Australian Government
Department of Health
Therapeutic Goods Administration

Risk management plan (RMP) compliance monitoring

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TGA Health Safety Regulation

Why does RMP compliance matter?

- RMPs aim to ensure that the benefits of a medicine outweigh its risks by the greatest achievable margin
- RMP document = written agreement applied as a condition of registration
- Compliance activities help to ensure that required risk management activities are conducted, and appropriate risk management systems maintained

RMP Compliance Monitoring Program

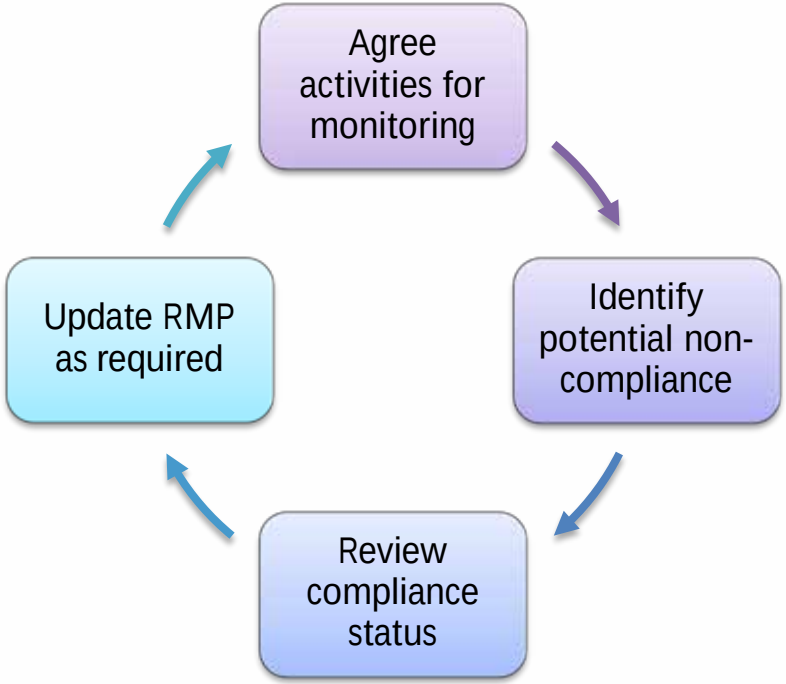
MMDR reform for enhanced medicines vigilance

…..has been operating since 1 January 2018

- complementary to other established TGA activities
  - RMP evaluation (2009)
  - PVIP (2018)

RMP Compliance monitoring program

- **Aim:** ensure timely implementation of RMP commitments
- **Approach:** cooperative compliance, aligned with the TGA's regulatory compliance framework



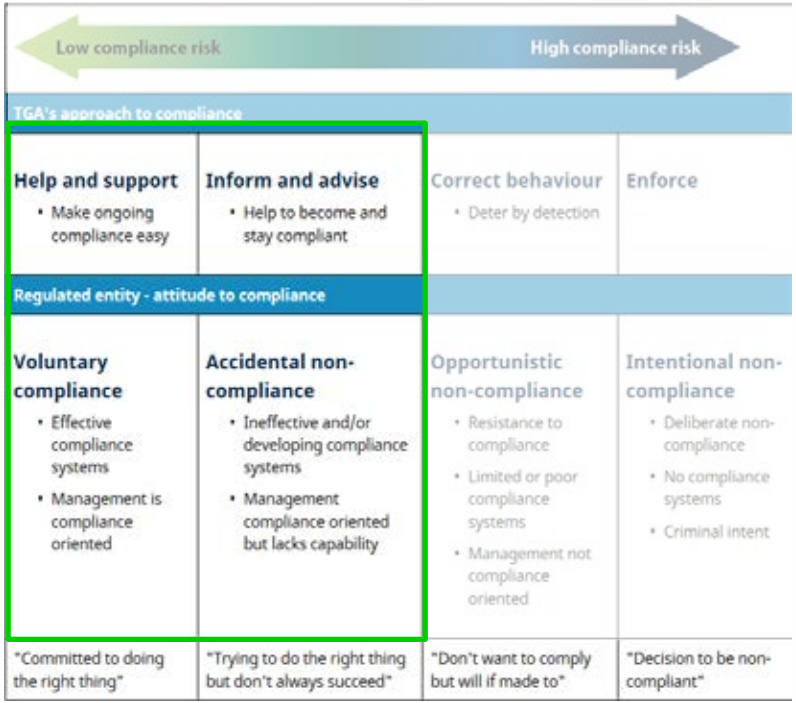
RMP Compliance – help & support, inform & advise

RMP evaluation will ensure RMP commitments are:

- clearly documented
- feasible and measurable

If we identify potential non-compliance, we will:

- contact you to clarify compliance status
- support you in developing a plan to achieve compliance
- continue to monitor to ensure future compliance



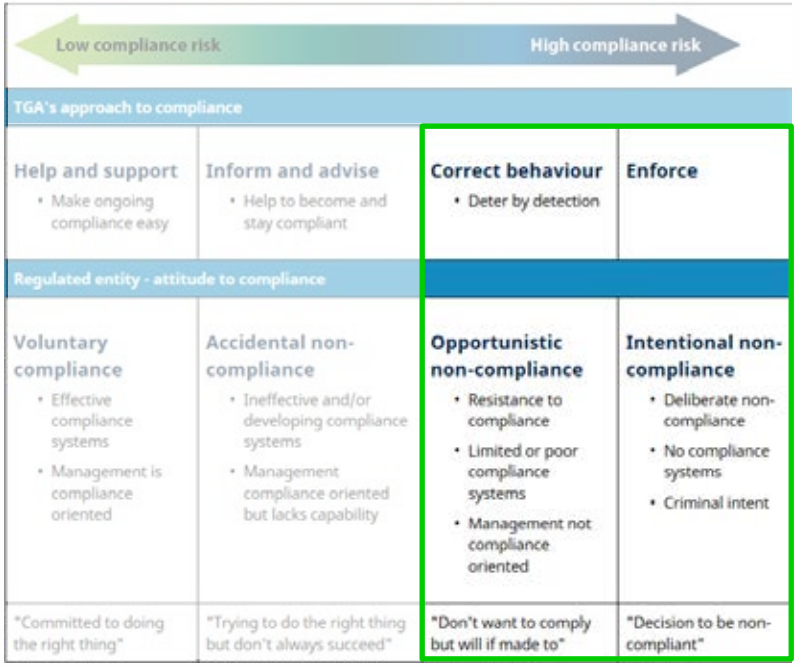
RMP Compliance – correct behaviour and enforce

If we identify continued non-compliance, we will:

- formally request information on how you will achieve compliance
- continue to monitor to ensure future compliance

Serious non-compliance will be referred internally to TGA enforcement area:

- outcomes of these regulatory actions may be published on the TGA website



Risk-based prioritisation

- High priority activities, subject to periodic desktop audit, may include:
  - Confirmatory studies for provisionally registered products
  - Local additional risk minimisation activities (e.g. providing educational materials for review)
  - Australian-specific additional pharmacovigilance
  - Local studies to measure effectiveness of additional risk minimisation
  - Some conditions of registration

Non-prioritised

- random desktop based audit of sponsors' RMP compliance to ensure non-prioritised requirements are met

General principles – 1 of 2

- Sponsor should ensure there is a clear mutual understanding of commitments at the time they are agreed
- Contact TGA to discuss any areas of uncertainty

ASA template – Record of the PV plan

Compliance Monitoring

Table 2: Ongoing and planned additional PV activities

Study and status	Summary of objectives	Safety concerns addressed	Study location; Australian patients?	Submission to TGA*	
				Required?	Deliverable and due date

ASA template - Record of implementation plan

Table 4: Australian implementation of additional risk minimisation activities

Additional risk minimisation activity	Target audience	Implementation details, including method(s) of dissemination	Timepoints for and frequency of dissemination

Compliance Monitoring

ASA template - Record of evaluation plan & deliverables

Table 5: Evaluation of additional risk minimisation activities

Additional risk minimisation activity	Evaluation plan and criteria for success	Submission of results to TGA: deliverable and timeframe

Compliance Monitoring

General principles – 2 of 2

- Situation may change in the post-registration setting
- Ensure proposed changes to agreed commitments are communicated to and agreed by TGA

Example
Supply educational guide to GP prescribers

Additional risk minimisation activity	Evaluation plan and criteria for success	Submission of results to TGA: deliverable and timeframe
Supply educational guide to GP prescribers	Initial and 2nd distribution completed to at least 90% of target audience EU survey of GP knowledge and awareness, predefined success criteria as per protocol in EU RMP	Evaluation report (EU survey outcomes and distribution information) to be submitted to TGA by May 2020

Educational guide to GP prescribers

- What does compliance look like?
  - sponsor submits EU survey outcome and report on local implementation by agreed date

  OR
  - sponsor contacts TGA in advance of the due date to request change to RMP, with robust justification

- Signals for potential non-compliance:
  - Sponsor does not submit by the due date, with no explanation
  - Sponsor submits EU survey results but no report on local implementation
    - § TGA contacts sponsor to determine status of commitment

Discussion

"TGA should provide more detail, including format of the periodic audits for RMP compliance and timelines to respond."

- there will not be periodic audits for all products
- desktop-based program
- risk-based program focused on highest priority activities and ensuring sponsors are aware of the need to comply
- there may also be random non-prioritised audits
- sponsors may be asked for evidence of meeting commitments during pharmacovigilance inspections
- sponsors will first be reminded of upcoming or due commitments
- opportunity to respond with plan to correct deficiency
- formal TGA notification in the event of non-compliance, expected course of action and timelines for responding stated

"Include guidance on what actions are required should RM measures prove to be ineffective."

- Action should be driven by the nature of the risk and criticality of the RM activity to address it
- Company should already be thinking about this in the initial design of RM
  - How critical is it that the measure proposed be viable and effective for patient safety?
  - What is the threshold criteria for success of a measure?
  - What is the plan if the measure proves ineffective?
- Communicate any negative outcome to TGA as soon as becomes known and provide information on your plan to address deficiencies

Feedback on RMP guidance

"Monitoring and compliance should be stated to apply to

- *Australia-specific RM activities*
- *implementation and effectiveness for Australia-specific RM activities*
- *outcomes of additional PV activities being the additional safety concerns identified by TGA*

This will avoid ambiguity as to whether the monitoring extends to EU-specific activities"

- TGA has published updated RMP Guidance and ASA template

Feedback on RMP guidance

"Provide additional guidance on the expected format of submission of the results of RM effectiveness measures."

- TGA has published updated RMP Guidance and ASA template

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