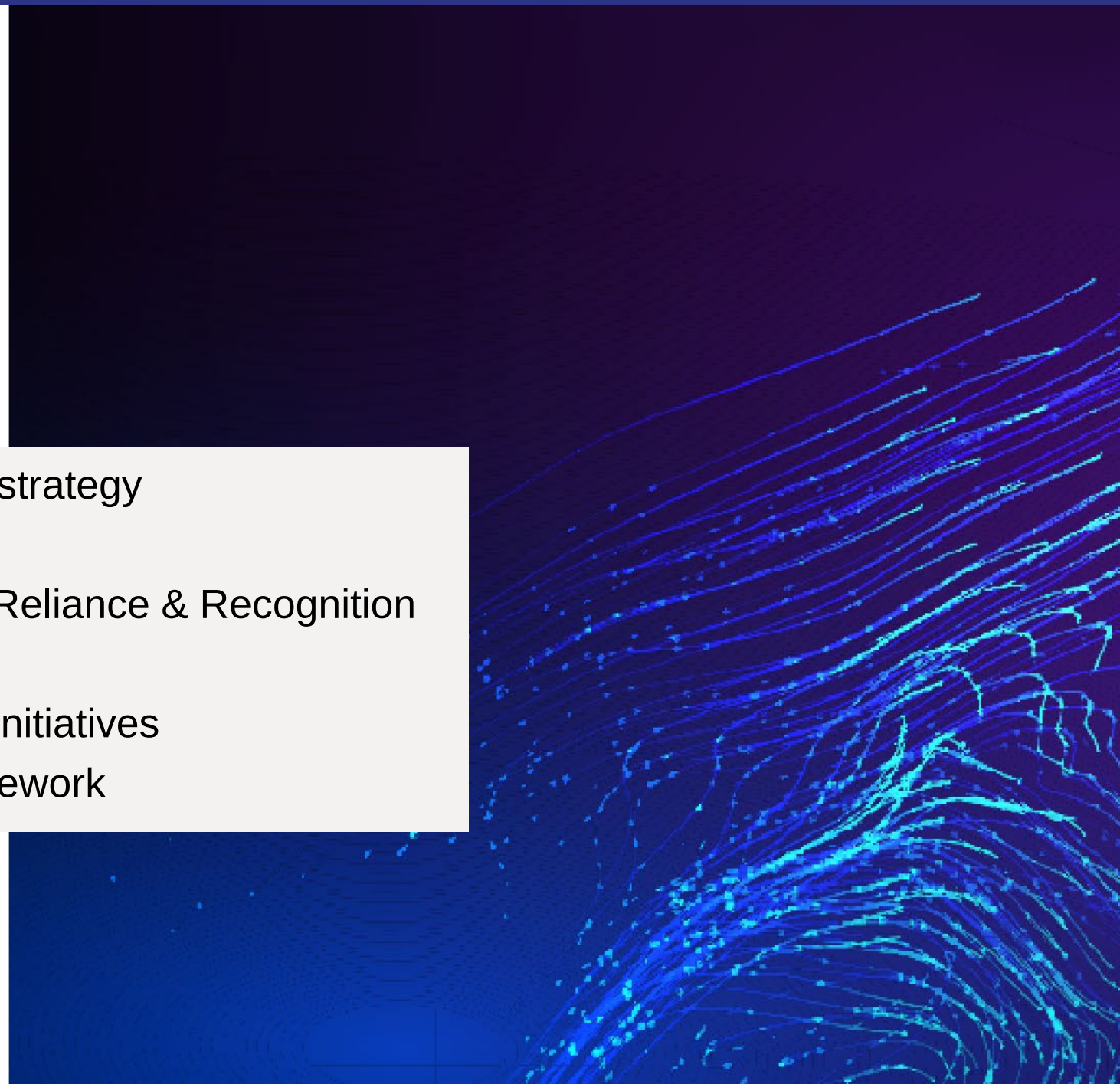
International GMP: Collaboration | Alignment | Harmonisation

Stephen Farrell
Manufacturing Quality Branch
Department of Health and Aged Care, TGA

GMP FORUM 2024

Agenda

- TGA International engagement strategy
- International agreements
- How these are used for GMP - Reliance & Recognition
- PIC/S
- Other international forums and initiatives
- GMP Inspection Reliance Framework



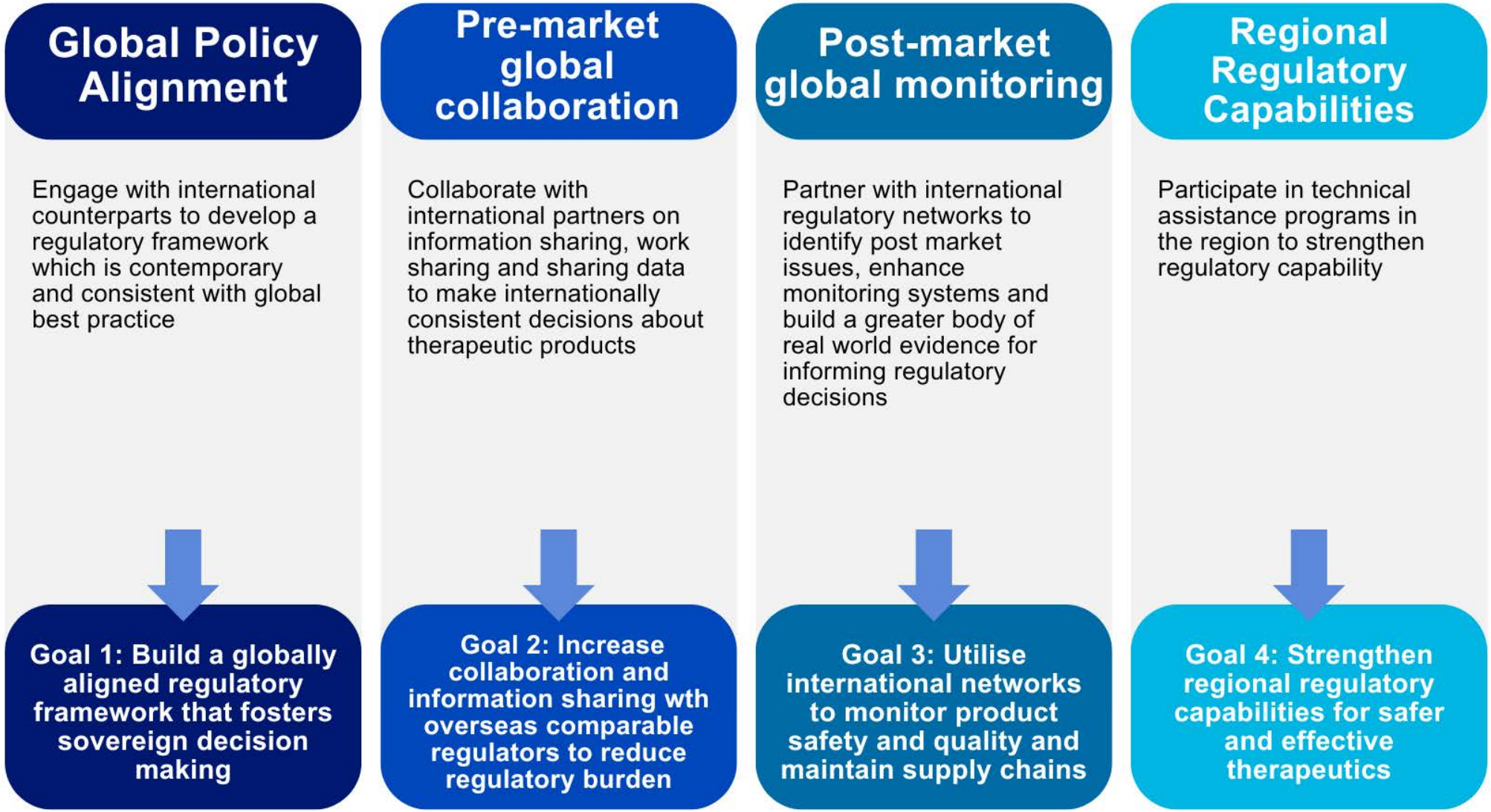
TGA's International Engagement Strategy

2021-2025

"more globally aligned regulatory framework"

"Australia will continue to make sovereign decisions…..but we will increasingly collaborate with other regulators to expedite and inform these decisions"

TGA's International Engagement Strategy



International Agreements

International Agreements

Why we have them

Facilitate trade

Underpin TGA's international engagement activities

Facilitate bi-lateral and multi-lateral forums

Outline the scope and type of collaboration

Underpin reliance activities

International Agreements

Release of Information

Release of information is outlined in section 61 of the Therapeutic Goods Act 1989

“The Secretary may release to a national regulatory authority of another country, or an international organisation, being another country or an organisation with which the Commonwealth has cooperative arrangements relating to the assessment or regulation of therapeutic goods, …….. the release of which is consistent with those arrangements”

International Agreements

GMP Reliance vs Recognition

Reliance:

- Leveraging information/effort from another Recognised Regulatory Authority (RRA) into our sovereign decision making
- Agreements are usually between authorities
- Non-binding

Recognition:

- Accepting the outcomes of a RRA
- Agreements are usually between countries
- Binding

International Agreements

Types of international agreements

Information sharing

- Exchange of letters
- Co-operative Agreements
- Memoranda of Understanding (MoU)

Trade

- Trade Agreements
- Mutual Recognition Agreements (MRA)

International Agreements

Exchange of letters / MoU

- Managed by TGA and used as information sharing agreements
- TGA has several agreements with regulators around the world
- Most do not include or are not used for GMP inspection reliance
- Exceptions are:
  - Swissmedic MoU
  - Health Canada MoU for Extra-Jurisdictional inspections

International Agreements

Trade agreements

- Managed by other government departments
- TGA input for medicines, biologicals and GMP/manufacturing
- Technical barriers to trade are considered to ensure trade is not adversely impacted
- Australia-India Economic Cooperation and Trade Agreement (ECTA)

International Agreements

Mutual Recognition Agreements

- Treaty level agreements for the mutual recognition of specific activities
- Each agreement may have different scopes due to differences in regulatory frameworks
- Australia has five MRAs
  - European Union (EU)
  - United Kingdom (UK)
  - Canada
  - Singapore
  - New Zealand
- All MRAs are limited to activities performed within each country’s borders

Word cloud

Who would you like us to have an agreement with?

Scan the QR code with your device to participate in this activity

PIC/S

Pharmaceutical Inspection Co-operation Scheme

PHARMACEUTICAL INSPECTION
CO-OPERATION SCHEME

PIC/S

Pharmaceutical Inspection Co-operation Scheme (PIC/S)

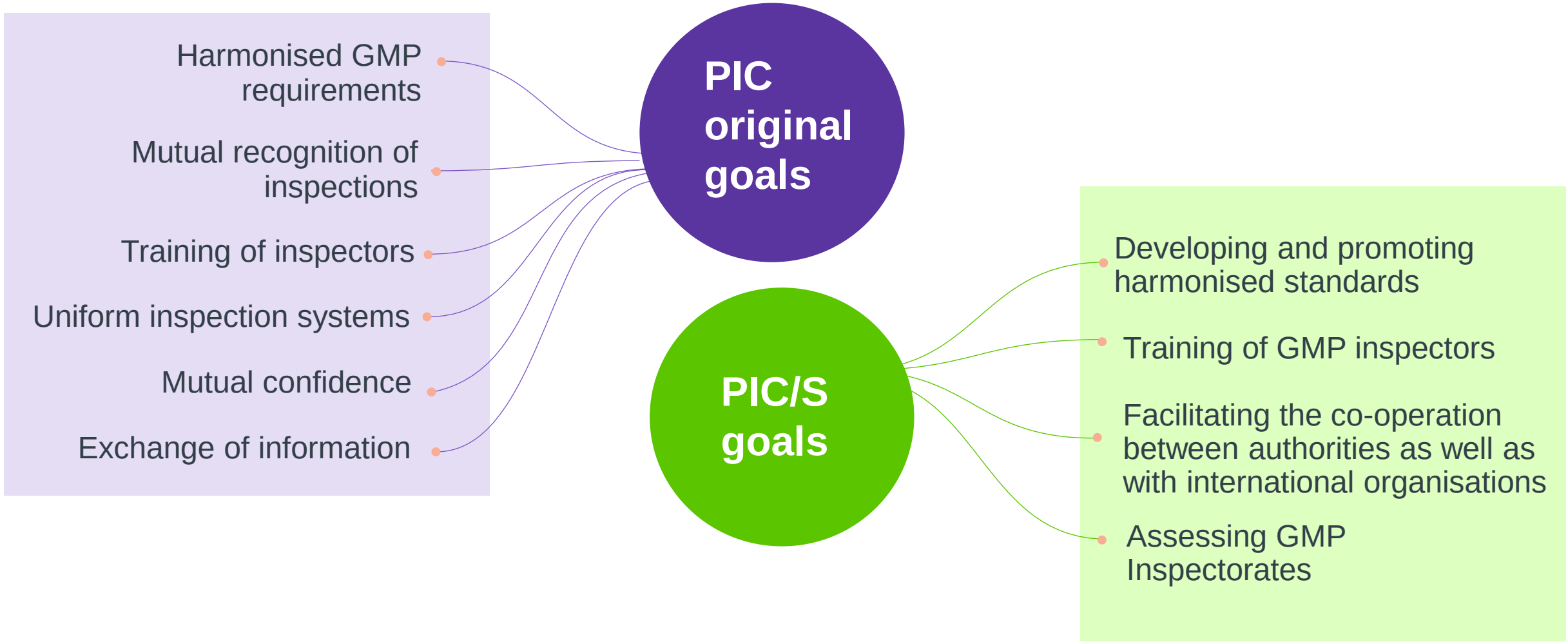
- Established in 1995 as an extension to the Pharmaceutical Inspection Convention (PIC) of 1970
- Non-binding, informal co-operative arrangement between Regulatory Authorities in the field of GMP of medicinal products
- Open to any Authority having a comparable GMP inspection system
- Relies on the voluntary exchange of information on GMP inspections. No obligation to accept inspection outcomes

PIC/S

PIC vs. PIC/S

PIC	PIC/S
Convention	Scheme
Between countries	Between agencies
A formal treaty	An informal arrangement
Legally binding	Legally non-binding
Focus on inspection	Focus on training & developing guidelines for inspectors/inspectorates
Mutual recognition of inspections	Exchange of information on inspections

PIC vs. PIC/S


Harmonised GMP requirements
Mutual recognition of inspections
Training of inspectors
Uniform inspection systems
Mutual confidence
Exchange of information
PIC original goals
PIC/S goals
Developing and promoting harmonised standards
Training of GMP inspectors
Facilitating the co-operation between authorities as well as with international organisations
Assessing GMP Inspectorates

PIC/S

56

Members (participating authorities)

6

Associated partners

4

Applicants

2

Pre-applicants

PIC/S

7 Expert Circles

20 Working Groups

Joint Reassessment programme

International Harmonisation

Joint Visit Programme

Inspectorates Academy (PIA)

Guides, recommendations & Quality systems

PIC/S

7 Expert Circles

- APIs
- Controlling Cross Contamination in Shared Facilities
- Human Blood, Tissues, Cells & ATMPs
- Quality Risk Management
- Good Distribution Practices
- Good Clinical Practices
- Good Pharmaco-Vigilance Practices

20 Working Groups

- Revision of Annex 1 (joint WG with EMA/EC and WHO)
- Revision of Annex 2
- Harmonisation of Classification of Deficiencies
- Data Integrity
- Controlling Cross-Contamination in Shared Facilities
- Revision of PI 006
- Unique Facility Identifiers (UFI)
- Inspector Travel Safety
- Veterinary Medicinal Products
- Quality Defects
- Informants
- Revision of Blood guidance documents
- Aide Memoire on Tissues and Cellular Therapy Products Inspections
- Computerised Systems
- Third Party Funding
- Revision of the PIC/S Aide Memoire on QRM Implementation
- ICH Q12 Training Material
- PIC/S Inspection Reliance
- Remote Assessment
- Revision of Inspection Report Format

Other international forums and initiatives

Other International forums and initiatives

Other international Forums

The International Coalition of Medicines Regulatory Authorities (ICMRA)

The International Council for the Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

ACCESS – Australia, Canada, Singapore, Switzerland and the United Kingdom Consortium

European Medicines Agency (EMA) GMDP Inspectors Working Group (IWG)

International Active Pharmaceutical Ingredient (API) Inspection Programme

Sterile Finished Dosage Form group

Other International forums and initiatives

ICMRA

- Informal group of leaders of medicines regulatory authorities
- Provides strategic direction for enhanced collaboration, communication and approaches
- Mission is to safeguard public health by facilitating strategic leadership and greater cooperation of international medicines authorities on shared regulatory issues and challenges
- 23 members, 15 associate members

Other International forums and initiatives

ICMRA – GMP

- Increased reliance in GMP was an early strategic initiative
- Inspection Reliance procedure developed by ICMRA working group
- Adopted by PIC/S in June 2018
- Pharmaceutical Quality Knowledge Management System (PQKMS) strategic initiative includes GMP components
- Collaborative pilot of hybrid GMP inspections between authorities

Other International forums and initiatives

ACCESS Consortium

- Formed in 2007 and known as “ACSS”
- Comprised of Australia, Canada, Singapore and Switzerland
- October 2020, the UK joined, and the name was changed to “Access”
- With combined populations of 150 million for the markets we regulate, the consortium aspires to be regulators of choice
- goal is to maximise international co-operation between partners, reduce duplication, and increase each agency’s capacity to ensure patients have timely access to high quality, safe and effective therapeutic products

Other International forums and initiatives

ACCESS consortium – GMP

- A GMP network exists that can be stood up as required for a product submission
- Evaluation of supply chains for each jurisdiction proposed
- Work sharing could consist of:
  - Joint inspections
  - Hybrid inspections
  - Reliance evaluations
  - Recognition
- Joint statement on GMP Inspection reliance and recognition was endorsed and published in November 2022.

Other International forums and initiatives

API inspection programme

Piloted between 2008-2010

Full programme since 2011

Monthly teleconferences discussing:

- **Inspection planning**
- **Non-compliance concerns**

Other International forums and initiatives

ICMRA - PQKMS

- Joint reflection paper from:
  - ICMRA
  - ICH
  - PIC/S
  - International Pharmaceutical Regulators Programme (IPRP)
- Streamlining post approval changes, reliance on PQS and life cycle management
  - ICH Q10, Q8, Q9, Q12
- Submission of same dossier to all jurisdictions
- Unique facility identifiers
- Revised inspection report format

Other International forums and initiatives

Single Inspection Program

- *TGA – Canada - MHRA*
- Limited to inspections outside of PIC/S member's jurisdiction - focus on India and China
- Sites preferably manufacture medicines for all three jurisdictions but sites who only supply two of the three can be considered

"This pilot aims to establish a coordinated approach to GMP inspections of overseas manufacturing sites of common interest. Using our collective inspection resources, each authority has agreed to extend the scope of an inspection to cover products of interest to one another, where possible, reducing the need for multiple inspections of the same site."

Other International forums and initiatives

How is the SIP different?

- Inspection Reliance Evaluations (IRE) are usually performed ‘after the fact’
- They require in depth gap-analysis on inspection scope and coverage
- Under the pilot SIP, some of the inspection reliance aspects are performed earlier in the process (Inspection planning)
- This allows for increased:
  - Reliance by facilitating an easier/abbreviated IRE
  - Greater recognition of inspection outcomes where supported by agreements

Other International forums and initiatives

SIP – Progress and next steps

Progress to date:

- Established framework and workplan
- Regular meetings since December 2023
- Sharing of inspection plans & creating ‘sites of common interest’ list
- Publication of joint web-statements announcing the pilot
- Three inspections performed

Next steps:

- Reflection on inspections performed
- Expand on inspection types and refine processes
- Expand to other regulatory authorities?

GMP Inspection Reliance Framework

“The demand for inspecting pharmaceutical manufacturing facilities far exceeds what any one National Competent Authority (NCA) can accomplish”

PIC/S GMP Inspection Reliance PI 048-1

GMP Inspection Reliance Framework

Determining equivalence

- Before we can rely on evidence from another regulatory authority, we evaluate that regulatory authority's GMP program and determine the level of equivalency to Australia's GMP requirements
- The combination of the agreements and arrangements in place, and the evaluation dictate the level of reliance and pathway for GMP Clearance
- This is performed using harmonised evaluation guides developed by Health Canada and used in EU and PIC/S evaluations

GMP Inspection Reliance Framework

Joint Audit Program (JAP) / Joint Re-assessment Program (JRP)

The EU JAP and PIC/S JRP are considered equivalent processes to evaluate GMP programs

TGA is audited by PIC/S and participates in other JRP audits

Both programs are used to compliment MRA maintenance activities as they occur

GMP Inspection Reliance Framework

Questions?

Scan this QR code with your device to submit a question

GMP FORUM 2024

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration