Australian Government
Department of Health
Therapeutic Goods Administration

Reporting significant safety issues

Changes to the Pharmacovigilance Guidelines for sponsors

Medicines Surveillance and Targeted Review
Pharmacovigilance Branch
Medicines Regulation Division

2022 ARCS Annual Conference

25 May 2022

TGA Health Safety Regulation

Overview

- Planned updates to the Pharmacovigilance Guidelines
- Safety issue reporting form (in development)
- Safety issues – to report, or not? (via conference app)
- Questions (via conference app)

Planned updates to the Pharmacovigilance Guidelines

"The PV guidelines do not clearly explain sponsor requirements with regard to SSI reporting"

Medicines Australia Regulatory Affairs Working Group &
Pharmacovigilance Expert Advisory Group - August 2020

Identified issues

- Unclear guidance results in varied interpretation of SSI reporting requirements
- Issues reported early with minimal detail
- Risk system will become saturated with less urgent information
- Single category with 72-hour timeframe

SSI guidance not fit for purpose

Unclear guidance results in varied interpretation of reporting requirements

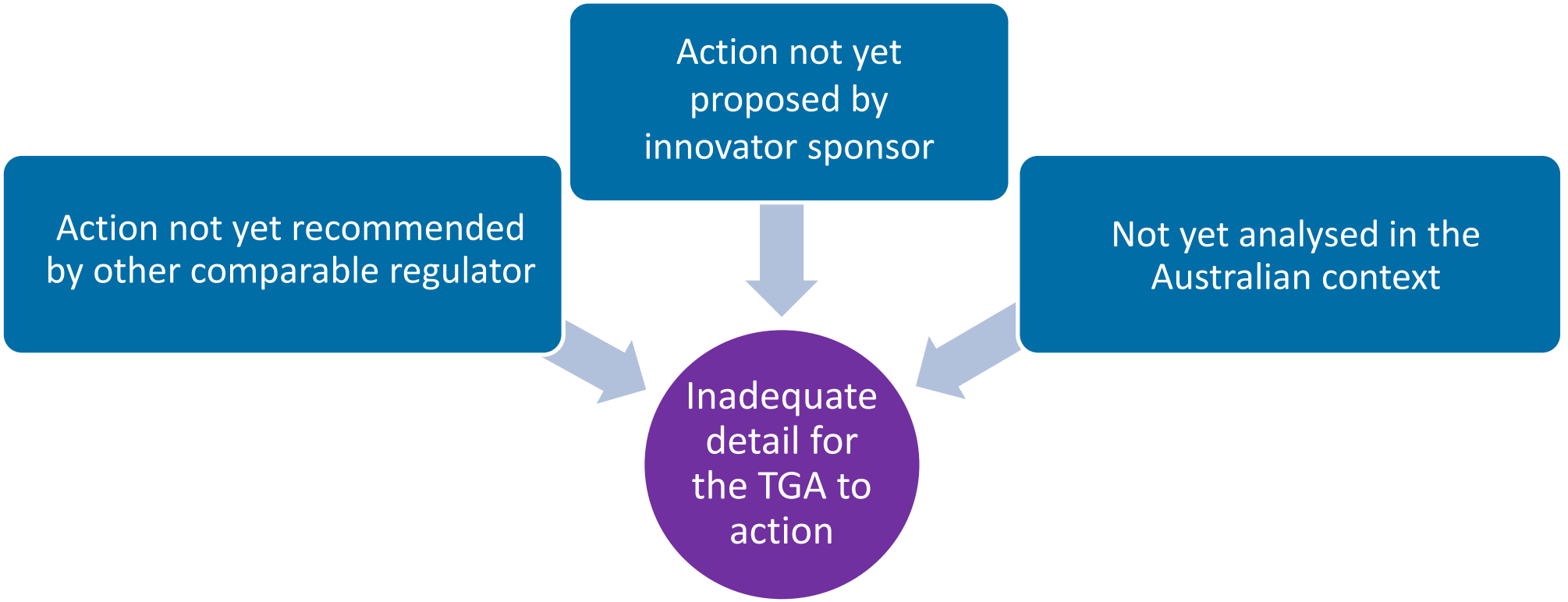
> A significant safety issue is a new safety issue or validated signal considered by you in relation to your medicines that requires urgent attention of the TGA. This may be because of the seriousness and potential major impact on the benefit-risk balance of the medicine and/or on patient or public health, which could warrant prompt regulatory action and/or communication to patients and healthcare professionals.

PV guidelines, Version 2.2, page 9

- Definition of SSI limited to issues requiring urgent attention of the TGA
- However, included examples result in subjective interpretation of what to report and when

Notifications lacking detail

- Many signals are notified to the TGA at the point of validation



Risk of system becoming saturated by less urgent issues

- Sponsors making notifications within 72 hour timeframe with inadequate information available to determine planned actions in Australia
- TGA triaging and investigating signals with inadequate information

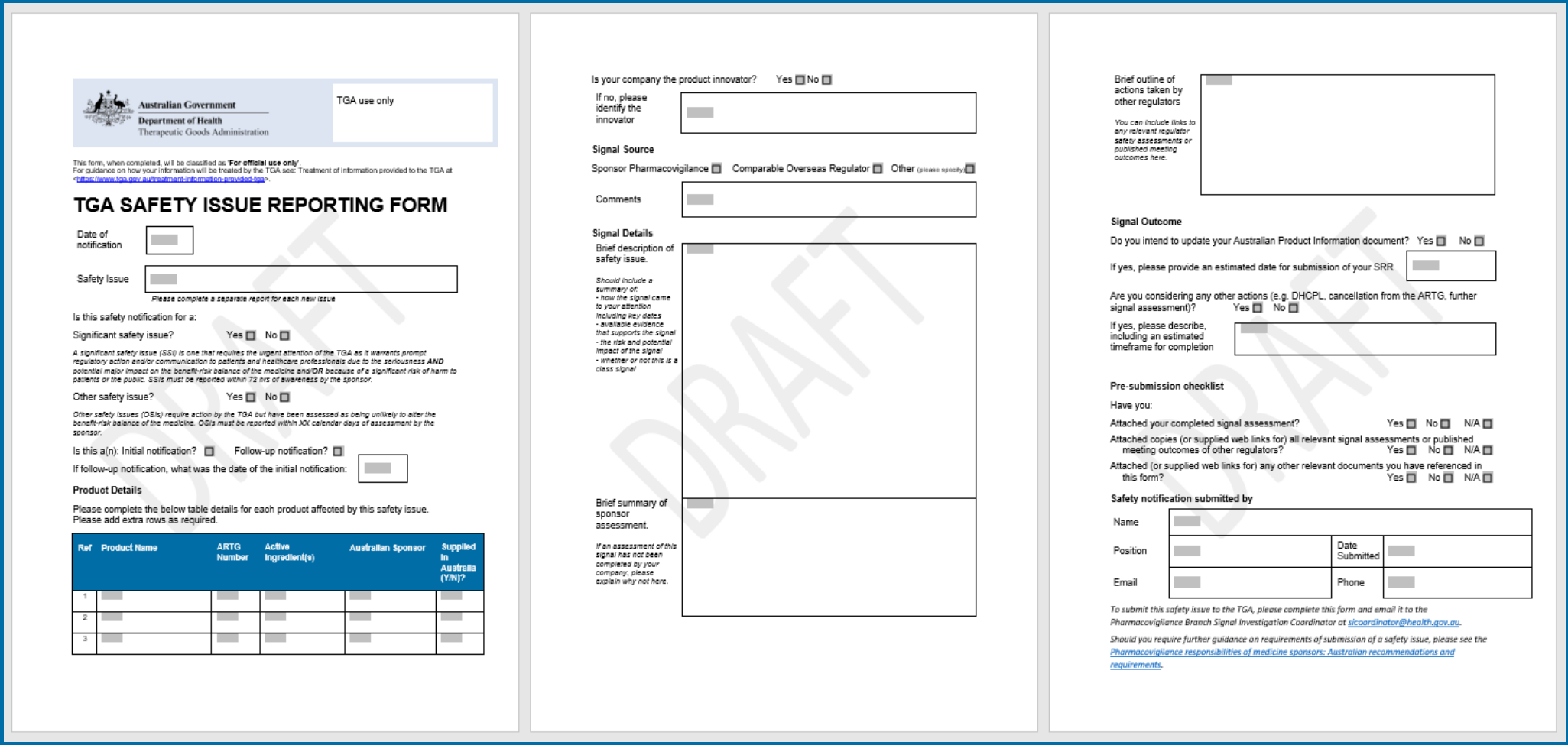
Proposed direction

- A tiered reporting system:
  - **Significant safety issues:** closely aligned with EMA's Emerging Safety Issue definition
  - **Other safety issues:** will require reporting within a longer timeframe (weeks/months following assessment completion). Examples:
    - Safety related changes recommended by comparable overseas regulators to the product information or label (that do not fit the definition of SSI)
    - Internally validated signals that have undergone signal assessment and subsequently been confirmed

Targeted consultation

- Planned for second half of 2022
- Currently on-hold due to caretaker conventions during Election period

Safety issue reporting form (in development)



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This form, when completed, will be classified as '**For official use only**'.
For guidance on how your information will be treated by the TGA see: Treatment of information provided to the TGA at <https://www.tga.gov.au/treatment-information-provided-tga>.

TGA SAFETY ISSUE REPORTING FORM

Date of notification

Safety Issue

Please complete a separate report for each new issue

Is this safety notification for a:

Significant safety issue? Yes ☐ No ☐

A significant safety issue (SSI) is one that requires the urgent attention of the TGA as it warrants prompt regulatory action and/or communication to patients and healthcare professionals due to the seriousness AND potential major impact on the benefit-risk balance of the medicine and/OR because of a significant risk of harm to patients or the public. SSIs must be reported within 72 hrs of awareness by the sponsor.

Other safety issue? Yes ☐ No ☐

Other safety issues (OSIs) require action by the TGA but have been assessed as being unlikely to alter the benefit-risk balance of the medicine. OSIs must be reported within XX calendar days of assessment by the sponsor.

Is this a(n): Initial notification? ☐ Follow-up notification? ☐

If follow-up notification, what was the date of the initial notification:

Product Details

Please complete the below table details for each product affected by this safety issue.
Please add extra rows as required.

Ref	Product Name	ARTG Number	Active Ingredient(s)	Australian Sponsor	Supplied in Australia (Y/N)?
1					
2					
3					

Is your company the product innovator? Yes ☐ No ☐

If no, please identify the innovator

Signal Source

Sponsor Pharmacovigilance ☐ Comparable Overseas Regulator ☐ Other (please specify) ☐

Comments

Signal Details

Brief description of safety issue.

Should include a summary of:
- how the signal came to your attention including key dates
- available evidence that supports the signal
- the risk and potential impact of the signal
- whether or not this is a class signal

Brief summary of sponsor assessment.

If an assessment of this signal has not been completed by your company, please explain why not here.

Brief outline of actions taken by other regulators

You can include links to any relevant regulator safety assessments or published meeting outcomes here.

Signal Outcome

Do you intend to update your Australian Product Information document? Yes ☐ No ☐

If yes, please provide an estimated date for submission of your SRR

Are you considering any other actions (e.g. DHCPL, cancellation from the ARTG, further signal assessment)? Yes ☐ No ☐

If yes, please describe, including an estimated timeframe for completion

Pre-submission checklist

Have you:

Attached your completed signal assessment? Yes ☐ No ☐ N/A ☐

Attached copies (or supplied web links for) all relevant signal assessments or published meeting outcomes of other regulators? Yes ☐ No ☐ N/A ☐

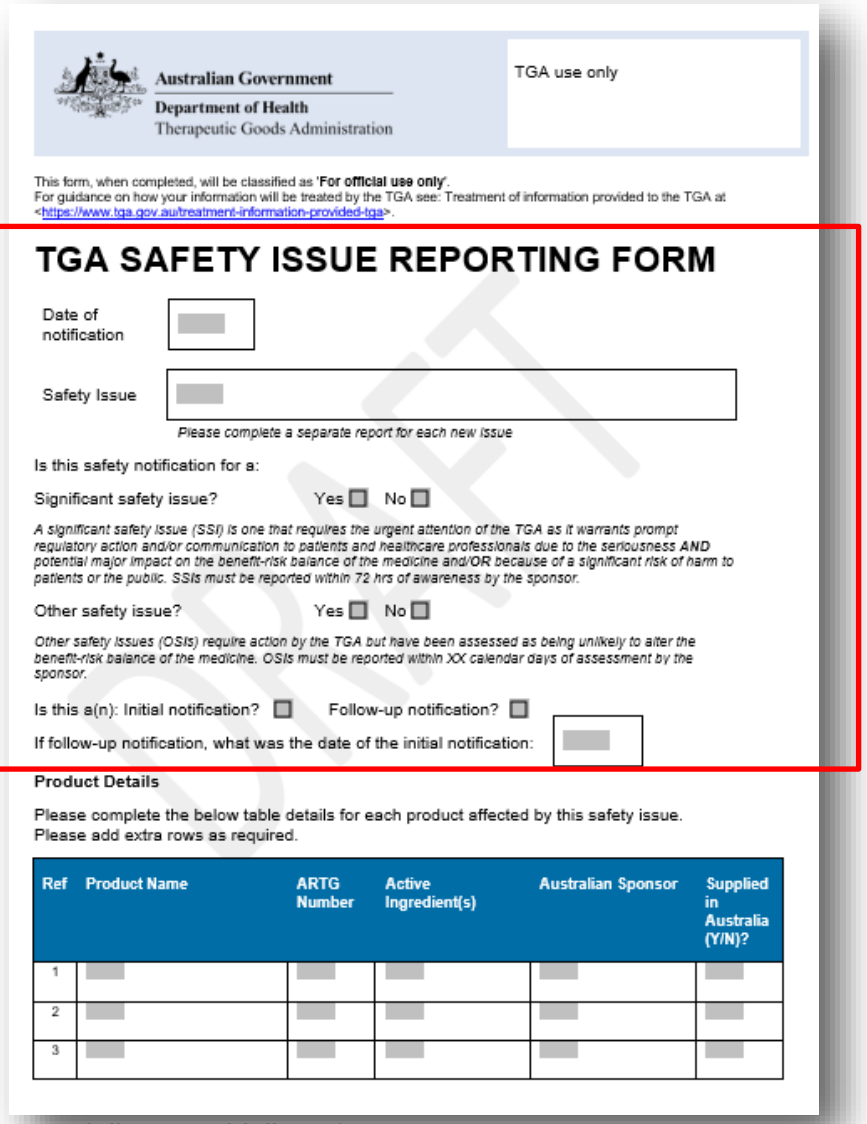
Attached (or supplied web links for) any other relevant documents you have referenced in this form? Yes ☐ No ☐ N/A ☐

Safety notification submitted by

Name			
Position		Date Submitted	
Email		Phone	

To submit this safety issue to the TGA, please complete this form and email it to the Pharmacovigilance Branch Signal Investigation Coordinator at sicoordinator@health.gov.au.

Should you require further guidance on requirements of submission of a safety issue, please see the Pharmacovigilance responsibilities of medicine sponsors: Australian recommendations and requirements.



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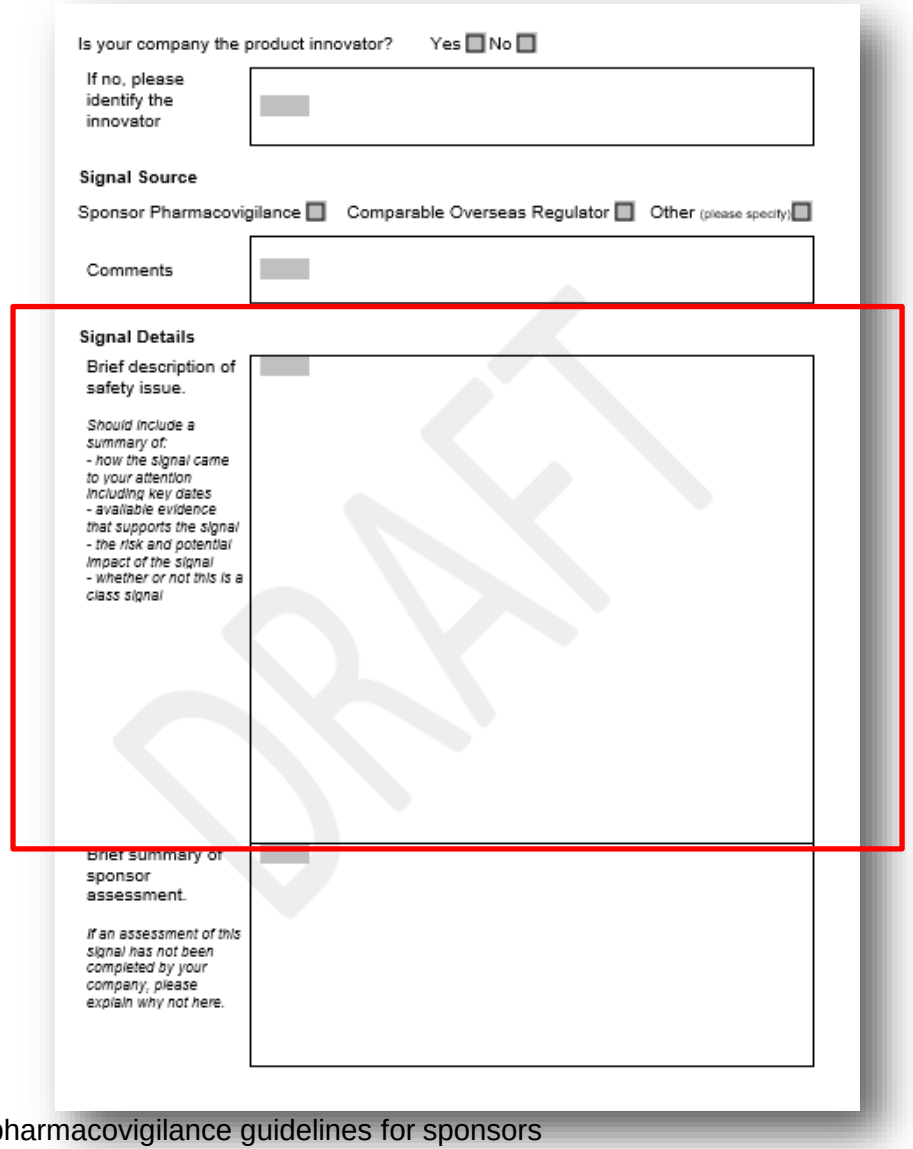

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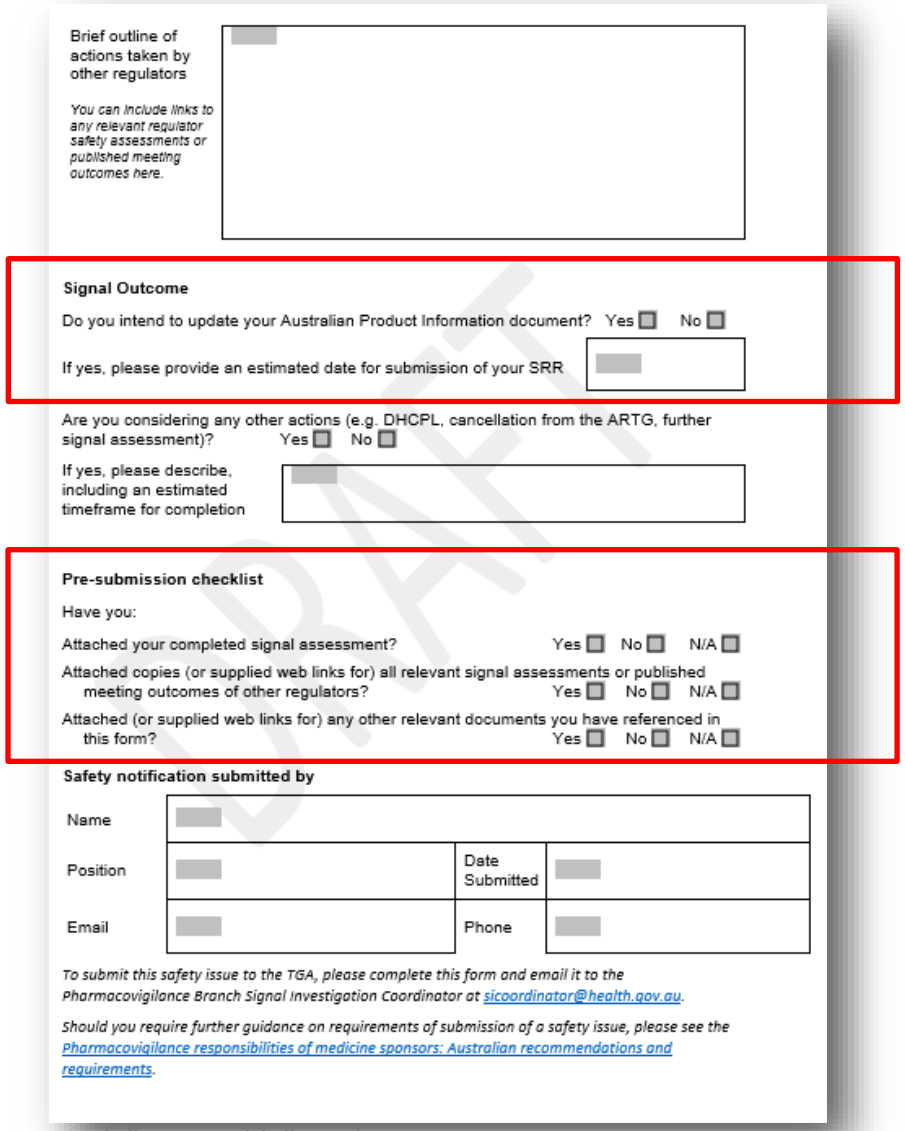

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Safety issues – to report, or not?

- Interactive questions via conference app

Question 1

Under the current PV guidelines would you report the following to the TGA as an SSI?

Scenario

You are the Australian sponsor of Drug A. You have received notification that the FDA has identified a Newly Identified Safety Signal (NISS) for *Drug A and hypertension*.

Answer

No – Notification of a comparable overseas regulator validating a signal does not, in itself, constitute an SSI. After initial assessment if you determine that there is no major impact on the benefit-risk balance of the medicine and/or on patient or public health you do not need to notify the TGA of this signal.

Question 2

Under the current PV guidelines would you report the following to the TGA as an SSI?

Scenario

You are the Australian sponsor of Drug B. You have become aware that Health Canada have requested the addition of a black box warning to the Drug B Product Monograph to include details of an increased risk of *fatal arrhythmias*.

Answer

Yes – This is a major safety-related action by a comparable overseas regulator. An issue such as an increased risk of fatal arrhythmias has a potential major impact on the benefit-risk balance of the medicine.

Question 3

Under the current PV guidelines would you report the following to the TGA as an SSI?

Scenario

You are the Australian sponsor of Drug C. Through your internal pharmacovigilance system, you have validated the following signal: *Drug C and leukocytoclastic vasculitis.* You are now planning to conduct a signal investigation.

Answer

No – You do not have to notify the TGA of every signal at the point of validation. If your initial review and analysis of the available evidence determines that there is no major impact on the benefit-risk balance of the medicine and/or on patients or public health then you do not need to notify us of this issue at this point in time.

Question 4

Under the current PV guidelines would you report the following to the TGA as an SSI?

Scenario

You are the Australian sponsor of Drug D. You have become aware that the Pharmacovigilance Programme of India have requested the following warning be added to the label and package insert of *Drug D* containing products:

- Use with caution in patients with conditions X, Y and Z.

Answer

No – The Pharmacovigilance Program of India is not considered a comparable overseas regulator by the TGA.

Question 5

Under the current PV guidelines would you report the following to the TGA as an SSI?

Scenario

You are the Australia sponsor of Drug E. Your global team has received an EMA PRAC request to perform a cumulative review of all cases of *Drug E associated with alopecia*.

Answer

No – A request for information from a comparable overseas regulator, while considered a validated signal, is not required to be notified to the TGA as an SSI. That is unless, following your review and analysis, you deem the issue to require urgent attention of the TGA because of the seriousness and potential major impact on the benefit-risk balance of the medicine and/or on patients or public health.

Questions – through conference app

In conclusion…

- The TGA will be making changes to the PV guidelines around SSI reporting
- Targeted consultation will occur later in 2022
- The focus will be on benefit-risk balance when identifying safety issues
- Please continue to observe the current PV guidelines for now
- We are working closely with our PV Inspection Program colleagues to ensure the guidelines for reporting align with parameters for inspection

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