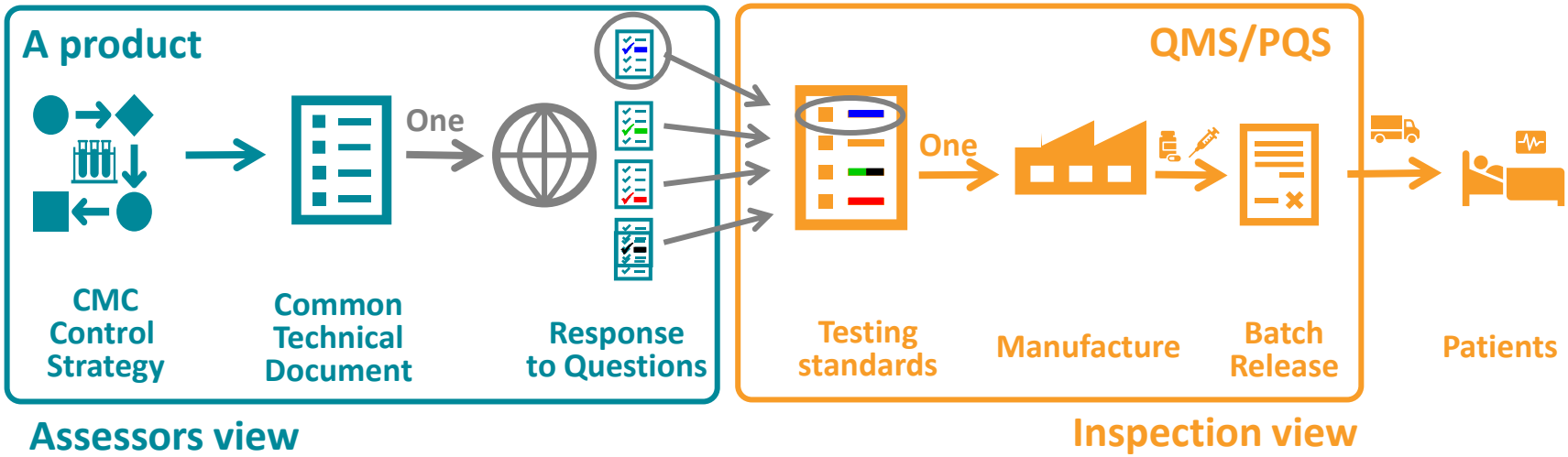
Inspectorates performing document inspections



Assessors in inspections

Roles and responsibilities of assessors (and inspectors)

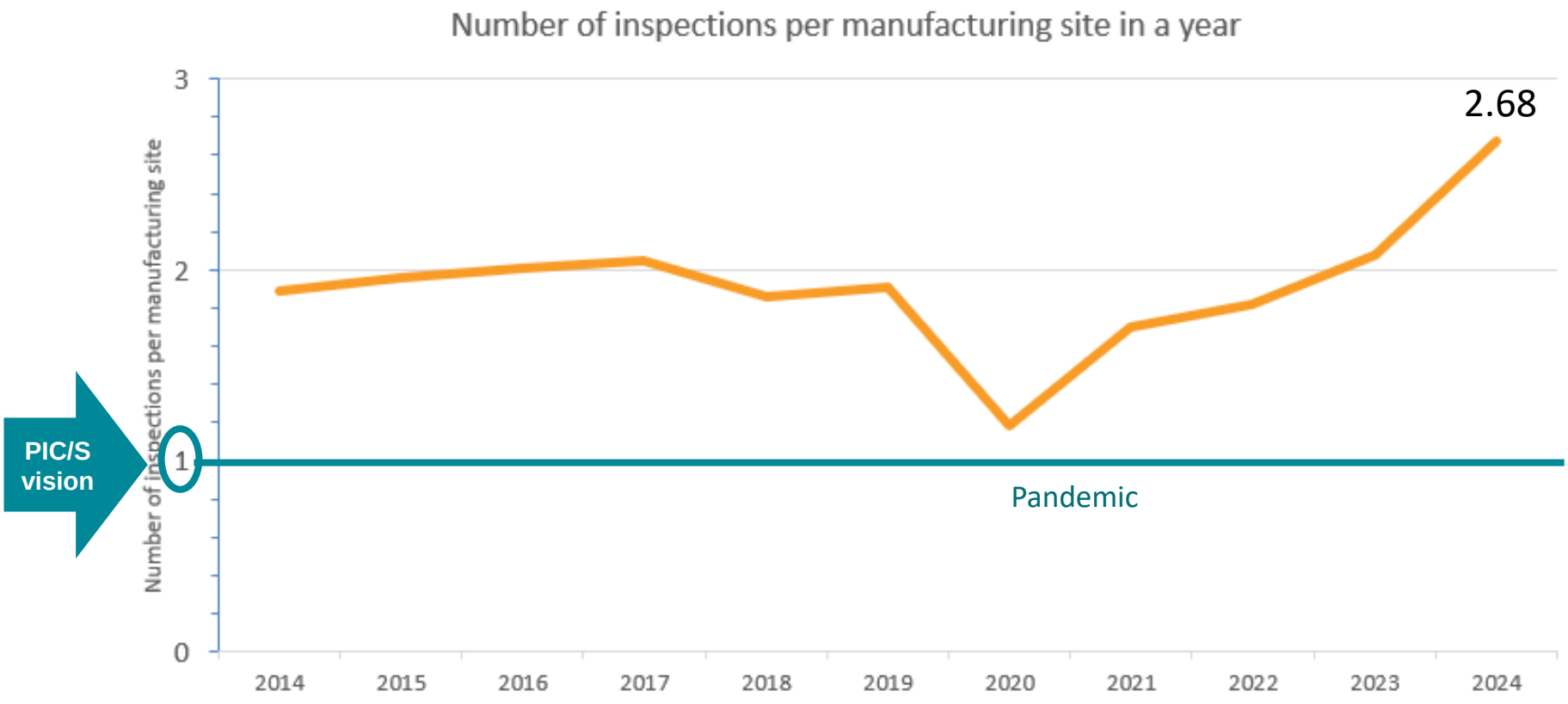
- Assessors should get a training on what inspectors are doing
- Enhancement of GMP activities understanding by assessors through firsthand insights for improving filing reviews.
- Assessors should focus on their mandate i.e., scientific consistency of dossiers (i.e., not acting as inspectors) while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



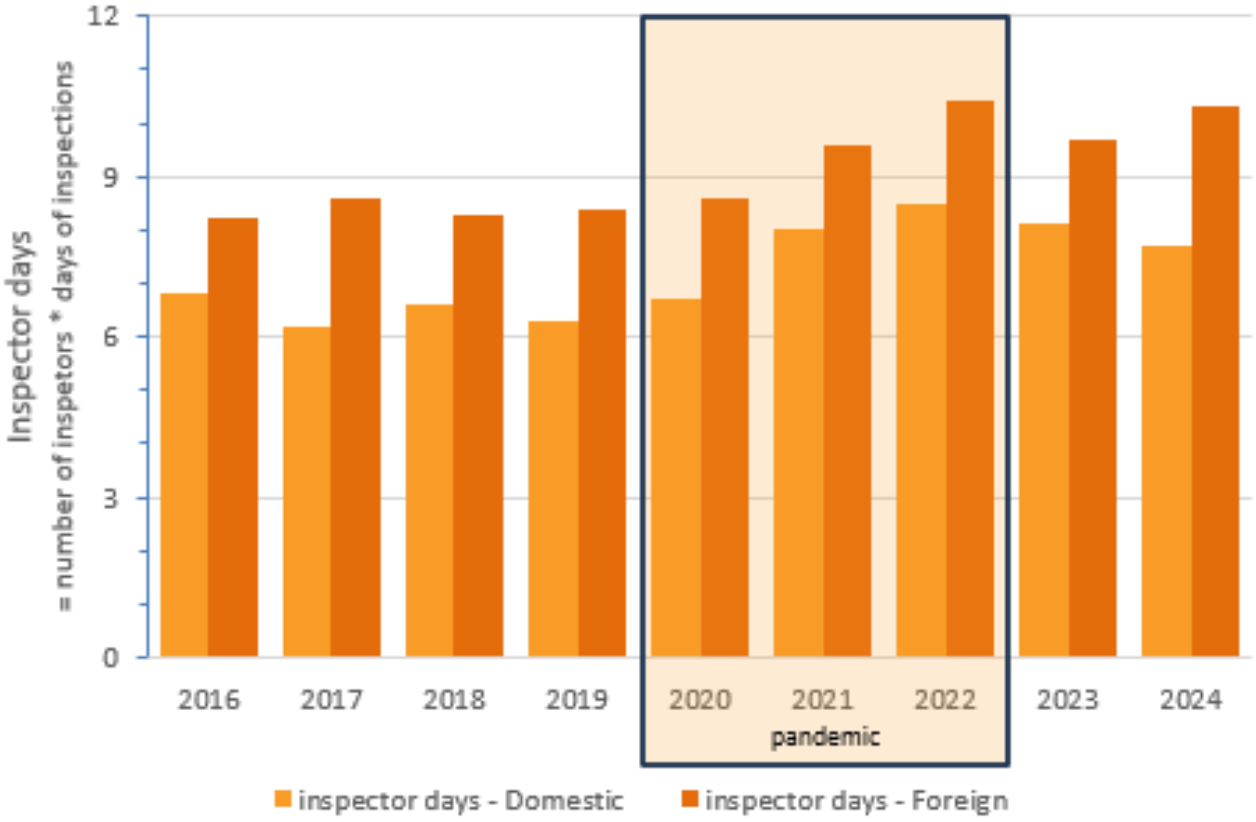
Green: what assessors see, Orange: what inspectors see view; Gray companies' activities
QMS/PQS: Quality Management System / Pharmaceutical Quality System

General Data

The number of inspections at a manufacturing site



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

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

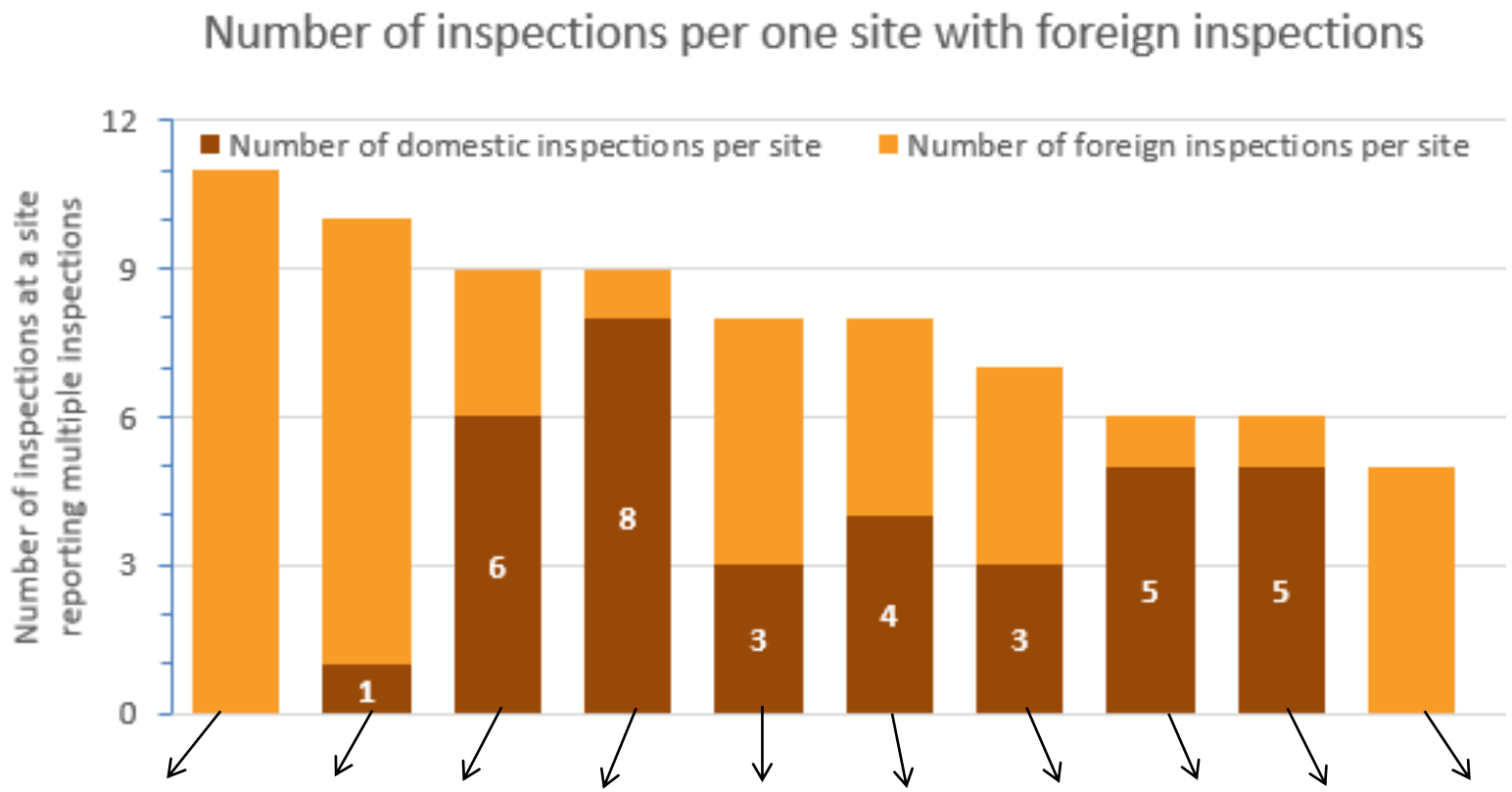
Resources

- 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

Multiple inspections at one manufacturing site (6 and more)



Denmark
- Japan (3)
- Rep. of Korea (3)
- Brazil
- Chinese Taipei
- Türkiye
- Kenya

Denmark
- Japan (4)
- Brazil (2)
- US-FDA
- Türkiye
- Kenya
- Chinese Taipei
- Rep. of Korea

Germany
- Japan
- Türkiye
- Belarus

Brazil
- Mexico

US
- AMA
- Tanzani
- Brazil
- Russia
- Türkiye

Germany
- US-FDA (2)
- Belarus
- Türkiye

Germany
- China
- Russia
- Türkiye
- Libya

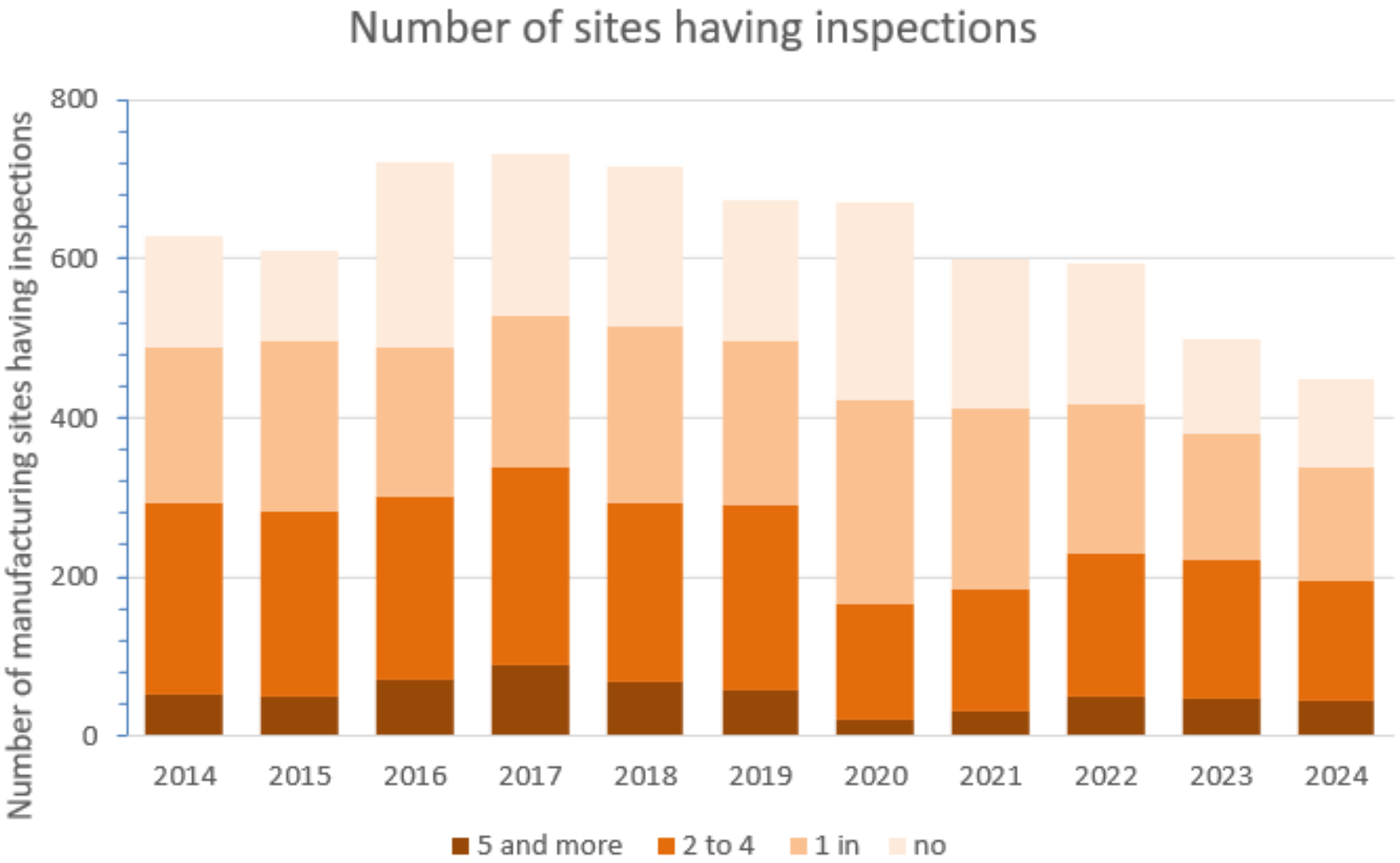
US
- Japan

Germany
- Russia

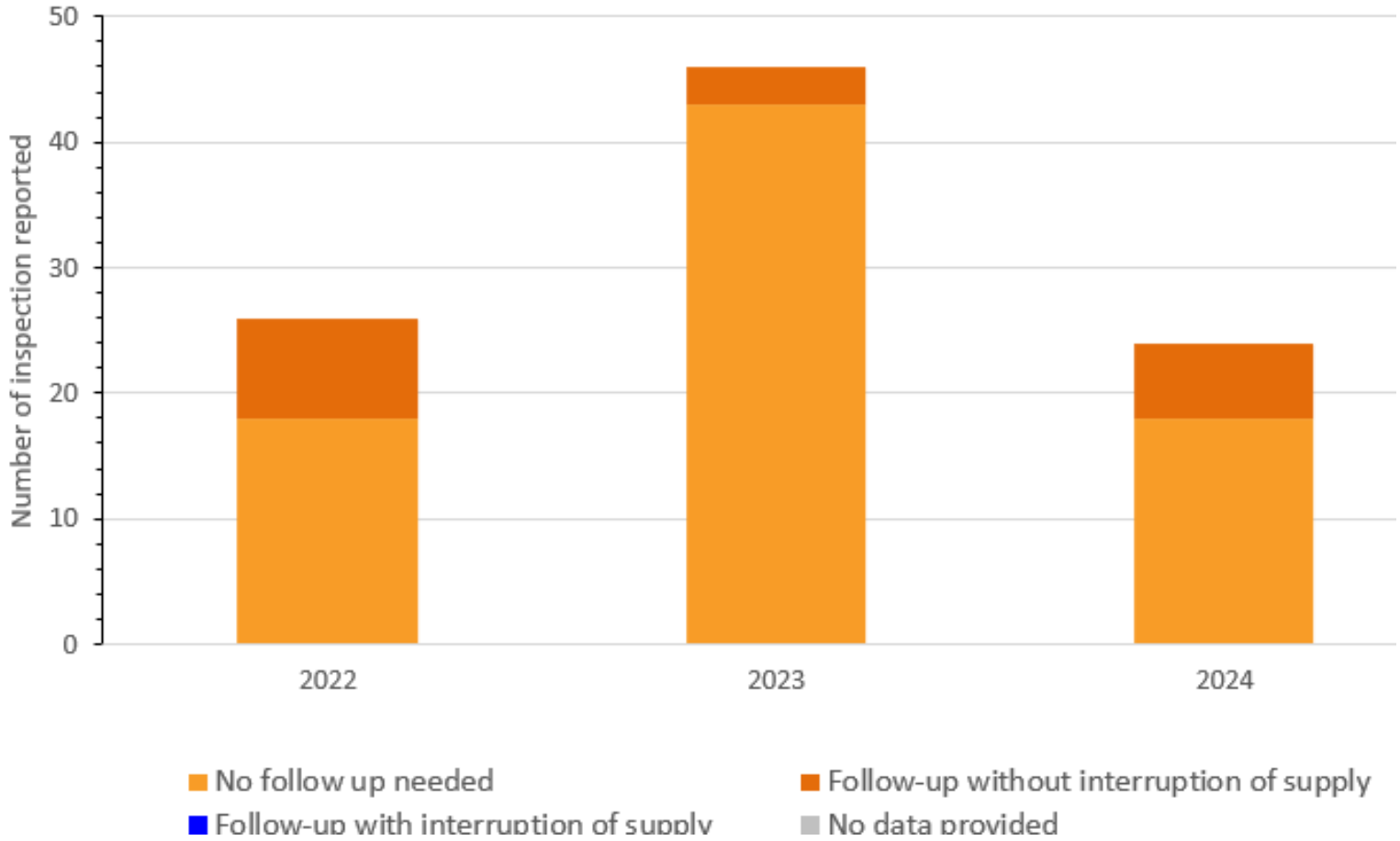
France
- US-FDA
- Türkiye
- Rep. of Korea
- China
- EAEU

Most sites exposed to multiple foreign inspections are in Germany (4) and Denmark (2)

Inspections at one manufacturing site

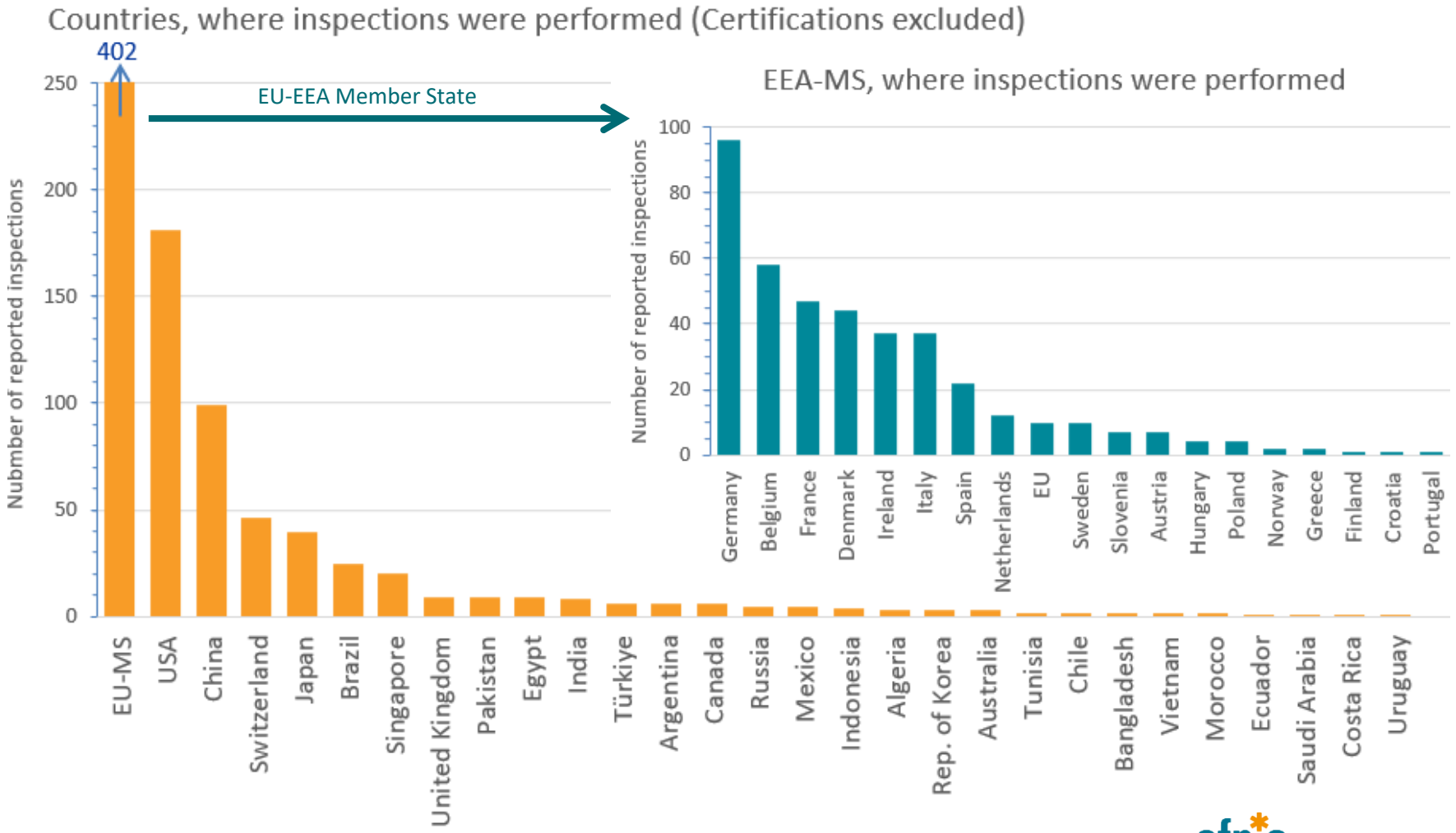


For cause inspections do not result in interrupted supply

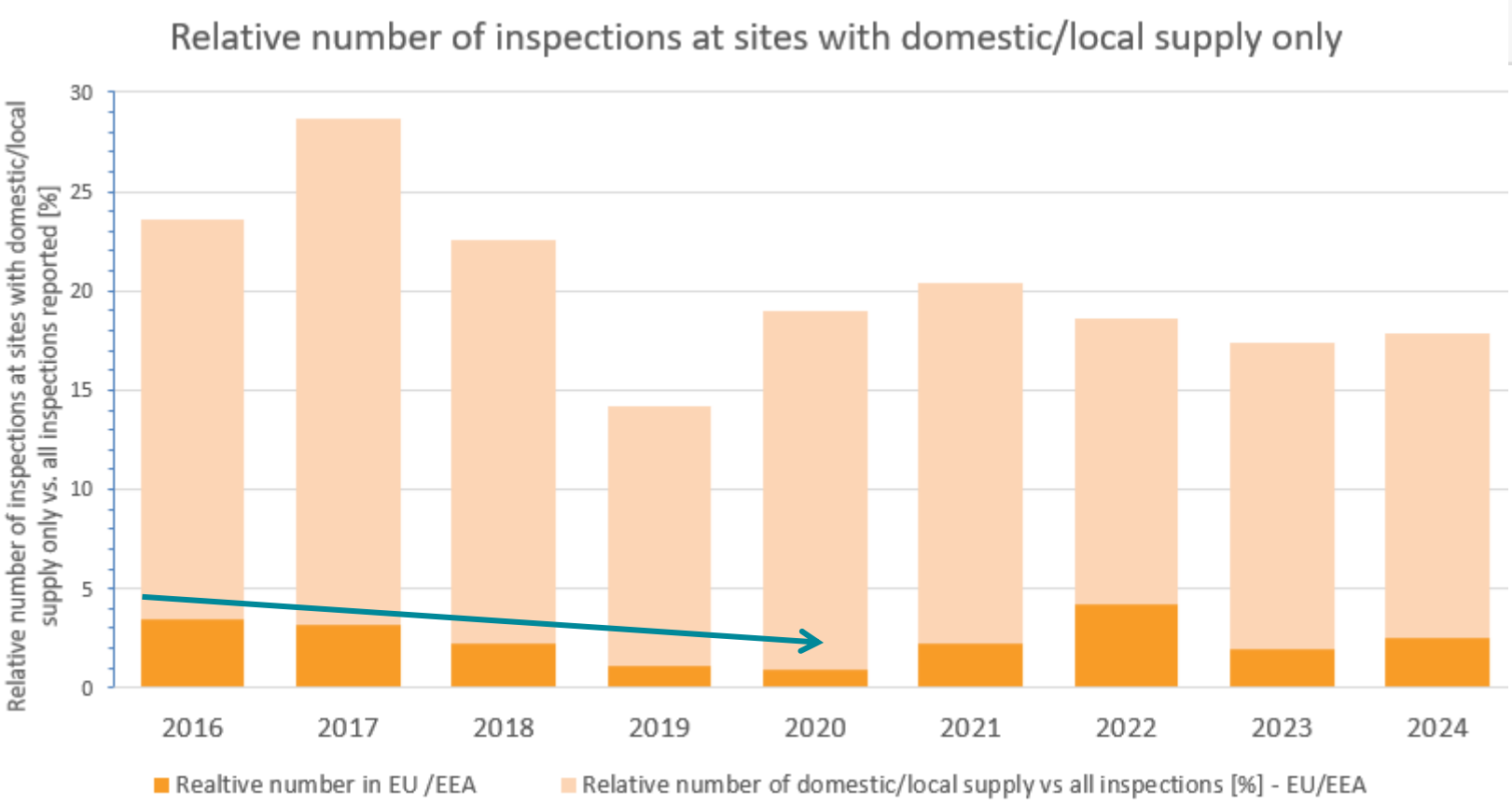


* The number of ‘for cause’ inspections had a peak in 2023

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

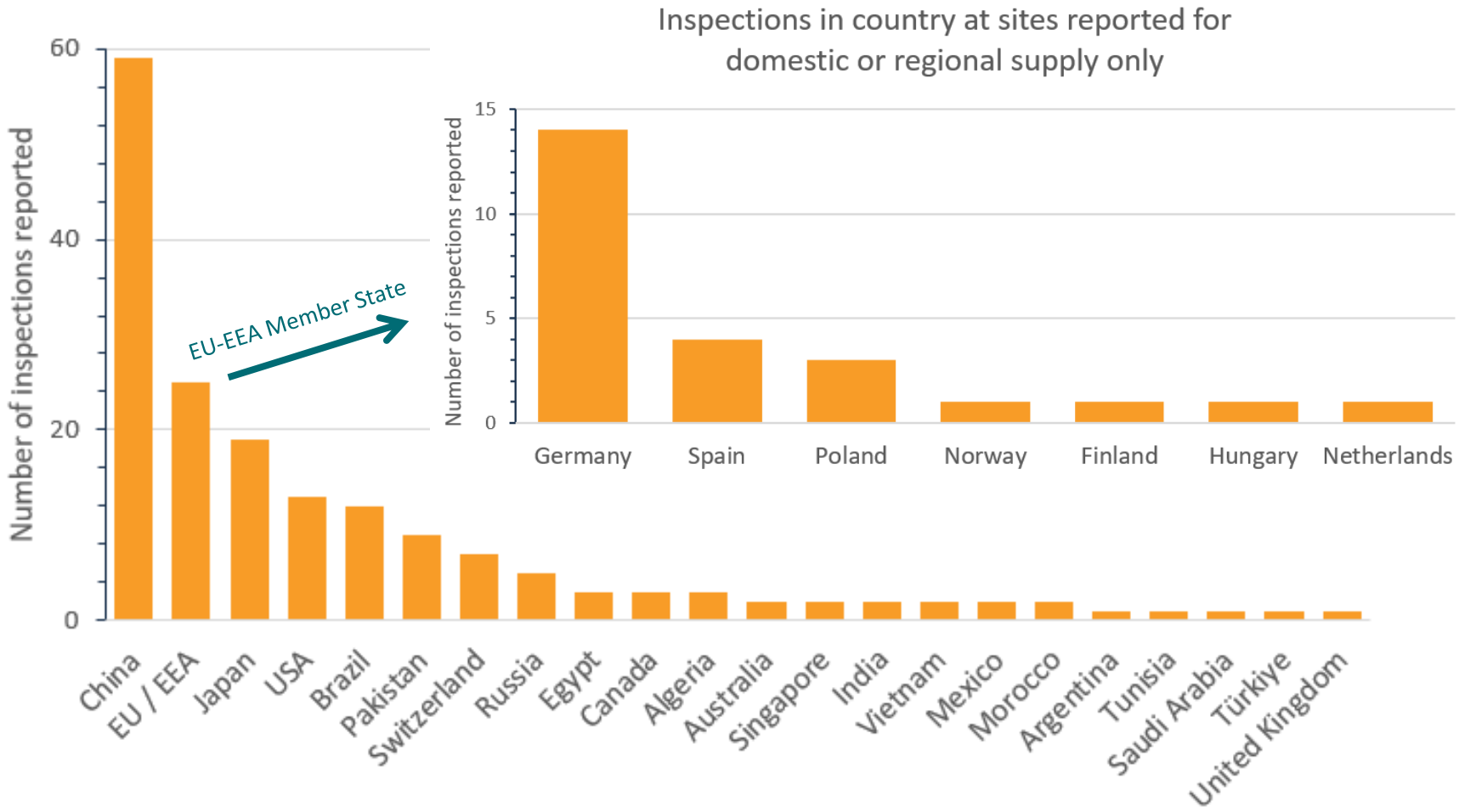


Inspections at sites with domestic/local supply only

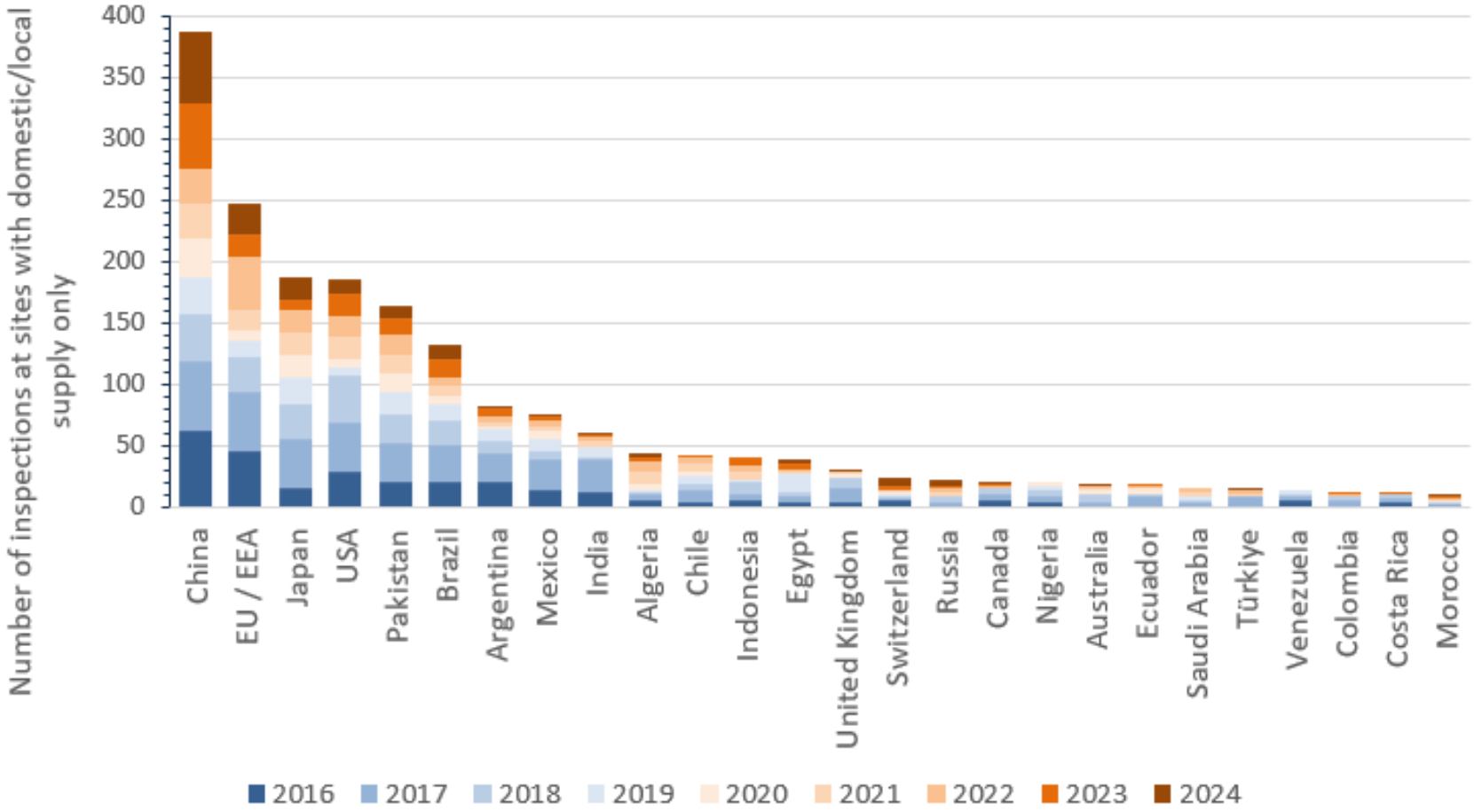


- **The data show a trend towards globalisation of manufacturing until 2020 i.e., the pandemic. After that, more sites manufacturing for local / regional supply are reported to be inspected**

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

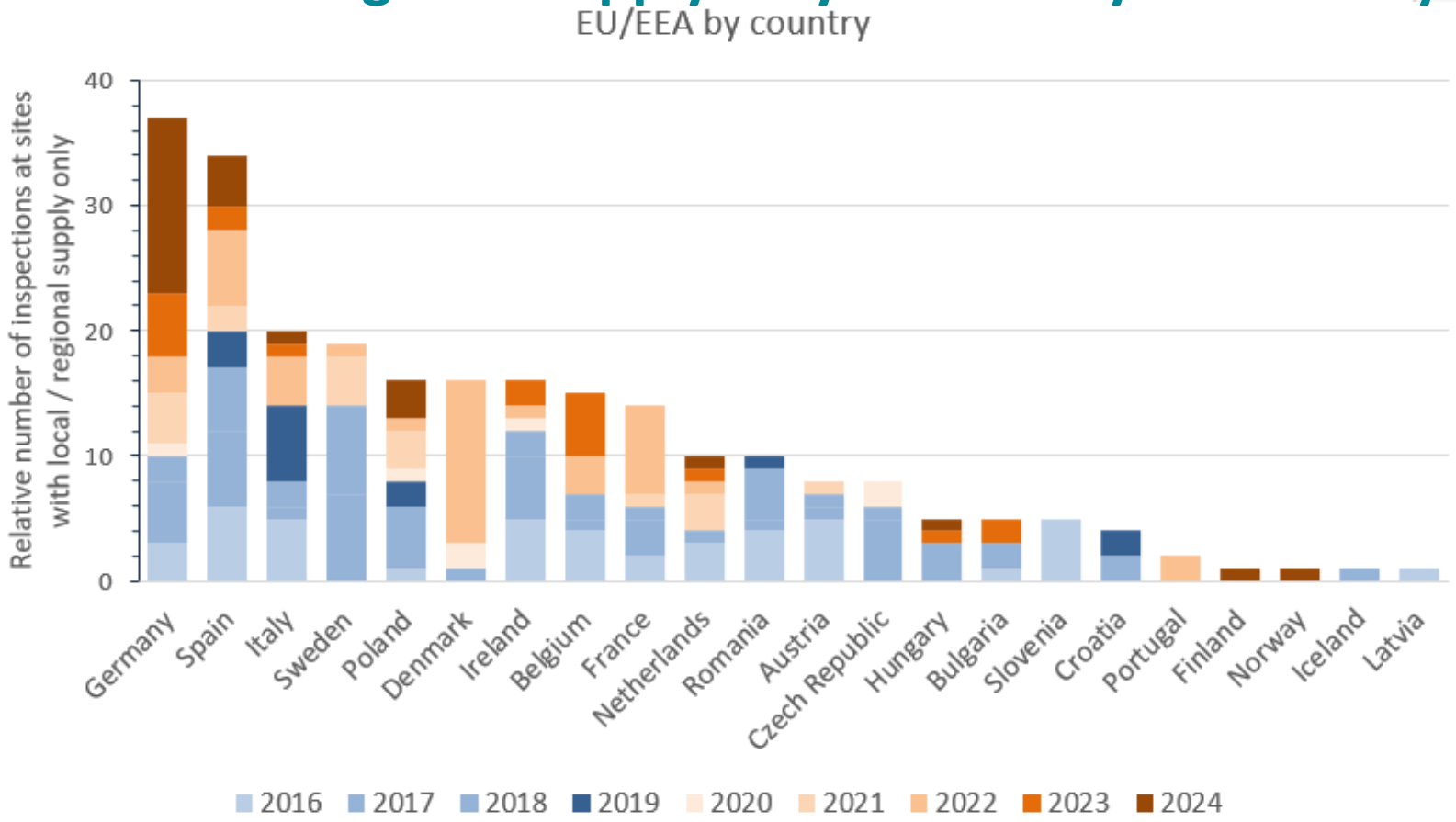


Inspections in country at sites reported for domestic or regional supply only – several years history



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

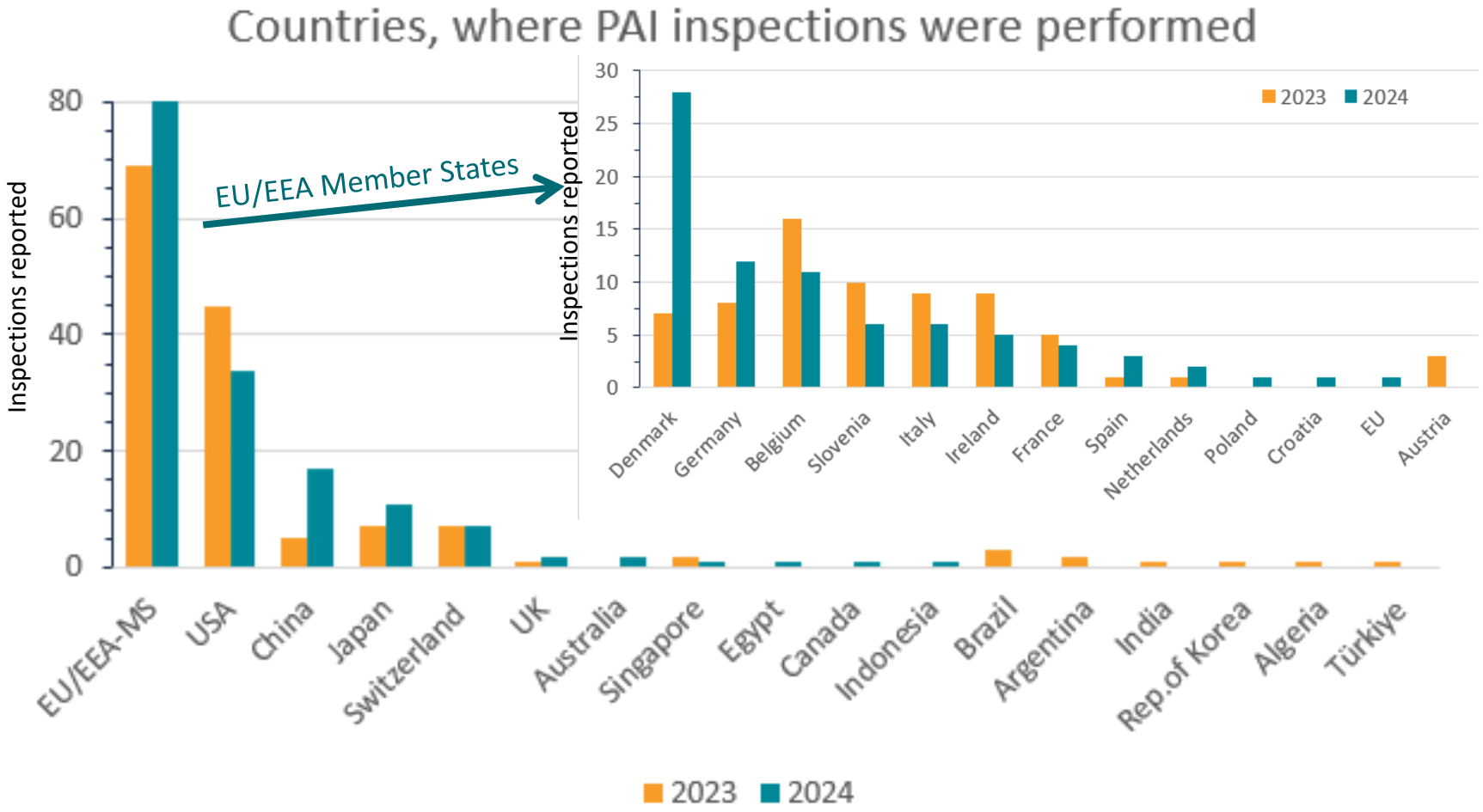
Inspections in country at sites reported for domestic or regional supply only – several years history



* **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**

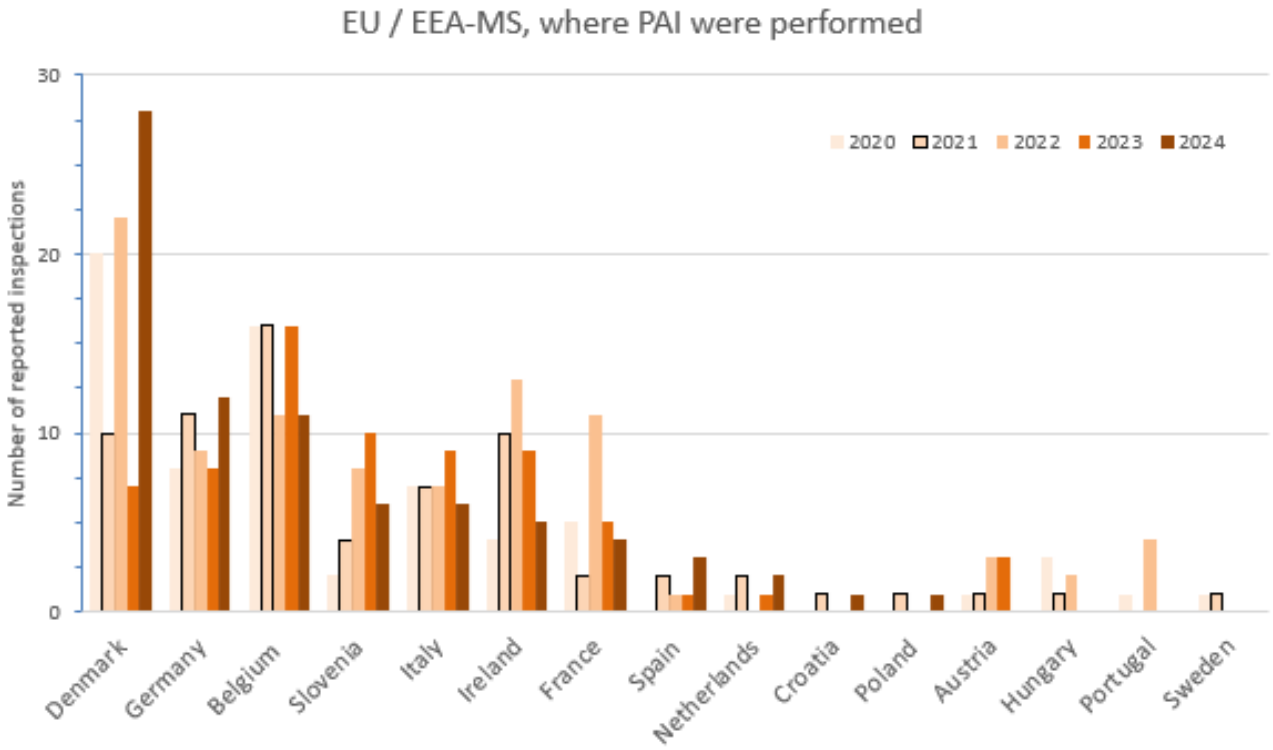
INSPECTIONS AT MANUFACTURING SITES - PAI

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



PAI: Pre-Approval Inspection

EU/EEA competitiveness where new innovative products are manufactured



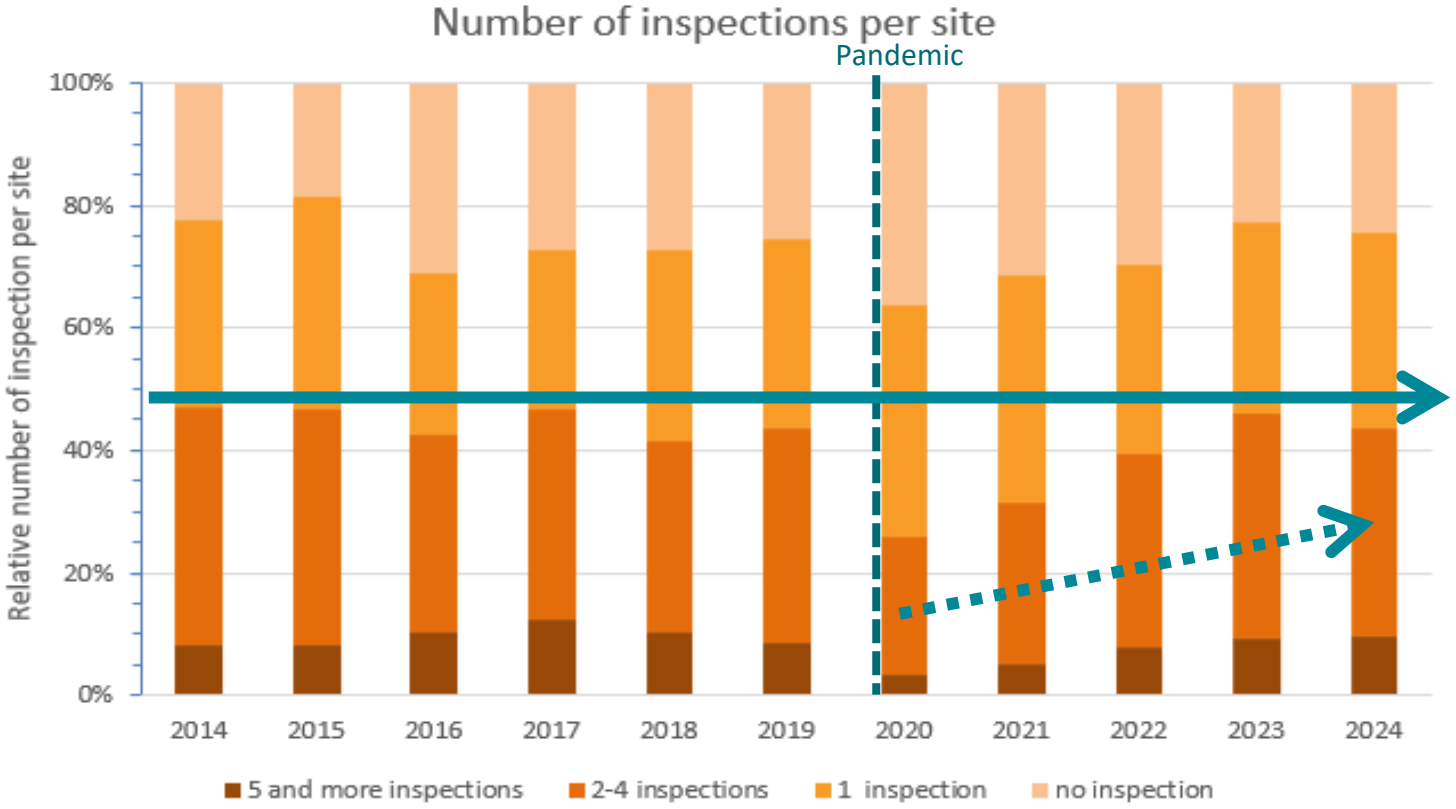
- **Member States where innovative products are manufactured include**
  - Denmark
  - Germany
  - Belgium
  - Slovenia
  - Italy
  - Ireland
  - France

PAI: Pre-Approval Inspection

Locations of inspected API manufacturing sites

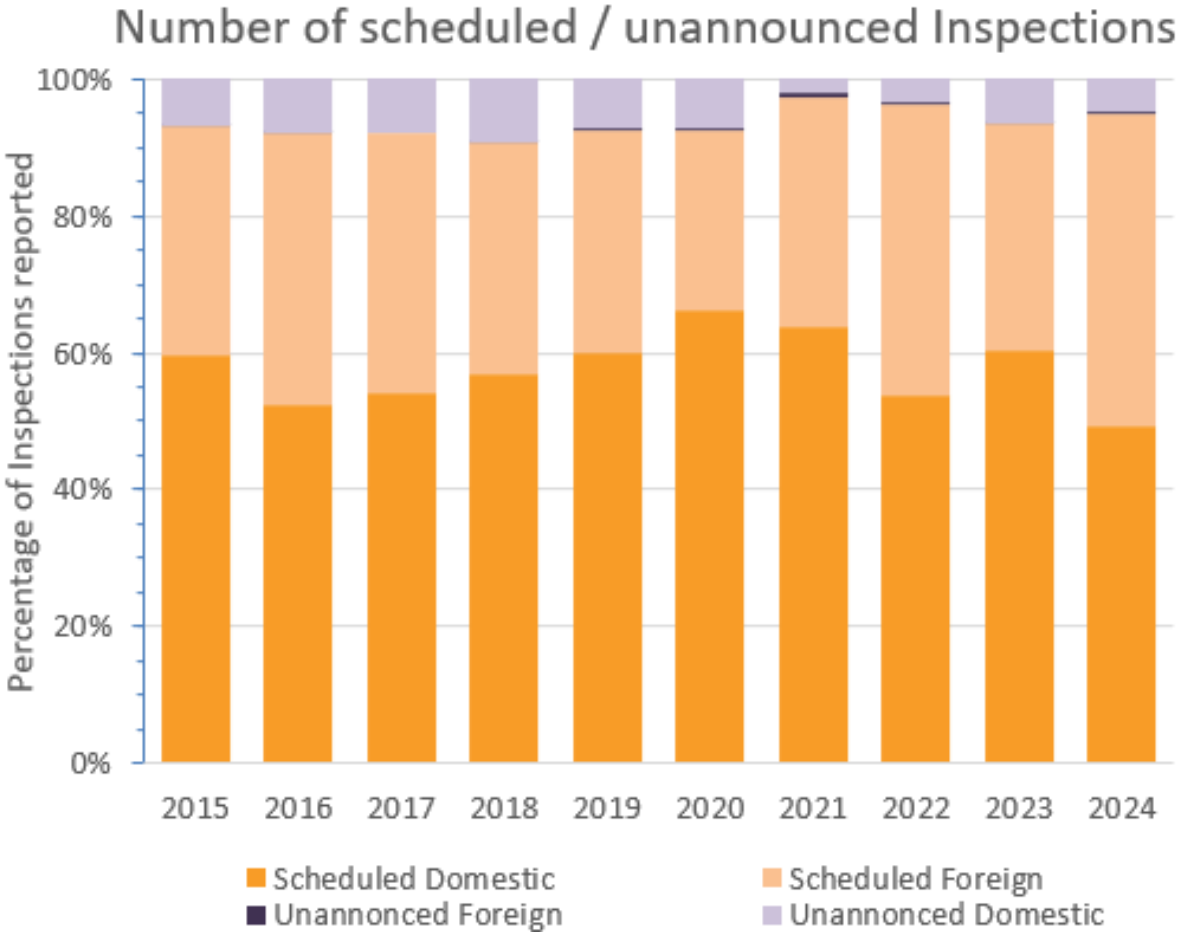
Inspections at API manufacturing sites are performed in the EU/EEA, US, Switzerland,, Singapore, and Pakistan; in the EU/EEA in Germany, Belgium, Ireland and Denmark

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

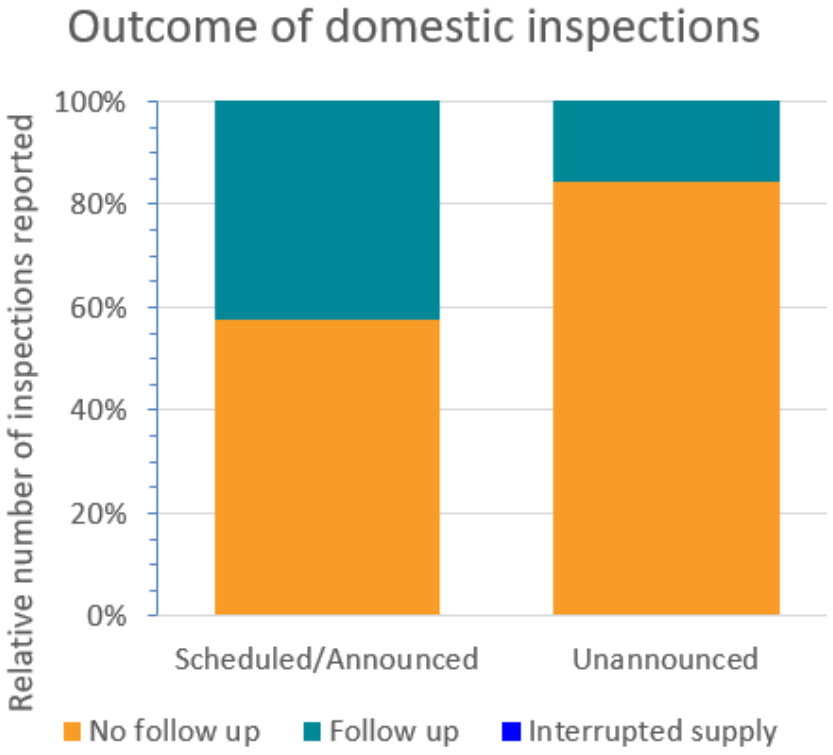
Scheduled versus unannounced inspections

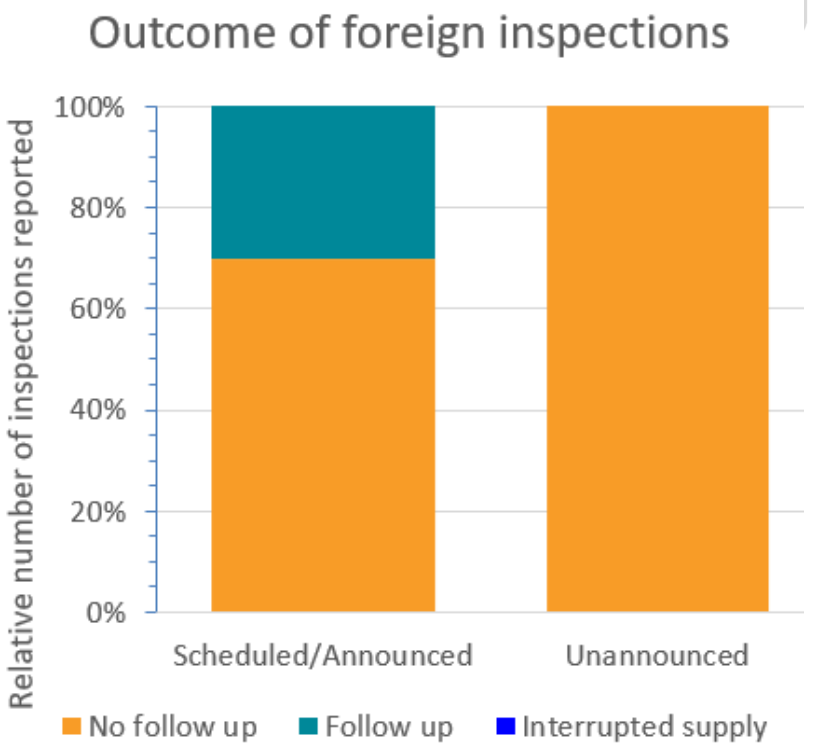


Inspectorate	Reported number of unannounced inspections in 2024
China / NMPA	21
USA / FDA	17
Notified Body	4
Japan / PMDA	2
Chile / ISP	2
Rep. of Korea / MFDS	1
Spain / AEMPS	1
Indonesia / BPOM	1
Brazil / ANVISA	1
Italy / AIFA	1

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

Outcome of scheduled versus unannounced inspections

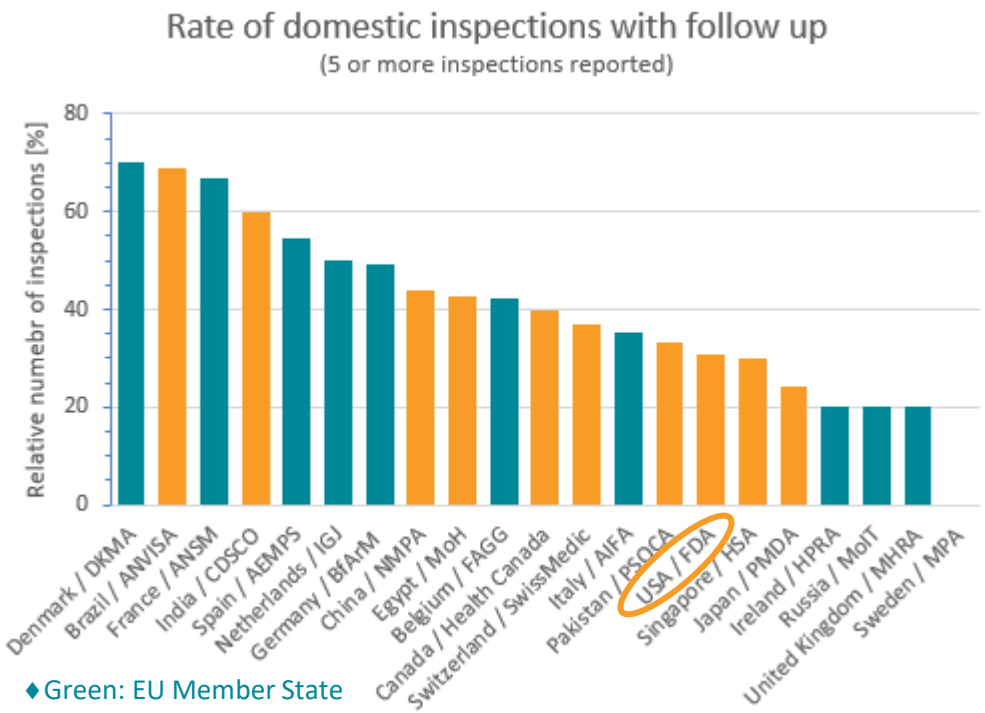




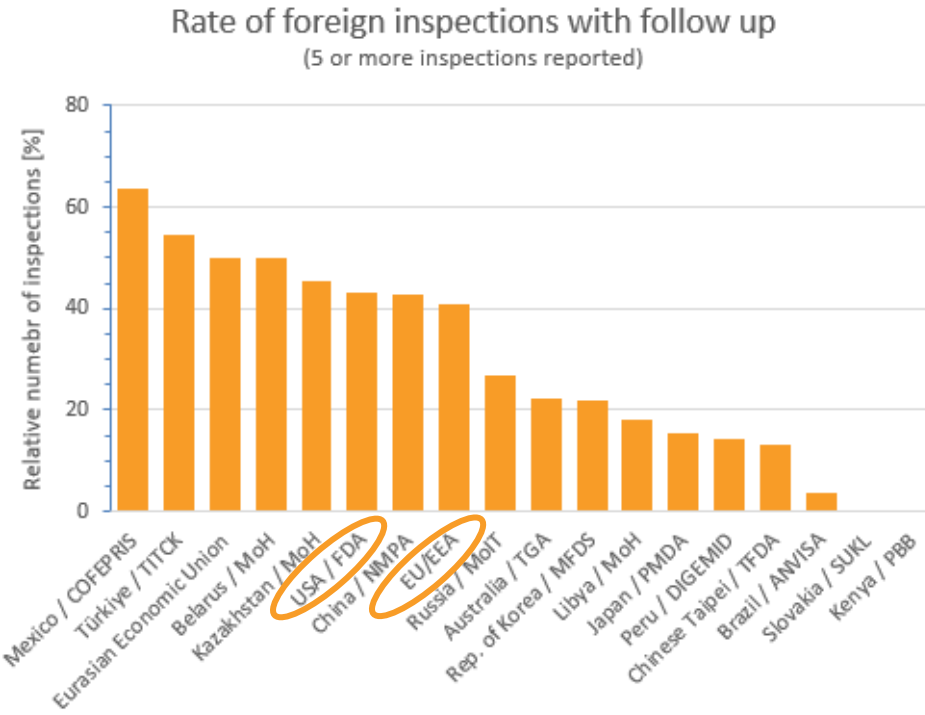
* **About 20% more follow up actions are reported with scheduled inspections compared to unannounced inspections (both foreign and domestic)**

Note: Non of the inspections ended with interrupted supply

Rate of inspections with follow-up actions

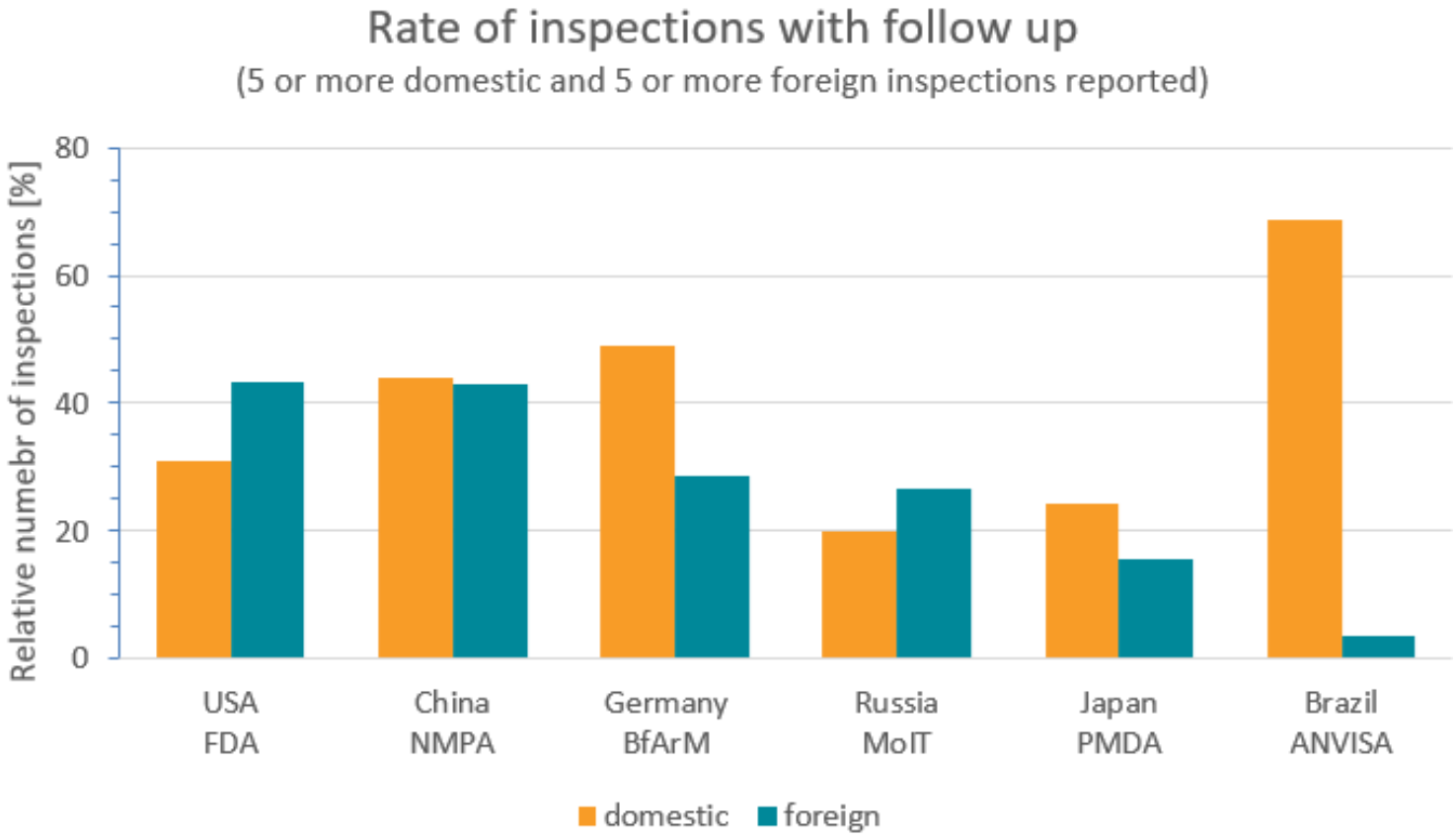


♦ Green: EU Member State



- **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?**

Rate of inspections with follow-up actions

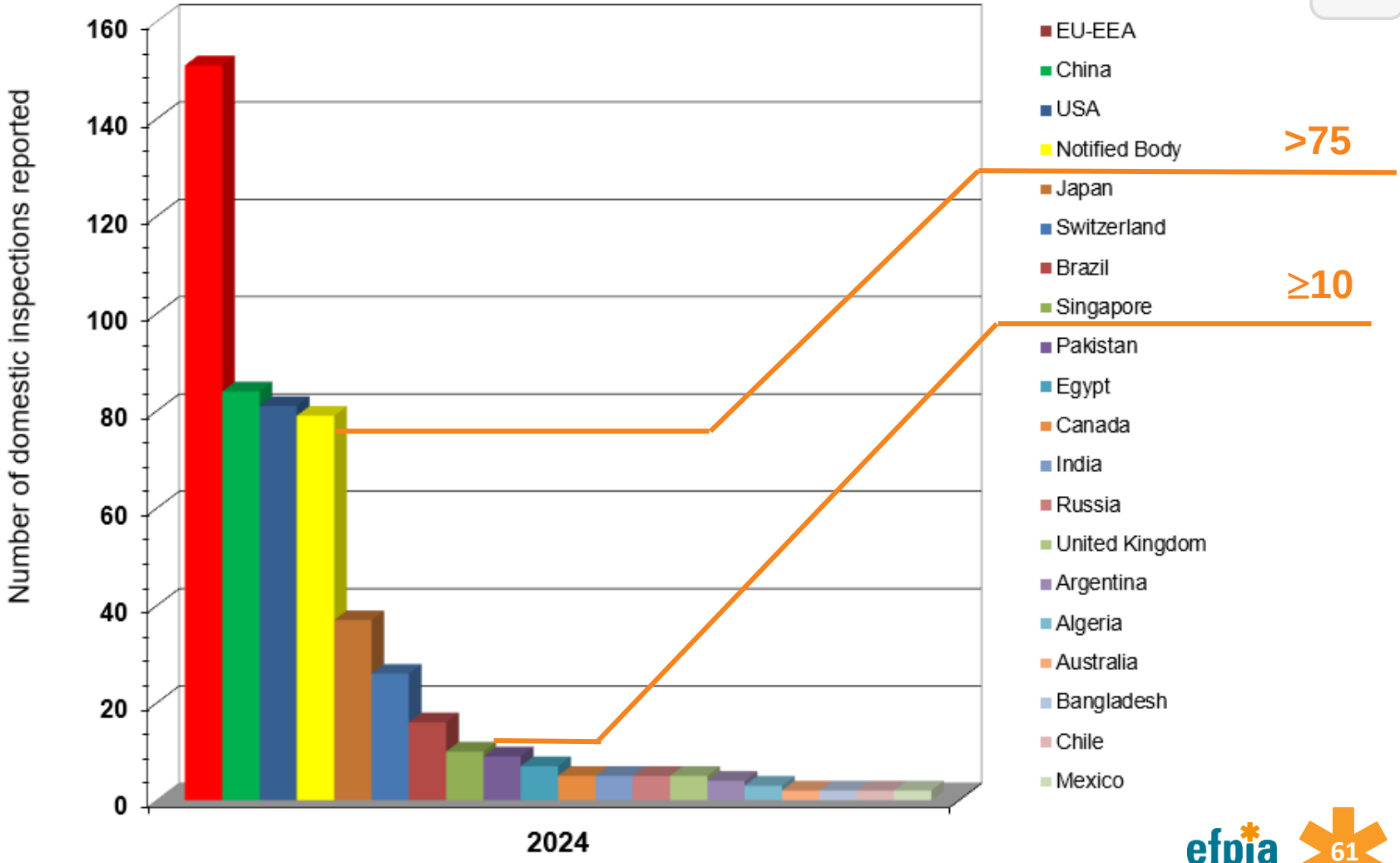


* **Even if FDA is doing announced foreign inspection companies report to have more inspections with follow up in 3rd countries than for sites in the US**

Domestic Inspection Activity

Number of domestic inspections

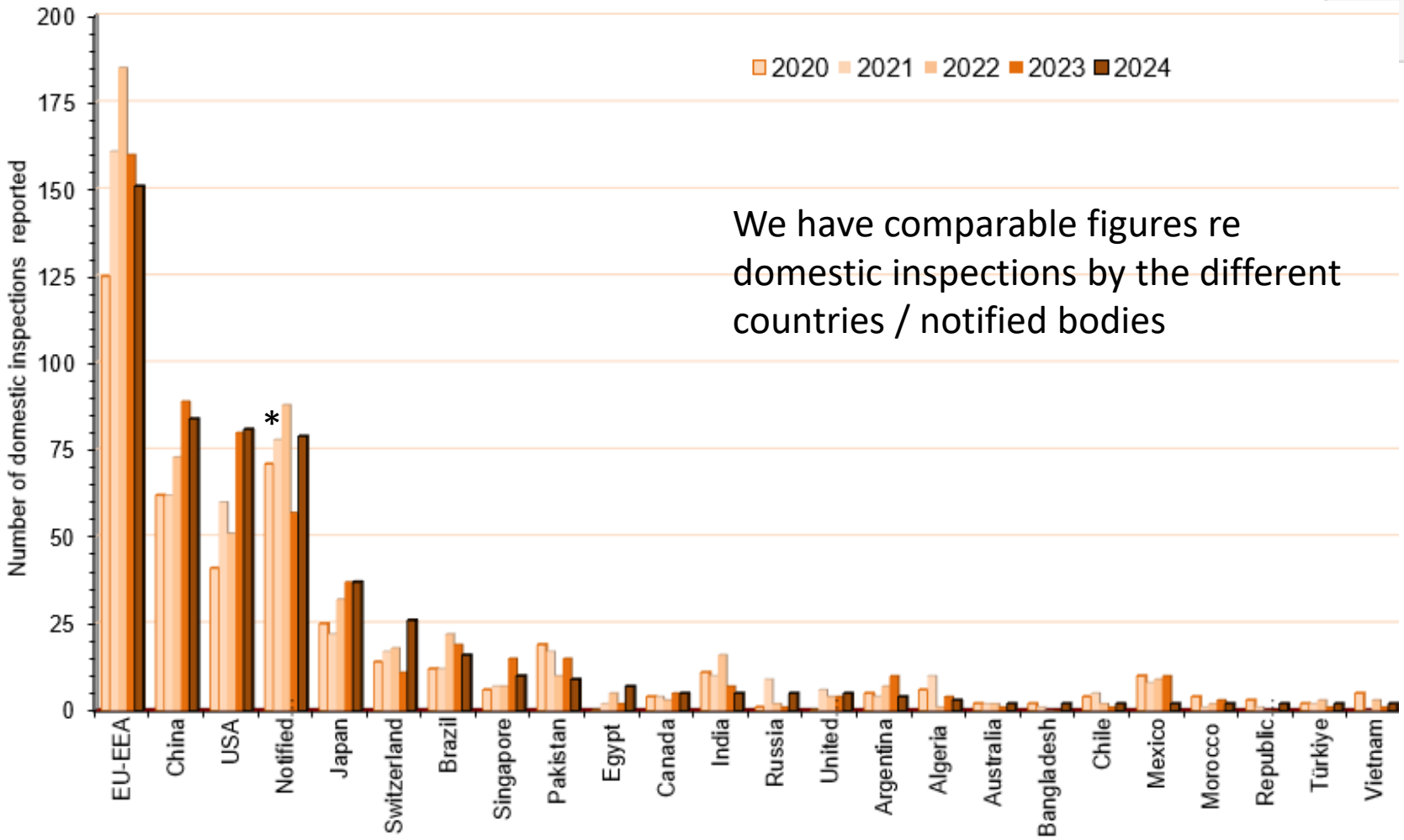
ordered by country (>1 inspections; EU/EEA as one entity; all modes)



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

DOMESTIC INSPECTIONS AT MANUFACTURING SITES

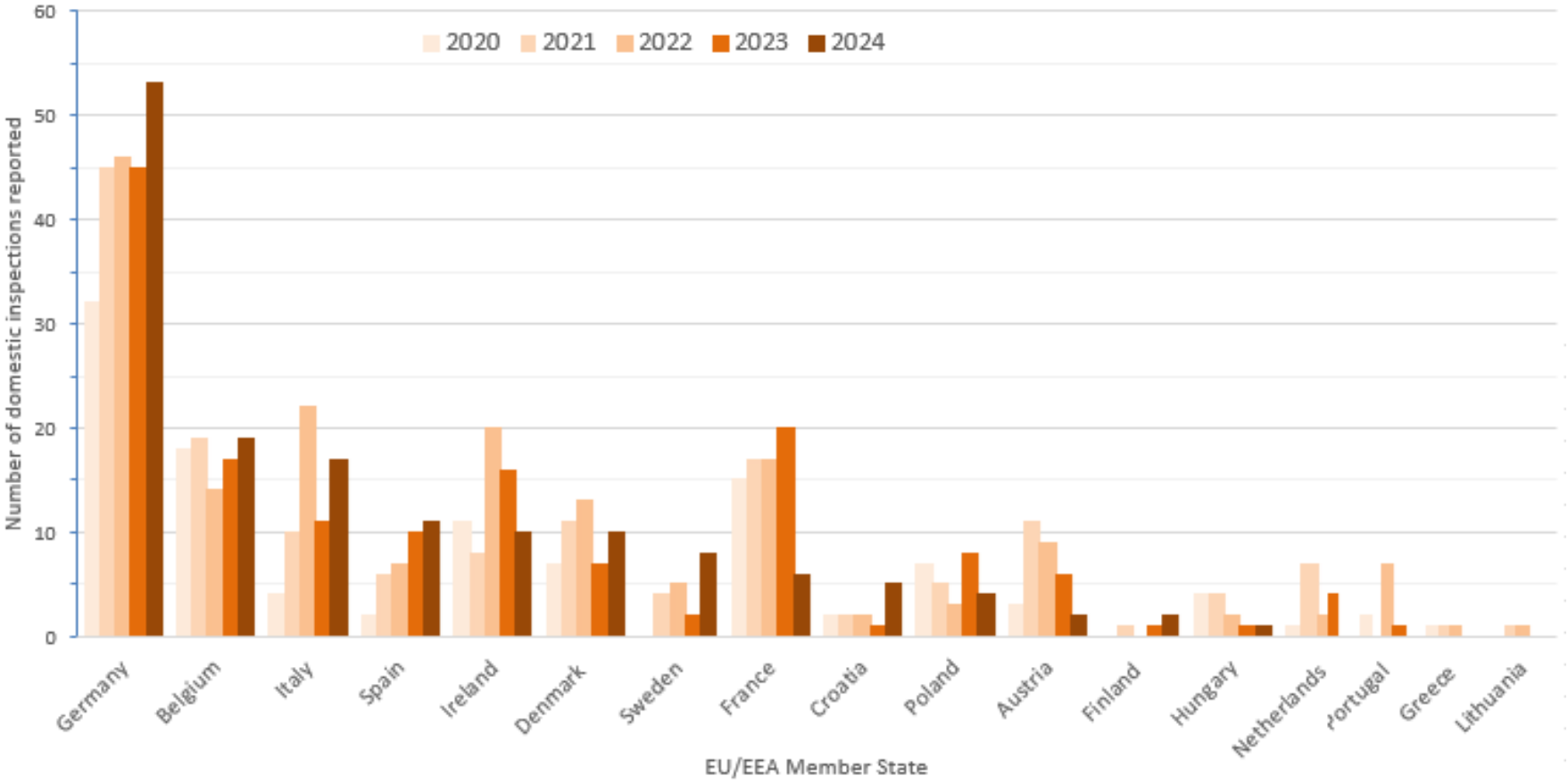
Number of reported domestic inspections



We have comparable figures re domestic inspections by the different countries / notified bodies

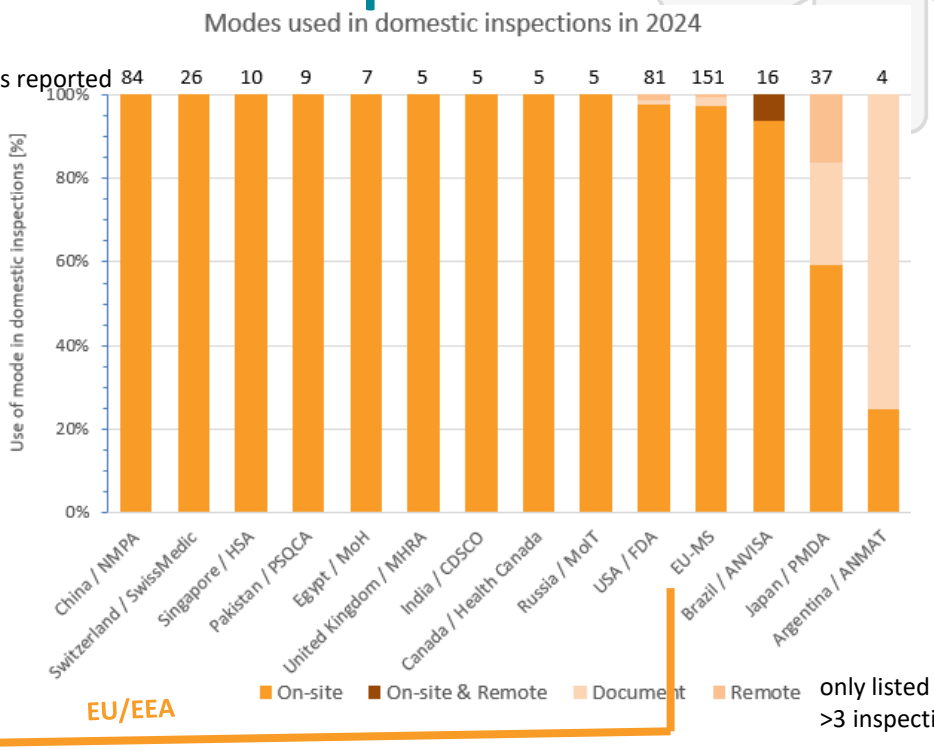
Only listed if more than 2 domestic inspections reported
Note: Notified Bodies doing certifications for devices included in Medicinal Products

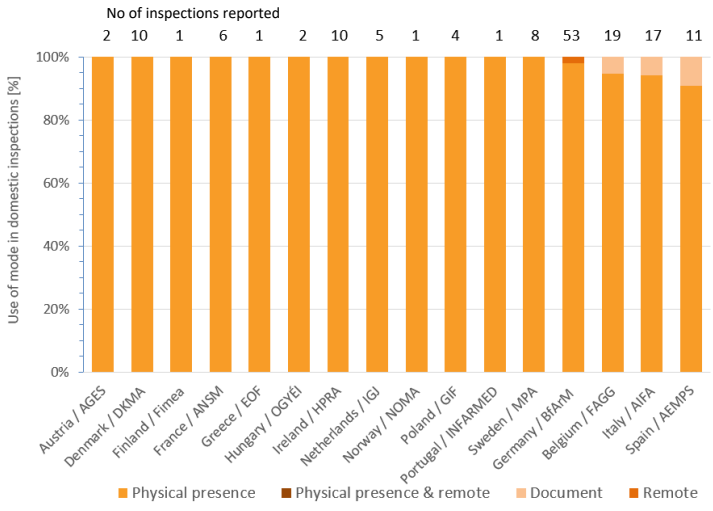
Number of reported domestic inspections by authorities in EU/EEA Member States



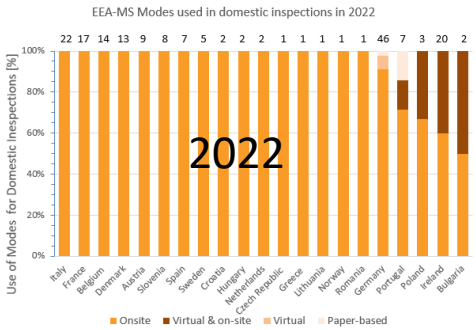
Inspection modes used in domestic inspections

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





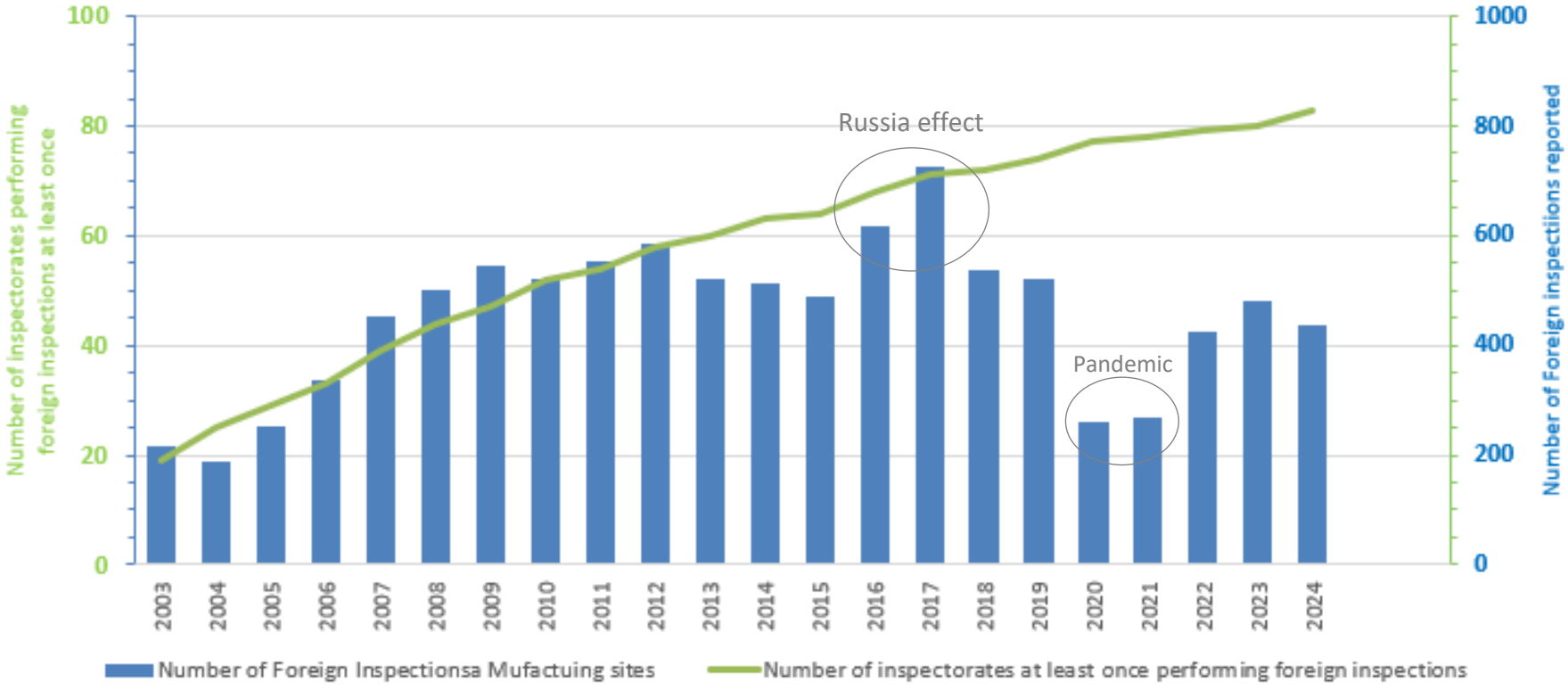
only listed if
>2 inspection



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

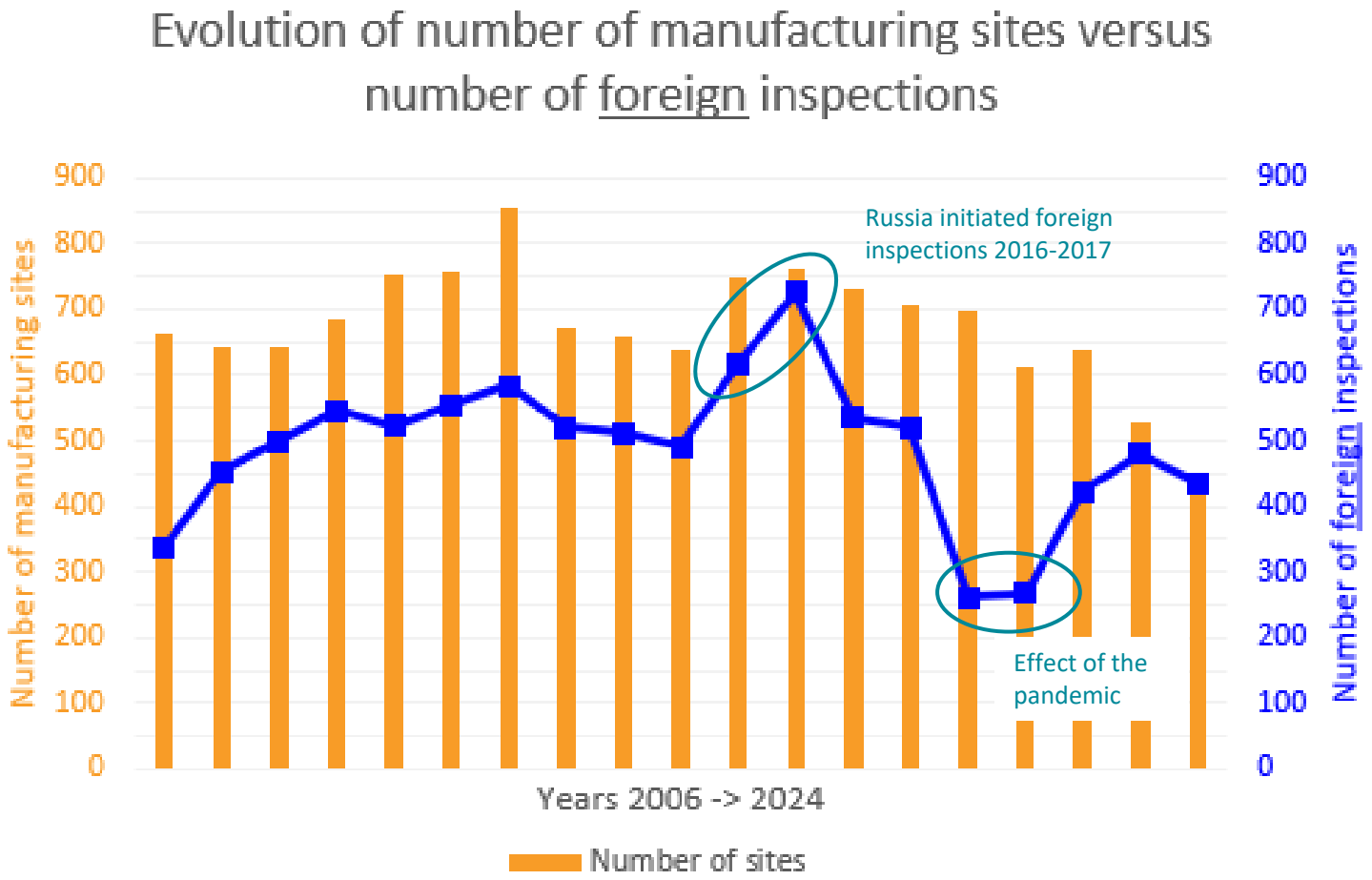
Foreign Inspection Activity

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

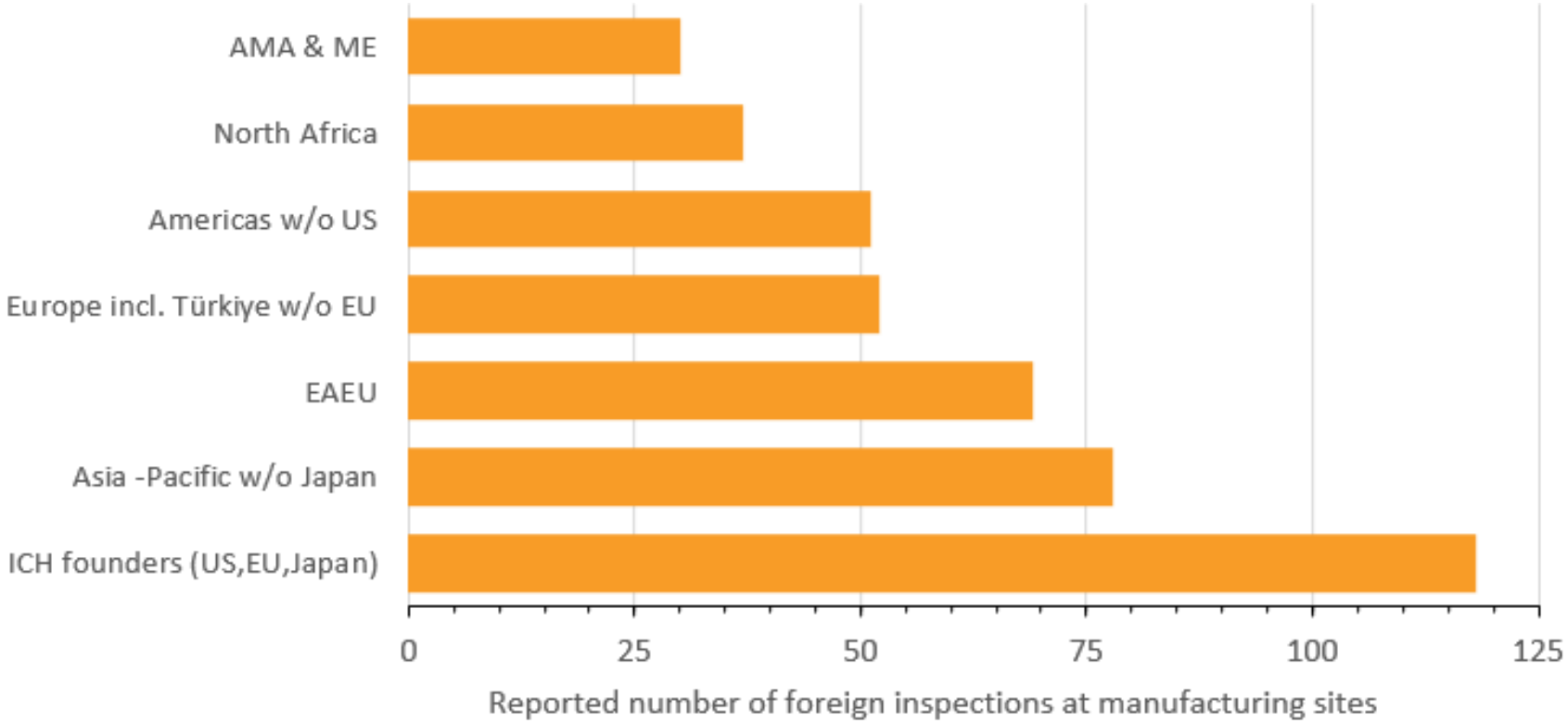
Number of foreign inspections at manufacturing sites



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

All inspections included independent of the mode used

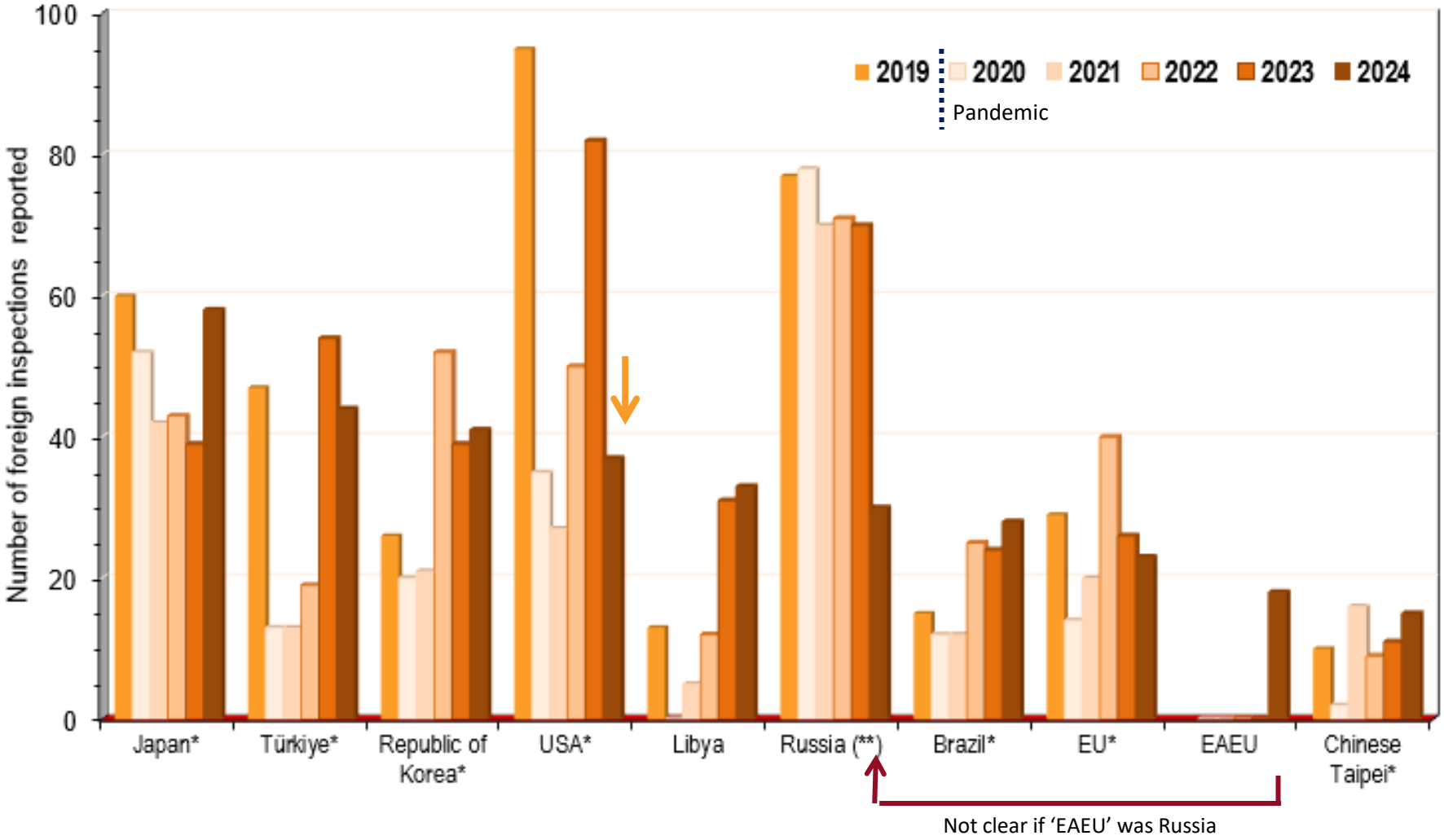
Number of foreign inspections at manufacturing sites by region of the inspectorate



* mostly driven by Rep. of Korea and Chinese Taipei

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

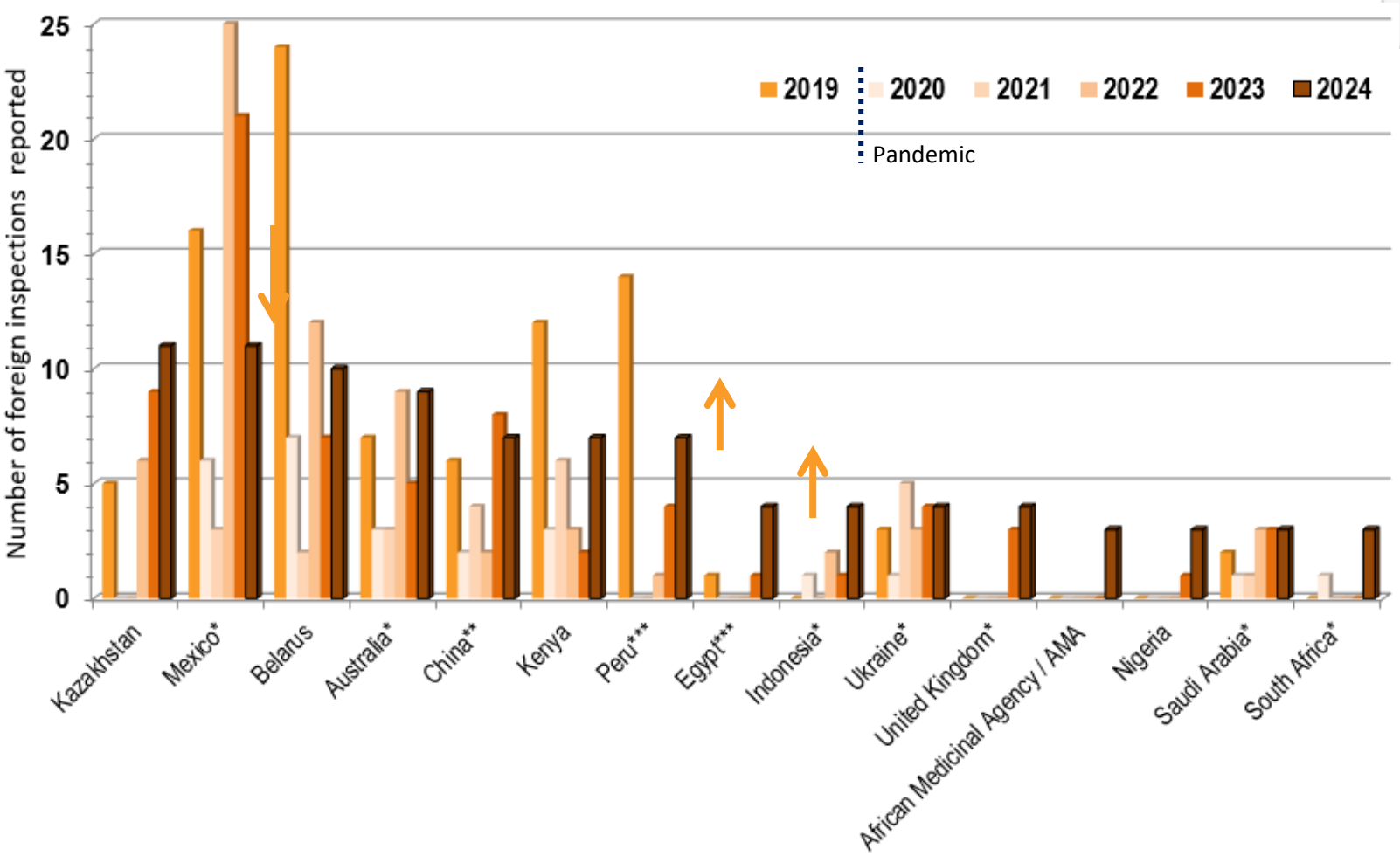
Number of foreign inspections by country 1/2



*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

Countries performing foreign inspections

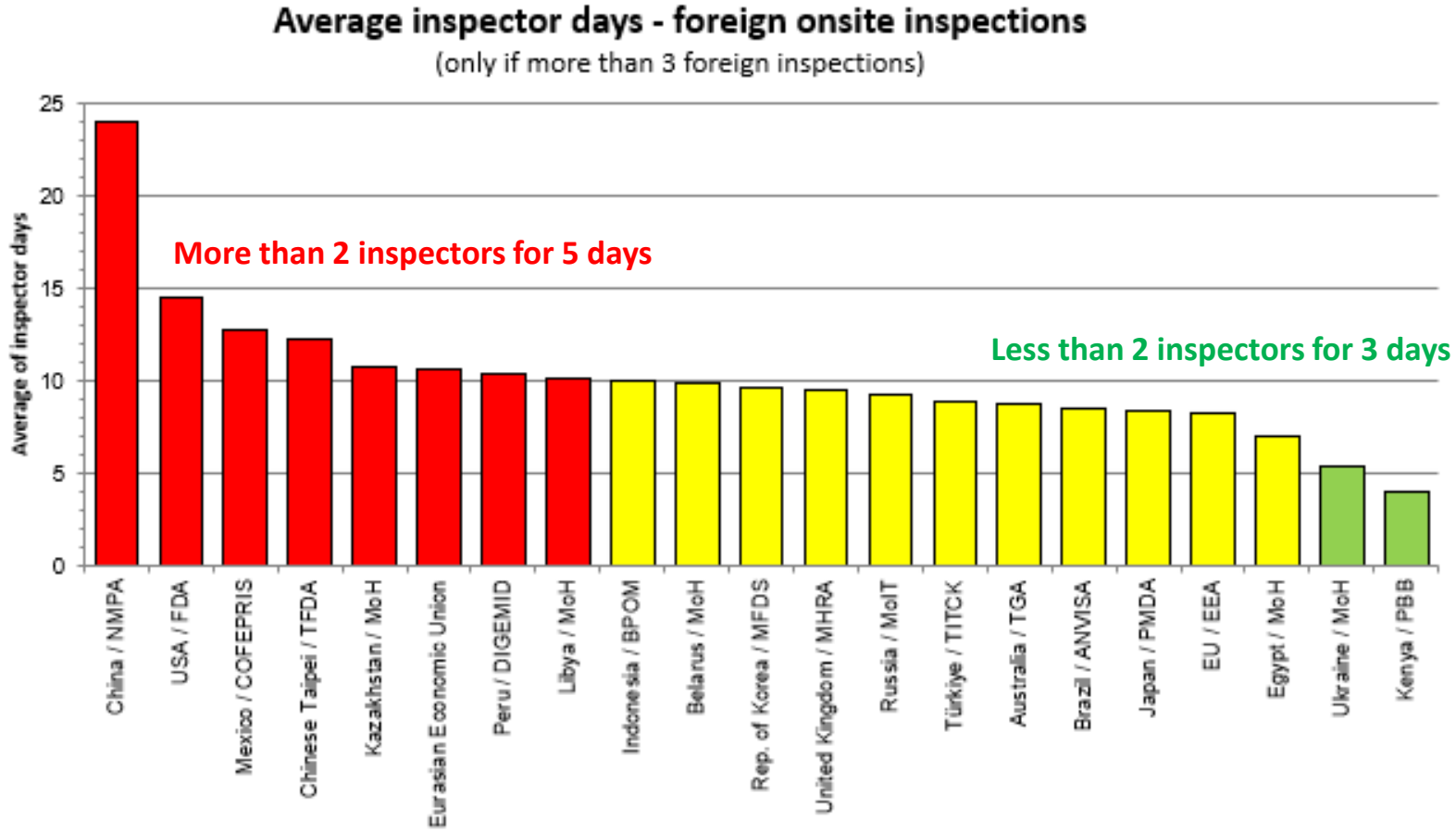
- 82 jurisdictions have performed foreign inspections from 2003 to 2024
- 38 jurisdictions performed foreign inspections in 2024

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

References:
a new in 2024
b EU/EEA countries as <u>one</u> 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

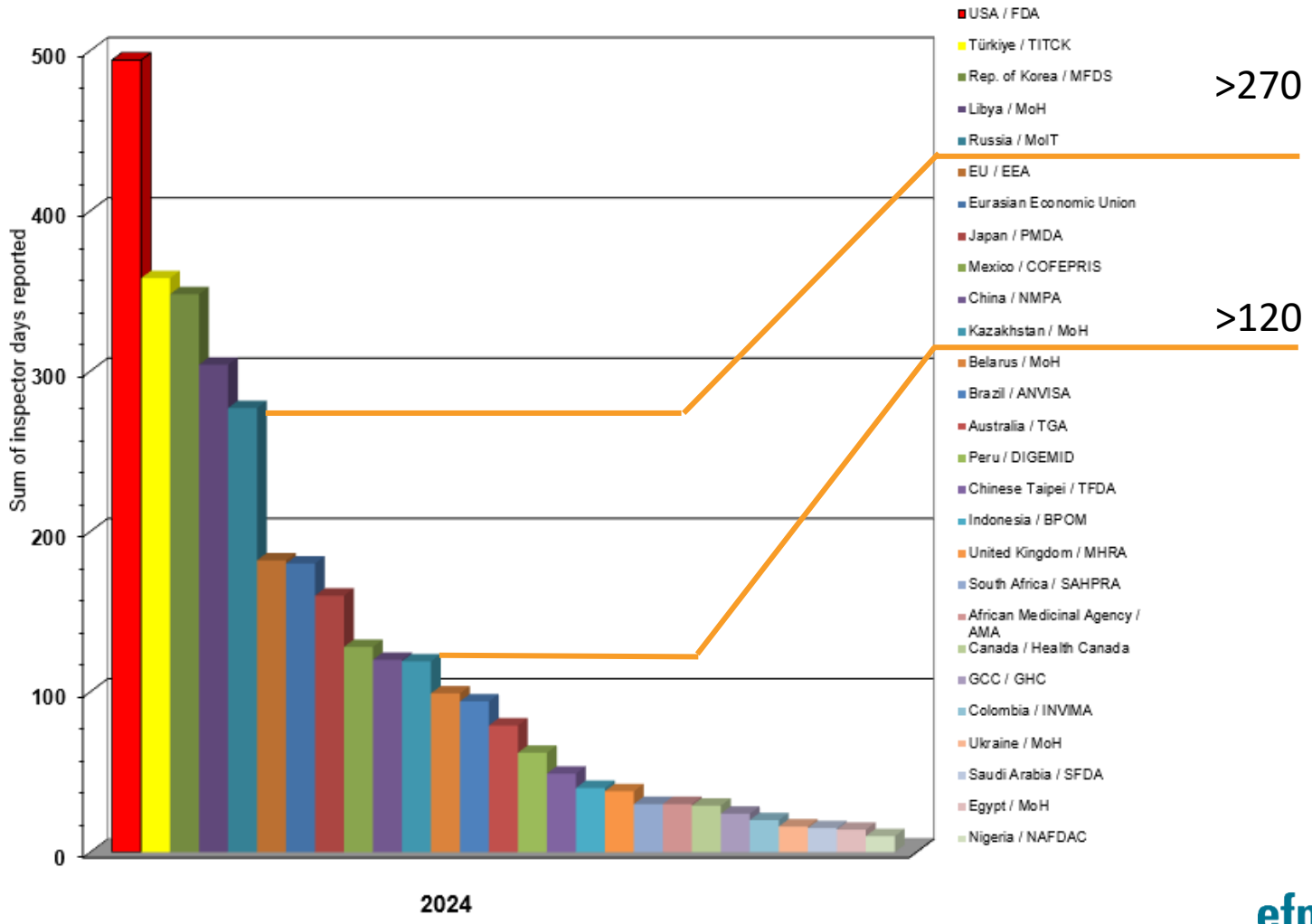
*Inspectorate is a PIC/S member **PIC/S applicant ***PIC/S pre-applicant

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



for China 4.5 inspectors in average – assumption: training of inspectors?

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

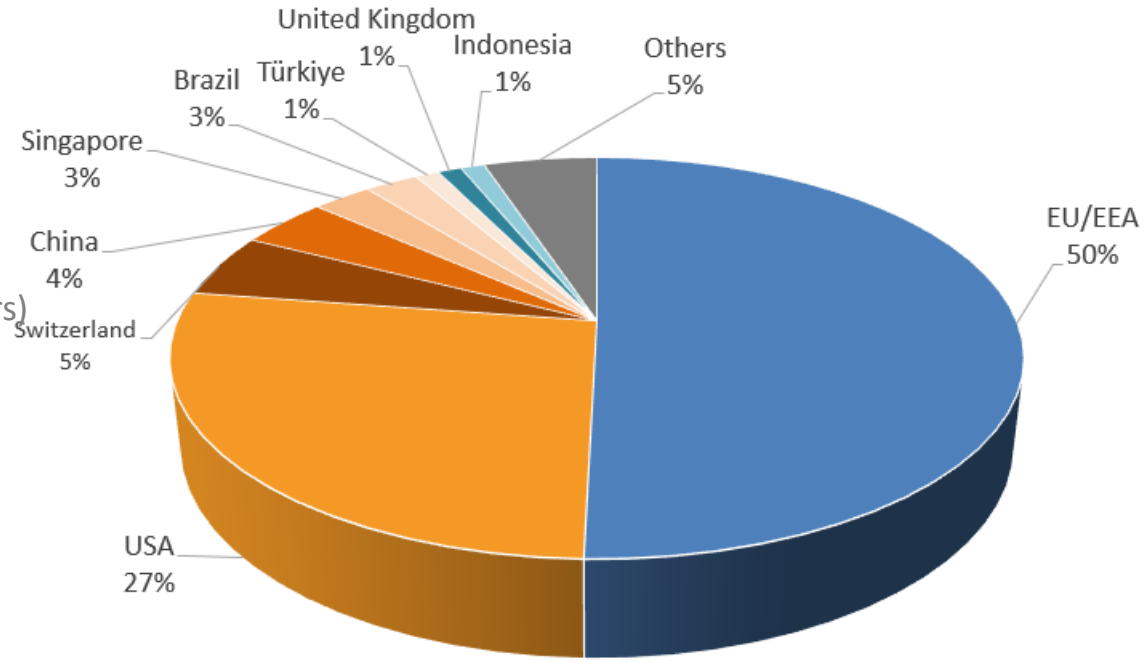


Excluded 6 inspectorates with < 10 days

Locations of manufacturing facilities hosting foreign inspections

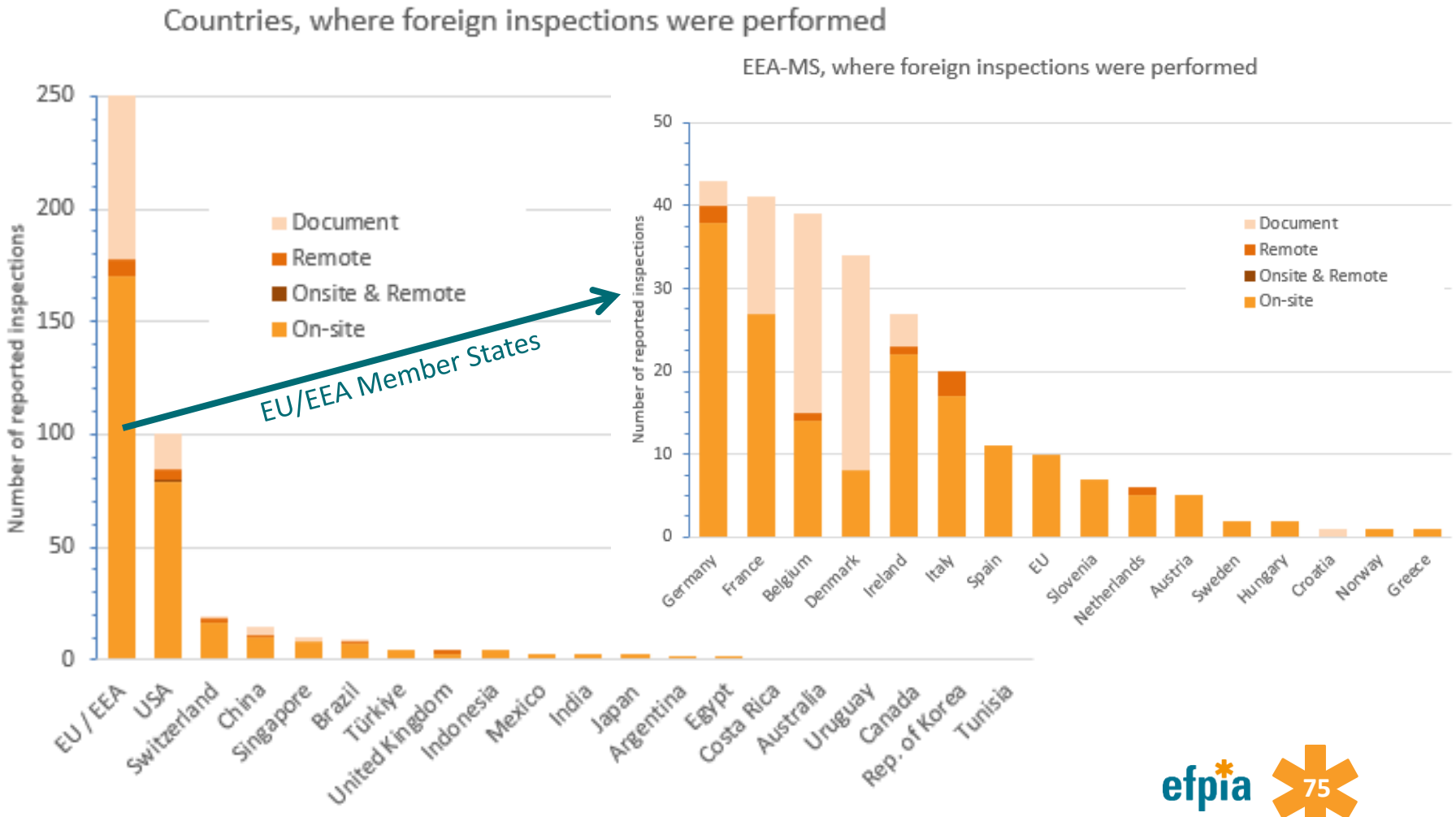
- **The location, where conducting foreign inspections, demonstrate that research-based manufacturers are mainly based in**
  - EU
  - US
  - Switzerland
  - China
  - Singapore

  (no change from previous years)

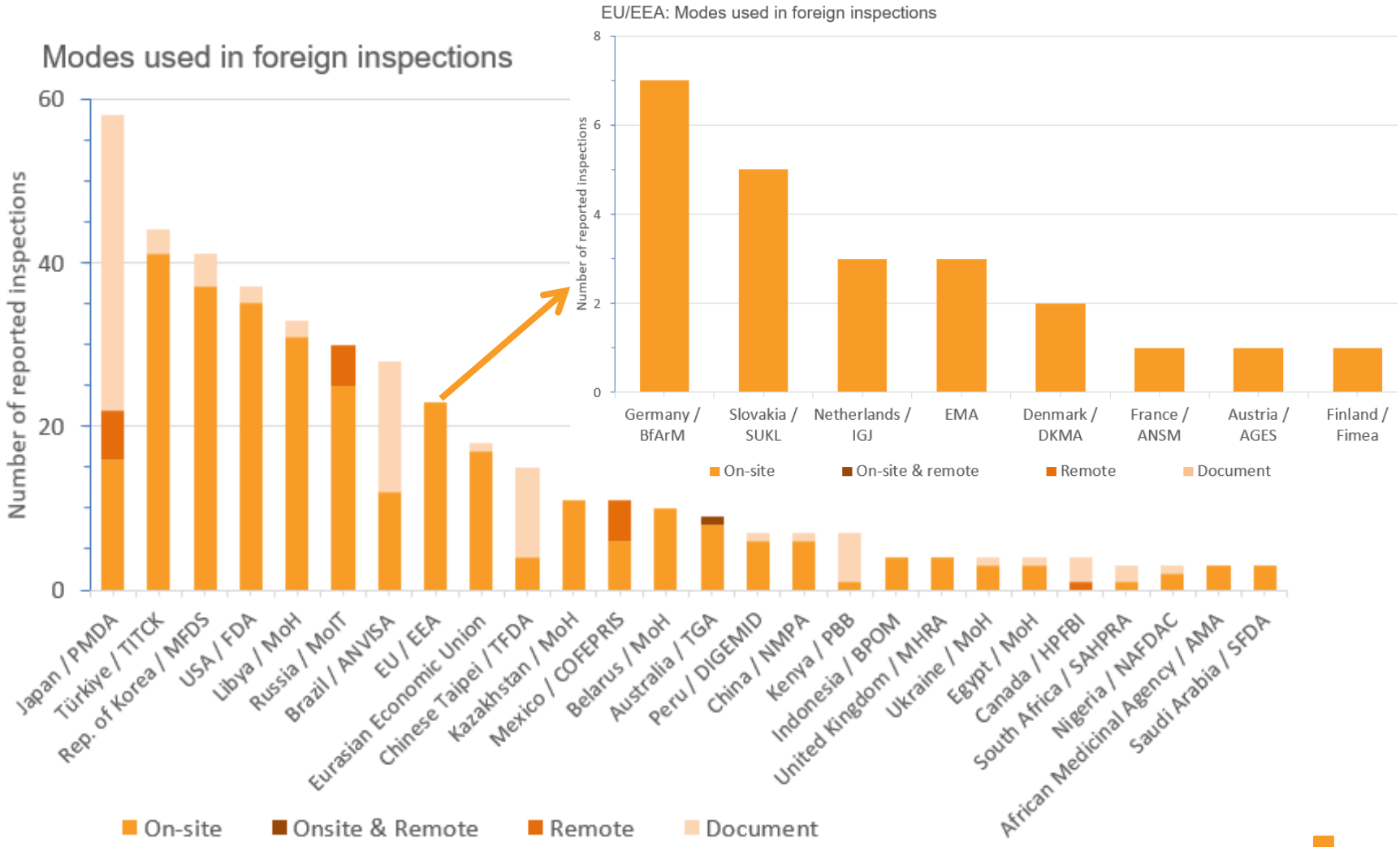


About 80% of the foreign inspections are conducted in EU/EEA, US and Switzerland

Locations of Manufacturing Sites Hosting Foreign Inspections

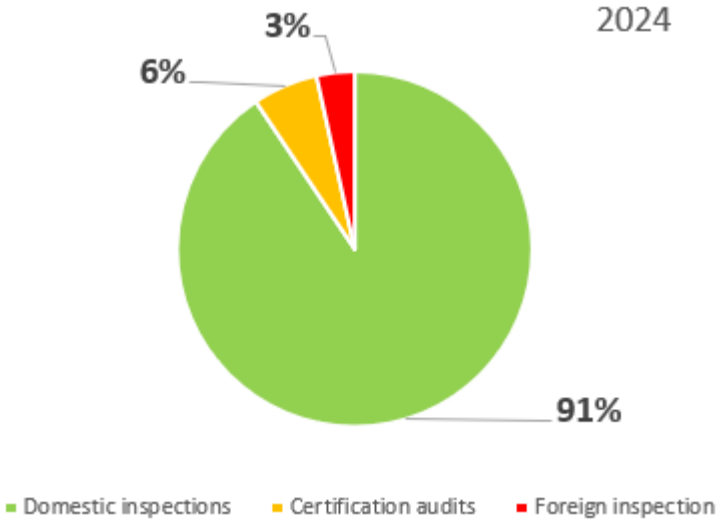


Modes used by inspectorates in foreign inspections

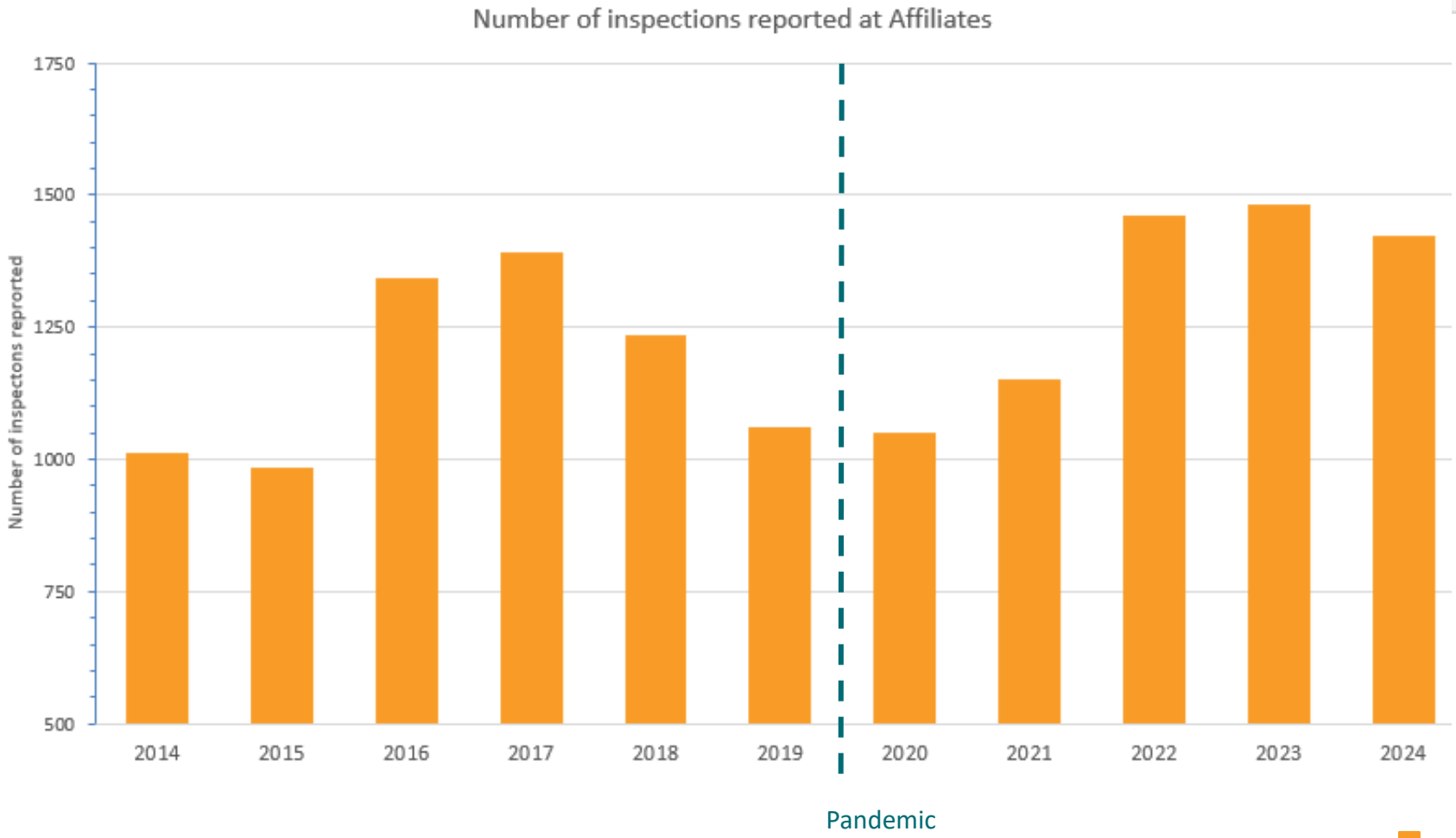


Only listed if 3 or more foreign inspections

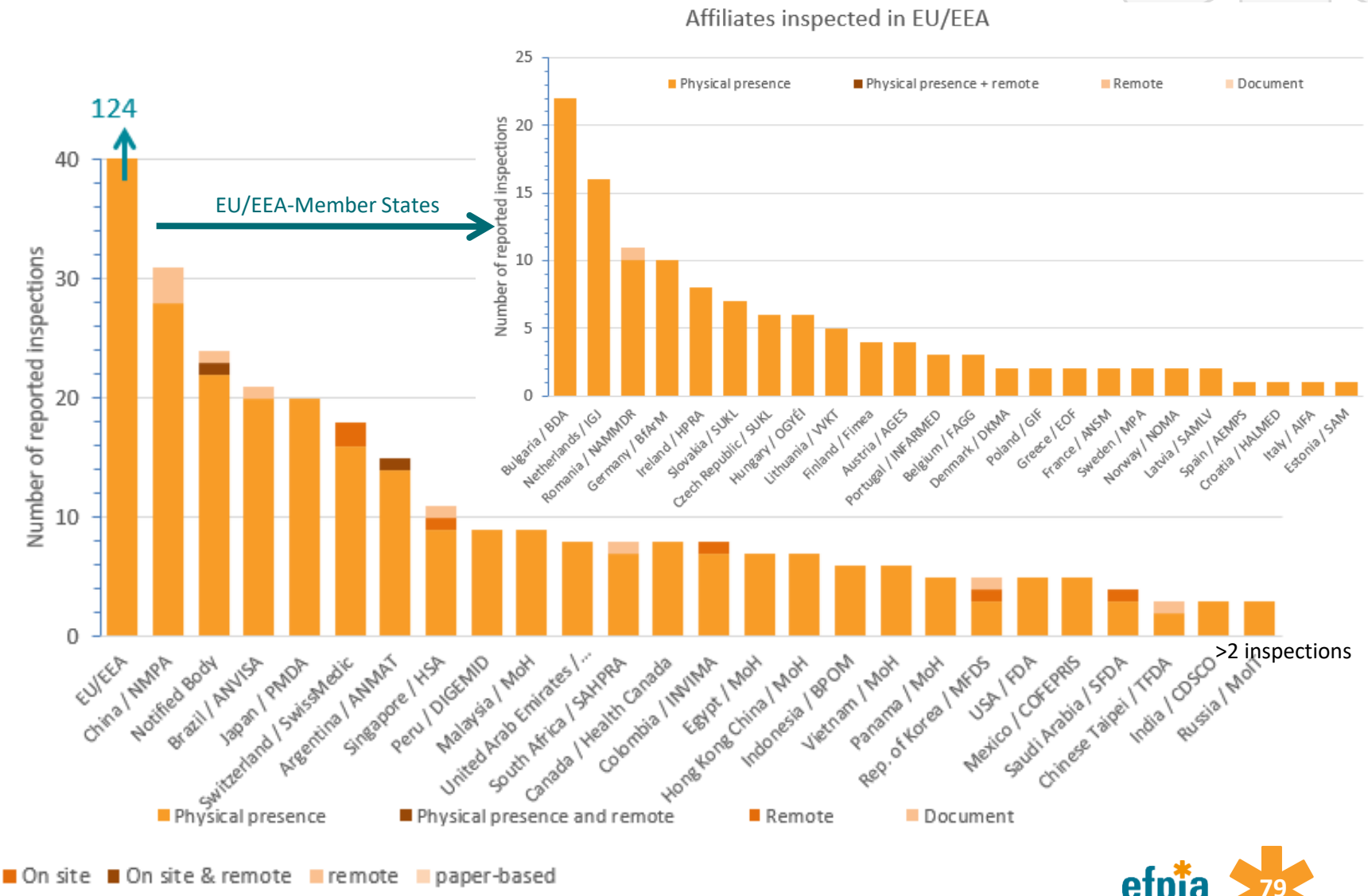
Inspections at Affiliates



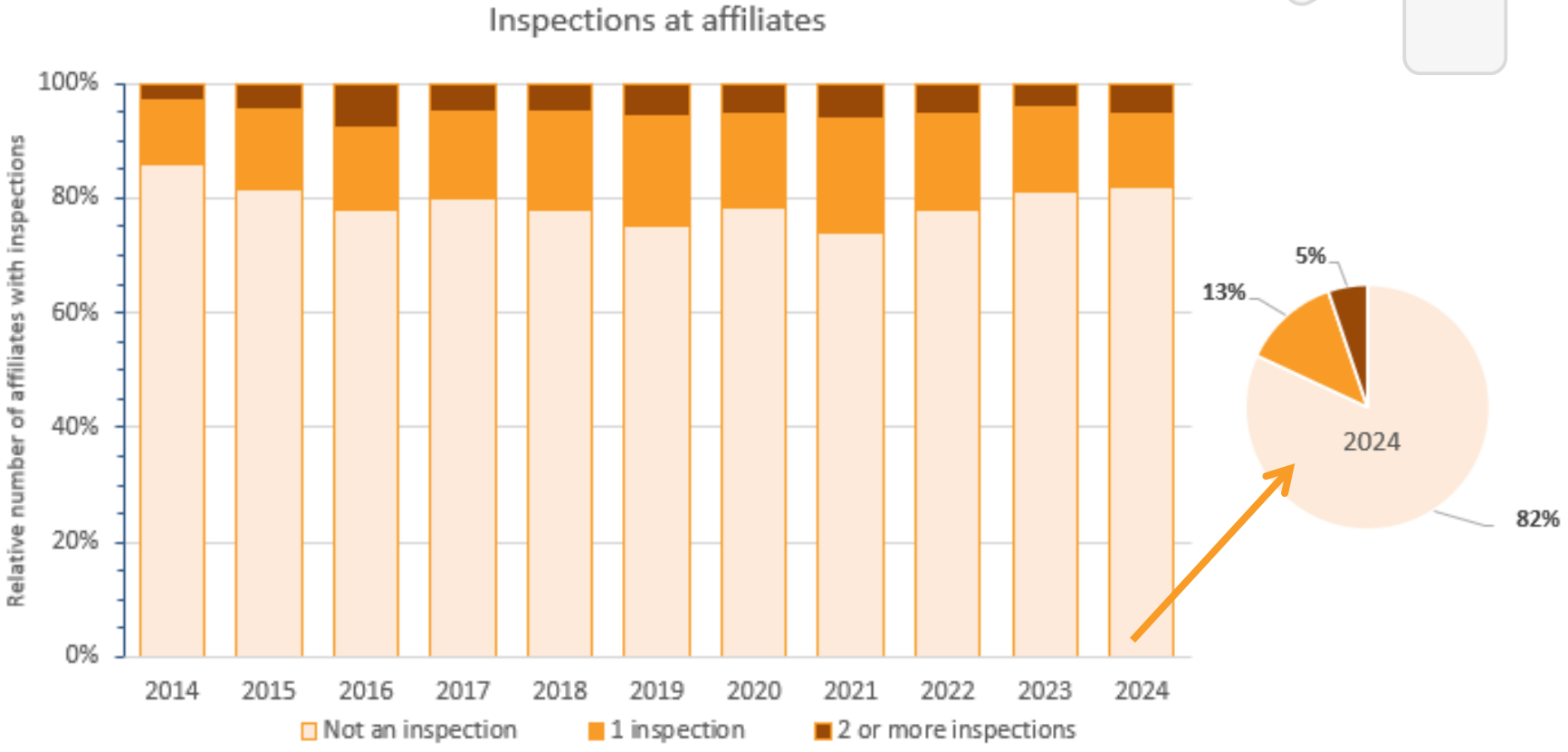
Constant level of inspections at affiliates with very limited influence by the pandemic



Local affiliates have received inspections - no trend by region



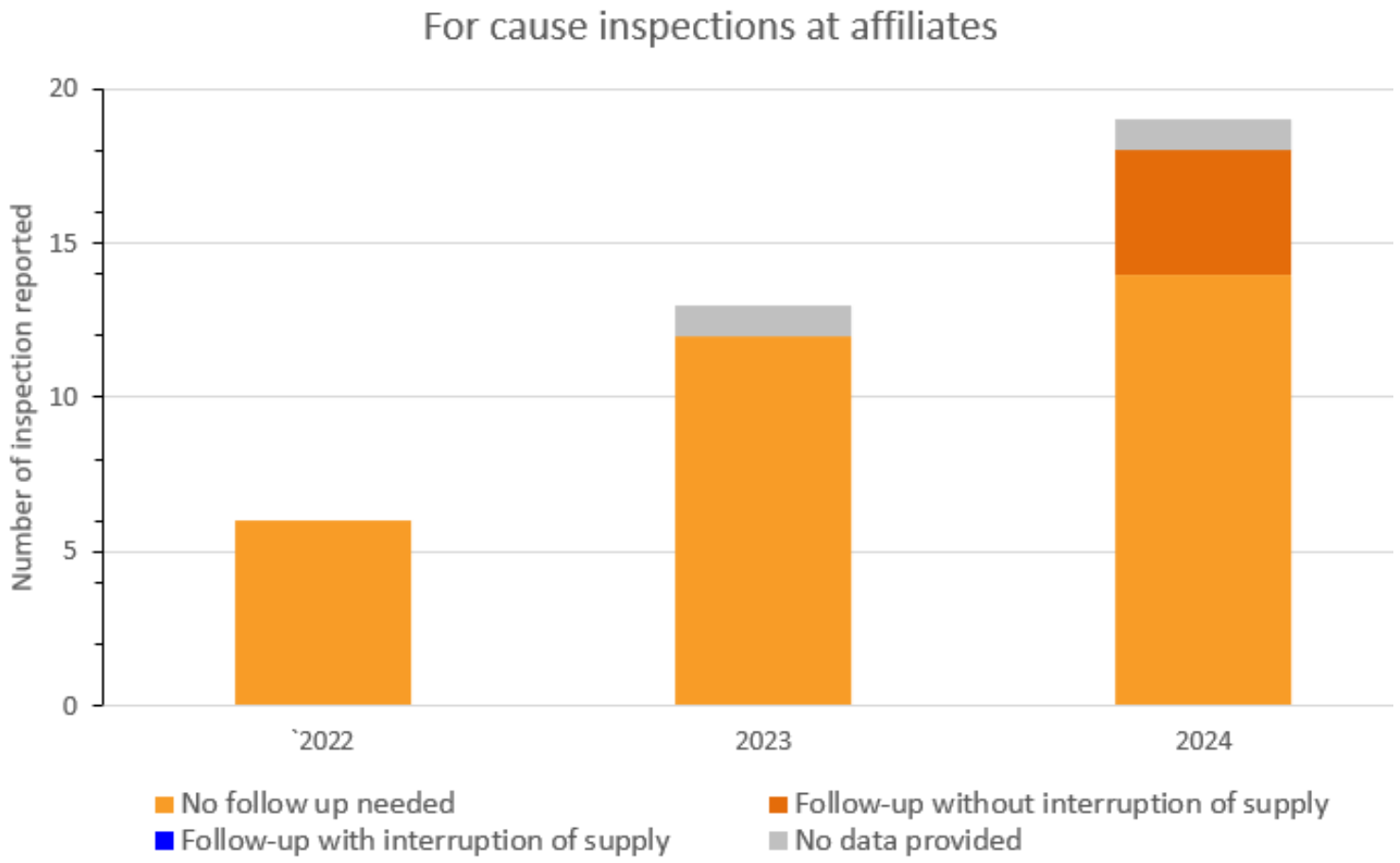
Number of affiliates inspected



Facts

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

For cause inspections do not result in interrupted supply



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

Specific Evaluations

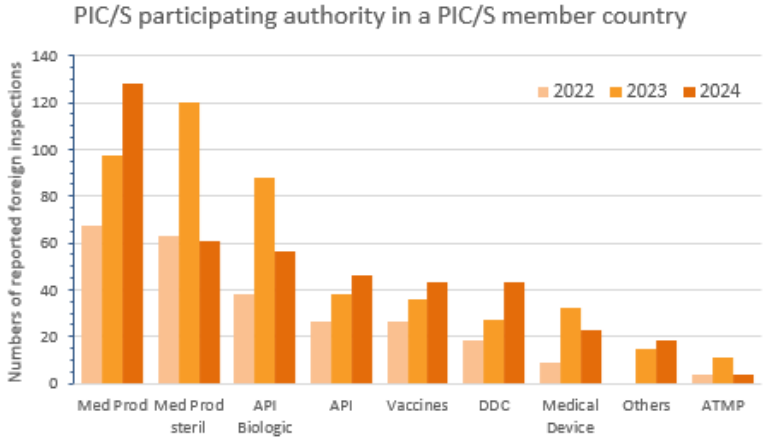
PIC/S

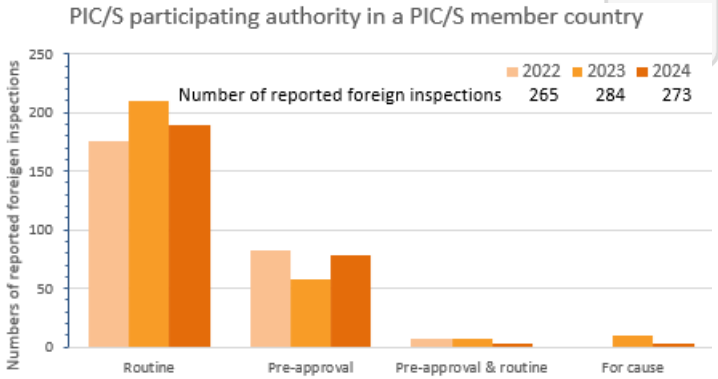
LEVERAGE TOOLS e.g.,

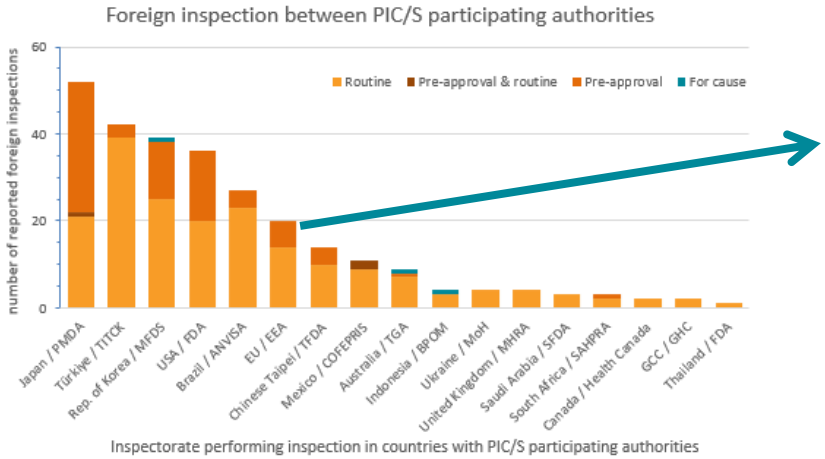
- **Risk-based inspection planning**,
  PIC/S guideline PI 037-1, 1 January 2012
- **GMP-Inspection reliance**,
  PIC/S guideline PI 048-1, 01 June 2018

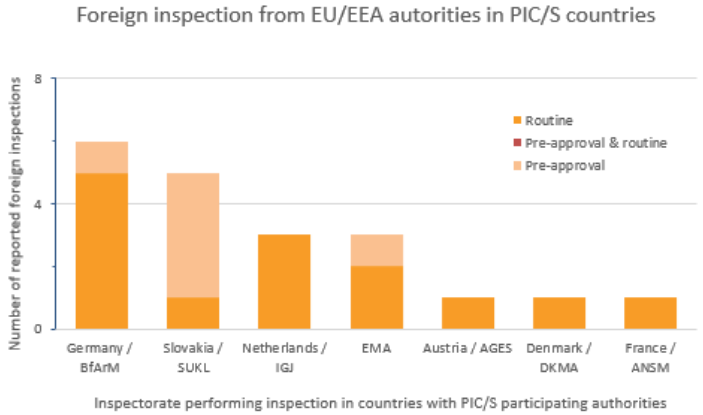
PIC/S Participating Authorities

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





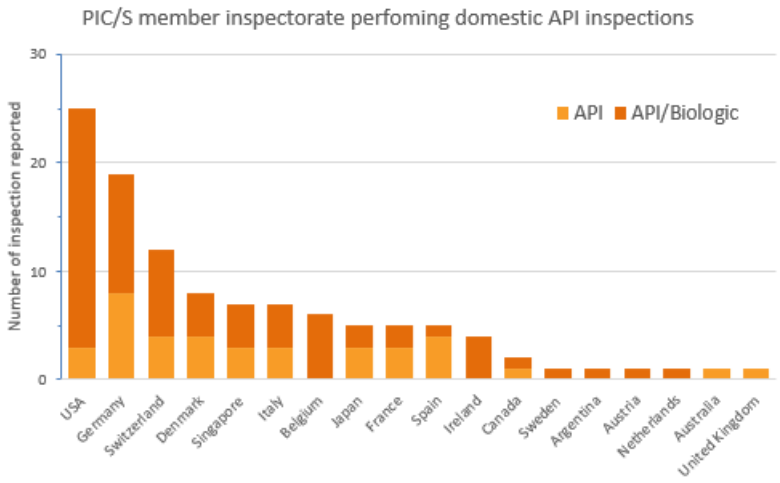




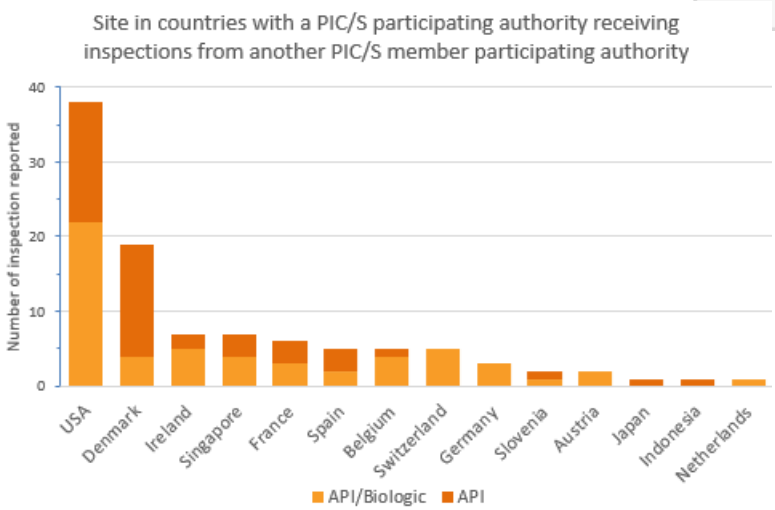
* **272/434 (2024: 62%; 2023: 62%; 2022: 63%) of the reported foreign inspections at manufacturing sites are amongst the PIC/S participating authorities**

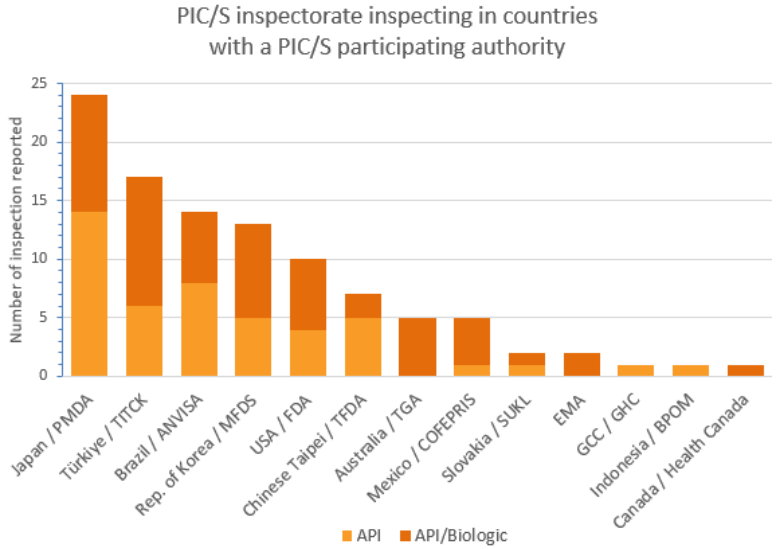
API inspections among PIC/S members

Domestic oversight by inspectorates

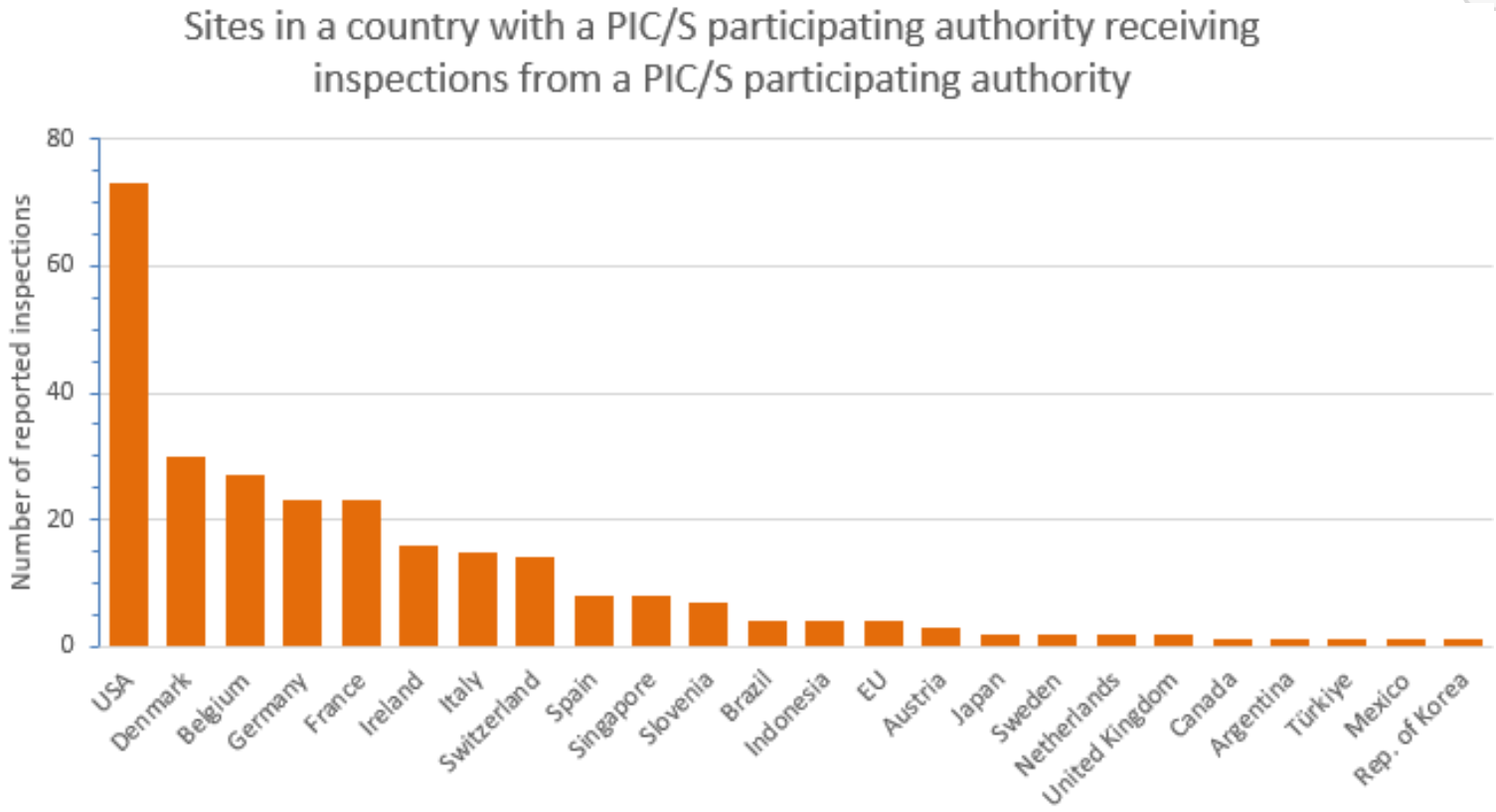


Sites receiving foreign inspections





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**

Applying reliance?!

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

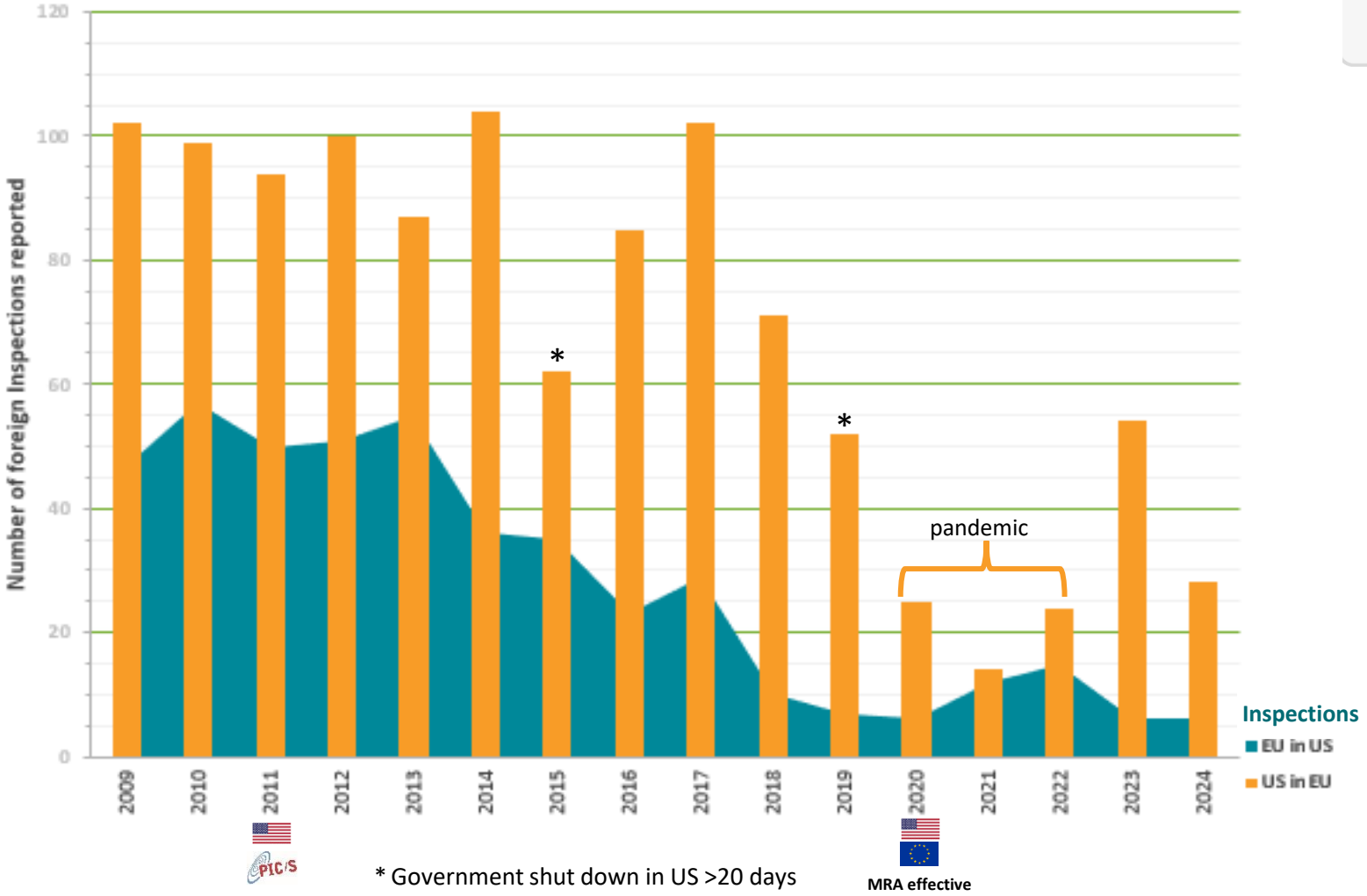
- Argentina / ANMAT
- Belgium / FAGG
- Greece / EOF
- Hungary / OGYÉI
- Ireland / HPRA
- Italy / AIFA
- Norway / NOMA
- Poland / GIF
- Portugal / INFARMED
- Singapore / HSA
- Spain / AEMPS
- Sweden / MPA
- Switzerland / SwissMedic

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

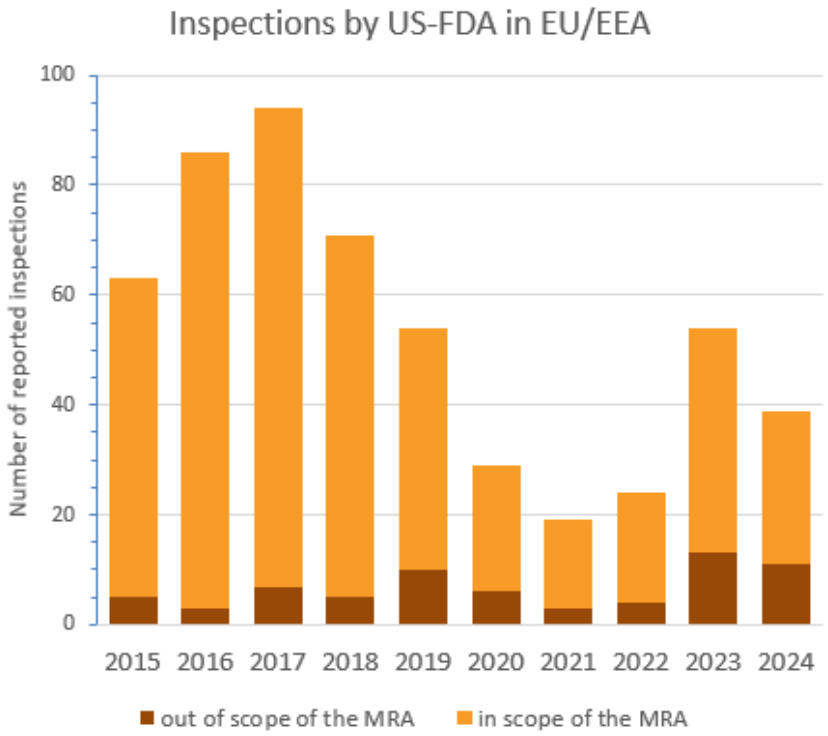
ANNUAL EFPIA INSPECTION SURVEY – MRA US/EU

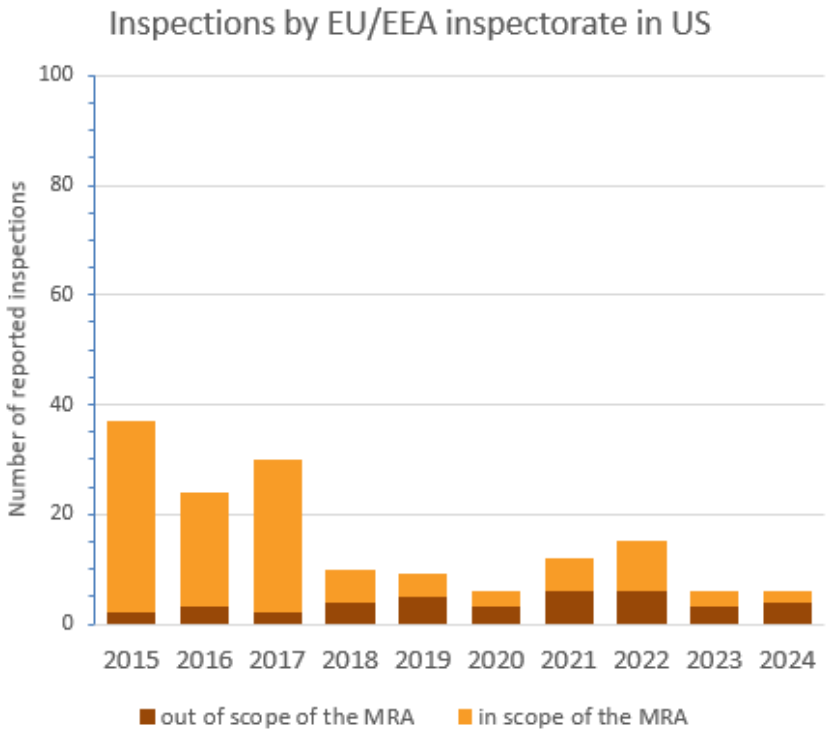
Full EU / US MRA implementation could leverage further benefits



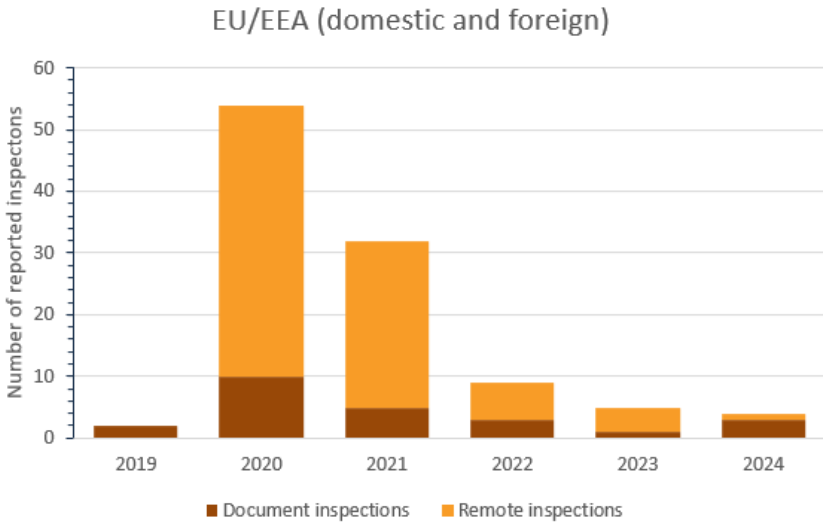
* Government shut down in US >20 days

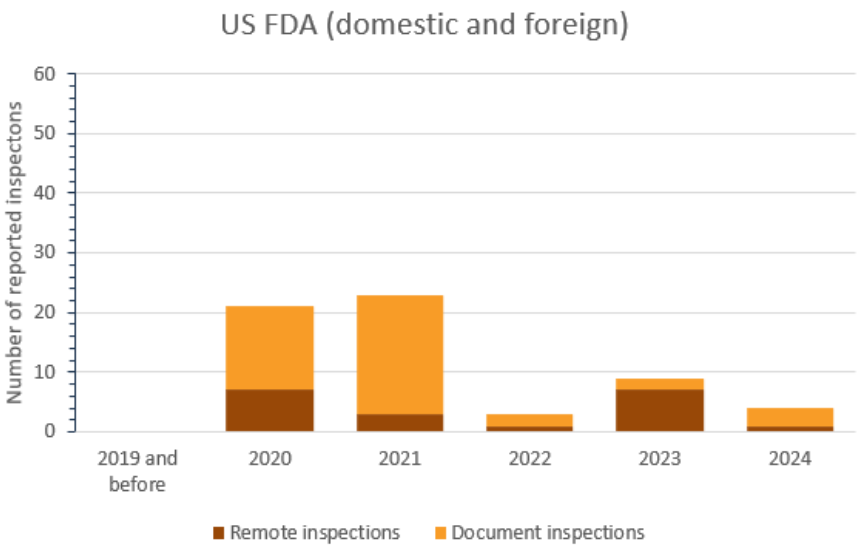
Inspections in each other territory as of scope





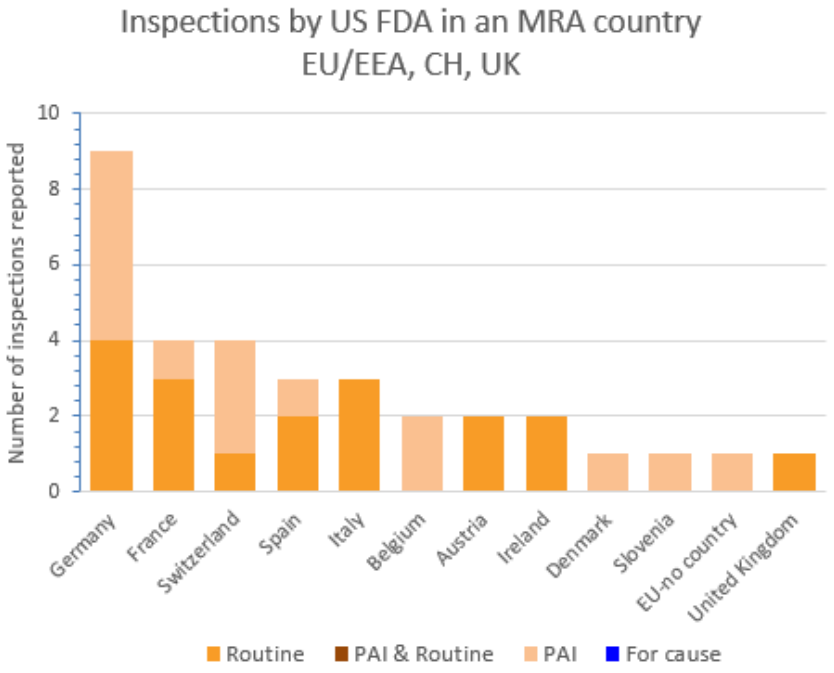
Remote (evaluations) and document inspections

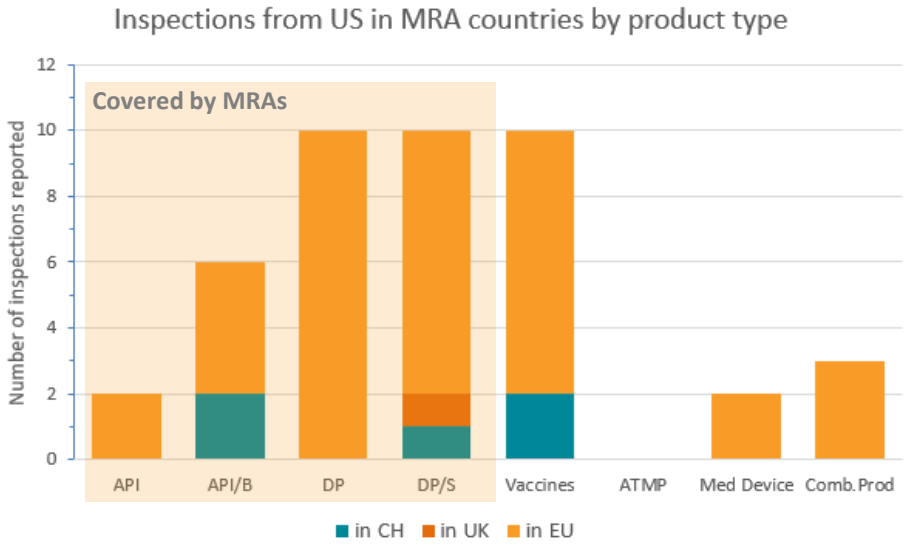




- EU/EEA: Trend of less remote inspections year by year after the pandemic
- US: No trend but slightly decreasing

Full MRA implementation could leverage further benefits





* **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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