Australian Government
Department of Health
Therapeutic Goods Administration

What's happening at the TGA's Manufacturing Quality Branch

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Manufacturing Quality Branch
Australian Government Department of Health, TGA
ARCS Annual Conference 2022

TGA Health Safety Regulation

The session will focus on 4 important activities within the Branch

- Medicinal cannabis reforms
- Recall Reforms Program
- Overseas remote GMP inspections
- GMP Clearances beyond the COVID-19 pandemic

Medicinal cannabis reforms

Jenny Burnett, Assistant Secretary, MQB

- GMP – a level playing field
- Labelling and packaging
- Microbiological requirements
- Compounding requirements

GMP – a level playing field

'each step of manufacture, in relation to a medicinal cannabis product, that occurs outside Australia must meet one of the GMP standards set out in section 13(2) of TGO 93'

- Requirement in Therapeutic Goods Order (TGO 93) – medicine must be manufactured under acceptable GMP
- Alignment with GMP requirements on Australian manufacturers
- Recognises equivalent GMP codes and comparable overseas jurisdictions
- If needed, acceptable GMP can be confirmed by TGA inspection

Obligation on sponsor

GMP – evidence

- Sponsor must obtain/hold acceptable written evidence (s13(2))
  - TGA will accept evidence from specified foreign regulators in country of manufacture
  - Other countries or evidence not available →request TGA inspection
- Clearances are **NOT** required
- Further countries may be added in the future

Labelling and packaging

- Child-resistant packaging
- More information on labels
  - Sponsor details
  - Active ingredient information
- Providing greater certainty to patients and prescribers, facilitating recall processes

Microbiological requirements

- Previously Therapeutic Goods Order (TGO) 100 and guidance documents
- Now in TGO 93
  - Clarity on requirements
  - Alternative pharmacopoeial monographs
  - Exemption in TGO 100

AUSTRALIA

Therapeutic Goods (Standard for Medicinal Cannabis) (TGO 93) Order 2017

made under subsection 10(1) of the
Therapeutic Goods Act 1989

Compilation No. 2

Compilation date: 28 March 2022

Includes amendments up to: F2022L00384

Prepared by the Department of Health, Canberra

Authorised Version F2022C00332 registered 28/03/2022

Compounded medicinal cannabis

- Alignment to supply of other medicinal cannabis products

- Pharmacists must ensure that prescriptions:
  - have Special Access Scheme approval or
  - were prescribed by an Authorised Prescriber

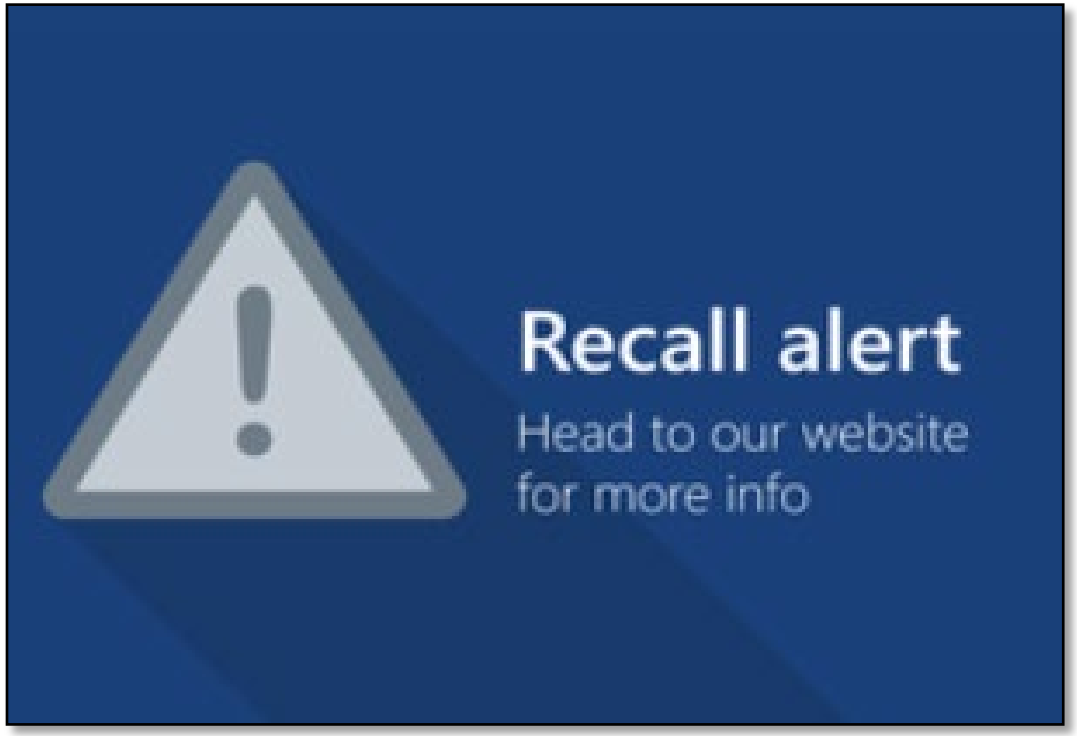
- Cannabis that is cultivated or manufactured **domestically** can be supplied for the extemporaneous compounding

Recall Reforms Program

Sharon Bennett, Assistant Director Recalls Section, MQB

- Overview of current processes
- Stakeholders and their roles
- Reforms Program
- Communication

Overview – The current recalls process and communication pathways



All recall stakeholders

Healthcare Sector

Health care facilities
Health care professionals
Professional guilds and associations e.g., Pharmacy Guild
Healthcare provider peak bodies e.g., NACCHO or Australian Private Hospitals
Professional media (scientific and medical)

Consumers

Patients and carers
Patient Advocacy Groups e.g., Diabetes Australia
Consumer peak bodies e.g., Consumer Health Forum or Choice
Consumer media

Government

Department of Health and TGA
Australian Government regulators e.g., Australian Competition and Consumer Commission
Other Australian Government agencies e.g., ACSQHC
State and territory government e.g., health departments and procurement agencies
International government regulators e.g., Medsafe

What the TGA does

- Provide a consistent approach via the
  Uniform Recall Procedure for Therapeutic Goods – 'URPTG'
- Assess proposed recall notifications
- Communicate and monitor progress of the recall
- Review the recall outcomes
- Monitor signals and regulatory compliance

URPTG: Version 2.2, December 2019 -
https://www.tga.gov.au/publication/uniform-recall-procedure-therapeutic-goods-urptg

What the sponsor/supplier does

- Responsible for responding to product defects / safety issues
- Notifies the TGA before commencing recall action
- Contact customers and monitor responses
- Perform any replacements or corrections
- Report outcomes to the TGA
- Implements measures so the issue does not re-occur

The End-To-End Recall Process

An issue with a therapeutic good is identified by consumers, healthcare providers, health departments, sponsors, manufacturers, labs, retailers, overseas regulators, research facilities, TGA, etc.

The sponsor submits a recall notice and works with the TGA to agree on the appropriate recall and communications strategy.

During recall strategy implementation, impacted customers are notified by the sponsor and/or health departments.

Customers notify impacted consumers, or they are informed through the media.

Key stages

Manage Emerging Issue → Submit Notification → Approve Recall → Implement Recall → Finalise Recall

The sponsor (in conjunction with the manufacture as needed) performs a risk assessment to determine the necessary actions to be taken

TGA reviews and assesses the documentation to ensure completeness, compliance and quality and publishes the recall to state and territory coordinators and the TGA website.

The sponsor notifies the TGA of the corrective action taken within the appropriate timeframe. If the report is satisfactory, TGA issues a close-out report and shares recall information other TGA stakeholders.

Recall Reforms

Why?

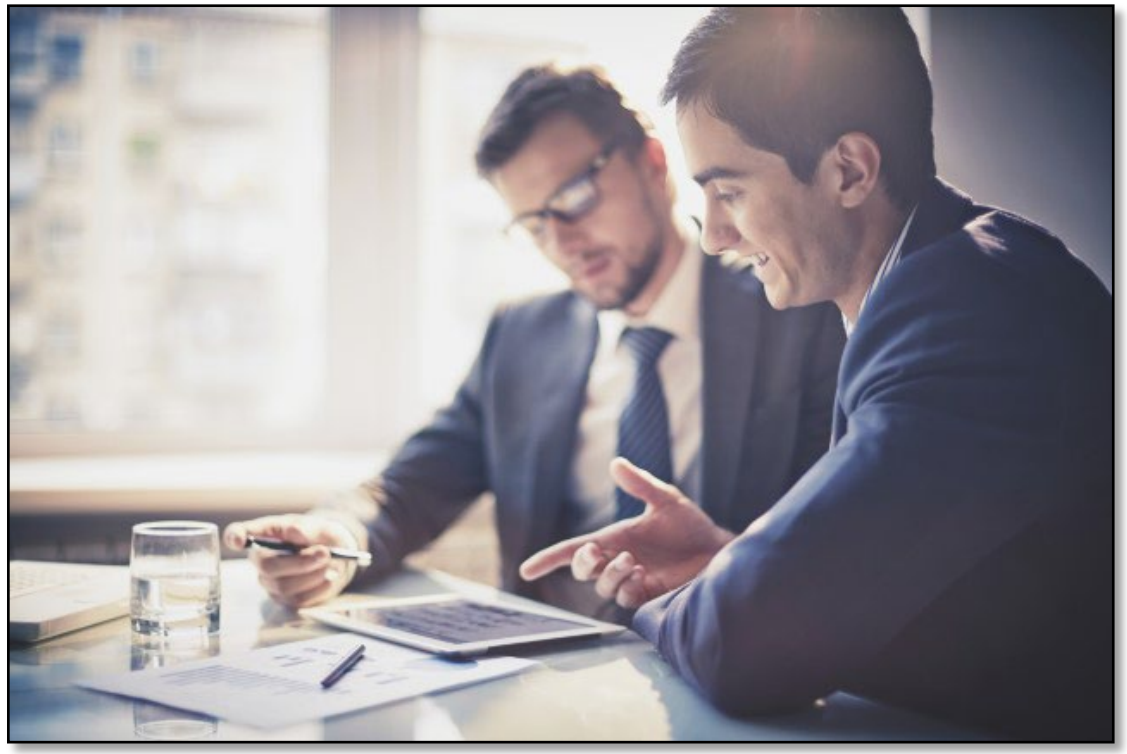
- Ensure clear and effective communication of safety related recall information to all stakeholders

- Faster responses to recall actions to reduce the risk of consumer / patient harm

Recall Reforms

What have we done so far?

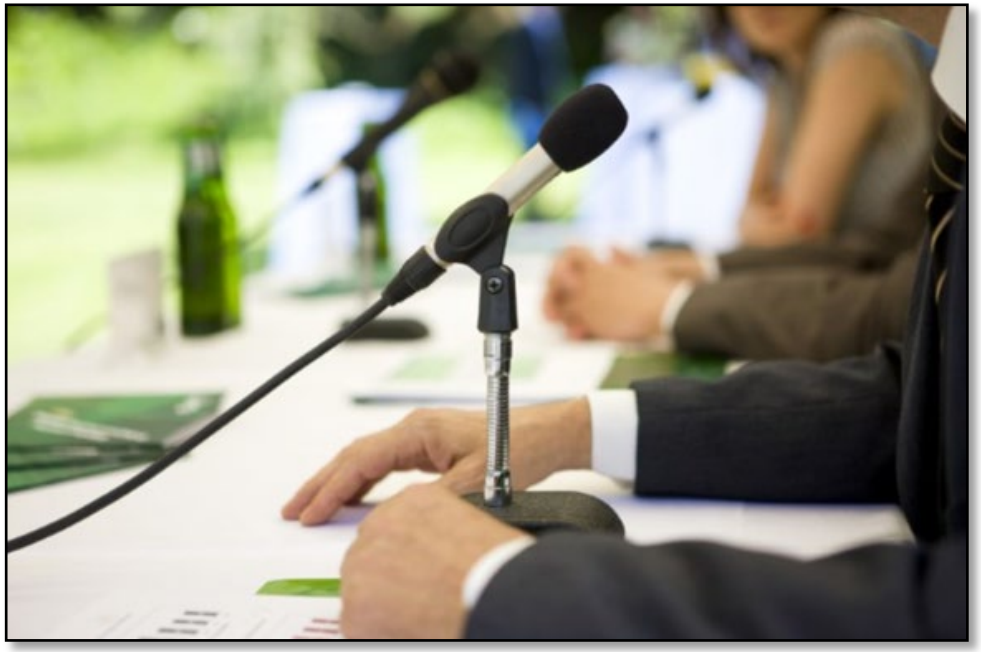
- Considered our IT options
- End to end process review
- Extensive consultation, feedback and discovery activities
- Established continuous improvement mechanisms
- Established the Recall Reforms Program



Recall Reforms

Themes already identified

- Information flow inefficiencies
- Difficulty at times identifying the precise product being recalled
- Duplication of effort
- Unclear roles and responsibilities
- Complexity of communication pathways across supply chains
- Difficulty reaching impacted customers
- Processes too manual
- Better education about recalls and recall terminology



Recall reforms

Next steps / what are we doing now?

- Recalls Data Model and Analytics
- Synthesising review recommendations & feedback from discovery activities
- Drafting Options Paper
- Standard Operating Procedures, Work Instructions and the QMS
- Robotic Process Automation (RPA)
- Recalls Education Material

Stay tuned for the Options Paper … we'll be in contact again.
Your views are very important to us!

Overseas remote GMP inspections

Maurice Makdessi, Team Leader Inspections Section, MQB

- Background
- Process and objectives
- Inspection Preparation
- Potential issues and solutions
- Tips

Background

Due to COVID-19 pandemic impact and travel restrictions:

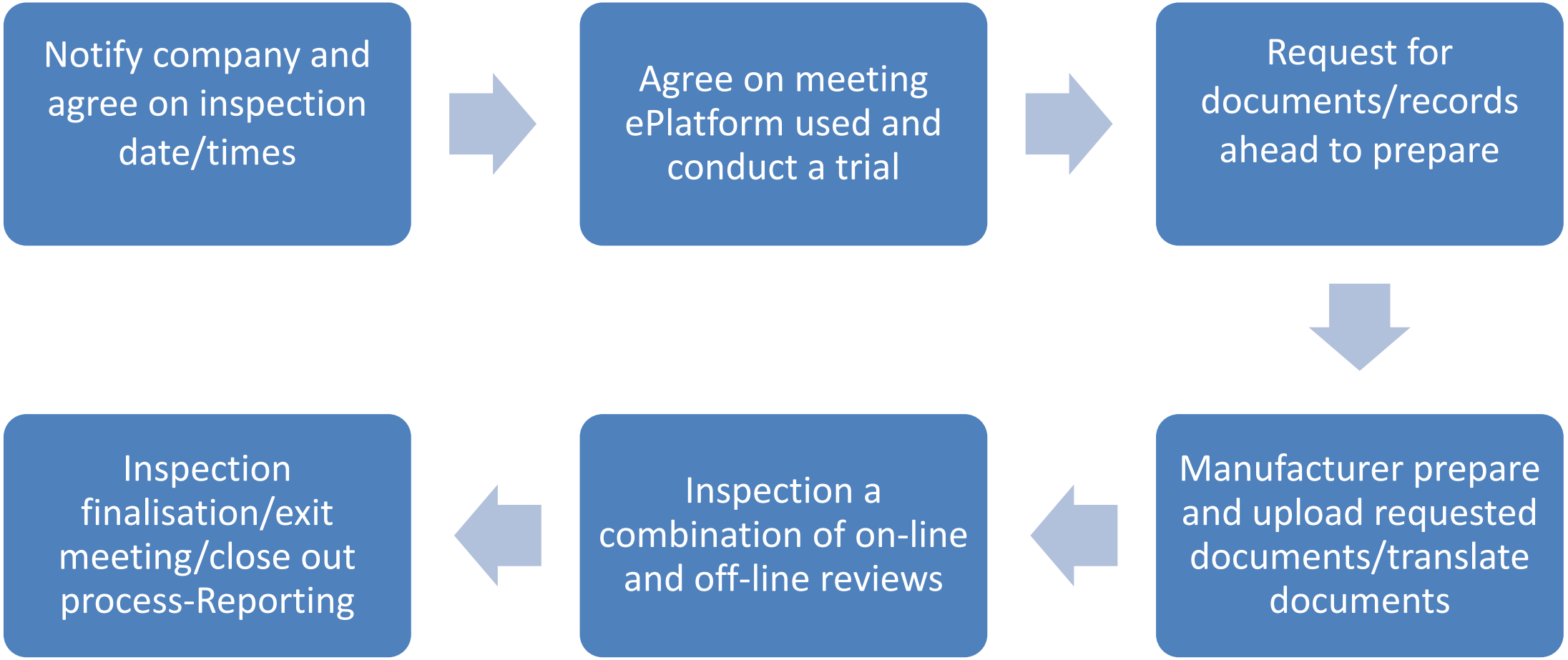
- Overseas on-site inspections ceased in February 2020
- Further collaboration with international information meetings/ closer communications with regulatory partners
- TGA commenced overseas **remote** inspections in August 2020

Objective of remote inspection

To ensure the ongoing supply of quality medicines, blood and human tissue products from overseas manufacturers in response to the COVID-19 pandemic, TGA undertook a broad range of activities to assist with ensuring their continued operation:

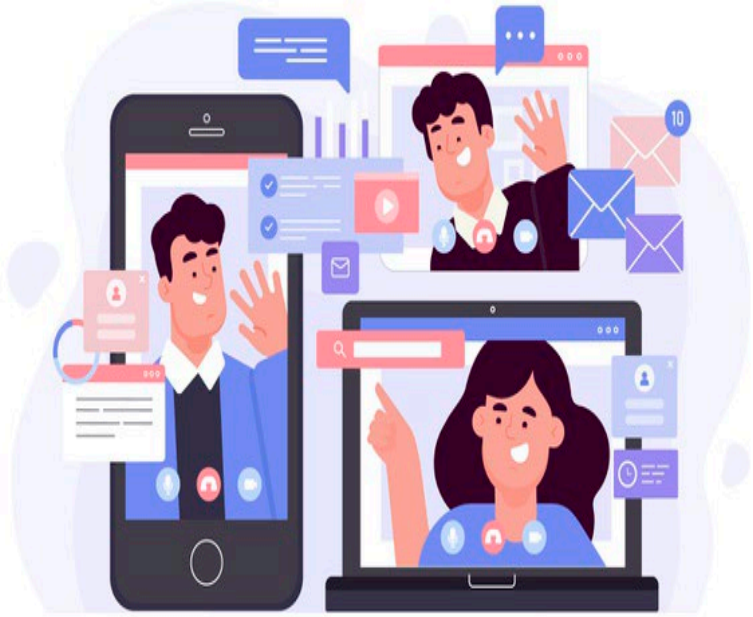
- Remote inspection program
- Overseas GMP clearance process

Process


Notify company and agree on inspection date/times
Agree on meeting ePlatform used and conduct a trial
Request for documents/records ahead to prepare
Manufacturer prepare and upload requested documents/translate documents
Inspection a combination of on-line and off-line reviews
Inspection finalisation/exit meeting/close out process-Reporting

Inspection preparation (Manufacturer/Sponsor)

Technology Options	• Effective internet/size/bandwidth • MS Team, WebEx • Share Drive accessibility set up • Phone/emails/pre-recorded videos/simulation
Document review	• Clarity of Document/on-line scanning • Upload documents - Share drive/eFiles • Translated documents • Scope of inspection/changes ahead of inspection
Facility/process review	• On-line camera/zooming functions • Pre-recorded



Potential issues/time constraints

Manufacturer's must be ready for inspection and be flexible

- Preparation for inspection:
  - availability of SMEs/relevant staff
  - availability of documents and records

- Inspector may require additional time
  - for focus areas
  - discussing potential deficiencies at the exit meeting

Time is Precious Please help the inspector to adhere to inspection plan

Tips for a successful remote inspection

A manufacturer/sponsor should ensure:

- Trial ePlatform set up
- Trial of digital camera in multiple areas/ scanning devices/document uploads of various formats as required.
- Availability of back up systems/camera/scanner/ WIFIs/associated compatible batteries
- Ensure agreed inspection times are appropriate/availability of SME’s

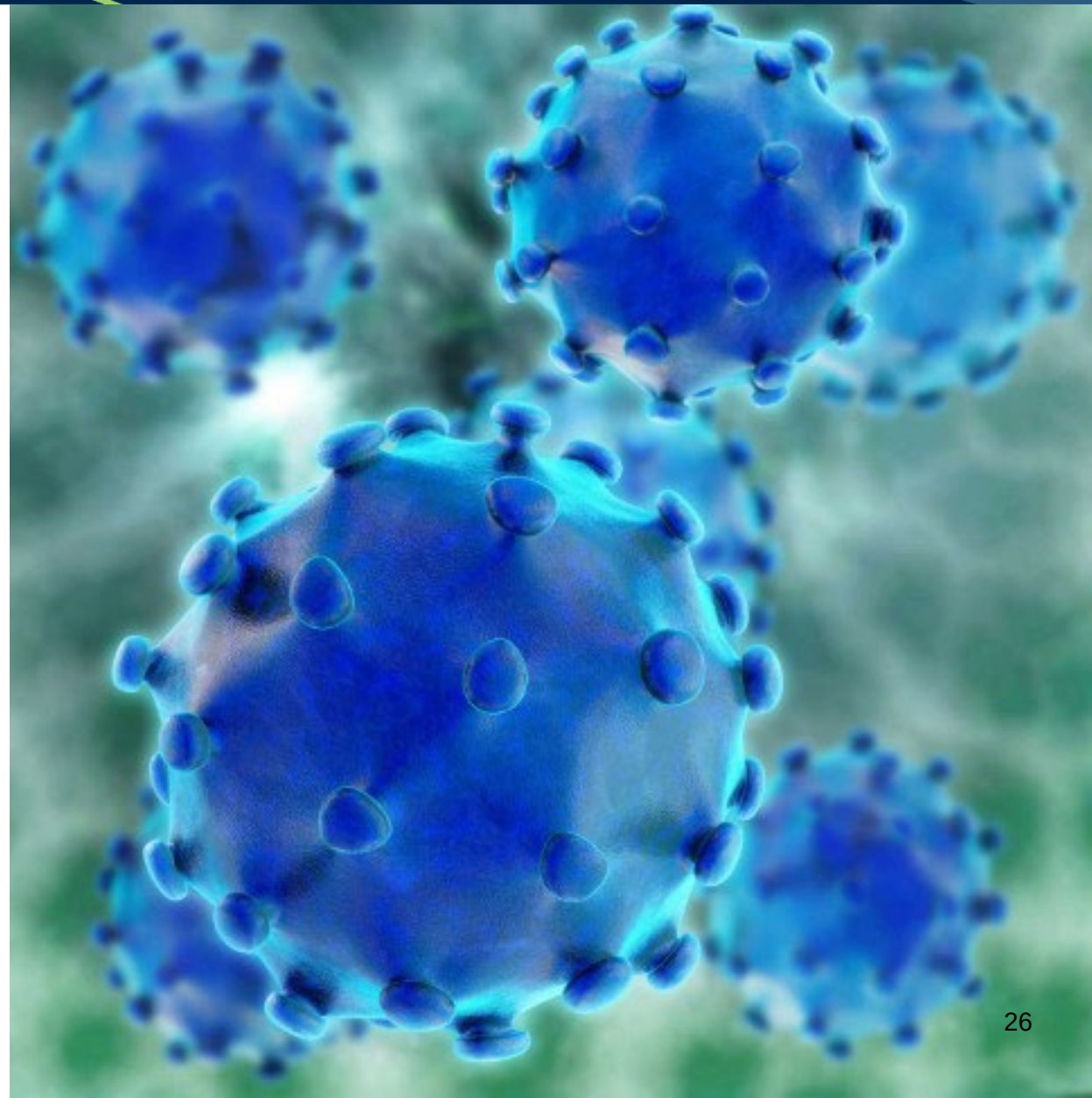
GMP Clearances beyond the COVID-19 Pandemic

Stephen Farrell, Director, GMP Clearance, MQB

- Recap of COVID-19 impact
- Recap of the TGA's Response
- Vaccines and Treatments
- Beyond the pandemic

Recap of COVID-19's impact

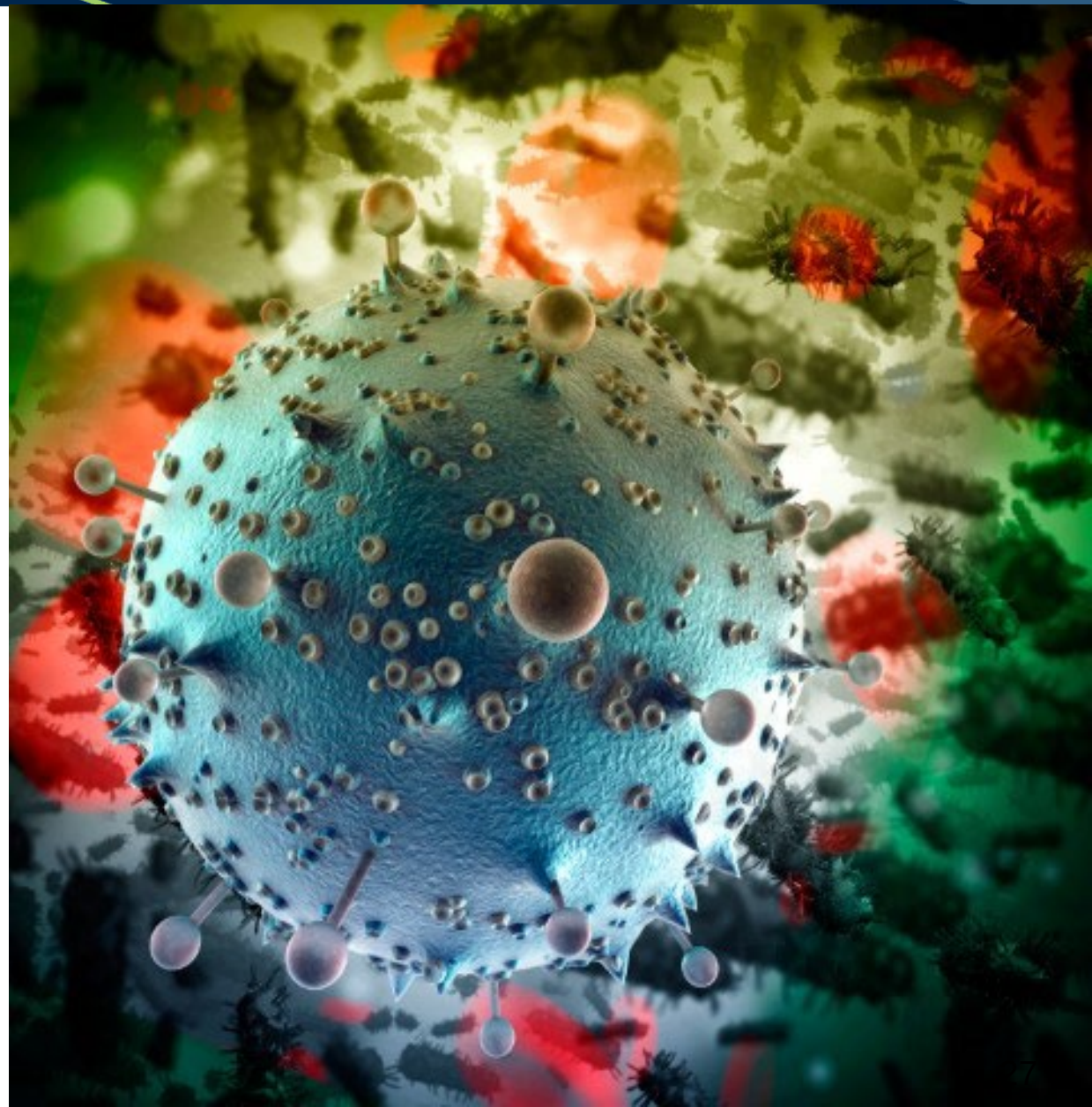
- Domestic and overseas on-site inspections postponed or cancelled
- Introduction of remote/virtual inspections or distant assessments
- Existing Mutual Recognition Agreements (MRA) tested
- Blanket extensions from other regulators



Recap of TGA's response

MRA Pathway:

- Increased collaboration & liaison with MRA partners
- Accepted 'distant assessment' GMP certificates
- Initially aligned expiry dates with MRA partners
- Developed risk-based approach to apply longer expiry dates



Recap of TGA's response

Compliance Verification (CV) pathway:

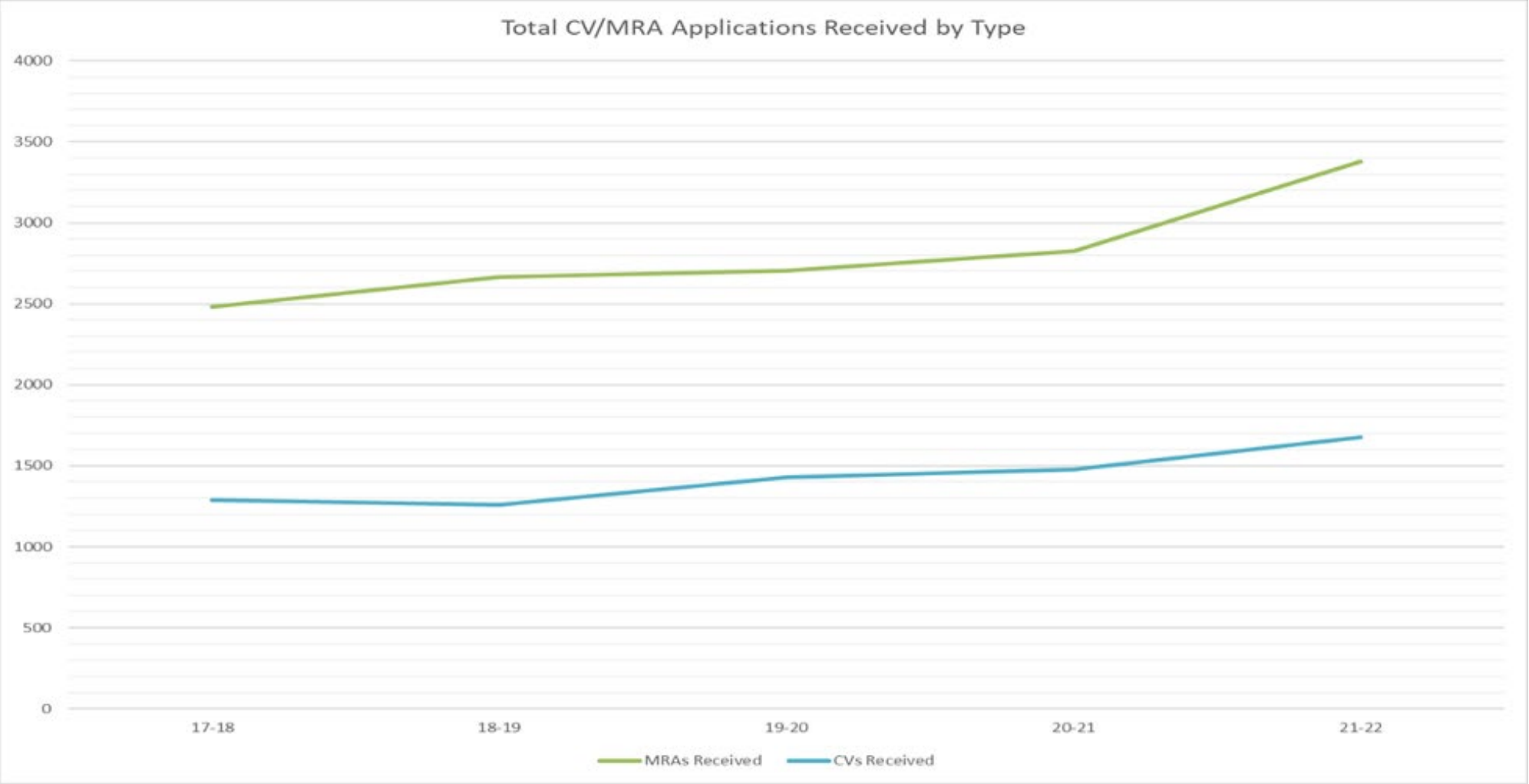
- Introduced GMP Clearance questionnaire
- Requested & assessed additional documents as required
- Allowed additional time for Sponsors and manufacturers to respond
- Accepted remote/virtual inspections in lieu of GMP questionnaire

COVID-19 Vaccines & Treatments

Vaccines	No. of sites	Treatments	No. of sites
Vaxzevria (AstraZeneca)	23	Remdesivir (Gilead)	5
Comirnaty (Pfizer)	30	Ronapreve (Roche)	2
Spikevax (Moderna)	15	Regdanvimab (Celltrion)	7
Jcovden (Janssen)	16	Molupiravir (MSD)	10
Nuvaxovid (Novavax)	21	Paxlovid (Pfizer)	6
Medigen (Grand Pacific CRO)	2	Evushield (AstraZeneca)	8

Over **140 manufacturing sites** required priority assessment

GMP Clearance applications received



MRAs beyond the pandemic

What do we keep?

- Existing risk-based approach to GMP Certificates with extended validity
- Continued acceptance of distant assessments & hybrid inspections

What else can we do?

- Re-open existing MRAs with lessons learnt and an eye on the future
- Increase the number of MRAs or agreements

CVs - beyond the pandemic?

What do we keep?

- GMP Clearance questionnaire can continue to be used in lower risk circumstances
- Requesting additional types of manufacturing documentation

What else can we do?

- Drive progress in global inspection reliance practices
- Update the GMP Clearance framework

GMP Clearance framework for the future

- New application types
- New flexible risk-based evidence requirements
- Improved fee structure and cost recovery
- Improved guidance and education
- Digital Transformation


Q&A

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