Update from the Pharmacovigilance Branch

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Reporting of significant safety issues

Changes to pharmacovigilance guidance

Pharmacovigilance inspection program insights

Common deficiencies and inspection tips

Signal detection and investigation and regulatory action for medicines and vaccines

Systems support and project management

RMP and PSUR evaluation

COVID-19 vaccine claims assessment

Adverse event collection

Complementary medicines and defect monitoring and action

Medicine shortages management

Safety and shortages communications

Good Clinical Practice Inspection Program

Clinical trials access pathways

Pharmacovigilance Inspection Program

Reporting of significant safety issues

Updates to pharmacovigilance guidance

Why we're making changes

To support timely responses by the TGA to new safety information

- ✓Clarifies requirements for urgent reporting
- ✓Expected to increase the quality of notifications
- ✓Will enable TGA to act on safety issues in a timeframe proportionate to the risk to public health

Our work so far

Consultation outcomes

- 99 stakeholders invited to participate, 44 submissions received
- Overwhelmingly positive responses to the 11 survey questions
- Important issues raised:
  - Reporting timeframes
  - Requirement to report safety issues from overseas regulators vs. comparable overseas regulators (CORs)
  - Quality defect issue reporting
  - Scope of Other Safety Issue (OSI) reporting
  - Administrative burden associated with downloadable safety issue reporting form
  - Issue of duplicate reporting not resolved

What to expect in PV Guidelines v3.0

Significant safety issues

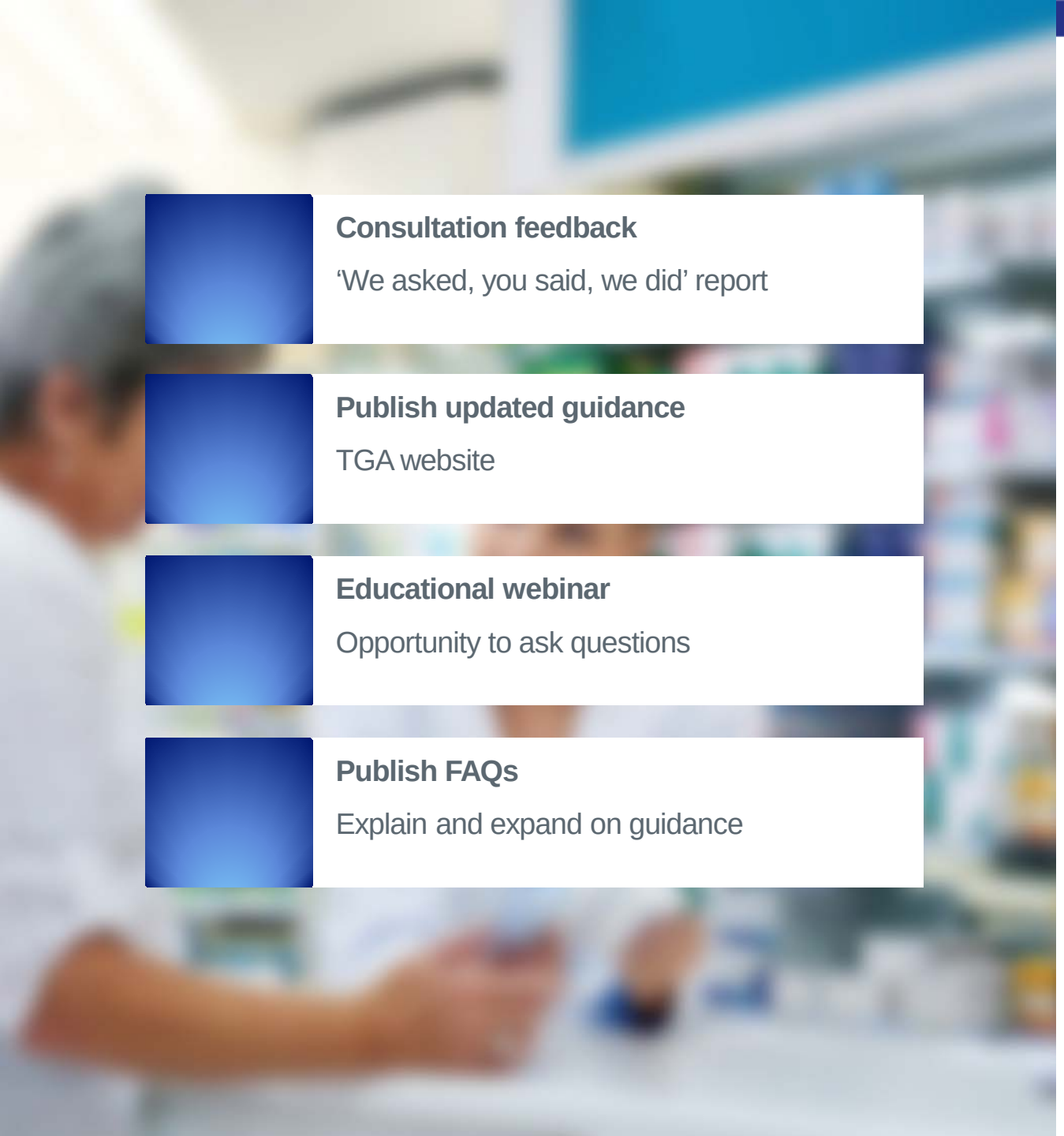
- Require the urgent attention of the TGA
- Closely aligned with the EMA 'Emerging Safety Issue'
- 72-hour reporting timeframe remains

Other safety issues

- Safety related changes recommended by CORs (that do not fit the definition of SSI)
- Safety issues from other sources that have been internally assessed and confirmed
- Report within 30 days

What to expect in PV Guidelines v3.0

- Regulator-identified safety issues only require notification if regulator is a **COR**
- **Quality defect issues** in scope of SSI reporting if serious/urgent
- **Alternative procedure for generic medicine sponsors to report COR-identified safety issues**
  - via timely SRR submission to align generic PI with the innovator PI
  - Obligation to identify and report other safety issues still remains
- **A safety issue reporting template** (for email) in place of a safety issue reporting form
- **A safety issue reporting decision tree** appended to the PV Guidelines



Consultation feedback

‘We asked, you said, we did’ report

Publish updated guidance

TGA website

Educational webinar

Opportunity to ask questions

Publish FAQs

Explain and expand on guidance

Next steps

- 6-month implementation period
- Education and communication

Pharmacovigilance Inspection Program findings

‘The aim of therapeutic product vigilance is to continually monitor and evaluate the safety and efficacy (performance) profile of therapeutic products and to manage any risks associated with individual products.’

PVIP process (routine announced inspections)

Pre-inspection (6-8 weeks)

- Notification and confirmation of inspection date
- Provision of Australian Pharmacovigilance System Summary (APSS) by the sponsor
- Development of inspection plan
- Pre-inspection document requests
- Pre-inspection call (1 week before inspection)
- Further document requests

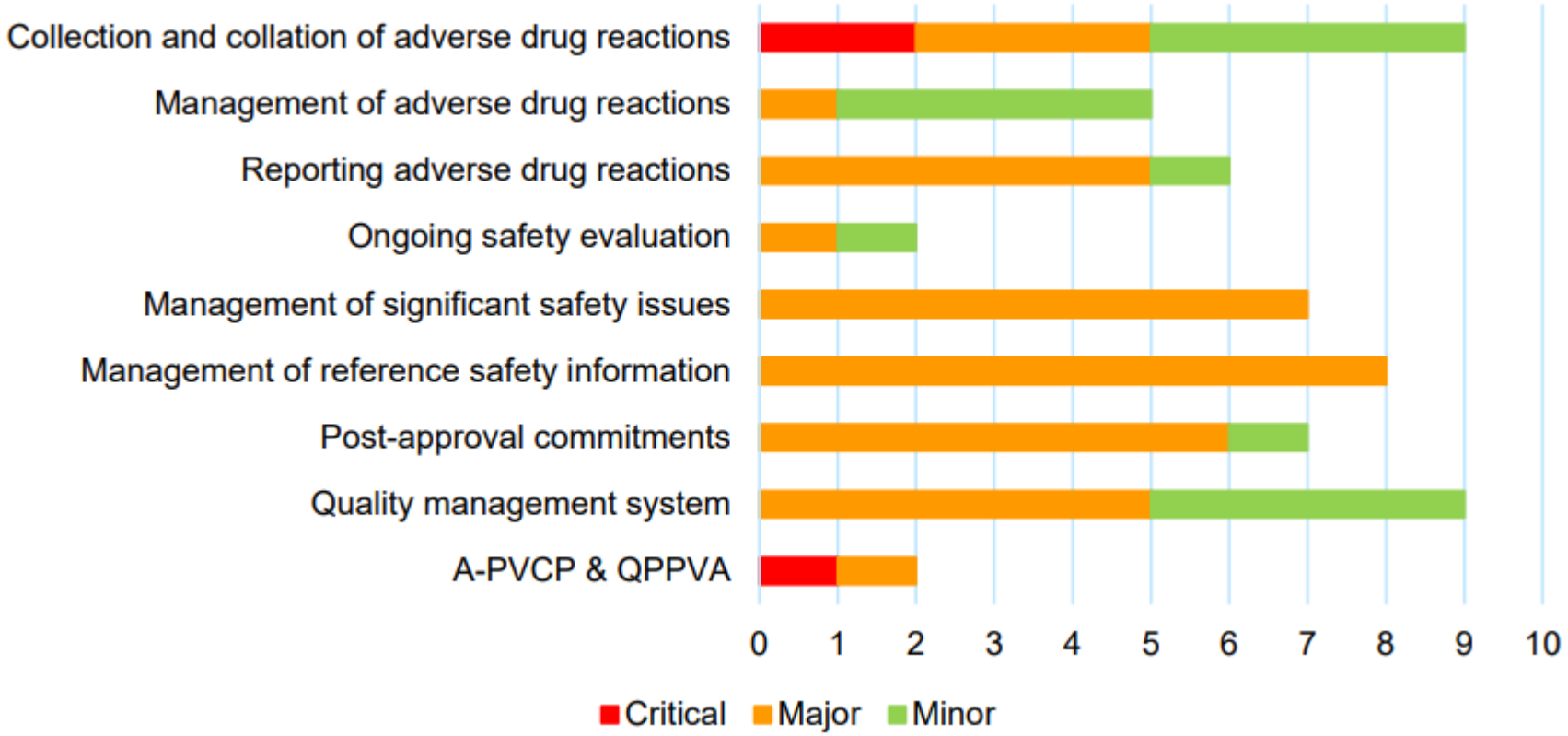
Inspection (≈3-4 days)

- Opening meeting
- Interviews and document requests and review
- On the final day: Closing meeting with presentation of preliminary deficiencies

Post-inspection

- Sponsor to prioritise outstanding document responses.
- Inspection report issued by the TGA (≤30 days)
- Initial Corrective and Preventative Action (CAPA) Plan provided by the sponsor (≤30 days from the issue of the inspection report)
- TGA evaluation and acceptance of CAPA Plan
- Close-out of the inspection

Number and grading of deficiencies in 2021



Common Major finding: Reference Safety Information (RSI)

Questions to support with self-evaluation of your compliance

- Where is the company sharing these materials? Including internally and externally and all formats.
- What is the process for maintenance of these materials? Including the removal of superseded materials and ongoing maintenance of these materials with new or revised safety information? What are the timelines and QPPVA oversight of these processes?
- Who has responsibilities in this process and are those responsibilities described in a procedure? Have all relevant staff been trained on those procedure(s)?
- Are there any gaps or non-alignments to the TGA requirements or recommendations?

Tips for sponsors

Follow the journey of a safety related update from first sponsor awareness of the need for a change. Assess the procedures in place and timelines for all subsequent steps.

Common Major finding: Post-Approval Commitments (PAC)

Questions to support with self-evaluation of your compliance

- Where is the sponsor recording all TGA approval letters and section 28 letters applicable to medicines on the ARTG and how are conditions of registration identified from these sources and tracked?
- Is there a process to verify ongoing compliance with all conditions imposed?
- Do timelines facilitate compliance?
- How does the QPPVA ensure oversight of these processes?
- Who has responsibilities in this process and are those responsibilities described in a procedure? Have all relevant staff been trained on those procedure(s)?
- Are there any gaps or non-alignments to the TGA requirements or recommendations?

Tips for sponsors

Follow the journey of an approval letter from first sponsor awareness through to completion of the commitments within. Assess the procedures in place and timelines for all subsequent steps.

Additional PVIP compliance activity

- Review of the TGA Business Services to identify sponsors who had not nominated an A-PVCP
- Most sponsors became compliant following education
- Three sponsors issued an infringement notice due to ongoing non-compliance

Inspection preparation

Tips for sponsors

- Engage support from internal functions EARLY including resources for document request management
- Consider how to manage BAU activities during inspection – what is the contingency plan?
- Consider engaging internal IT support for the inspection
- Respond to document requests promptly
- Prompt and clear communication with the inspector

Inspection conduct

Tips for sponsors

- We request a presentation (20-30 mins) during the opening meeting to provide an overview of the sponsor company
- Consider the use of a ‘scribe’ during interviews
- Ask questions during the interview for clarification/education
- Don’t guess an answer to an interview question
- Continue prompt and clear communication with the inspector and use Webex chat to communicate outside of interviews

Post-inspection

Tips for sponsors

- Aim to provide any outstanding document responses ASAP after the closing meeting
- Provide a thorough root cause analysis to document why the deficiencies occurred, as this will facilitate a quality CAPA Plan
- The CAPA Plan needs to:
  - Outline corrective actions to rectify any identified non-compliance
  - Outline preventative action to avoid/minimise the risk of the non-compliance occurring again
- It is not possible in an inspection, with limited time, to identify every area of the system that requires attention, so the sponsor must establish, implement and maintain effective systems and procedures to comply with their pharmacovigilance responsibilities

Pharmacovigilance resources and link references

Current pharmacovigilance requirements in Australia Pharmacovigilance responsibilities of medicine sponsors Australian recommendations and requirements version 2.2 of January 2021	https://www.tga.gov.au/resources/resource/guidance/pharmacovigilance-responsibilities-medicine-sponsors
For topics not covered by the guidelines Frequently Asked Questions (FAQs), based on enquiries submitted to the TGA mailbox: pharmacovigilance.enquiries@health.gov.au since 2019	https://www.tga.gov.au/resources/resource/guidance/pharmacovigilance-obligations-medicine-sponsors
For further information on Pharmacovigilance Inspection Program • PVIP: Guidance for medicine sponsors version 1.0, September 2017 • Annual inspection program metrics report	https://www.tga.gov.au/resources/publication/publications/pharmacovigilance-inspection-program-guidance-medicine-sponsors
For any other enquiries, not covered in PV Guidelines and FAQs email pharmacovigilance.enquiries@health.gov.au	pharmacovigilance.enquiries@health.gov.au
For enquiries related to specific inspections, email pharmacovigilance.inspections@health.gov.au	pharmacovigilance.inspections@health.gov.au

1. Know the pharmacovigilance requirements and recommendations that apply to your medicines
2. Integrate your pharmacovigilance system
3. Use available resources to continually review and improve your pharmacovigilance system
4. If you are selected for inspection, maximise the educational opportunity

Do not wait for an inspection to review your pharmacovigilance system.

- Take time to **proactively understand** the TGA pharmacovigilance requirements and recommendations applicable to your medicines and build a pharmacovigilance system to achieve compliance.
- Pharmacovigilance should be **integrated** into the sponsor company – it is not a standalone function.
- Review PVIP Metrics Reports and compare your pharmacovigilance system against the deficiencies previously identified.
- TGA pharmacovigilance inspectors aim to work with sponsors and provide education to improve compliance and protect public health.

Therapeutic Goods Administration (TGA)

Exhibition booth **No.1**

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Therapeutic Goods Administration