Update on PQ Inspections

2022-2023 highlights & Importance of being inspected by WHO PQT

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Structure of this presentation

Our objectives and structure
Clear procedures, timelines and standards
Ensuring transparency for all
Working with sites to reach GXP compliance
Maximum efficiency & leverage of resources
Recognition of inspection outcomes by others
What we help prevent
Closing remarks

Cross Cutting Services

MEDICINE

VECTOR CONTROL

VACCINES

IVD

INSPECTION SERVICES

Onsite Inspection Timelines

- Initial inspection: within 6 months from dossier acceptance for assessment or from site confirming it is ready for inspection
- Notification: 1 – 6 months before inspection
- Onsite days: 2 – 5 days based on scope and complexity
- Report: 30 days from last date of inspection
- CAPAs: 30 days from receipt of report (max 2 rounds, comprehensive, soft and not hard copies)
- Closing of inspection: 6 months from inspection
- Follow-up inspection: 6 months from inspection
- Routine inspection: 1 – 3 years from the previous inspection

Notes: timelines for remote assessments are similar.

Composition of the inspection teams

For onsite inspections

1.**WHO representative**
Qualified inspector from PQT Inspection Services

2. Co-inspector
Qualified inspector from a well established inspectorate (e.g. PIC/S)

3. WHO Assessor
(for vaccines or diagnostics only)

4. Observer
National inspector(s) invited to participate and observe the inspection

5. Co-Inspector
from the rotational program

6. Observer
nominated by a recipient and or developing WHO member state

TRANSPARENCY FOR ALL: WHOPIRS

They are **detailed** and publicly available inspection reports for sites that are found to be compliant.

They are used by procurement agencies to verify the level of GMP compliance of sites prior to purchases

They are published within 30 days of the date of closure of an inspection, desk assessment or remote assessment.

See: https://extranet.who.int/pqweb/inspection-services/whopirs

TRANSPARENCY FOR ALL: NOTICES OF CONCERN

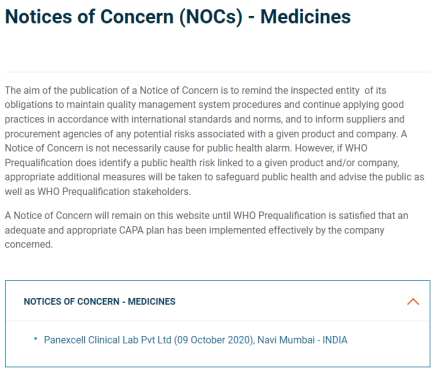
6 major or more
OR
critical deficiency
+
Marketed products

Letter is drafted to the site – the site is given 10 days to respond.

The letter may be rescinded depending on the response and published to the WHO website if issues are not adequately resolved in 10 day timeframe

It is shared by email with our international partners and with member states

Removed from WHO website only once issues are adequately resolved



Available at: https://extranet.who.int/pqweb/inspection-services/notice-concern

Working with Medicines sites towards GXP compliance

If the initial inspection is non-compliant

- the site is given a detailed list of non-conformities.
- Meetings with PQT INS upon request to further explain the issues & to ensure they are well understood.

Referral to LPA for qualifying sites

CAPA

- Feedback provided on CAPA plans.
- Flexible approach when certain CAPA may take time to be implemented.

For sites that are borderline GMP compliant after CAPA

- Follow-up inspections or routine reinpections at a closer time (depending on the level of risk)
- PQT INS has significant experience with this, especially for local production and critical products based on risk/benefit.

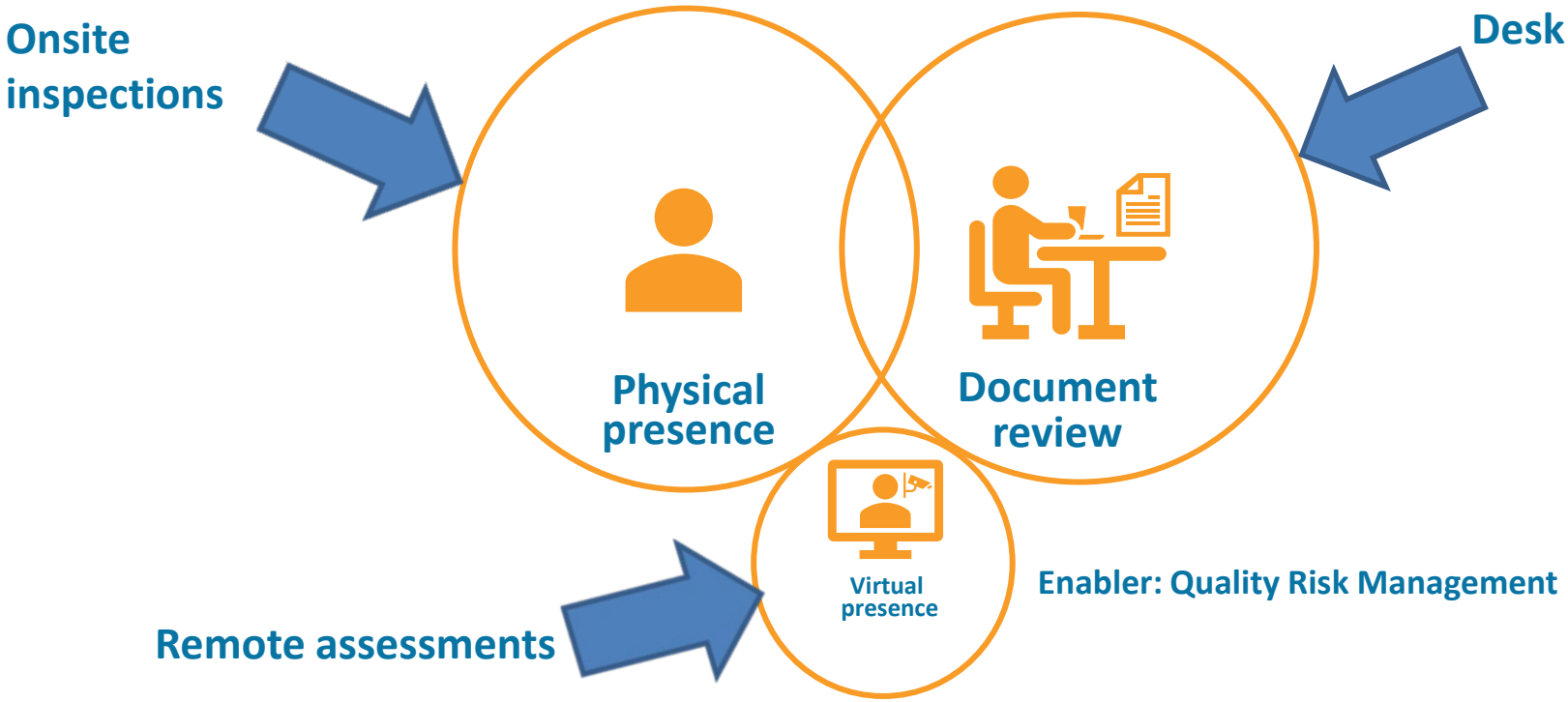
51 sites received a follow-up inspection after having been found initially non-compliant or "follow-up inspection required" upon closing of the initial inspection since 2002. 35 sites (57% found compliant).

415 sites found non-compliant during the initial inspection since 2002, an additional 25 sites were closed with "follow-up inspection required"

*Not counting vaccine sites

How

Use of different regulatory tools to verify adequacy and compliance

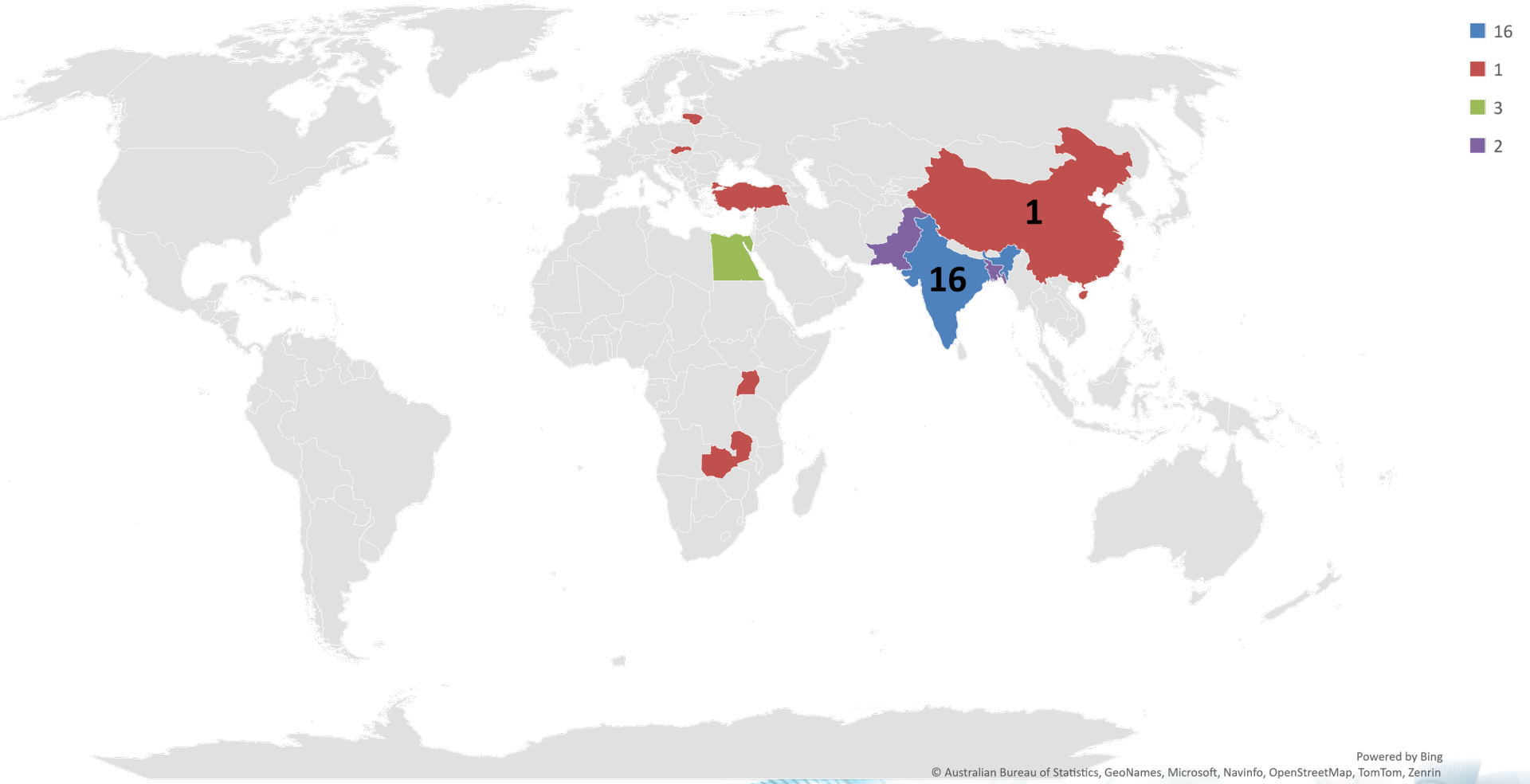


Tools are not equivalent
Each has challenges and opportunities

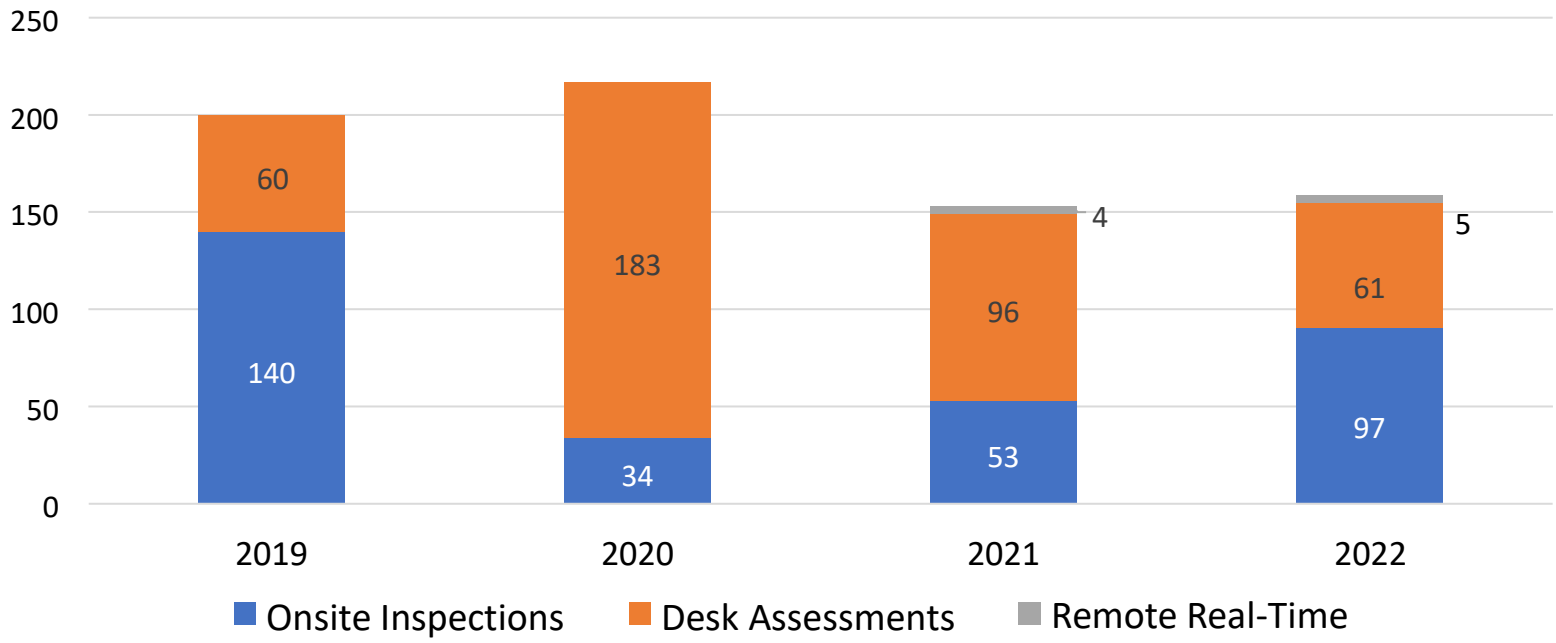
*Good reliance practices in the regulation of medical products: high level principles and considerations, WHO, *TRS 1033, Annex 10,* **2021,** 237-267.

Diagrams partially taken from Annual Inspection Survey 2020, EFPIA, May 2021

Countries of focus for onsite inspections in 2022 (Medicines)



Inspection Statistics (all streams combined)



Number of sites inspected in total in First half of 2023 – All streams

	FPP	API	CRO	QCL	Vax	IVDs	VCPs	Totals
Onsite	18	6	9	7	6	16	8	**70**
Remote	0	0	0	0	0	0	0	**0**
Desk assessments	3	4	0	0	0	5	5	**17**
Totals	21	10	9	7	6	21	13	**87**

WHO PQT Inspections:

Reliance & importance of establishing effective & strategic Partners to increase regulatory efficiency

- Pharmaceutical Inspections Cooperation Scheme (PIC/S)
- EMA GMDP IWG – GMP related activities
- EMA GCP IWG – GCP and BE activities
- FDA EMA MHRA TGA HC ANVISA WHO WG – API sites
- International Group on Nitrosamines
- IAPG – Interagency Pharmacist Group (Partners and UN agencies)
- NRA's – individual (Confidentiality agreements)
- ICMRA – GMP Digitalization working group
- MDSAP – Sharing of audit findings by Notified bodies (for IVDs)
- Concept of WHO Listed authorities – Global benchmarking tool

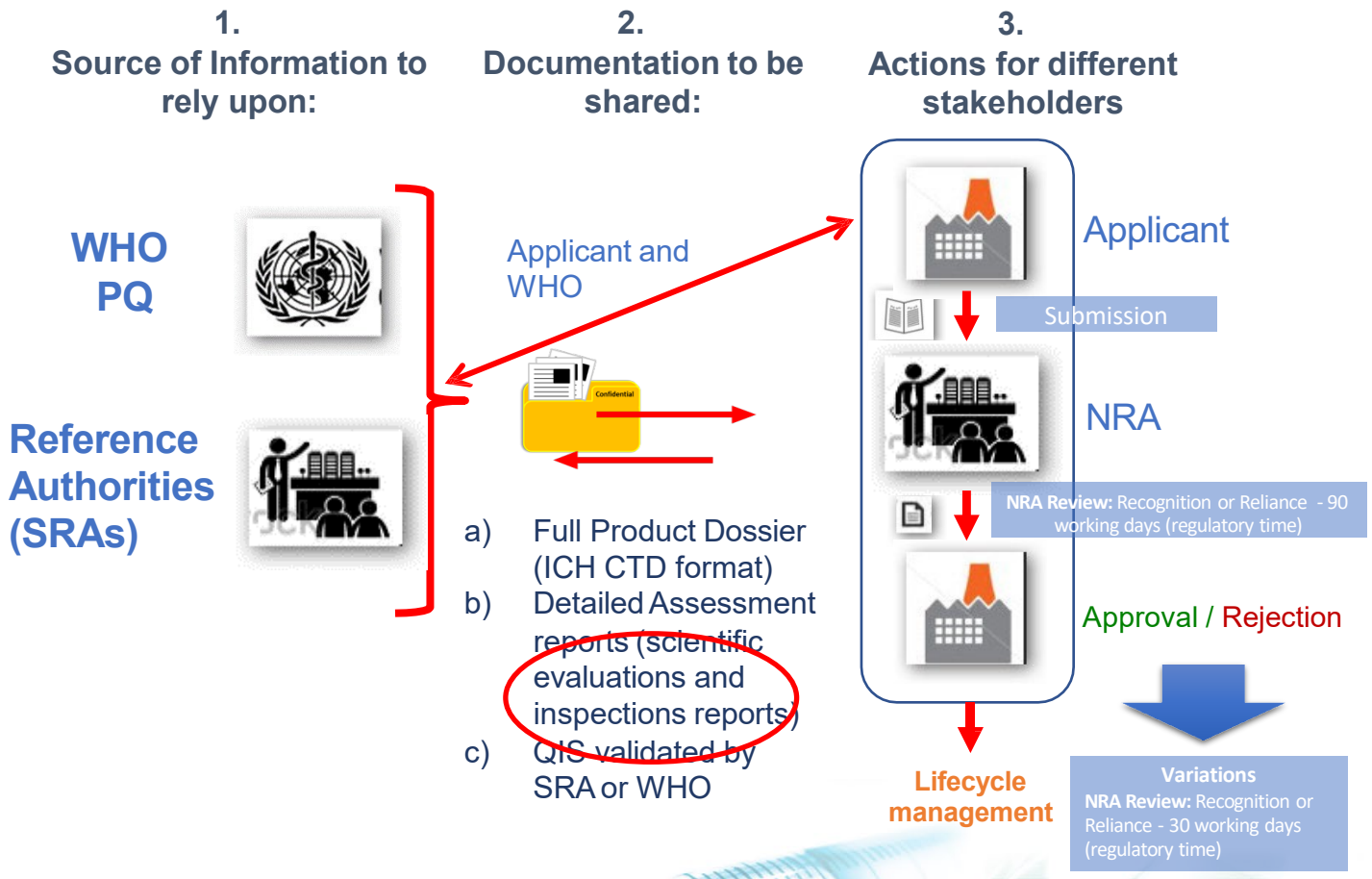
Focus on risk analysis to prioritize inspections and to avoid duplication of inspections:

Factors taken into consideration include:

- Type of site (Sterile aseptic higher risk than terminal sterilization, higher risk then solid dosage forms, higher risk than APIs, higher risk than QCLs, etc…)
- Number of products per site
- Past compliance history: This includes verification of internal GMP compliance records + EUDRAGMDP, COMSTAT, API Masterlist and other regulatory tools.
- Information sharing amongst authorities through regular meetings on potential contamination with nitrosamines, whistleblower, intelligence, etc.
- Number and nature of complaints received re site's products.
- Internal triggers, such as many variations, assessor remarks, data integrity concerns.

Leverage of WHO PQT Inspection work through CRP

CRP Process (PQ CRP or SRA CRP)

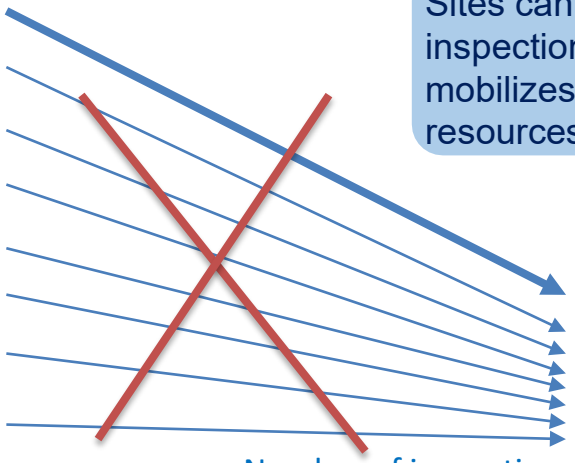


The importance of reliance and/or recognition

For onsite inspections

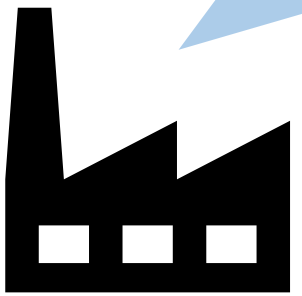
- National regulatory authority A
- National regulatory authority B
- National regulatory authority C
- National regulatory authority D
- National regulatory authority E
- National regulatory authority F
- National regulatory authority G
- National regulatory authority H

X 194 WHO Member States



Number of inspections

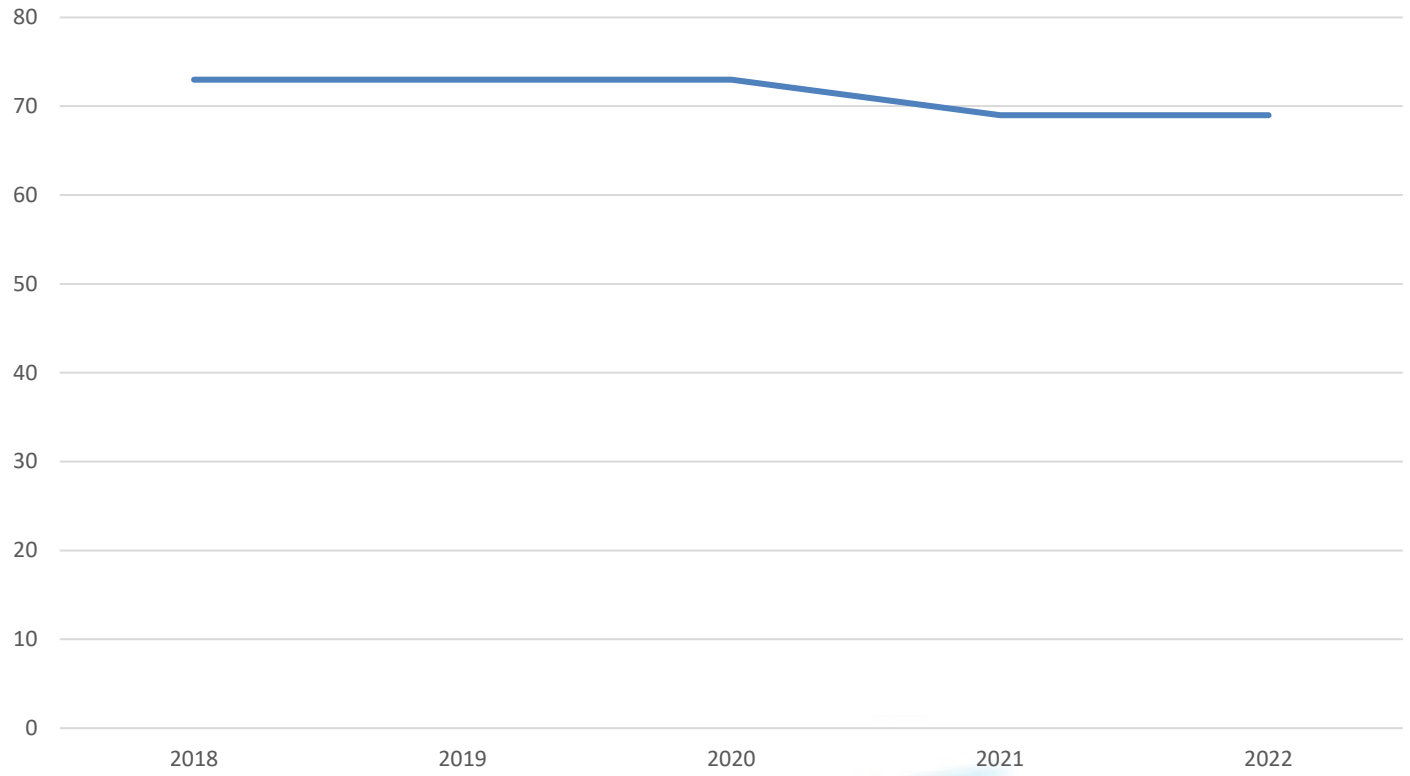
Sites can usually accommodate only 1 inspection at a time as each inspection mobilizes significant personnel and resources



Manufacturing site

It is crucial to be able to rely on the work best performed by others for decision-making because it is not realistic or useful to repeat each other's inspections.

Percentage of sites found compliant after onsite inspections performed 2018-2022



*does not include vaccines

CONCLUSION

WHO PQT inspections are beneficial to manufacturers, procurement agencies, partners & patients:

- ✓ Performed using a standardized & fair approach
- ✓ Through the use of enhanced collaboration, it enables recognition of GXP compliance on wider basis.
- ✓ Provide opportunities for improvement to companies and reinforcement of their compliance
- ✓ Increased market access of products across Member States when applicants opt to participate in the CRP & eliminates or reduces the need for additional inspections.
- ✓ Strong use of regulatory flexibility
- ✓ Emphasis on local production

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

FDA Commissioner Scott Gottlieb, M.D. October 31, 2017.

For a more detailed discussion:
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