Australian Government
Department of Health
Therapeutic Goods Administration

Recalls annual report 2019-20

Version 1.0, November 2020

TGA Health Safety Regulation

Contents

What we do

The Therapeutic Goods Administration (TGA) safeguards and enhances the health of the Australian community through effective and timely regulation of therapeutic goods. The Manufacturing Quality Branch (MQB) works to ensure manufacturers of medicines, as well as blood and blood components, human tissue and cellular therapy products, meet appropriate Good Manufacturing Practice (GMP) quality standards.

This involves both the physical inspection of manufacturing facilities in Australia and abroad as well as the desktop assessment of facilities facilities where suitable inspections have been carried out by comparable overseas regulators and where necessary, initiation of appropriate regulatory action to ensure compliance with the quality standards.

A critical component of this work is also the management of recall actions for therapeutic goods in Australia. This report focusses on that body of work while a separate report has been produced covering other aspects of the work of the MQB.

Recalls

The coordination and management of recall and non-recall actions of therapeutic goods in Australia involves liaison with the sponsor/supplier of the therapeutic good and the relevant regulatory area/s within the TGA. The outcomes of these interactions may also result in the treatment of the matter as a non-recall action or its referral to another stakeholder, internal or external to the TGA.

Recall is an action taken to resolve a problem with therapeutic goods already supplied to the market for which there are established deficiencies in quality, efficacy, safety, presentation or performance. A therapeutic goods recall might be initiated following notification by the sponsor, a request by the TGA or as a result of reports referred from a variety of sources.

All notifications are typically finalised within 7 clear working days, with the day of notification being day zero, and these are completed according to the priority of the issue at hand, based on the risk to public health and safety.

Ensuring the safety of therapeutic goods

The information in this report provides insights into therapeutic goods safety regulatory activity for our recalls program. This program makes a key contribution to Outcome 5: Regulation, Safety and Protection in the Health Portfolio Budget Statements 2019-20, and TGA business plan 2019-20 objectives, particularly in regard to the removal of products from the market which pose an unacceptable risk to consumers.

Key statistics

We coordinated 790 recall actions during the 2019-20 financial year, up from 768 in 2018-19.

Table 1: All recalls by product type

Product type	2018-19	2019-20
Medicine recalls	41	60
Medical device (including IVDs) recalls	596	614
Blood product recalls	102	100
Biological product recalls	29	16
Total	**768**	**790**

Overall, the total number of recall actions rose by almost 3 per cent in 2019-20. However, there was a significant increase (46 per cent) of recall actions performed for medicines. This was mainly due to a high number of recalls performed for ranitidine products in September - October 2019, regarding trace amounts of N-nitrosodimethylamine (NDMA) impurities in the tablets.

In contrast, recall actions for biological products decreased this financial year, from 29 to 16. Of these, 15 were Implant Hazard Alerts, 13 of which were for femoral head allografts. The remaining action was for a Class III (non-safety related) Product Defect Correction for a freeze-dried musculoskeletal allograft.

The following tables provide further detail on the recall actions for each of the product types in 2019-20.

Table 2: Medicine recalls by reason for recall

Reason for recall	2018-19	2019-20
Adverse reactions	2 (5%)	1 (2%)
Foreign matter	5 (12%)	0
Illegal supply	2 (5%)	2 (3%)
Impurity and degradation	4 (10%)	13 (22%)
Labelling and packaging	14 (34%)	18 (30%)
Micro-organisms	2 (5%)	4 (7%)
pH	0	0
Potency	1 (2%)	4 (7%)

Reason for recall	2018-19	2019-20
Sterility	0	7 (12%)
Other[a]	11 (27%)	11 (18%)
Total	**41 (100%)**	**60 (100%)**

[a] 'Other' includes dissolution, physical defects, observed differences, variable content, diagnostic inaccuracy and wrong product, disintegration/dissolution, GMP non-compliance, transport/storage, bioavailability, preservative efficacy and therapeutic inefficiency.

Table 3: Medical device (including IVDs) recalls by reason for recall

Reason for recall	2018-19	2019-20
Adverse incidents	5 (0.8%)	6 (1%)
Diagnostic inaccuracy	66 (11%)	70 (11%)
Electrical defect	23 (4%)	28 (5%)
Illegal supply	1 (0.2%)	2 (<1%)
Labelling and packaging	131 (22%)	136 (22%)
Mechanical and physical defects	203 (34%)	182 (30%)
Software defects	130 (22%)	151 (25%)
Sterility	3 (0.5%)	3 (<1%)
Other[a]	34 (6%)	36 (6%)
Total	596 (100%)	614 (100%)

[a.] 'Other' includes bioavailability, disintegration/dissolution, microbial contamination, variable content, foreign matter, impurity, wrong product, therapeutic inefficiency, observed differences, GMP non-compliance, transport/storage, and potency.

Table 4: All recalls by hazard classification

Hazard classification	2018-19	2019-20
Class I	91 (11.8%)	96 (12.2%)
Class II	579 (75.4%)	606 (76.7%)
Class III	98 (12.8%)	88 (11.1%)
Total	**768 (100%)**	**790 (100%)**

Class I recalls are the most serious safety-related, a situation in which there is a reasonable probability that the use of, or exposure to, the deficient therapeutic good(s) will cause serious adverse health consequences or death.

Class II recalls are urgent safety-related, a situation in which use of, or exposure to, the deficient therapeutic good(s) may cause temporary or medically reversible adverse health consequences, or where the probability of serious adverse health consequences is remote.

Class III recalls are the lowest risk actions, a situation in which use of, or exposure to, the deficient therapeutic good(s) is not likely to cause adverse health consequences.

For more information on Recall hazard classification please see the Uniform Recall Procedure for Therapeutic Goods (URPTG).

Overall, the majority (over 75 per cent) of recalls performed in 2019-20 were classified as "Class II", which are urgent, safety related actions. The remaining actions were split fairly evenly between Class I (most serious) and Class III (lowest risk). The spread of recalls by hazard classification remained consistent in 2019-20 compared with 2018-19.

Table 5: All recalls by action level

Action level	2018-19	2019-20
Wholesale	5 (0.7%)	4 (0.5%)
Hospital	686 (89.3%)	711 (90.0%)
Retail	50 (6.5%)	43 (5.4%)
Consumer	27 (3.5%)	32 (4.1%)
Total	**768 (100%)**	**790 (100%)**

The action level (or depth) of a recall describes who will be notified of the recall action.

The TGA will endeavour to recall therapeutic goods to the depth of supply and as such, only affected parties need to be notified of an action as detailed in the customer or distribution list.

For more information on Recall action level please see the Uniform Recall Procedure for Therapeutic Goods (URPTG).

Overall, the vast majority (90 per cent) of recalls performed in 2019-20 were Hospital level actions, which includes public and private hospitals, nursing homes, and other healthcare institutions.

Recall levels are performed in a cascading order, for example, for Retail level actions, customer letters are also sent by the sponsor to affected wholesalers and hospitals by default. Consumer level actions, which are frequently wide reaching and/or high profile, accounted for 4.1 per cent of the recalls we processed in 2019-20. The spread of recalls by action level in 2019-20 remained fairly consistent compared with 2018-19.

Table 5: All recalls by action category

Action category	2018-19	2019-20
Recall	307 (40.0%)	323 (40.8%)
Product Defect Correction	406 (52.9%)	419 (53.0%)
Hazard Alert	46 (6.0%)	42 (5.3%)
Product Defect Alert	9 (1.2%)	6 (0.8%)
Total	**768 (100%)**	**790 (100%)**

There are four main types of recall action category. For more information on Recall action level please see the Uniform Recall Procedure for Therapeutic Goods (URPTG).

Product Defect Corrections are the most common type of recall action, accounting for 53% of all recall actions in 2019-20. This type of action is often utilised for medical devices (which account for around 80 per cent of all actions) where the product can continue to be used if there is a robust risk mitigation procedure put in place until a permanent correction can be performed.

A straight recall (accounting for 41 per cent of all recall actions in 2019-20) is conducted to remove therapeutic goods permanently from the market or from use, and is performed for all types of products. Hazard Alerts and Product Defect Alerts make up the small remainder of actions (around 6 per cent in 2019-20).

The above data does not include the assessment of non-recall actions, 'no action' assessments, assessment of overseas recall notifications or recall close-out activity.

Impact of COVID-19 on product recalls

During the initial months of the COVID-19 pandemic in early 2020, the number of sponsor recall notifications remained consistent with the number received during other periods. Some recall actions involved products[1] used for the treatment of COVID-19 patients and /or the protection of health care professionals and other members of the community. In these cases, as with all recall actions, risk-benefit considerations were taken into account to balance the risk posed by the product defect relative to the risk of the product not being available for treatment or use at all and/or a shortage situation being created.

[1] Products included intensive care ventilators, infrared thermometers and various types of personal protective equipment.

Uniform Recall Procedure for Therapeutic Goods

The Uniform Recall Procedure for Therapeutic Goods (URPTG) assists sponsors to conduct recall and non-recall actions using a standardized process. It enables sponsors to respond efficiently and effectively to issues with a therapeutic good that has, or may pose a risk to public health and safety.

As part of our commitment to review and improve our guidance material, as referred to in the TGA Business Plan 2019-20, the TGA in December 2019 published the latest version (V2.2) of the URPTG on its website. The main updates in this version included:

1. additional clarity on the provision of surgeon contact details for implanted therapeutic goods
2. amendments related to the online notification of recall and non-recall actions (including the use of GS1 Australia's Recall Health portal)
3. removal of the placeholder referring to the "National Patient Contact Principles for Patients with Implanted Medical Devices subject to Hazard Alerts"
4. a second example template for the sponsor's customer letter.

There are four distinct **recall actions** available to sponsors - recall, product defect correction, hazard alert and product defect alert.

Recall - a recall is conducted to remove therapeutic goods permanently from the market or from use when there are deficiencies or potential deficiencies in safety, quality, efficacy, performance or presentation.

Product defect correction - undertaken to correct a specific or potential deficiency and includes repair, modification, adjustment or re-labelling of a therapeutic good.

Hazard alert - a hazard alert is issued for an implanted therapeutic good with a deficiency or potential deficiency relating to its safety, quality, performance or efficacy because implanted goods (medical devices or biologicals or medicines) cannot be recalled.

Product defect alert - allows for the informed, continued use of defective but critical therapeutic goods, raises awareness of the issue and describes the precautionary actions that clinicians or patients may take to mitigate any associated risk.

The URPTG also defines and provides guidance on four types of **non-recall actions**:

Safety alert – provides information on the safe use of therapeutic goods in certain situations where, although meeting all specifications and therapeutic indications, its use could present an unreasonable risk of harm if certain specified precautions are not followed. A safety alert is generally used for reiterating specific precautions or instructions regarding use of the goods.

Product notification – provides information about a therapeutic good in a situation that is unlikely to involve significant adverse health consequences.

Quarantine action – suspends further supply and distribution of the goods pending investigation of an issue or incident. The outcome of the investigation will determine further actions. Consideration should be given to initiating a quarantine of goods if a defect is identified in released goods which has the potential to raise issues related to safety, efficacy (medicines / biologicals) or performance (medical devices).

Product withdrawal – used to withdraw products for reasons that are not related to safety, quality, efficacy, performance or presentation e.g. removing a previous model from the market when a new model has been released

System for Australian Recall Actions (SARA)

Since July 2012, summaries of Australian recall actions are available from the TGA website via the publicly accessible and searchable System for Australian Recall Actions (SARA) database.

A new enhancement was added to the SARA database in June 2020 which allows users to extract individual search data into editable, MS Excel spreadsheets, and includes all of the existing available data in this easy to use format. The project was undertaken in response to requests from industry and other external stakeholders to provide better access to TGA recall data. This provides enhanced access and transparency through users acquiring a 'self-serve' style, ready access to large volumes of recall action data.

Online recall notification form

On 31 October 2019, the TGA launched a new, online form for sponsors to use when notifying new recall and non-recall actions. The online form is accessible via the TGA Business Service portal.

Further advice on submitting recall information is included at Step 7 in Version 2.2 of the Uniform Recall Procedure for Therapeutic Goods (URPTG). This version was published on 12 December 2019 and includes advice that the online form is now the **preferred** method of submitting new notifications. Whilst sponsor uptake of the form was initially a little slow, usage rates have increased through to 30 June 2020. Recalls staff look forward to continuing to receive sponsor notifications via the online form (rather than via the outdated method of sending emails which leads to double handling of sponsor information).

Confirmation of sponsor contact details

Sponsors are requested to verify that their relevant staff contact details listed in the TGA's TBS Portal are accurate and up to date, as per the guidance published on the TGA website. TBS enquiries may be directed to - ebs@health.gov.au or 1800 010 624 (freecall within Australia).

Stakeholder engagement

During 2019-20, recalls staff continued to engage and consult with a wide range of stakeholders on issues relating to the recall of therapeutic goods. This has included the hosting of, and attendance at various stakeholder meetings, stakeholder consultation on proposed amendments to the URPTG, regular engagement with health professionals and consumers (including peak representative bodies) and participation in stakeholder educational activities, a key commitment in the TGA Business Plan 2019-20 to the education of industry. Specific examples include:

- attendance and presentations at meetings of the TGA Industry Working Group of GMP (TIWGG) and RegTech which comprise representatives of the peak therapeutic goods industry associations
- attendance at the 'TGA Café' which was part of 2019 GMP Forum and provided the opportunity for attending delegates to speak with TGA staff on any issues of importance to them
- maintaining lines of communication on recall policy issues and processes between the Commonwealth (TGA and the Australian Commission on Safety and Quality in Healthcare) and key jurisdictional stakeholders (state and territory health departments, including their nominated recall coordinators)
- meetings with GS1 Australia (and peak industry associations) to continue discussions on how best to address current sponsor confusion relating to 'who' and 'where' recall actions should be notified to; and how to address industry concerns about duplication of effort when notifying recall actions to the TGA when they are also required to notify recalls via GS1 Australia's Recall Health system (due to a state based requirement)
- working collaboratively and effectively with key internal colleagues, including those in the TGA's post-market, clinical and laboratory testing business areas.

Some notable recall actions in 2019-20

The action level (or depth) of a recall describes who will be notified of the recall action. 'Consumer level' recall actions are the highest level with notifications made to patients and other consumers as well all other levels of the supply chain, including 'retail', 'hospital' and 'wholesale'.

The recall levels in cascading order are:

Wholesale - includes wholesalers and state/territory purchasing authorities.

Hospital - includes public and private hospitals, nursing homes and other healthcare institutions, hospital pharmacists, ambulance services, blood and tissue banks and pathology laboratories as well as wholesale as appropriate.

Retail - includes retail pharmacists, medical, dental and other health care professionals, supermarkets, health food stores and online stores as well as wholesale and hospital as appropriate.

Consumer - includes patients and consumers, as well as wholesale, hospital and retail levels as appropriate.

For example, in a Retail level recall action, letters are also to be sent by the sponsor to affected wholesalers and hospitals by default.

The TGA will endeavour to recall therapeutic goods to the depth of supply and as such, only affected parties need to be notified of an action as detailed in the customer or distribution list.

The level of recall is determined by having regard to the following factors:

- channels by which the product has been distributed
- extent of the distribution
- potential risks to a user because of the issue
- likelihood of the issue with the goods occurring
- ability of the consumer, health professional or caregiver to identify the issue
- whether the good is outside the manufacturer's specifications
- availability of a replacement or alternative good, or the risk associated with not providing treatment if a replacement or alternative good is not available
- whether a recall (if a medicine) will cause a medicine shortage.

Throughout 2019-20, some of the more notable recall actions included the following:

- **Jin Gui Shen Qi Wan (oral pills) – 5 September 2019**

  Class I, Consumer Level Recall

  TGA Laboratory testing found toxic aconitum alkaloids being present at a level placing the product into Schedule 4 ("prescription-only medicine") of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), including for use in adults. Aconitum alkaloids are toxic to humans. Poisoning with these compounds may affect the heart, the nervous system and the gastrointestinal system. Children are particularly at risk, as toxicity can occur at normal doses of Jin Gui Shen Qi Wan pills. An accidental overdose could be fatal in a small child.

  The labelling of AUST L 217716 does not restrict the medicine's use to adults, which is a requirement for exemption from Schedule 4 of the SUSMP. Instead, the labelling states 'Not to be used in children under two years of age without medical advice', which promotes unrestricted use in children aged two years and above. These pills were subsequently cancelled from the Australian Register of Therapeutic Goods (date of effect – 16 January 2020) as it was determined the goods were not eligible for listing.

- **Ranitidine (multiple products and sponsors) – September 2019, October 2019 and April 2020**

  Multiple Class II, Retail Level Recalls

  Several ranitidine-containing products were removed from the Australian market due to contamination with an impurity called N-nitrosodimethylamine (NDMA).

  NDMA is a type of N-nitroso compound. N-nitroso compounds are commonly found in low levels in a variety of foods, particularly smoked and cured meats, as well as in some drinking water and in air pollution. Long-term exposure, over years, can increase an individual's risk of developing cancer.

  The additional risk posed by NDMA from ranitidine, at the levels identified to date, is considered to be very low. However, such contamination is considered unacceptable for a medicine. The actual health risks depend on dose and will vary from person to person. The risks from short-term use of ranitidine are expected to be extremely low.

  Ranitidine tablets and oral liquids are now in short supply as a number of commonly-used brands have been recalled from pharmacies, hospitals, wholesalers, and other retail outlets, such as supermarkets and online stores.

- **Arthrem capsules – 19 September 2019**

  Class II, Retail Level Recall

  Arthrem Capsules have been identified as a possible cause of abnormal hepatic function and the product was therefore removed from sale.

  The health risk associated with this issue was highlighted following a review of adverse reactions experienced by users in New Zealand. The adverse reactions range from reports of increased liver enzymes to jaundice and hepatitis.

  At the time of recall, there had been no adverse events reported in Australia.

- **Breast implants and breast tissue expanders (multiple products and sponsors) – September 2019, November 2019 and May 2020**

  Multiply Class I, Hospital Level Hazard Alerts and/or Recalls

  Recalls of unimplanted stock and/or Hazard Alerts for macro- and micro-textured implants and smooth implants were issued following the recent TGA evaluation suggesting there is an increased risk of Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL).

  The Hazard Alerts, as well as TGA web publications, advised implanted patients if they have breast implants and notice swelling or a lump in their breast or armpit, or have any other concerns with the implants, they should seek medical attention.

  Implanting surgeons were advised by the sponsors to be alert to this issue and also requested to review the relevant literature in the context of their particular patients on a case-by-case basis.

- **Accu-Chek Guide and Accu-Chek Performa blood glucose meters - Product defect correction – 14 November 2019**

  Class II, Consumer Level Product Defect Correction

  Roche Diabetes Care identified that the Accu-Chek Guide and Performa blood glucose meters may show the following power-related issues: Display E-9 Errors (indicating batteries need to be replaced), unexpectedly show the low battery icon, have unexpected short battery life, and not power on.

  These failures could cause a delay in therapy decisions and may potentially lead to a serious medical condition. Roche advised customers to follow the instructions provided in the customer letter and the following warnings: Always have a spare set of high quality batteries, battery life may vary due to factors such as temperature, and have a back-up testing method available.

- **Brauer Teething Gel – Recall – 29 November 2019**

  Class I, Consumer Level Recall

  Consumers and health professionals were advised that Brauer Natural Medicine recalled one batch of Brauer Teething Gel 20 g due to bacterial contamination.

  Brauer Teething Gel is used to reduce the discomfort caused by teething in babies.

  Testing found that some samples from this batch were contaminated with *Burkholderia spp*, a bacteria commonly found in soil, water and the general environment. They are capable of causing infections in healthy hosts, but in particular affect those with compromised immune systems. These bacteria can be also spread through person-to-person contact.

- **Palexia SR 100 mg tapentadol sustained release tablets – 14 February 2020**

  Class II, Consumer Level Product Defect Correction

  PALEXIA 100 mg SR tablets are packaged in four blister foils contained in a product carton. Printed on the blister foil is the name and strength of the product along with batch number and expiry date details. There is a possibility that some blisters of PALEXIA 100 mg SR tablets may have these details missing or the print appears faded or partially absent. This anomaly will not be evident until the product carton is opened and the blister foil inspected.

  Seqirus confirmed there was no defect with the quality, safety or efficacy of the tablets themselves.

This Product Defect Correction was initiated as a precautionary measure as the absence of product information on the blister foil compromises the identity of the product and theoretically presents the risk of a product mix-up and overdose in novel circumstances where a patient may be using more than one strength of this product at the same time.

- **Blackmores Professional Duo Celloids S.C.F. tablets – 13 May 2020**

  Class II, Consumer Level Recall

  A number of batches of Blackmores Professional Duo Celloids S.C.F. Tablets were identified via consumer complaints as having microbial mould growth appearing on tableted product. This appears to have occurred after some time in storage and was visible to the naked eye as black or brown patchy spots.

  At the time of recall, no adverse events had been reported in relation to this issue.

Recalls related web statements for each of these actions were published on the 'Alerts' pages of the TGA website and summary recall information is available from the System of Australian Recall Actions (SARA) database.

Further information

For any further enquiries about Australian recall actions or the URPTG, readers should contact the TGA's Recalls Section by telephone - 02 6232 8935 or via email - recalls@health.gov.au.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Manufacturing Quality Branch	November 2020

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