Reporting requirements for safety issues

Proposed changes to *Pharmacovigilance responsibilities of medicine sponsors: Australian recommendations and requirements*

"We asked, you said, we did" – Outcomes of the targeted consultation

August 2023

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Introduction

The targeted consultation: Reporting requirements for safety issues – Proposed changes to *Pharmacovigilance responsibilities of medicine sponsors: Australian recommendations and requirements* opened on Monday 24 October 2022 for a period of 6 weeks, concluding on Monday 5 December 2022. This consultation was published to the Australian Government Department of Health and Aged Care online consultation hub, Citizen Space, in the form of an 11-question, multi-part survey.

A total of 99 stakeholder organisations were invited to participate in the consultation survey and 44 submissions were received.

Following analysis of the consultation submissions and consideration of the major issues raised by respondents, the *Pharmacovigilance responsibilities of medicine sponsors: Australian recommendations and requirements* (PV Guidelines) update has now been finalised and republished as version 3.0.

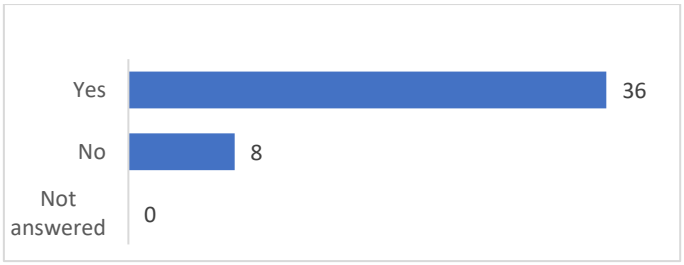
This report provides a summary of the consultation responses, outlines the major issues raised, and provides the rationale behind the final changes made to the PV Guidelines.

Consultation responses

The following feedback was received in response to the consultation survey questions. See appendix for the full list of survey questions.

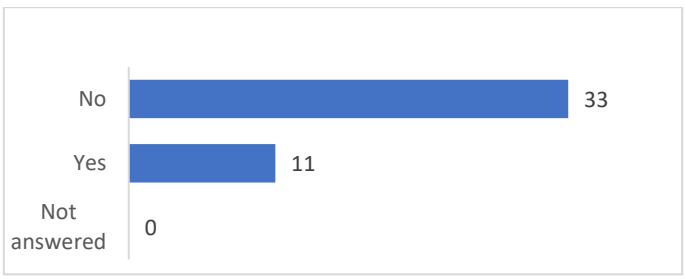
Two-tiered reporting system

Do you believe the proposed two-tiered reporting system for safety issues is suitable and practicable?



82% of respondents believe the proposed two-tiered reporting system for safety issues is suitable and practicable.

Do you have any concerns with the two-tiered reporting system not addressed at the previous question?

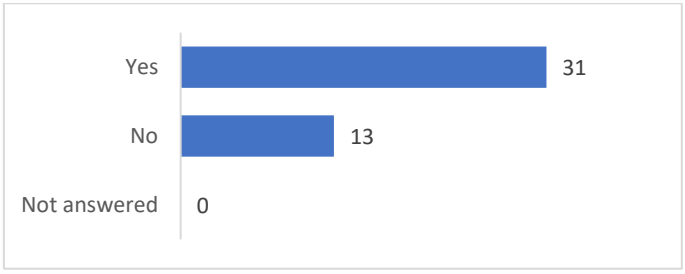


75% of respondents have no concerns with the two-tiered reporting system not addressed at the previous question.

Significant safety issues (SSIs)

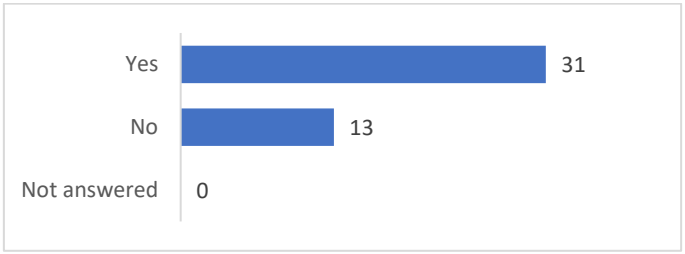
With reference to the information on SSIs in the 'Proposed changes to the PV Guidelines, version 2.2: Changes to safety issue reporting requirements' document:

Are the definitions and reporting requirements for SSIs clear and comprehensive?



70% of respondents believe the definition and reporting requirements for SSIs are clear and comprehensive.

Are the provided examples of SSIs sufficiently clear?



70% of respondents believe the provided examples of SSIs are sufficiently clear.

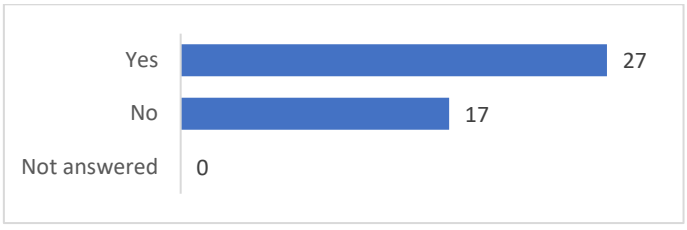
Do you agree with the proposed timeframe for the reporting of SSIs?

57% of respondents agree with the proposed timeframe for the reporting of SSIs.

Other safety issues (OSIs)

With reference to the information on OSIs in the 'Proposed changes to the PV Guidelines, version 2.2: Changes to safety issue reporting requirements' document:

Are the definitions and reporting requirements for OSIs clear and comprehensive?

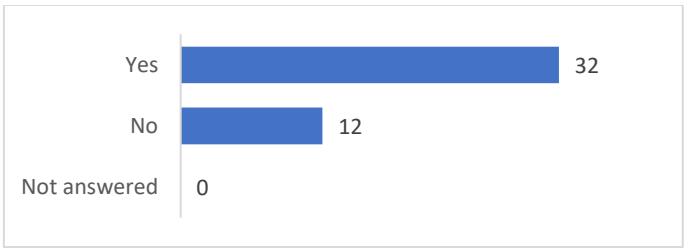


61% of respondents believe the definitions and reporting requirements for OSIs are clear and comprehensive.

Are the provided examples of OSIs sufficiently clear?

57% of respondents believe the provided examples of OSIs are sufficiently clear.

Do you agree with the proposed timeframe for the reporting of OSIs?

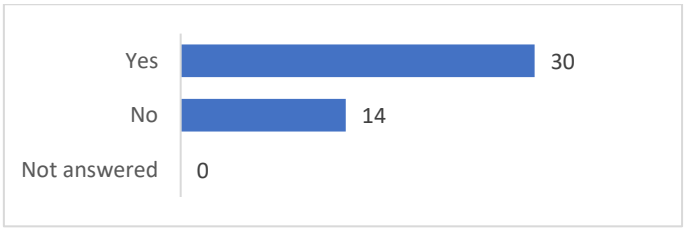


73% of respondents agree with the proposed timeframe for the reporting of OSIs.

Safety issue reporting form

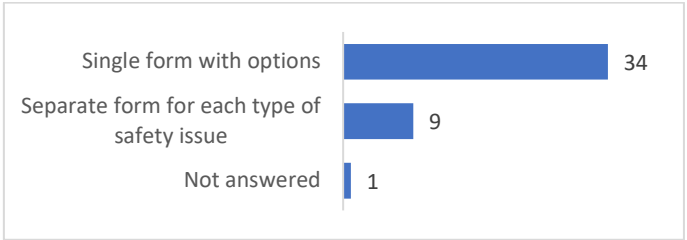
With reference to the draft safety issue reporting form:

Is this form clear and practical?



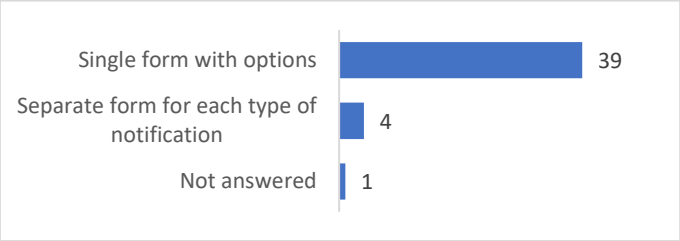
68% of respondents believe the draft safety issue reporting form is clear and practical.

Would you prefer a single form (with options for SSI or OSI notification) OR separate forms for each type of safety issue?



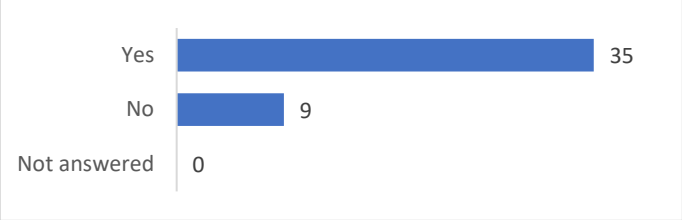
77% of respondents would prefer a single form (with options for SSI or OSI notification) over a separate form for each type of safety issue.

Would you prefer a single form (with options for initial or follow-up notification) OR separate forms for each type of notification?



89% of respondents would prefer a single form (with options for initial or follow up notification) over a separate form for each type of notification.

Do you think 3 months is an acceptable transition period, following which time the form will become mandatory for reporting safety issues?

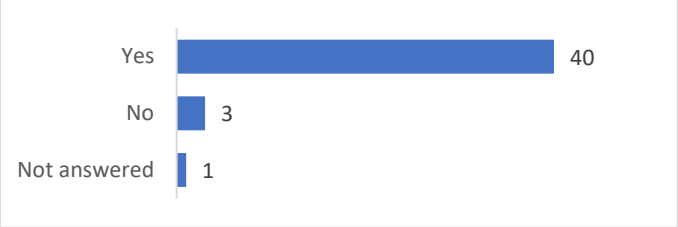


80% of respondents think that 3 months is an acceptable transition period.

Safety issue reporting decision tree

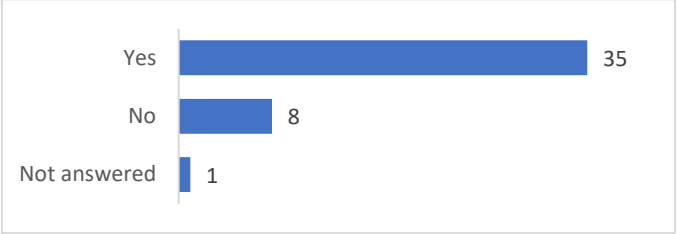
With reference to the safety issue reporting decision tree:

Is the decision tree a useful addition to the PV Guidelines?



91% of respondents agree that the safety issue reporting decision tree is a useful addition to the PV Guidelines.

Is the decision tree clear and easy to follow?



80% of respondents believe that the decision tree is clear and easy to follow.

Proposed TGA workshops on safety issue reporting

Would you be interested in attending any TGA workshops on safety issue reporting/PV Guidelines updates following publication of the revised PV Guidelines?

100% of respondents are interested in attending TGA workshops on safety issue reporting/PV Guidelines update.

Post-consultation changes to PV Guidelines

Despite the overwhelmingly positive response to the targeted consultation, a number of issues were raised that required further consideration by the TGA before changes to the PV Guidelines were finalised.

A summary of the major issues raised, and the rationale for any changes to the draft PV Guidelines, or reason for no change, are outlined below:

'Overseas regulators' amended to 'comparable overseas regulators'

Initial proposed changes to the PV Guidelines included a requirement to report safety-related actions imposed by all overseas regulators.

To avoid an increase in regulatory burden for both sponsors and the TGA, the requirement to notify other regulators' safety-related actions will be limited to those of comparable overseas regulators (CORs).

Clearer definitions of SSI and OSI with examples in a separate FAQ document

The definitions of SSI and OSI have both been refined and clarified in response to feedback.

In addition, clarification in the PV Guidelines that OSIs should only be reported to the TGA following completed sponsor assessments should ensure safety issues are reported at the right time, and reduce the chance of overreporting.

A separate PV FAQs document will include illustrative specific examples of both SSIs and OSIs. This will allow for timely updates to examples without the need to revise the PV Guidelines document.

Day 0 for reporting of OSIs aligned with *Day 0* for SSIs

Day 0 for the reporting of OSIs has been amended from the initially proposed:

> *the day that your internal signal assessment is completed*

to:

> *the day that any personnel of your Australian sponsor (including any third parties, vendors or partners that have been delegated pharmacovigilance responsibilities) are made aware of an* ***assessed*** *safety issue.*

This change aligns *Day 0* for OSI reporting with *Day 0* for SSI reporting. It should also reduce subjective interpretation resulting from differences in global company procedures.

This change will also ensure that, following identification of an OSI, sponsors have sufficient time to provide the TGA with all the information required in the safety issue reporting template.

Quality defect issues returned to definition of SSI reporting

The PV Guidelines have been amended to include specific reference to *serious* quality defect issues within the domain of SSI reporting. This is to ensure that the TGA is notified where the defect issue is likely to require prompt regulatory action because of potential major impact to the benefit-risk balance of the medicine and/or public health. The guidelines now include the following bullet point, under the subsection *Significant safety issues* (p.16):

> *Serious quality defect issues which may lead to an immediate risk to public health.*

Additionally, quality defect issues have been added to the safety issue reporting decision tree.

Duplicate reporting

Inclusion of an alternative procedure for generic sponsors to report COR-identified safety issues has been added to the PV Guidelines. This new procedure allows sponsors of generic medicines to meet their reporting obligations for COR-identified safety issues with the timely submission of an application to align their product information document with the innovator product information document. This inclusion will result in reduction in the number of duplicate reports received.

Safety issue reporting form amended to online reporting webform

The proposed *Microsoft Word* safety issue reporting form has been replaced with an online webform. This is a significant improvement to the TGA's safety issue reporting capabilities and will facilitate complete and correct safety issue notification.

Management of follow up information

Follow-up information can be supplied to the TGA via submission of an additional webform which references the initial notification date. Explicit guidance regarding when and what follow-up information is required will be provided in the FAQs document.

Transition period for implementation of new guideline requirements

The proposed 3-month transition period for implementing the new pharmacovigilance requirements contained in the revised PV Guidelines has been extended to 6 months. This will allow for the integration of changes into sponsors' internal processes and subsequent staff training.

Further harmonisation with the EMA's GVP Module IX

A number of respondents suggested further alignment with the EMA's safety issue reporting requirements, per GVP module IX. Due to inherent differences between the EMA and the TGA including signal detection processes and legislation, further harmonisation with GVP module IX cannot be considered further at this time.

SSI reporting timeframe: 72 hours versus 3 working days

A number of respondents requested that the TGA reconsider the 72-hour timeframe for reporting of SSIs, proposing that the timeframe be changed to '*as soon as possible and no later than 3 working days from awareness*'.

A change in the timeframe for SSI reporting is not supported by the TGA as it would delay communication of the most urgent safety issues. However, following the redefinition of SSI, there should be considerably fewer safety issues that require reporting to the TGA within 72-hours.

Timeframe for communication of SSIs from global to Australian affiliate

A 3-calendar day timeframe for SSI communication from global to the Australian sponsor has been included in the PV Guidelines (v3.0). Several respondents requested extending this timeframe to ≥5 calendar days or ≥3 working days.

As with the timeframe for SSI reporting between the Australian sponsor and the TGA, the proposal to extend this timeframe is not supported as this would delay receipt of the most urgent safety issues to the TGA.

Expectation to report same issue if actioned by different regulators sequentially

Multiple respondents raised the issue of different overseas regulators acting on the same safety issue and sponsors' obligations to report each of these actions. Respondents proposed that in such circumstances it be sufficient to inform the TGA of the safety issue only once.

While multiple overseas regulators may identify a safety issue and take regulatory action, their assessments of the issue and resultant actions may not be the same. Therefore, sponsors are required to notify the TGA of each separate overseas regulator action.

'To be determined'/'Under assessment' option in the *Safety Issue Reporting Form*

Some survey respondents proposed that the question '*Do you intend to update your Australian PI document?*' on the safety issue reporting form include a third option *'To be determined'/'Under assessment'*.

One of the key goals of implementing a safety issue reporting form is to facilitate the clear reporting of safety issues once internal sponsor assessments are complete – this includes a decision on whether the sponsor intends to update their Australian PI. Including an option for *'To be determined'/'Under assessment'* would result in the submission of incomplete safety reports, therefore this option will only be available for initial reporting of SSIs where this information may not yet have been determined within the 72-hour timeframe.

Appendix – consultation survey questions

1. What is your name?
2. What is your email address?
3. What is your organisation?
4. Do you believe the proposed two-tiered reporting system for safety issues is suitable and practicable?

   If you answered no, please indicate why and provide comment regarding a possible alternative system.
5. Do you have any concerns with the two-tiered reporting system not addressed at the previous question?

   If you answered yes, please outline these.
6. With reference to the information on SSIs in the 'Proposed changes to the PV Guidelines, version 2.2: Changes to safety issue reporting requirements' document:

   Are the definitions and reporting requirements for SSIs clear and comprehensive?

   If you answered no, please indicate why.

   Are the provided examples of SSIs sufficiently clear?

   If you answered no, please comment including any additional examples that you feel should be included.

   Do you agree with the proposed timeframe for the reporting of SSIs?

   If you answered no, please indicate why.

   Please include any comments or suggestions regarding SSI reporting requirements not captured elsewhere.
7. With reference to the information on OSIs in the 'Proposed changes to the PV Guidelines, version 2.2: Changes to safety issue reporting requirements' document:

   Are the definitions and reporting requirements for OSIs clear and comprehensive?

   If you answered no, please indicate why.

   Are the provided examples of OSIs sufficiently clear?

   If you answered no, please comment including any additional examples that you feel should be included.

   Do you agree with the proposed timeframe for the reporting of OSIs?

   If you answered no, please indicate why.

   Please include any comments or suggestions regarding OSI reporting requirements not captured elsewhere.
8. With reference to the draft safety issue reporting form:

   Is this form clear and practical?

   If you answered no, please indicate why.

Would you prefer a single form (with options for SSI or OSI notification) OR separate forms for each type of safety issue?

Would you prefer a single form (with options for initial or follow-up notification) OR separate form for each type of notification?

Do you think 3 months is an acceptable transition period, following which time the form will become mandatory for reporting safety issues?

If you answered no, please indicate why.

Please include any comments or suggestions regarding the safety issue reporting form not captured elsewhere.

9. With reference to the safety issue reporting decision tree: Is the decision tree a useful addition to the PV Guidelines?

   If you answered no, please indicate why.

   Is the decision tree clear and easy to follow?

   If you answered no, please indicate why.

   Please include any comments or suggestions regarding the decision tree not captured elsewhere.

10. Would you be interested in attending any TGA workshops on safety issue reporting/PV Guidelines updates following publication of the revised PV Guidelines?

11. Do you have any final comments or suggestions on the proposed updates to the safety issue reporting requirements or the PV Guidelines?