Australian Government

Department of Health

Therapeutic Goods Administration

Therapeutic Goods Administration

Half Yearly Performance Snapshot

1 July to 31 December 2018

Contents

About the Therapeutic Goods Administration

The Therapeutic Goods Administration (TGA) is part of the Department of Health and is responsible for assessing whether therapeutic goods available for supply in Australia are safe and fit for their intended purpose. Approved therapeutic goods can be lawfully manufactured and supplied in Australia and include prescription medicines, over-the-counter medicines, complementary medicines, biologicals, and medical devices.

Products for which therapeutic claims are made are entered on the Australian Register of Therapeutic Goods.

Some examples of goods that the TGA regulates the supply of include:

- medicines prescribed by a doctor or dentist
- medicines available from supermarkets, the general pharmacy or from behind the pharmacy counter
- vaccines
- complementary medicines, including vitamins, herbal and traditional medicines
- medical devices, from simple devices like bandages to complex technologies like heart pacemakers
- tampons and disinfectants
- products used to test for various diseases or conditions (in vitro diagnostic devices [IVDs]), such as blood tests
- blood, blood components and biologicals (cells and tissues).
- We also play a regulatory role in overseeing the manufacturing process and advertising of therapeutic goods.

More information about how therapeutic goods are regulated can be found on the TGA website at www.tga.gov.au.

Introduction

The TGA prepares an annual TGA Business Plan, which identifies the priority activities being undertaken over the financial year and is available on the TGA website. This Half Yearly Performance Snapshot provides statistical information for 1 July to 31 December 2018 in relation to our regulation of therapeutic goods, tracking our progress against the priorities we have identified for the year. This data will be incorporated into our Annual Performance Statistics Report for the 2018-19 financial year, to be published on the TGA website in the second half of 2019.

As part of our annual Business Plan we continue to implement the Australian Government response to the Review of Medicines and Medical Devices Regulation (MMDR) involving a significant program of work. Throughout 2018-19 we will continue to roll out reforms in a staged approach with the majority of activities set to conclude by the end of the financial year. Some longer term reforms are scheduled to commence later to allow time for transition processes to be put in place.

Performance highlights

The TGA has maintained a high level of activity while also implementing regulatory reforms over the reporting period, 1 July to 31 December 2018. Highlights are as follows:

Regulatory Reforms

Australia-Canada-Singapore-Switzerland (ACSS) New Chemical Entity (NCE) Work-sharing pilot

Building on the successful Generic Medicines Work-Sharing Trial ACSS established a NCE work-sharing pilot that allowed for shared evaluation of a NCE application with the aim of enhancing efficiencies for the regulators, reducing the regulatory burden on sponsors and the opportunity to contribute to advancing regulatory innovation. In July 2018, the first medicine under the pilot was registered on the Australian Register of Therapeutic Goods (ARTG) after undergoing joint assessment by the TGA and Health Canada. The medicine also utilised TGA's new priority review pathway. The approval time taken for the evaluation was well within the priority review target timeframe.

Reporting of medicine shortages

While the reporting of medicine shortages was voluntary during this reporting period, work was undertaken in preparation for the 1 January 2019 implementation of mandatory reporting requirements. This included making the necessary changes to the *Therapeutic Goods Act 1989* (the Act). From 1 January 2019, sponsors of prescription medicines and some over-the-counter medicines will be required to report all shortages or discontinuations of their products to the TGA. IT system improvements to facilitate this reporting were undertaken late in 2018 in close consultation with industry stakeholders. Information and resources were published on the TGA website in November and December 2018.

Comparable Rating Scheme for listed medicines

In November 2018 we implemented a Compliance Rating Scheme for listed medicines as part of ongoing enhancements to our post-market compliance monitoring program. The scheme standardises how we rate listed medicines that have been reviewed in terms of any non-compliance

with regulatory requirements and the associated risks to consumers. The scheme provides predictability for sponsors about our approach to compliance, and will underpin increased transparency for consumers about the safety and efficacy of self-selected medicines on the market. Following a transition period of six months, we will begin to release the ratings assigned to individual medicines under the Scheme as part of publishing the overall outcomes of each review on the TGA website.

Medicines

Prescription medicines

We recently implemented five new processes and the revised orphan drug designation criteria for the registration of a prescription medicine. During this reporting period we finalised applications using the new orphan criteria and four of the new processes, including:

- nine orphan drug designations;
- four priority determinations and seven priority approvals for registration, with a median approval time of 122 working days
- four provisional determinations, and
- one approval for registration after undergoing Comparable Overseas Regulator (COR)-A review within the legislative timeframe of 120 working days; and

In addition, over the same period a large number of standard registration applications were processed through the standard pathways. Over the reporting period, 177 standard Category 1 (including 20 NCE and 41 new generic medicines) and 697 Category 3 applications were approved. This is consistent with the equivalent period in 2017 (166 Category 1 and 695 Category 3 applications). Mean and median approval times were below the statutory timeframes.

Consistent with the intent of the MMDR, we also initiated a program of work investigating possible reforms to the registration process for generic medicines.

Over-the-counter medicines

We approved 139 new over-the-counter medicine applications (N1 to N5) during this period, which was an increase on the previous 6 months (87) and on the corresponding period in 2017 (126).

The number of approved applications to change existing medicines (C2 to C4; 225) was consistent with the previous 6 months (219) and an increase on the corresponding period in 2017 (170).

One of three approved C3 applications took longer than the target time. For all other application types, more than 80% of applications were completed within target timeframes.

Listed medicines

The number of new listed medicines has remained similar to previous years with 943 new listed medicines in this period compared to 916 new listed medicines in the same period in 2017.

The number of new ingredients permitted for use in listed medicines dropped from 42 to five in this period. The high figure in the corresponding period in 2017 was primarily due to an unusually large number of sunscreen excipients permitted for use that year.

There was a significant decrease in the number of post market compliance reviews completed in the July to December 2018 period. This was due to undertaking a number of time intensive, extensive and complex targeted reviews, notably completing the review of 94 listed sunscreens and

commencing the review of products making indications that directly or indirectly refer to macular degeneration.

Medical devices

All conformity assessment applications were processed within target timeframes despite the increased numbers of applications, and resources, being focussed on to the medical device reform projects.

We also continued to process a large number of ARTG inclusion applications for medical devices, including in vitro diagnostic medical devices (IVDs). The number of inclusion applications chosen for audit remained steady when compared with the same reporting period in 2017.

The number of medical device incident reports completed was comparable to the same reporting period last year. While the average TGA processing time (33 days) was higher than last year, it was still significantly lower than the target timeframe (90 days).

The implementation of the Medical Device Single Audit Program (MDSAP) has enabled a reduction in the overall number of overseas on-site audits required for the verification of Quality Management System Compliance. Verification for these sites is achieved through an assessment of an MDSAP Audit Report. This has enabled the TGA to reduce both a cost and time burden on Australian sponsors and overseas manufacturers in cases where MDSAP reports contain sufficient evidence for regulatory decision making. In addition, there has been a significant improvement in the compliance rating of both domestic and overseas manufacturers when compared with the same reporting period in 2017.

Biologicals and Blood components

Two Class 4 biologicals were included on the ARTG. These were the first Class 4 biologicals and the first gene therapy products to be approved.

Exports

The procedure of Free Sale and Export Certificates for medical devices was updated, resulting in a streamlined application procedure, guidance material and updated certificate appearance that has received positive feedback from stakeholders.

Access to unapproved therapeutic goods

There were 35,829 completed applications/notifications for medicines through the Special Access Scheme (SAS), 3,870 for medical devices and 1089 for biologicals. There were significant increases in the number of notifications for medicines and medical devices through the Category C notification pathway as compared to the same period last year (9315 in 2018 compared to 4,732 in the equivalent period of 2017), and 452 notifications for medical devices in this period in 2018 compared to one in this period in 2017. These increases reflect increased use of this pathway since its introduction on 3 July 2017.

During this time, there were a total of 686 approvals for Authorised Prescribers (418 for medicines, and 268 for medical devices).

Clinical trials

During this period, there were 494 notifications for new clinical trials, which is comparable to the same reporting period in 2017 of 481.

Licensing and manufacturing

Initial inspections are performed when a manufacturer has applied for a new Good Manufacturing Practice (GMP) licensed site in Australia or when sponsors have requested a GMP certificate for a new overseas manufacturing site. Initial inspections continue to be performed within the target dates for Australian manufacturers (88% within three months of the application) and there was an increase in the number of initial inspections for overseas manufacturers performed within the target dates (78% within six months of the application compared to 53% for the equivalent period in 2017).

Re-inspections are undertaken when licenses and certificates are to be extended, with a risk-based approach used to determine how frequently these inspections need to occur. There was an increase (from 68% in 2017 to 78% for the equivalent period in 2018) of inspections performed for Australian manufacturers within the six month timeframe.

The overall compliance of Australian and overseas manufacturers was similar compared to the same period in 2017, however there was a small increase in the number of Australian manufacturers with marginal compliance (19% in 2018 compared to 10% for the equivalent period in 2017). Notably, no inspections completed in this period found that the manufacturers had unacceptable compliance.

Medicine and vaccine adverse event reports

A new Adverse Event Management System was introduced in June 2018. Due to differences in the way adverse event report data is recorded in the new system, the data included in this report is not directly comparable to previous reports.

During this period, we received a total of 10,619 medicine and vaccine adverse reaction reports (1,830 reports related to vaccines). Of these, 9978 were accepted and 641 rejected or withdrawn. Of the accepted cases, 62% (6171) were submitted by pharmaceutical companies and 19% (1897) were made by health professionals. The most prolific reporters among health professionals were pharmacists (including hospital pharmacists) with 884 reports submitted. The mean number of reports received by the TGA weekly was 408.

Regulatory compliance

In collaboration with the Australian Border Force (ABF), over 1 million units of unapproved and counterfeit therapeutic goods were destroyed in 2018 calendar year.

We continued ongoing communications with the ABF to streamline processes. Operation Pangea XI was held from 9-16 October 2018 to target and identify trends in the types of counterfeit and illicit medicines being imported and exported. This resulted in seizures and destructions of unapproved and counterfeit therapeutic goods, warning letters and safety alerts being issued.

We continue to build capability through strategic relationships, training in new competencies, and the ongoing development of our intelligence function. A strategic threat assessment was completed that identified the areas of highest threat of therapeutic goods non-compliance. There was a strong focus on two compliance targets: Operation Antlia for offences in the industry for cosmetic procedures, and Operation Centaurus for offences related to performance enhancing drugs. These two operations resulted in search warrants, seizure of goods, destruction of goods, infringement notices issued, and briefs of evidence being prepared for the Commonwealth Director of Public Prosecutions.

Advertising complaints

On 1 July 2018, the TGA became the sole body for handling complaints about the advertising of therapeutic goods to the Australian public. To support this scheme, we implemented a case management system and compliance framework with key performance indicators (KPIs) to ensure performance can be measured. For this period we received a large number of complaints about non-compliant advertising, which generated 1,039 cases. This represents a significant increase in the volume of advertising complaints compared with the previous scheme.

Further information about the first six months of the new advertising complaints framework is available at: https://www.tga.gov.au/first-six-months-embedding-tga-advertising-reforms.

Recalls

Activity regarding biological recalls has shown a significant increase from previous reporting periods (17 in 2018 compared to zero for the equivalent period in 2017) as a result of the implementation of an updated Uniform Recall Procedure for Therapeutic Goods, to provide further clarification regarding the notification of Biological issues. The number of medicine and medical device recalls has remained relatively consistent across the two reporting comparable reporting periods (19 in 2018 compared with 21 in 2017 for medicines and 268 in 2018 compared with 284 in 2017 for medical devices).

Laboratory testing

The Pacific Medicines Testing Program is a joint program between the Department of Foreign Affairs and Trade and the TGA. Under the Program we test the quality of at least five medicines per participating Pacific Island Country per year (2017-2021). The focus of the Program is medicines for non-communicable diseases such as high blood pressure and diabetes, as well as antibiotics and medicines purchased in high volumes. The first two testing campaigns commenced in 2018, with the second testing campaign, a series of insulin products, falling within the reporting period for this snapshot (July to December 2018). To date, medicines have been tested on behalf of 10 Pacific Island Countries.

Pharmacovigilance Inspection Program

During this period, we inspected a total of five medicine sponsors (four innovator sponsors and one generic sponsor). Inspections were scheduled using a risk-based approach and included an internal assessment of the sponsor's pharmacovigilance system, product portfolio and regulatory compliance history. Deficiencies were identified in each inspection with a total of 25 major deficiencies and 17 minor deficiencies. No critical deficiencies were identified during this period.

Risk Management Plan evaluations

During this period, 44 evaluations of Risk Management Plans (RMPs) were completed.

Processing and approval times

Processing and approval times are defined as the number of working days from the acceptance of the application until the formal notification of decision, unless otherwise specified. These exclude times where we were unable to progress the application until the sponsor provided additional information or completed payment of fees, unless otherwise specified. Under the Act the TGA working days exclude public holidays and weekends.

The timeframes applicable to many of our activities are mandated by legislation. For non-mandated activities we self-impose target timeframes to ensure that we perform our functions efficiently and in a timely manner. Target timeframes are subject to ongoing review.

1. Prescription medicines

Applications to register new or vary existing prescription medicines are accompanied by supportive scientific data and evaluated with timeframes underpinned by legislation and/or associated business rules.

The framework for prescription medicines includes the following categories:

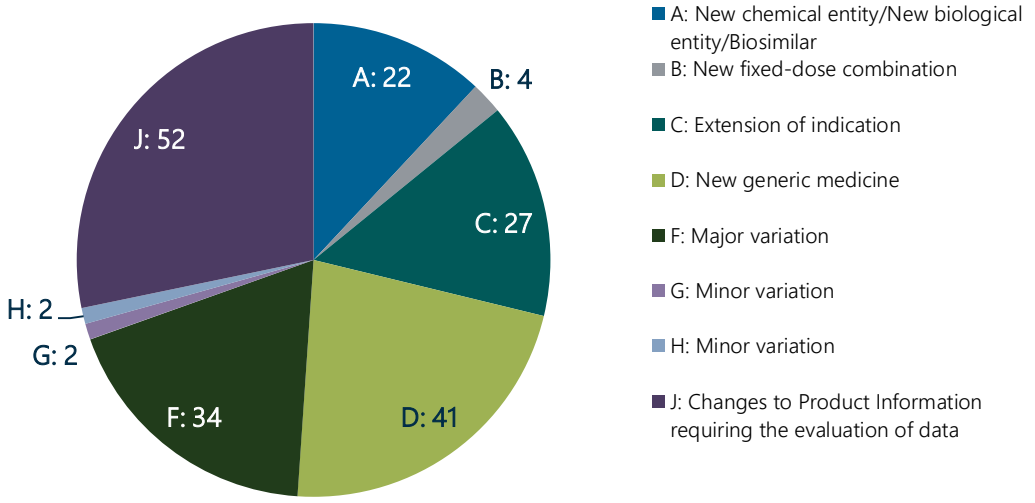
Application category	Description	Timeframe in working days
Category 1	An application to register a new prescription medicine (other than an additional trade name) or to make a variation to an existing medicine that involves the evaluation of clinical, pre-clinical or bio-equivalence data. For example, NCE, extensions of indication, and new routes of administration.	Legislated timeframe: 40 working days for notification of whether the application has passed preliminary assessment and 255 working days for the completion of the evaluation and notification of the decision.
Note: The timeframes quoted above are statutory timeframes. The new priority review pathway (applicable to Category 1 applications only) has the same statutory timeframe as other Category 1 applications, but the target timeframe is 150 working days.		
Comparable Overseas Regulator (COR) report-based process	An application accompanied by an un-redacted assessment report package from a comparable overseas regulator.	Legislated timeframe: 40 working days for notification of whether the application has passed preliminary assessment. The timeframe to notify the applicant of the decision depends on the COR pathway: COR-A[a]: 120 working days COR-B[a]: 175 working days

[a] Under COR-A, the TGA regulatory decision will be based on a critical review of the COR assessment reports and an evaluation of the Australian label, Product Information (PI) and where required, the Risk Management Plan (RMP). Under the COR-B approach, the TGA regulatory decision will still be mostly based on a critical review of the COR assessment reports. The amount and type of additional data requiring evaluation will determine whether the application is best processed under the COR-B approach or as a Category 1 application

Category 3	An application to register or to vary the registration of a prescription medicine where the application does not require the support of clinical, pre-clinical or bio-equivalence data. For example, broader changes to the product specifications, manufacturing and labelling or a change in trade name.	Legislated timeframe: 45 working days to notify the applicant of the decision.
Correction to, or completion of, a Register entry	An application to vary the registration of a prescription medicine to correct or complete information that was inadvertently recorded incorrectly or omitted from the Register entry. For example, errors to product information, or quality-related documentation.	No legislated timeframe: TGA processes as soon as possible.
Safety-related request	An application to vary the registration of a prescription medicine to either: reduce the patient population that can receive the medicine, or add a warning or precaution.	No legislated timeframe: TGA processes as soon as possible.
Notification request to vary an ARTG entry	An application to vary the registration of a prescription medicine, where the application has been determined to pose a very low risk under certain conditions. For example, the removal of a redundant manufacture site.	No legislated timeframe: automatic approval on submission of e-form and full payment of fee.
Self-assessable request	An application to register or to vary the registration of a prescription medicine where the application does not require the support of clinical, pre-clinical or bio-equivalence data and where no data is necessary or where the data can be self-assessed by the applicant. For example, certain changes to the pack size or approved product label.	Legislated timeframe: 45 working days for notification of acceptance or rejection of an application, completion of evaluation and notification of the decision.
Additional Trade Name	An application for an additional trade name for a registered prescription medicine.	Legislated timeframe: 45 working days.

Figure 1 Number of approved Category 1 submissions by type for July to December 2018

Prescription medicine submissions may include a number of applications submitted at the one time. The data presented below relates to the number of submissions as this best reflects the evaluation and decision-making processes.



A: Includes two submissions processed via the priority review pathways

C: Includes five submissions processed via the priority review pathway

1.1. Approval times

Table 1 Prescription medicine standard registration application approval time

			Approval time (TGA working days) Jul to Dec 2018		
Application Type	**Submissions approved**	**Legislated timeframe**	**Mean**	**Median**	**Range**
Category 1					
A: New chemical entity/New biological entity/Biosimilar[a]	20	255	206	204	147 - 241
B: New fixed-dose combination	4	255	217	216	191 - 246
C: Extension of indication[b]	22	255	189	184	130 - 253
D: New generic medicine	41	255	177	168	96 - 254
F: Major variation	34	255	188	193	67 - 253
G: Minor variation[c]	2	255	189	189	139 - 239
H: Minor variation[c]	2	255	81	81	59 - 102
J: Changes to Product Information requiring the evaluation of data	52	255	138	146	4 - 221
Comparable Overseas Regulator (COR)-A					
C - Extension of indications	1	120	40	40	40 - 40
Additional trade name (ATN)					
E: Additional trade name	24	45	38	41	13 - 46

[a] Application type A figures do not include two submissions processed via the priority review pathway.

[b] Application type C figures do not include five submissions processed via the priority review pathway.

[c] The type G minor variations differ from type H minor variations in that they result in a new ARTG entry.

Table 2 Prescription medicine median approval time comparisons

Application Type	Legislated timeframe	Median approval time (TGA working days)	
		Jul - Dec 17	Jul - Dec 18
Category 1			
A: New chemical entity/New biological entity/Biosimilar[a]	255	212	204
B: New fixed-dose combination	255	178	216
C: Extension of indication[a]	255	189	184
D: New generic medicine	255	185	168
F: Major variation	255	196	193
G: Minor variation	255	250	189
H: Minor variation	255	168	81
J: Changes to Product Information requiring the evaluation of data	255	129	146
Comparable Overseas Regulator (COR)-A			
C: Extension of indication[d]	120	N/A	40
Additional trade name (ATN)			
E: Additional trade name	45	27	41
Minor Variations			
Category 3			
G: Minor variation[b]	45	40	42
H: Minor variation[c]	45	33	38
Safety-related request [SRR]	N/A	28	35
Self-assessable request [SAR]	45	38	40
Minor editorial change [MEC]	45	22	32
Correction [9D(1)]	N/A	40	54

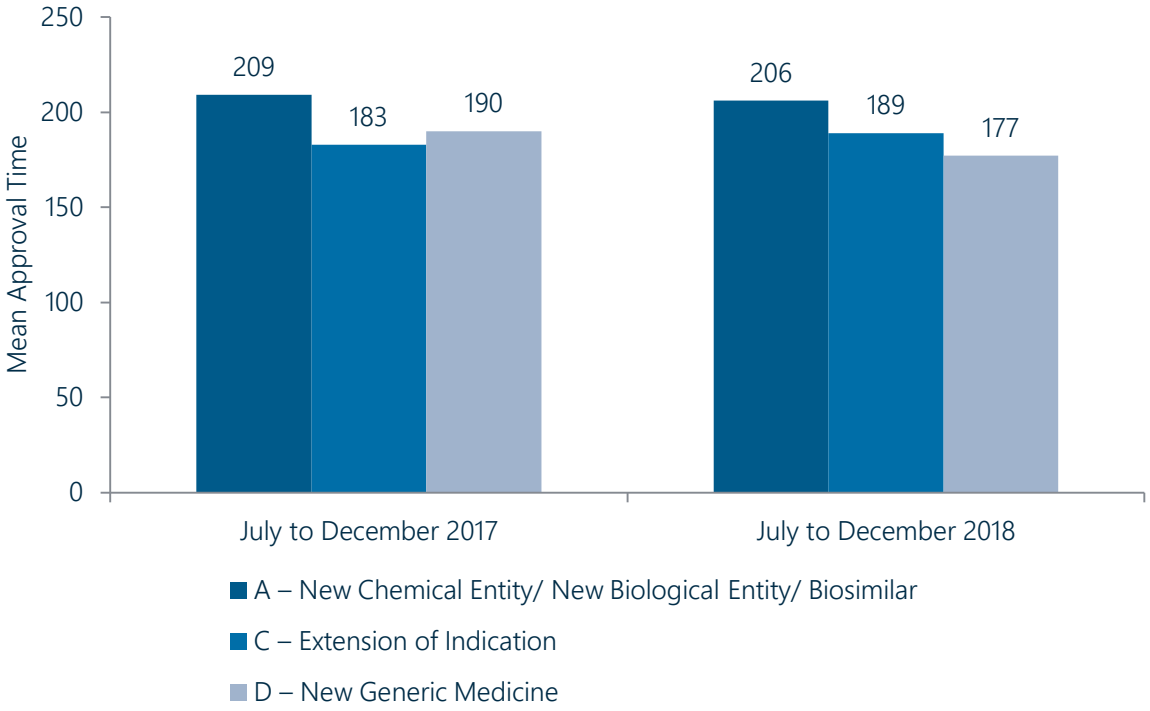
[a] Median working days does not include submission processed via the priority review pathway.

[b] The type G minor variations differ from type H minor variations in that they result in a new ARTG entry.

[c] The minor variations (type H) included in the table above refer to applications to change the formulation, composition or design specification or the container for the goods or any other attribute that results in the goods being separate and distinct. These applications are typically 'Category 3' changes, unless the supporting scientific package contains non-clinical or clinical data in which case the application is a 'Category 1' application.

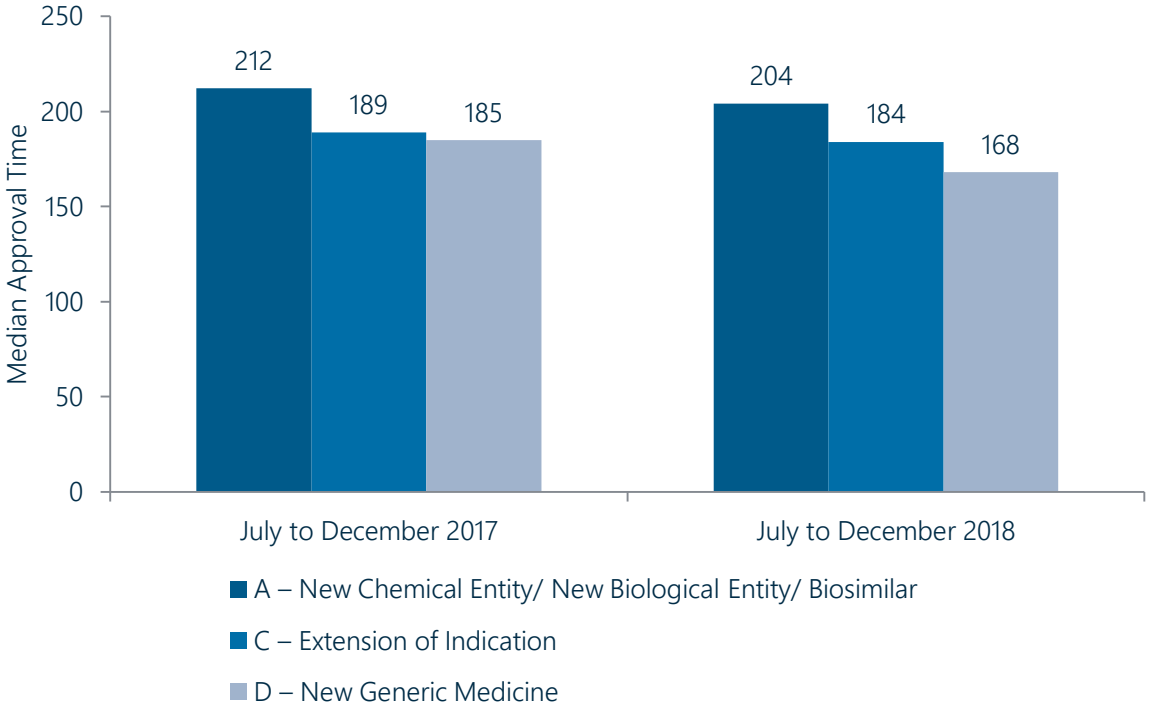
[D].COR extension of indications was implemented for the first time in 2018.

Figure 2 Prescription medicine standard registration[a] mean approval times



[a] Does not include submissions processed via the priority review or COR-A pathways.

Figure 3 Prescription medicine standard registration[a] median approval times



[a] Does not include submissions processed via the priority review or COR-A pathways.

1.2. Submission outcomes

Table 3 Number of completed prescription medicines submissions[a] by type and outcome for July to December 2018

Submission Type	Approved	Withdrawn	Rejected	Total
A: New chemical entity/New biological entity/ Biosimilar	22	1	0	23
B: New fixed-dose combination	4	0	1	5
C: Extension of indication [Category 1]	27	4	1	32
C: Extension of indication [COR]	1	0	0	1
D: New generic medicine	41	4	1	46
E: Additional Trade Name	24	0	0	24
F: Major variation	34	1	0	35
G: Minor variation [Category 1]	2	0	0	2
G: Minor variation [Category 3]	75	2	0	77
H: Minor variation [Category 1]	2	0	0	2
H: Minor variation [Category 3]	622	7	1	630
J: Changes to Product Information	52	0	0	52
Safety-related request [SRR]	474	8	0	482
Self-assessable request [SAR]	438	6	0	444
Minor editorial change [MEC]	64	3	0	67
Correction [9D(1)]	79	8	0	87
Notification	771	0	0	771
Total	2732	44	4	2780

[a] Includes submissions processed via the priority review and COR-A pathways.

1.3. Other applications

In accordance with the legislation, registered medicines must comply with numerous standards at the time they are registered and throughout their lifecycle. Following an appropriate application and review of the scientific data and safety considerations, approval to supply a product when it does not meet a particular standard may be granted.

Table 4 Number of other prescription medicine submissions for July to December 2018

Exemptions to comply with a standard (S.14)	Submissions
Approved	28
Rejected	1
Total	29

1.4. Orphan drug program

The objective of the orphan drug program is to provide an incentive to sponsors to provide medicines for a small population and make medicines available to patients who would not otherwise be able to access them. The incentive is in the form of a waiver of application and evaluation fees. Orphan drug designation step precedes lodgement of the registration application. A prescription medicine must have a valid orphan drug designation to be eligible for a waiver of application and evaluation fees.

Table 5 Orphan drug designations granted for July to December 2018

Application Type	Granted
A: New chemical entity/New biological entity/Fixed dose combination	4
C: Extension of Indications	5
Total	9

Table 6 Orphan drug registrations for July to December 2018

Application Type	Number Approved	Median approval time (TGA working days)
A: New chemical entity/New biological entity/Biosimilar	4	150
C: Extension of Indications	4	176
F: Major Variation	4	191
Total	12[a]	176

[a] One new biological entity was registered under the new orphan drug program and the priority review pathway.

1.5. Priority review pathway

Priority review involves faster assessment of vital and life-saving prescription medicines for which a complete data dossier is available. The target timeframe of 150 working days is up to three months shorter than the standard prescription medicines registration process. The priority review pathway operates with flexible business processes in order to facilitate faster assessment for registration, while maintaining our high standard for efficacy, safety and quality. The priority review determination step precedes lodgement of the registration application. A prescription medicine must have a valid priority review determination before it can be evaluated for registration under the priority review pathway.

Table 7 Priority determinations granted for July to December 2018

Application type	Granted
A: New chemical entity/New biological entity	2
C: Extension of indications	2
Total	4

Table 8 Medicines approved through the priority review pathway[a] for July to December 2018

Application Type	Number Approved	Median approval time (TGA working days)
A: New chemical entity/New biological entity/Biosimilar	2	105
C: Extension of Indications	5	122
Total	7	122

[a] The target timeframe for the priority review pathway is 150 working days.

1.6. Provisional approval pathway

This pathway allows sponsors to apply for time-limited provisional registration on the ARTG on the basis of preliminary clinical data, to allow access to certain promising new medicines where we assess that the benefit of early availability of the medicine outweighs the risk inherent in the fact that additional data are still required.

Provisional registration is limited to a maximum of six years and will automatically lapse at the end of a specified period unless sponsors are able to demonstrate that they have met the conditions imposed on the provisional registration. Sponsors may apply for full registration when sufficient clinical data to confirm the safety and efficacy of the medicine is available. The determination step precedes lodgement of the registration application. A prescription medicine must have a valid provisional determination before it can be evaluated for registration under the provisional pathway.

This pathway was introduced on 20 March 2018. Although a number of determinations have been granted, no applications for provisional registration have been approved as at 31 December 2018.

Table 9 Provisional determinations granted for July to December 2018

Application Type	Granted
A: New chemical entity/New biological entity/Fixed dose combination	2
C: Extension of Indications	2
Total	4

2. Over-the-counter medicines

Over-the-counter (OTC) medicine applications are categorised as new medicine (N) or change (C) applications and are further categorised by risk (N1 and C1 are lowest risk, N5 and C4 are highest risk).

Application category	Definition
N1	An application submitted as a 'Clone'.
N2	An application which complies with an OTC medicine monograph.
N3	New application for a 'generic' medicine other than those 'generic' applications in levels N1, N2 or N4.
N4	An application for a 'generic' medicine where the medicine: • requires supporting safety and/or efficacy (clinical/toxicological) data or a justification for not providing such data; and/or • requires a higher level of assessment due to the umbrella branding segment of the product name; and/or • has not been previously registered as an OTC medicine following • down-scheduling.
N5	An application for a new product that is an extension to a 'generic category' product or an application for a product containing a new chemical entity as an active ingredient.
CN	'Notification' changes, where their implementation would not impact the quality, safety or efficacy of a medicine. Includes quality and non-quality changes classified as 'negligible risk'.
C1	Quality and non-quality changes classified as 'negligible risk'.
C2	Quality and non-quality changes classified as 'low risk' – no safety and/or efficacy data required; quality data may be required.
C3	Quality and non-quality changes classified as 'low risk' – safety and/or efficacy data required unless justified; quality data may be required. Umbrella branding segment of new name requires a higher level of assessment.
C4	Non-quality changes classified as 'moderate risk' – safety and/or efficacy data required unless justified.
Requests for consent under section 14/14A of the Act	Request for consent by the Secretary under sections 14 and 14A of the Act to the import, export or supply of therapeutic goods that do not comply with an applicable standard.
B1	Request for advice in relation to a registered OTC medicine for the purpose of listing of listing the medicine as a pharmaceutical benefit that does not contain clinical data.
B3	Request for advice in relation to a registered OTC medicine for the purpose of listing the medicine as a pharmaceutical benefit that contains clinical data or a justification as to why such data is not needed.

Table 10 OTC medicine application processing time for approved applications for July to December 2018

		Total approved	Target Approval time (days)	Mean	Median	Range	Percentage within target
New medicine applications							
N1	Lower risk	98	45	30	30	3-51	90%
N2		14	55	46	49	30-55	100%
N3		15	150	87	75	57-153	93%
N4		8	170	78	76	18-153	100%
N5	Higher risk	4	210	148	136	121-198	100%
Change applications							
C1	Lower risk	92	20	6	4	0-22	98%
C2		222	64	42	45	0-121	88%
C3		3	120	130	92	84-214	67%
C4	Higher risk	0	170	N/A	N/A	N/A	N/A

Table 11 Other OTC medicine applications processed

Other application types that we process include notification changes, where their implementation would not impact the quality, safety or efficacy of a medicine, and requests for advice for the purpose of listing a medicine as a pharmaceutical benefit. In accordance with the legislation, registered goods must comply with numerous standards at the time they are registered and throughout their lifecycle. Following an appropriate application and review of the scientific data and safety considerations, we may grant an exemption from a particular standard for a product.

	Jul-Dec 2017	Jul-Dec 2018
Notification changes, where their implementation would not impact the quality, safety or efficacy of a medicine		
CN	83	101
Request for advice for the purpose of listing a medicine as a pharmaceutical benefit		
B1	0	2
B3	0	0
Requests for consent under section 14/14A of the Act to import, export or supply therapeutic goods not complying with an applicable standard		
Approved	5	17
Rejected	0	0

3. Complementary medicines

3.1. Registered complementary medicines

Table 12 Number of approved registered complementary medicine applications

	Jul – Dec 2017	Jul – Dec 2018
New registered medicines	1	2
Variation to registered medicines	7	12

3.2. Listed complementary medicines

Table 13 Number of new ingredients permitted for use in listed medicines

	Jul – Dec 2017	Jul – Dec 2018
New permitted ingredients	42	5[a]

[a] The decrease in new ingredients numbers for Jul to Dec 2018 is primarily due to an unusually large number of applications of sunscreen excipients received in 2017.

Table 14 Number of new listed medicines

	Jul – Dec 2017	Jul – Dec 2018
New listed medicines	916	943

Table 15 Number of listed medicine reviews by type

	Jul – Dec 2017	Jul – Dec 2018
Reviews initiated		
Random reviews[a]	90	6
Targeted reviews[a]	29	1
Total	119	7
Reviews completed		
Random reviews	32	45
Targeted reviews	86	12
Total	118	57

[a] During 2018 there was a considerable decrease in reviews as we undertook intensive targeted reviews of listed sunscreens, and commenced a review of products making indications referring to macular degeneration.

Table 16 Number of completed listed medicine reviews by outcome

	Jul – Dec 2017	Jul – Dec 2018
Compliance status determined		
Medicines with no compliance breaches	37	5
Medicines with verified compliance breaches	45	45
Sub-total	82	50
Compliance status unable to be determined		
Medicines cancelled by sponsors after request for information	24	7
Medicines not yet manufactured or information unavailable	6	0
Other	3	0
Sub-total	33	7
Product not a therapeutic good	3	0
Total completed	118	57

4. Biologicals and blood components

Blood, blood components, plasma derivatives, tissue and cellular products, tissue and cell based derivatives, and other emerging biological therapies are regulated under the Act.

Table 17 Number of completed biological applications

	Jul – Dec 2017	Jul – Dec 2018
Technical Master File (TMF) new	0	0
TMF annual updates	1	2
TMF variations	6	7
TMF notifications	4	3
Plasma Master File annual updates	7	6
Biological Class 2 – new applications	0	1
Biological Class 3 – new applications	2	0
Biological Class 4 – new applications[a]	N/A	2
Biological Class 2 – variations	1	8
Biological Class 3 – variations	1	2
Biological Class 4 - variations[a]	N/A	0
Total completed	22	31

[a] Class 4 biologicals and gene therapy products were included on the ARTG for the first time in 2018

5. Medical devices

The regulatory framework for medical devices spans the life cycle of these products, including conformity assessment, inclusion on the ARTG and post-market monitoring.

Table 18 Number of completed applications and processing time for conformity assessments of medical devices (including IVDs)

	Jul – Dec 2017	Jul – Dec 2018
New devices		
Total completed	44	48
Percentage processed within target processing timeframes	100%	100%
Mean TGA processing time (working days)	128	177
Median TGA processing time (working days)	183	197
Changes to recertification		
Total completed	88	96
Percentage processed within target processing timeframes	100%	100%
Mean TGA processing time (working days)	115	115
Median TGA processing time (working days)	115	98

The TGA is required to complete conformity assessment applications within 255 working days.

Table 19 Number of completed applications for inclusion of medical devices and IVDs on the ARTG

	Jul – Dec 2017	Jul – Dec 2018
Class I medical devices	1545	1013[a]
Class I measuring medical devices	22	12
Class I sterile medical devices	127	109
Class IIa medical devices	607	634
Class IIb medical devices	328	304
Class III medical devices	189	204
Class III Joint Reclassification medical devices	63	5
Active Implantable Medical Devices (AIMD)	28	10
Class 1 IVDs	45	27
Class 2 IVDs	47	33
Class 3 IVDs	19	24
Class 4 IVDs	10	26
Total	3030	2401

[a] Changes to Class 1 medical devices reporting were introduced in October 2018 to include export only applications.

Table 20 Number of application audits completed and processing time for medical devices and IVDs for July to December 2018

	Total completed	Processing times	
		Mean	Median
Medical devices			
Auto-included applications[a]	843		
Applications completed without audit[b]	1165	10	9
Non-compulsory audits[c]	99	89	34
Level 1 compulsory audits	49	26	18
Level 2 compulsory audits	135	89	68
IVDs			
Auto-included applications[a]	27		
Applications completed without audit[b]	52	5	5
IVD non-compulsory audit	3	39	20
IVD compulsory audit	28	97	98

[a] Class I and Class 1 IVDs (with some exception) are automatically included medical devices and are not subject to audits before inclusion. Separate post-market monitoring is undertaken for these goods.

[b] These figures do not include applications for Class I and Class 1 IVD auto-included devices. These applications are completed within 20 working days.

[c] Non-compulsory audit – estimate for the audit processing time does not include applications for reclassification of joint replacement medical devices received during transitional period (Class III Joint Reclassification medical devices), and applications supported by European Community certificates issued by certain notified bodies (for details see Increased application audit requirements for some medical devices applications).

6. Exports

Table 21 Number of approved applications for export-only medicines and export certifications and relevant processing time for July to December 2018

	Total approved	Target processing time (days)	Average Processing time (days)
Export-only medicines			
New application	135	30	20
Variation	47	30	18
Export certificates			
Medicine applications	872	15	10
Medical device assessments	230	10	5

7. Access to unapproved therapeutic goods

7.1. Special Access Scheme

Table 22 Number of completed applications and notifications for the Special Access Scheme

	Jul – Dec 2017	Jul – Dec 2018
Medicines		
Category A	16824	19178
Category B	5968	7336
Category C[a]	4732	9315
Total	27524	35829
Medical devices		
Category A	2014	2343
Category B	1692	1075
Category C	1	452
Total	3707	3870
Biologicals		
Category A	22	60
Category B	371	780
Category C	242	249
Total	635	1089

[a] There has been a significant increase in the use of SAS Category C since this pathway was introduced on 3 July 2018.

7.2. Authorised prescribers

Table 23 Number of authorised prescriber approvals for medicines and medical devices

	Jul – Dec 2017	Jul – Dec 2018
Medicines	355	418
Medical devices	114	268
Total	469	686

7.3. Clinical trials

Table 24 Number of notifications for new clinical trials received by therapeutic good type

	Jul – Dec 2017	Jul – Dec 2018
Medicine only	223	220
Medical device only	77	71
Biological only	4	10
Medicine and medical device	171	193
Medical device and biological	1	0
Medicine and biological	2	0
Medicine, medical device and biological	3	0
Total	481	494

A trial may be notified with more than one phase type and not all trials are notified to the TGA by phase, therefore there may be a discrepancy between the numbers in Tables 24 and 25.

Table 25 Number of notifications for new clinical trials received by phases

	Jul – Dec 2017	Jul – Dec 2018
Phase 1	120	118
Phase 1 and 2 in combination	24	24
Phase 2	89	102
Phase 2 and 3 in combination	6	2
Phase 3	126	131
Phase 4	32	36
Bioavailability / equivalence	5	9
Other phases in combination	5	1
Device only	74	71

8. Licensing and manufacturing

Number of manufacturing inspections by outcome

Table 26A Medicines and blood, tissue and cellular therapies

Applicants often submit applications for GMP licences and certifications before finalising all of their systems and processes. The TGA works with the applicant to ensure an inspection is not conducted before the manufacturing facility is ready. It is therefore not uncommon for inspections to be conducted later than the target dates.

	Jul – Dec 2017	Jul – Dec 2018
Outcomes of inspections of Australian manufacturers		
Number of inspections conducted	96	104
Satisfactory compliance (of completed inspections) [a]	89%	81%
Marginal compliance (of completed inspections) [a]	10%	19%
Unacceptable compliance (of completed inspections) [a]	1%	0%
Close-out in progress	11%	18%
Processing time		
Initial inspections conducted within 3 months of application	92%	88%
Re-inspections conducted within 6 months of due date	68%	78%
Outcomes of inspections of overseas manufacturers		
Number of inspections conducted	49	39
Satisfactory compliance (of completed inspections) [a]	83%	85%
Marginal compliance (of completed inspections) [a]	13%	15%
Unacceptable compliance (of completed inspections) [a]	4%	0%
Close-out in progress	6%	13%
Processing time		
Initial certification inspections conducted within 6 months of application	53%	78%
Certification re-inspections conducted within 6 months of due date	60%	52%

[a] Compliance data for this period is aligned with data reported for the 2016 Jul-Dec period and excludes 'Close-out in progress' in calculation of percentages i.e. the percentages reported are limited to those inspections that are completed.

Table 26B Medical Devices

We conduct assessments of applications received for Conformity Assessment Certification. It may be determined that an audit of one or more manufacturers included in the Conformity Assessment Application is required. The timeframes used below for calculation of conducted audits are from the date of notification of this requirement.

The implementation of the MDSAP has enabled a reduction in the overall number of internal on-site audits required, substituted by a desktop assessment based on the MDSAP audit report.

	Jul – Dec 2017	Jul – Dec 2018
Quality Management System Audits (domestic manufacturers)		
Number of audits conducted	22	15
Satisfactory compliance (of completed audits)	17%	60%
Marginal compliance (of completed audits)	33%	13%
Unacceptable compliance (of completed audits)	0%	0%
Close-out in progress	50%	27%
Processing time		
Initial audits conducted within 3 months of application	66%	0%[a]
Re-audits conducted within 6 months of due date	56%	35%
QMS Audits (overseas manufacturers)		
Number of audits conducted	12	18
Satisfactory compliance (of completed audits)	17%	67%
Marginal compliance (of completed audits)	33%	0%
Unacceptable compliance (of completed audits)	0%	0%
Close-out in progress	50%	33%
Processing time		
Initial certification audits conducted within 6 months of application	38%	55%
Certification re-audits conducted within 6 months of due date	50%	0%[b]

[a] During the Jul-Dec 2018 reporting period only one domestic initial audit was conducted. This audit was completed within 4 months of application.

[b] Due to the increased demand for overseas initial audits and assessments of MDSAP Auditing Organisations, and a temporary reduction in the number TGA auditors, all overseas certification re-audits (7) were conducted between 7 and 12 months past due date for the Jul-Dec 2018 reporting period. These manufacturers are typically subject to regular surveillance MDSAP or Notified Body audits.

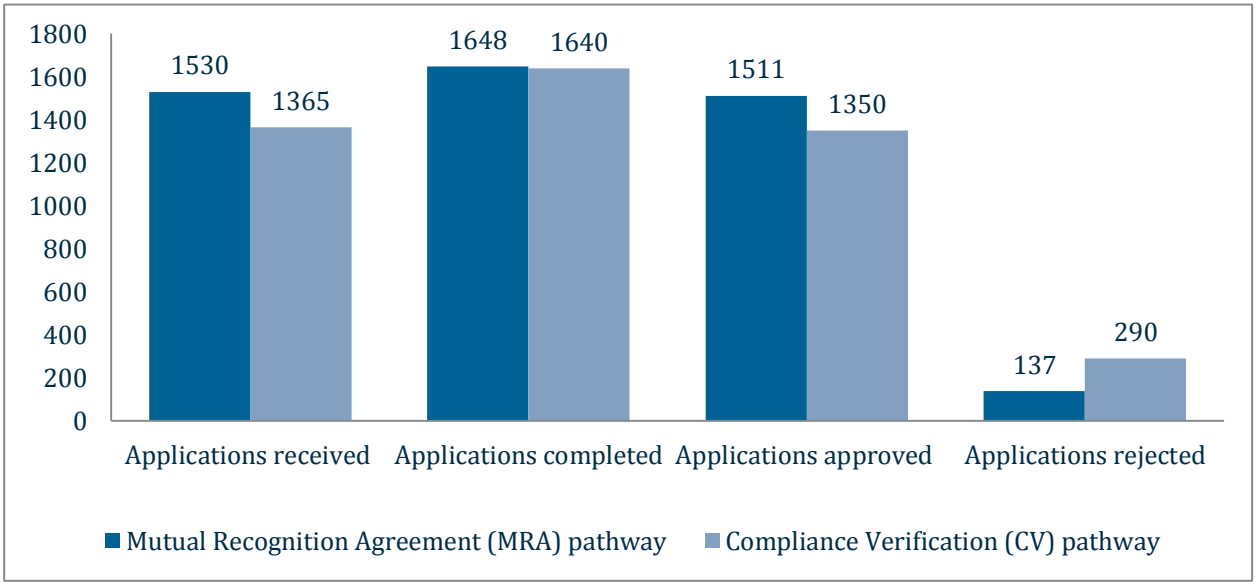
Table 27 Number of GMP clearance applications

GMP clearance is required for all medicines supplied in Australia (unless exempt), including for products supplied to sponsors by overseas manufacturers.

	Jul – Dec 2017	Jul – Dec 2018[a]
Applications received	2909	2895
Approved	2780	2861
Rejected	167	427
Total completed	2947	3288

[a] A change in the reporting method from 2017 now captures additional application types (e.g. extensions, variations etc.). It followed updates to the GMP Clearance application e-forms in September 2017 and has resulted in variations to some figures when comparing the two reporting periods.

Figure 4 Number of GMP clearance applications actioned by pathway from July to December 2018



9. Laboratory testing

Table 28 Number of samples tested by type of therapeutic good and percentage which failed

	Jul – Dec 2017		Jul – Dec 2018	
Product type	Total	% fail	Total	% fail
Prescription medicines	482	1.0%	496	0.2%
OTC medicines	9	0.0%	17	0.0%
Complementary medicines	123	16%	149	21%
Medical devices	42	38%	81	41%
External/contract[a]	31	16%	28	14%
Pacific Medicines Testing Program[b]	N/A	N/A	9	0%
Unregistered[c]	109	51%	67	57%
Total samples (excluding AHQ samples)[e]	796	13%	838	13%
Total samples (including AHQ samples)[e]	915	11%	991	11%
Total number of products tested[f]	415	N/A	415	N/A

[a] Performed on request for overseas regulators or aid agencies and encompasses medicines and medical devices.

[b] The Pacific Medicines Testing Program is a joint program between the Department of Foreign Affairs and Trade and the TGA and commenced in 2018.

[c] 'Unregistered' refers to products that meet the definition of therapeutic goods but are not included on the ARTG or otherwise specifically exempted from this requirement in the legislation. This often includes adulterated complementary medicines or counterfeit products.

[d] Accreditation, harmonisation and quality control (AHQ) samples.

[e] The TGA may test a number of samples of each product per reporting period.

10. Medicine and Vaccine Adverse Event Reporting

Table 29 Source of notifications of medicine and vaccine adverse reaction

	Jul – Dec 2017	Jul – Dec 2018
Accepted cases total	10091	9978
Reports by health professionals (total)	1994	1897
Medical practitioners	387	460
Pharmacists [a]	569	884
Nurses	85	216
Others [b]	2	156
Unknown [b]	951	181
Patients/consumers[b]	580	332
Pharmaceutical companies	6069	6171
Other source	1448	1578
Rejected/withdrawn cases	1407	641
Total received	11498	10619
Mean number of reports received weekly	442	408
Vaccine reports included in this table	1846	1830

[a] In 2018 the increased number of reports submitted by the pharmacists from the NPS MedicineWise phone service – a service for consumers to report adverse events and seek clinical advice from pharmacists - may explain the increased number of reports submitted by pharmacists and the decreased number of reports submitted by consumers.

[b] The Adverse Drug Reaction System (ADRS) legacy data captured limited information regarding the type of health professional reporter.

11. Medical device incident reports

Table 30 Number of completed medical device incident reports and processing time

Processing time is defined as the number of working days from receipt of the notification until the incident has been investigated and resolved.

The target timeframe for processing of medical device incident reports is 90 working days. The doubling of the mean processing time is due to the length of time taken to close several investigations that required complex testing in the laboratories and many rounds of expert advice.

	Jul – Dec 2017	Jul – Dec 2018
Reports completed	2771	2661
Mean TGA processing time	15	33
Percentage processed within target timeframe	95%	91%

12. Regulatory compliance

Data in relation to investigations may appear in multiple tables as compliance matters may be captured under several categories.

Table 31 Number of products investigated by product type

	Jul – Dec 2017	Jul – Dec 2018
Prescription medicines	1413	2308
Medical devices	70	60
Biological and blood products	8	16
OTC medicines	14	229
Complementary and homeopathic medicines	197	61
Other	41	262
Total	1743	2936

Table 32 Number of offence outcomes

	Jul – Dec 2017	Jul – Dec 2018
Criminal prosecution	1	2
Infringement notices	0	5
Warning letters issued[a]	1394	2613
Advertisements removed from online trading platforms[b]	0	47
Goods released under the Personal Importation Scheme	165	445
Referred to external entity	24	81
No offence identified	70	193
Total completed	1654	3386

[a] The category 'warning letters issued' can include goods destroyed as prohibited imports and goods re-exported. In the 2018 reporting period 970 certificates (2017-870) were issued for the destruction of 516,818 (2017-363,763) units.

[b] This figure does not include those offences reviewed by the Advertising Compliance Section.

Table 33 Number of offence types completed

	Jul – Dec 2017	Jul – Dec 2018
Import	1600	3187
Supply	137	272
Manufacture	5	16
Export	1	4
Total completed	1743	3479

13. Advertising complaints

The *Therapeutic Goods Advertising Code (No 2) 2018* was issued in this period, and a comprehensive education campaign conducted. The first meeting of the Therapeutic Goods Advertising Consultative Committee was also held.

We received a large number of complaints about non-compliant advertising of therapeutic goods, which generated 1,039 cases. The following data reflects the time to action and time to close cases that were finalised within the reporting period. The time to action and close complaints is measured against KPIs, which we use to measure our complaints handling performance.

The time to action a complaint is the period of time starting from when a complaint is received, including categorisation and ending on initial engagement with the advertiser. The time taken to close a case means the period of time from when a complaint was received, categorised and progressed as a case, to when no further action is required and the case is closed. The target period of time that will apply for the TGA to action or close a complaint will depend on the categorisation of the complaint. Further information about the categorisation of advertising complaints is available at: https://www.tga.gov.au/publication/complaints-handling-advertising-therapeutic-goods-australian-public. The data is based on cases that were closed in the period.

Table 34 Number of advertising cases meeting time to action and time to close KPIs

	Jul – Dec 2018
Low	
Total completed cases	693
Time to Action (target 95% in 14 days)	623 (90%)
Time to Close (target 90% in 20 Days)	667 (96%)
Medium	
Total completed cases	47
Time to Action (target 95% in 40 days)	35 (74%)
Time to Close (target 90% in 90 Days)	47 (100%)
High	
Total completed cases	1
Time to Action (target 95% in 20 days)	1 (100%)
Time to Close (target 90% in 90 Days)	1 (100%)
Critical	
Total completed cases	5
Time to Action (target 100% in 10 days)	4 (80%)
Time to Close (target 90% in 60 Days)	5 (100%)

In this period, one direction notice was issued. Further information is available at: https://www.tga.gov.au/direction-about-advertisement-gumby-gumby-capsules. We also initiated Federal Court proceedings, seeking both an injunction and the imposition of civil penalties, against an advertiser for advertising contraventions.

14. Recalls

Table 35 Number of therapeutic goods recalls

	Jul – Dec 2017	Jul – Dec 2018
Medicines	21	19
Medical devices (including IVDs)	284	268
Biologicals	0	17
Bloods	38	43
Total recalls	343	347

15. Pharmacovigilance Inspection Program

Table 36 PVIP inspections undertaken and deficiencies identified from July to December 2018

	Jul – Dec 2018
Total completed	5
Total with completed findings	5
Critical deficiencies [a]	0
Major deficiencies [b]	25
Minor deficiencies [c]	17
Average deficiencies per inspection	5 major 3.4 minor

[a] A deficiency in pharmacovigilance systems, practices or processes that adversely affects the rights, safety or well-being of patients or that poses a potential risk to public health or that represents a serious violation of applicable legislation and guidelines. Deficiencies classified as critical may include a pattern of deviations classified as major. A critical deficiency also occurs when a sponsor is observed to have engaged in fraud, misrepresentation or falsification of data.

[b] A deficiency in pharmacovigilance systems, practices or processes that could potentially adversely affect the rights, safety or well-being of patients or that could potentially pose a risk to public health or that represents a violation of applicable legislation and guidelines. Deficiencies classified as major may include a pattern of deviations classified as minor.

[c] A deficiency in pharmacovigilance systems, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients. A deficiency may be minor either because it is judged as minor or because there is insufficient information to classify it as major or critical.

16. Reporting of medicine shortages

Table 37 New medicine shortage reports by month[a]

	Number received
2018	
July	28
August	25
September	47
October	58
November	71
December	174

[a] New reports only, does not include updates of previously reported shortages. All reports are submitted voluntarily, with mandatory reporting of all shortages of prescription medicines and select over-the-counter medicines commencing 1 January 2019.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Reporting and Collaboration Services	12/03/2019

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Reference/Publication D19-5095952