REGULATORY PRACTICE COMMITTEE

Agenda Item No. 3.3

Date: **Thursday 28 November 2019**

Sponsor: [redacted]
Assistant Secretary – Complementary & OTC Medicines Branch

Subject: **Prioritisation and Handling Model for Listed Medicines Compliance Leads**

RECOMMENDATION

That the Committee:

1. **ENDORSES-in-principle our proposed model for prioritising and handling leads about non-compliance of listed medicines, including the:**
   a. **risk-based categorisation of deficiencies**
   b. **relative priorities for resolution and target times for action**
   c. **enforcement actions**
2. **NOTES that the model prioritises issues that pose a likely or potential risk to consumer safety or public health over other non-compliance.**
3. **NOTES that LCS intends to finalise implementation of the handling model with the development of joint operating procedures with partner business areas**

BACKGROUND

- The Listing Compliance Section (LCS) receives signals of potential non-compliance related to listed medicines in the form of complaints/allegations from consumers or industry, and referrals from other areas within the TGA or external stakeholders. We refer to these collectively as **compliance leads**. Approximately 90 leads are received each year with a third of these pertaining to more than 3 medicines.
- In approximately 90% of the cases the perceived non-compliance results in a confirmed breach and some of those pose/may pose a risk to consumer safety. Frequently the allegations relate to lack of efficacy of the product.
- The LCS' current practice for handling leads involves a basic triage, followed by an investigation and risk-assessment to choose and prioritise enforcement action. The majority of leads in relation to which non-compliance of a medicine is determined to be likely on the basis of the information received give rise to a targeted post-market compliance review, irrespective of the risk of the non-compliance.
- While leads where the alleged non-compliance could pose an imminent safety risk to consumers are immediately actioned, the majority are queued for review pending evaluator availability, and there are no target timeframes associated with its initiation.
- The compliance review is the usual means, in non-urgent circumstances, to formally investigate the signal including obtaining information from the sponsor; determine definitively whether a breach of regulatory requirements has occurred (including providing an opportunity for the sponsor to respond to our findings); and take

necessary enforcement action. Information requested from the sponsor can include labelling, manufacturing documents or the evidence the sponsor holds in support of indications for their medicine.

ISSUES TO BE CONSIDERED

Historical approach

- The LCS' current singular enforcement approach to resolve leads where likely non-compliance is identified (a targeted post-market compliance review):
  - is resource-intensive;
  - can delay the voluntary resolution of non-compliance by a sponsor;
  - may not be proportionate to low-risk non-compliance;
- Although prioritisation for enforcement action is based on a risk assessment, it is relative to the other leads in the queue awaiting compliance review—i.e. the order timing of reviews depends on other leads in the queue according to risk score rank order. This can unacceptably delay the initiation of a compliance review pending evaluator availability.
- The risk assessment process for prioritising enforcement action is time consuming and relies on information that is frequently unavailable as part of the lead, such as the volume of a particular product in the market. This has meant inconsistent prioritisation and resolution of similar issues for different medicines.
- The lack of predictability on determining the level of priority that should be assigned to a given lead and the corresponding course of action for resolution, results in lack of transparency for our internal stakeholders around actions and timeframes.

Proposed solution

- The LCS is seeking to implement a model for systematic and predictable handling of leads that uses a risk-based selection and timely completion of enforcement actions. The model is depicted at **Attachment 1**.
- The proposed model leverages:
  - the categorisation of most legislative breaches according to the level of risk to consumers;
  - the spectrum of options that are available under the *Therapeutic Goods Act 1989* ('the Act') for enforcing compliance, rather than a one-size-fits-all approach;
  - a recently-established team that is responsible for managing leads; and
  - the new data analytics tools (i.e QLIK Sense applications) to visualise current and historical data related to compliance reviews and lead investigations.
- The model specifically links the risk of alleged breaches and other relevant factors to an appropriate enforcement action and corresponding level of priority for resolution (**Attachment 1**). The relevant factors include:
  - the 'lead background', incorporating (a) the sponsor compliance history from compliance reviews, (b) the relative frequency of leads related to that sponsor, and (c) the number of past investigations into the medicines that are the subject of the lead; and/or
  - the credibility or level of confidence in the source of the lead; and/or
  - the level of certainty regarding the breach occurrence (lead quality).
- The specific objectives of the model are:

  - To increase predictability and transparency for our internal stakeholders around timeframes and resultant enforcement actions when a lead is sent to the LCS
  - To use all enforcement options available in a risk-based manner to foster a culture of compliance among listed medicine sponsors
  - To expedite enforcement actions in cases where the detected deficiencies pose or may-pose a risk to consumer safety
  - To provide sponsors the opportunity to take proactive steps to bring all of their goods into compliance in cases where the detected deficiencies are not expected to adversely affect consumer safety, consistent with the TGA's enforcement model
- Key differences offered by the new model compared with the previous model are:
  - Use of prescribed prioritisation and actions according to risk categories, rather than a ranking system which is highly variable depending on the other leads in the queue.
  - Use of a light touch enforcement action (**Obligation Notices)** to conclude investigations where the suspected deficiency(ies) are determined to be non-safety related (i.e. minor or efficacy-related). This approach reduces the need to undertake post-market compliance reviews where the issues identified are minor in nature. It also provides sponsors an opportunity to proactively bring their product into compliance.
  - Consideration to using Infringement Notices in relation to sponsors with a persistently poor compliance history where the non-compliance is immediately verifiable without the need of initiating a compliance review (e.g. Detection of prohibited substance verified by the TGA's Laboratories Branch).
  - Application of internal timeframes to triage and action all leads investigations.
  - Formally requesting information from a sponsor and providing them with details of the alleged breach while a lead with high-risk alleged deficiencies is still under investigation. Our recent trial suggests this compels the sponsor to proactively and voluntarily resolve potential deficiencies and expedites resolution should the lead need to progress to a formal review.
- The intended outcomes of the model are:
  - Improved consistency with prioritisation and enforcement actions
  - Increased capacity within the LCS to focus resources on higher risk leads and leads that involve serial non-compliant sponsors
  - Increased capacity for investigations and reviews
- The operation of model is illustrated by way of examples in **Attachment 2**.

Outcomes of the pilot of the proposed model

The proposed leads priorisation and handling model has been successfully trialled for 2 months (September - October 2019.) So far a total of 20 leads that were received in this period have been closed according to the model. A summary of the numbers of leads actioned by the enforcement actions and outcomes is as follows:

Leads actioned Sep-Oct 2019 by outcome					
		Enforcement action			
		Obligations Notice	Compliance review	Proposal to Cancel	Other
Equivalent Risk from non-compliance	Low (neither safety nor efficacy deficiencies)	7	-	-	-
	Medium (efficacy-related deficiencies)	3	3 - Queued	-	-
	High (safety-related deficiencies)	-	2 - Sponsor cancellation 3 - Concluded 28 – In progress 8 - Queued	-	-

The Leads Manager and team have observed the following benefits during the trial period:

- More timely transition of leads regarding higher-risk to compliance review.
- Greater clarity and consistency for the section regarding lead prioritisation and handling.
- Less processing time for LCS staff to determine priority and suitable actions
- Improved transparency and incentive for sponsors to resolve alleged non-compliance due to the use Obligations Notices and formal requests for information under Section 31 of the Act.

Key identified risks

Identified risk	Control measure
Incorrect, inappropriate or inconsistent categorisation or prioritisation of leads	All leads follow 3 control points: • **Lead receipt:** All leads are received and read by two members of the leads team. This happens before official logging into the system. Leads that may pose an imminent risk to consumers' safety are generally picked up and prioritised at this stage. • **Lead triage:** A triage process occurs while the lead is logged into the system. This process is usually undertaken by a Scientific Officer who makes a quick assessment of

	the non-compliance risk of the alleged breaches with the information available at the time. If the breach is determined to be safety-related, the officer arranges for immediate investigation. All other leads with alleged minor or efficiency-related breaches are discussed at the next leads team meeting before the investigation is initiated. • **Lead investigation**: Scientific Officers and Evaluators who undertake lead investigations prepare a written file summarising their findings and recommending an enforcement action. This document is cleared and approved by the Leads Manager before the actual enforcement action is initiated. In addition, the LCS has key mechanisms in place to aid consistency in decision making that equally apply to leads handling, including: 1. Extensive internal guidance within our Quality Management System (QMS) 2. Regular peer review meetings 3. A database to record the outcomes and rationale for decisions 4. Data analytics applications in Qlik Sense to interrogate past leads
Sponsors do not address non-compliance in response to Educational or Obligation Notices because they may not feel compelled to do so	The LCS is currently developing a compliance assurance program, within which a proportion of sponsors that have received Education or Obligations Notices each quarter, whether associated with a lead or a compliance review, will be randomly selected for follow-up. Sponsors will also be informed with receiving an Education or Obligations Notice that further action may be taken if further signals are received about potential non-compliance of their product.

RESOURCE IMPLICATIONS

Can the proposal be implemented within existing resources?	YES
Are changes required to existing work practices or workflow?	YES
Are new/changed fees and charges required?	NO

LEGISLATIVE IMPLICATIONS

Is the proposed change consistent with existing legislation?	YES
If 'no', is policy approval required?	N/A
Are there any time constraints that need to be taken into account?	NO

IT IMPLICATIONS

Does this proposal require changes to TGA's Online business systems?	NO
If 'yes', has a statement of the business requirements been considered by TGA's IT Section?	N/A
Was the work foreshadowed in the current/future year's IT work?	N/A
If 'no', are funds and IT Section resources available?	N/A

COMMUNICATIONS IMPLICATIONS

Will this work require any of the following activities?

• Publishing information on the TGA website (www.tga.gov.au)?	NO
• A public event or conference participation?	NO
• Graphic design work?	NO
• Editorial or writing advice?	NO
If 'yes' to any of the above, has the Communications and Education Section been contacted and provided advice on standards and guidelines?	N/A
Have you developed a communications strategy?	N/A

PAPERS

Is there any reason why this Agenda Papers should not be placed on the TGA intranet?	NO

CONSULTATION

We have not consulted internally or externally because the model:

- relies upon greater/improved use of existing, rather than new, regulatory and human resources;
- represents an alignment with existing TGA models for comparable purposes, in particular the advertising complaints handling model;
- pertains to activities that mostly terminate with the LCS;
- represents an increase in service to other business areas of the TGA in terms of transparency and timeliness, but otherwise does not impact the core activities of other business areas within the TGA;
- represents a decrease in regulatory burden for most sponsors of listed medicines, that is those who are not serially non-compliant; and
- will be overlayed with specific joint operating procedures that the LCS intends to soon develop collaboratively with its key internal stakeholders as part of continued

implementation of its Quality Management System (QMS). Discussions about these have already commenced with the Advertising Complaints and Investigations Section (ACIS) and the Adverse Events and Medical Defects Section (AEMDS).

Does this issue relate to an external consultation activity?	NO
Will the consultation to appear on the consultation forecast?	NO

ATTACHMENTS

- Attachment 1 – DRAFT Priorisation and Handling Model for Listed Medicines Compliance Leads
- Attachment 2 – Application of the Priorisation and Handling Model for Listed Medicines Compliance Leads– Examples

CONTACT

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