The Australian Pharmacovigilance Inspection Program
Overview, objectives and what to expect

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Overview

• Background
• MMRD Review
• Objectives of the pharmacovigilance inspection program (PVIP)
• Relevant legislation
• Inspection process
  – Inspection types
  – Scheduling of inspections (including risk factors)
  – Conduct of inspection (including pre- and post-inspection activities)
  – Publication of inspection metrics
• Further Information
## Background to the PVIP

### Overseas pharmacovigilance (PV) inspections

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Type of Inspections</th>
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<tbody>
<tr>
<td>European Medicines Authority (EMA)</td>
<td>• risk based inspections</td>
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<td>Corresponding EU regulators (i.e. MHRA, BfArM)</td>
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<tr>
<td>US Food and Drug Administration</td>
<td>• for cause and routine inspections</td>
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<tr>
<td>Swissmedic</td>
<td>• for cause and routine inspections</td>
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The Australian Pharmacovigilance Inspection Program
Background to the PVIP

• In May 2016, the TGA completed a successful pilot of a PV Inspection Program.
  – Ten sponsors volunteered to participate in the pilot – ranging from large multinational companies to small Australian owned and based companies, biotechnology companies and complementary/herbal medicine companies.
  – Pilot PV inspections were modelled on the TGA’s Good Manufacturing Practice (GMP) inspections and the UK MHRA inspections.
  – Successful with generally positive feedback especially regarding the increased visibility and importance of pharmacovigilance in Australia as a result of the inspection.
Expert Review of Medicines and Medical Devices Regulation (MMDR review)

• The review was conducted by an expert panel and made 58 recommendations relating to the regulation of medicines, medical devices, post-market monitoring, complementary medicines and advertising of therapeutic goods.
• On 15 September 2016, the Australian Government released its response to the MMDR review.
• The response included the increasing flexibility for registration pathways and enhanced post-market monitoring for prescription medicines.
• Senate inquiry into Therapeutic Goods Amendment Bill 1 – strong interest in ensuring that changes to legislation do not compromise patient safety.
• PVIP being implemented as part of an enhanced vigilance framework.
Objectives of the PVIP

- PV inspections will enable us to:
  - **verify** sponsor compliance with their pharmacovigilance requirements (reporting AEs, significant safety issues) and other related legislative requirements;
  - **educate** sponsors to assist them to meet their requirements; and
  - **promote** continuous improvement in pharmacovigilance
  - **safeguard patient safety** by ensuring the ongoing positive risk benefit balance of a medicine in the Australian context
    - collect and collate current information on the safety and efficacy of your medicines(s)
    - assess the risk/benefit balance of your medicine(s)

- The inspection will monitor your compliance with Pharmacovigilance responsibilities of medicine sponsors – Australian recommendations and requirements (the PV guidelines) and relevant legislation
Implementation details

• **Implementation from 1 September 2017:**
  – we will be running in depth information sessions later in the year and **no** inspections will occur until these information sessions have been run

• PVIP will apply to Sponsors of:
  – prescription medicines
  – over-the-counter medicines

• Risk-based prioritisation of sponsors for inspection, considering:
  – the risk that non-compliance is occurring, and
  – the potential consequences of this

• In addition to routine inspections, sponsors may be selected for random or “for cause” inspections
Scheduling of inspections

Risk based scheduling

• Routine inspections prioritised based on the risk we have assigned to you or your pharmacovigilance system.

• How we assess your risk:
  – Internal intelligence: including whistleblower information, information from regulatory compliance, previous PV inspection history, overseas agency data
  – Non-compliance to other TGA requirements: PSUR submission, RMP commitments, GMP findings, PV reporting requirements, updating PIs
  – Product risk profile
  – Planned PV risk assessment survey
    ▪ Biannual (and ad hoc) electronic report on your pharmacovigilance system.
    ▪ Completing the requested fields of this form will help us assign your risk and prioritise you.
    ▪ If you do not complete the report as requested, we will assign you the highest risk!
The inspection process

<table>
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<tr>
<th>Step</th>
<th>Description</th>
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<tbody>
<tr>
<td>Notification</td>
<td>Notification issued to the Australian Contact Person</td>
</tr>
<tr>
<td>Inspection preparation</td>
<td>Dates agreed on, the development and dissemination of an inspection plan and initial document requests</td>
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<tr>
<td>Inspection</td>
<td>Interview and document review</td>
</tr>
<tr>
<td>Inspection Report</td>
<td>Issued 30 days after inspection completed</td>
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<tr>
<td>Sponsor CAPA</td>
<td>Agreement of CAPA and review of ongoing actions where required</td>
</tr>
<tr>
<td>Close out of inspection</td>
<td>The inspection report and close out record will be signed as final and issued to the sponsor</td>
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Notification

• Routine inspection: **six to eight weeks’ notice**
  – Allow you to make logistic arrangements
  – ensure key personnel are available
  – gain access to relevant data

• ‘For cause’ inspections: can be **nil or short notice for exceptional circumstances**

• We will issue an inspection notification to your Australian pharmacovigilance contact person and may request further information on your pharmacovigilance system
Inspection preparation

1. Agree on suitable dates and venues

2. Prepare and distribute an inspection plan, outlining the areas to be inspected and the schedule

3. Request documents prior to the inspection to allow pre-inspection analysis and inspection planning.
The inspection

Interviews and document reviews

The inspection will consist of

• **Interview sessions** designed to gain an understanding of your pharmacovigilance system
  – interview appropriate staff members
  – examine relevant computers, electronic systems and databases

• **Document request and review** to analyse specific examples of the pharmacovigilance system/processes. This may include review of relevant:
  – company or contracted organisation policies and procedures
  – adverse event case documentation
  – internal and external communication
  – product-related documentation
  – staff training records

• **Opening and closing meeting** to discuss the inspection and any findings
The Inspection report

- You will be issued an inspection report **within 30 days** of completing the inspection
- The inspection report consists of:
  1. Inspection details
  2. Introduction and summary of the inspection activities
  3. Inspection observations and findings
  4. Deficiencies observed during the inspection
  5. Name and signature of the person authorising the report on behalf of the TGA
Close-out record

• We attach a close-out record with the inspection report to provide your response- This is the CAPA plan
• The close-out record documents:
  – any deficiencies identified *(completed by inspector)*
  – the root cause of the deficiencies
  – your proposed corrective and preventative actions (CAPA) plan to the root cause
  – corrections to observed examples (if relevant)
  – objective evidence provided (if relevant)
  – proposed completion dates
  – inspector assessment and any comments on your CAPA plan *(completed by inspector)*
  – the final response acceptance *(completed by inspector)*
• Return the close-out record within 30 days of receiving the inspection report.
• We will then liaise with you to agree on the corrective and preventative actions and corresponding dates
Close out of the inspection

• Once the CAPA plan has been agreed by the inspector, the inspection report and close out record will be signed as final by the lead inspector and issued to the sponsor.

• Follow-up actions to the inspection may be initiated if required (e.g. progress reports on corrective actions, updating PI documents, re-inspection to assess CAPA implementation)
How to prepare for an inspection *(a few pointers)*

- Ensure you have nominated an Australian contact person for PV to the TGA
- Ensure an appropriate quality management system is in place as a basis for an effective PV system— including up to date SOPs, training and auditing
- Ensure all potential sources are being monitored for ADRs— including but not limited to marketing programs, medicines information, product quality complaints, literature, company sponsored internet sites and social media, post market clinical trials etc.
- Ensure you have a robust and secure system to collect, process and analyse safety data
- Ensure all serious Australian ADRs are being reported to the TGA within required timeframes
- Ensure ongoing monitoring for safety signals is occurring on a regular basis
How to prepare for an inspection *(a few pointers)*

- Ensure there are procedures in place to receive notification of significant safety issues from global counterparts and report to the TGA within required timeframes, where required.
- Ensure you have safety agreements in place with required partners and contractors.
- Ensure PSURs are complete and submitted on time.
- Ensure any RMP commitments are being met.
- Ensure the Australian person responsible for PV has appropriate oversight of the system.
- Ensure CAPA from any previous PV inspection has been completed.
- Ensure all safety data is being held indefinitely for the life of the product and for 10 years after its removal from the ARTG.
Further information

• New guidelines currently in draft (due for release September 2017):
  – Pharmacovigilance responsibilities of medicine sponsors – Australian recommendations and requirements (Pharmacovigilance guidelines)
  – Pharmacovigilance Inspection Guidelines
• Information sessions on the inspection are currently being scheduled in capital cities form sept 2017 (see TGA events page for PVIP information session dates.)

• New PVIP web page will be implemented 1 September 2017
  – the PVIP guidelines
  – FAQ
  – inspection metrics (in the future)
  – Risk survey information when available