Australian Government
Department of Health
Therapeutic Goods Administration

# Performance Statistics Report

## July 2015 to June 2016

TGA Health Safety Regulation

# Contents

# Executive summary

The TGA provides information on our regulatory performance to our stakeholders through detailed statistical information. The following statistics cover the period 1 July 2015 to 30 June 2016. This is the first report following a review of our reporting framework and the development of the *TGA key performance indicators under the Regulator Performance Framework*.

The performance statistics provided in this report should be read in conjunction with the Key Performance Indicator Report which outlines performance against our broad strategic intent, as required under the Government's Regulator Performance Framework.

## Key observations: July 2015 to June 2016

Key observations for 2015-16 are summarised below, including trends and notable changes from previous reporting periods.

### Prescription medicines

Over the past three years, the number of submissions received across some Category 1 application types has been relatively stable. Applications for new generic medicines and Extension of Indications (EOI) in 2015-16 were comparable to those received in 2013-14, following a slight drop in 2014-15. While New Chemical Entity (NCE) submissions were higher in 2015-16 than in 2014-15, they remained down on the high number received in 2013-14.

All Category 1 submissions processed in 2015-16 were within the legislated 255 working day timeframe with a modest decrease in average approval times for NCE, EOI and generic medicine applications. Median approval times for all application types were lower than previous years, including Additional Trade Name applications which reduced to 35 TGA working days following the introduction of a 45 day legislated timeframe from 1 July 2015.

### Over-the-counter medicines

The total number of new medicine applications received in 2015-16 was lower than in 2014-15, primarily due to a drop in the number of low risk (N1) applications.

The number of applications received to vary existing medicines and median approval times for the majority of application types remained largely consistent with previous periods. There was, however, a significant increase in approval times for N3 (new 'generic' medicine) and C4 (non-quality change) applications, likely influenced by varying application complexity.

### Complementary medicines

The number of new ingredients permitted for use in listed medicines increased, primarily due to finalisation of the Permitted Ingredients List project which resulted in the approval of 10 new ingredients.

Compliance activity for complementary medicines increased during 2015-16. The number of compliance reviews more than doubled, largely the result of business process improvements to streamline the overall review process and improve review timelines. The number of investigations initiated also increased, driven by external factors including complaints and referrals.

Medicines with verified compliance breaches were 80% for 2015-16 compared to 73% for 2014-15, suggesting that the overall rate of non-compliance has remained high despite the significant increase in compliance reviews.

Labelling, advertising and evidence continued to be the major compliance breaches for listed medicines. In 2015-16, 13 products were found to have safety related issues, compared to no products in 2014-15. This increase in 2015-16 was largely a result of targeted work undertaken on safety of ingredients.

### Biologicals

During 2015-16 there was a significant increase in applications received for variations to approved biologicals (Class 2). This was the result of transitional arrangements during 2014-15 to reflect new requirements under the regulatory framework for biologicals that commenced in May 2011.

### Medicine and vaccine adverse event reports

Overall, adverse events reports in 2015-16 were similar to those in 2014-15. While the number of adverse event reports from pharmacists fell, reflecting a change to pharmacist reporting classifications during reporting periods, adverse event reporting from members of the public increased. This was likely the result of activity to promote adverse event reporting from consumers.

### Medical devices

During 2015-16 we received 2,816 medical device applications for inclusion on the Australian Register of Therapeutic Goods (ARTG) (excluding the 2,685 Class I medical devices automatically included). A total of 3,266 applications were completed (including a number on hand at the commencement of the reporting period), with 92% of these approved. Two transition periods – for joint reclassification and commercial In-Vitro Diagnostics (IVDs) – ended on 30 June 2015. While high numbers of applications for these medical devices were received in 2014-15, the end of the transition period has seen an end to these applications.

Processing times for conformity assessment applications for new devices were well within the 200 TGA target days. However, processing times for Level 2 compulsory audits of applications were well above the target 60 TGA working days. Delays were due to a significant wait time for commencement of the clinical assessment component.

Post-market reviews for 83 devices were completed. The drop in activity was largely due to a number of device reviews that required a detailed clinical review.

An increase in the number of device incident reports may have been due to the inSite program (to improve awareness about medical device adverse event reporting) and increased vigilance within the medical community. As figures were collected at a point in time, the apparent disconnect between received and completed reports was likely the result of data crossing annual boundaries.

The IVD regulatory framework transition period for commercial IVDs ended on 30 June 2015. Application numbers for 2014-15 were higher due to extra applications associated with the transition. In 2015-16 application numbers fell, and were more representative of expected ongoing numbers.

### Access to unapproved therapeutic goods

There was an increase in the number of Special Access Scheme Category B applications for biologicals in 2015-16, due to an increase in applications by dental practitioners for access to a dental product for bone grafts.

In relation to clinical trials, data for 2015-16 reflects the transition of the Clinical Trials Notification to an online system on 1 July 2015. During the transition process there was a parallel paper-based notification system. In addition, there were some differences between the

previous paper-based system and the online form in the capturing and reporting of clinical trial information.

## Medicines and biologicals manufacturing

Demand for Good Manufacturing Practice (GMP) clearance increased with 5,657 applications received in 2015-16. Major contributing factors included sponsors sourcing more products from new and multiple manufacturers, globalisation and company mergers, and overseas regulatory agencies undertaking more inspections in other countries, creating opportunities for evidence to be used in support of Australian GMP clearance applications. The increase in applications reduced the number of on-site inspections as evidence could be relied upon in lieu of an inspection.

There was an increase in the number of licences revoked at the request of manufacturers. The majority of these were the result of the relocation of services by The Australian Red Cross Blood Service.

## Recalls

There was an increase in the number of recalls for medicines and medical devices that corresponded with an increase in the number of ARTG entries.

## Laboratory testing

There was a significant increase in the number of unregistered products tested. This category of products traditionally has a high rate of failure due to counterfeiting and adulteration. The increase in testing of unregistered products also increased the overall percentage fail rate for all products tested in 2015-16.

## Regulatory compliance

Regulatory compliance actions almost doubled in 2015-16 due to an increased number of referrals by the Australian Border Force, increased awareness through publication of safety alerts relating to specific unapproved products, and educational materials including videos about the risk of buying unapproved products online.

# 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 which are subject to legislated timeframes:

- **Category 1 application:** 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, new chemical entities, extensions of indication and new routes of administration.

  The legislated timeframes for the two stages of a Category 1 application are: 40 working days for notification of acceptance or rejection of the application and 255 working days for the completion of the evaluation and notification of the decision.

- **Category 2 application:** An application accompanied by two independent evaluation reports from comparable overseas regulators in whose jurisdiction the product is approved for the same indication.

  The legislated timeframes for the two stages of a Category 2 application are: 20 working days for notification of acceptance or rejection of an application and 175 working days to notify the applicant of the decision.

- **Category 3 application:** 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, a change in the site of manufacture, a change to the synthetic route, a change in the product specifications, a change in the steps of manufacture or a change in trade name.

  The legislated timeframe for a Category 3 application is 45 working days for notification of acceptance or rejection of an application, completion of evaluation and notification of the decision.

## 1.1. Approval times

Once an application has been accepted by the TGA, the approval time is defined as the number of TGA working days until a decision is made. As detailed above, this timeframe is underpinned by legislation and excludes public holidays, weekends, the time allocated to the applicant to provide responses to requests for information and 'mutual clock stop' periods agreed with the applicant.

In accordance with the *Therapeutic Goods Regulations 1990*, a 'submission' may include a number of applications submitted at the one time. The data presented below relates to submissions as this best reflects the evaluation and decision-making processes.

**Table 1 Prescription medicine approval times for July 2015 to June 2016**

| | | Approval time (days) | | | |
|---|---|---|---|---|---|
| **Application type** | **Legislated timeframe** | **Mean** | **Median** | **Minimum** | **Maximum** |
| A: New chemical entity | | | | | |
| Category 1 | 255 | 193 | 199 | 94 | 253 |
| B: New fixed-dose combination | | | | | |
| Category 1 | 255 | 169 | 167 | 138 | 220 |
| C: Extension of indication | | | | | |
| Category 1 | 255 | 186 | 195 | 86 | 230 |
| D: New generic medicine | | | | | |
| Category 1 | 255 | 170 | 158 | 108 | 255 |
| E: Additional trade name (ATN) | | | | | |
| Category 1 | 255 | 212 | 219 | 129 | 254 |
| ATN | 45 | 33 | 35 | 19 | 54 |
| F: Major variation | | | | | |
| Category 1 | 255 | 181 | 183 | 42 | 255 |
| G: Minor variation | | | | | |
| Category 1 | 255 | 163 | 163 | 147 | 179 |
| Category 3 | 45 | 20 | 19 | 6 | 40 |
| H: Minor variation | | | | | |
| Category 1 | 255 | 156 | 146 | 110 | 212 |
| Category 3 | 45 | 22 | 20 | 2 | 84 |
| J: Changes to Product Information requiring the evaluation of data | | | | | |
| Category 1 | 255 | 133 | 134 | 14 | 211 |

**Table 2 Prescription medicine median approval time comparisons**

| | | Median approval time (days) | | |
|---|---|---|---|---|
| **Application type** | **Legislated timeframe** | **2013-14** | **2014-15** | **2015-16** |
| A: New chemical entity | | | | |
| Category 1 | 255 | 211 | 215 | 199 |
| B: New fixed-dose combination | | | | |
| Category 1 | 255 | 190 | 188 | 167 |
| C: Extension of indication | | | | |
| Category 1 | 255 | 186 | 200 | 195 |
| D: New generic medicine | | | | |
| Category 1 | 255 | 170 | 170 | 158 |
| E: Additional trade name (ATN) | | | | |
| Category 1 | 255 | 186 | 194 | 219 |
| ATN | 45 | N/A[a] | N/A[a] | 35 |
| F: Major variation | | | | |
| Category 1 | 255 | 176 | 189 | 183 |
| G: Minor variation[b] | | | | |
| Category 1 | 255 | 184 | 0[b] | 163 |
| Category 3 | 45 | 24 | 18 | 19 |
| H: Minor variation[c] | | | | |
| Category 1 | 255 | 137 | 143 | 146 |
| Category 3 | 45 | 22 | 19 | 20 |
| J: Changes to Product Information requiring the evaluation of data | | | | |
| Category 1 | 255 | 134 | 143 | 134 |

[a] In July 2015, a new process was introduced for ATN submissions to which a 45 working day legislated timeframe was introduced. During the reporting period relevant to this report, these applications were under both the Category 1 framework with a legislated timeframe of 255 working days and the new ATN submission framework with a legislated timeframe of 45 working days.

[b] The type G minor variations differ from type H minor variations in that they result in a new Australian Register of Therapeutic Goods entry. No type G Category 1 applications were approved in 2014-15.

[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.

**Figure 1 Submissions Received 2013-14 to 2015-16**

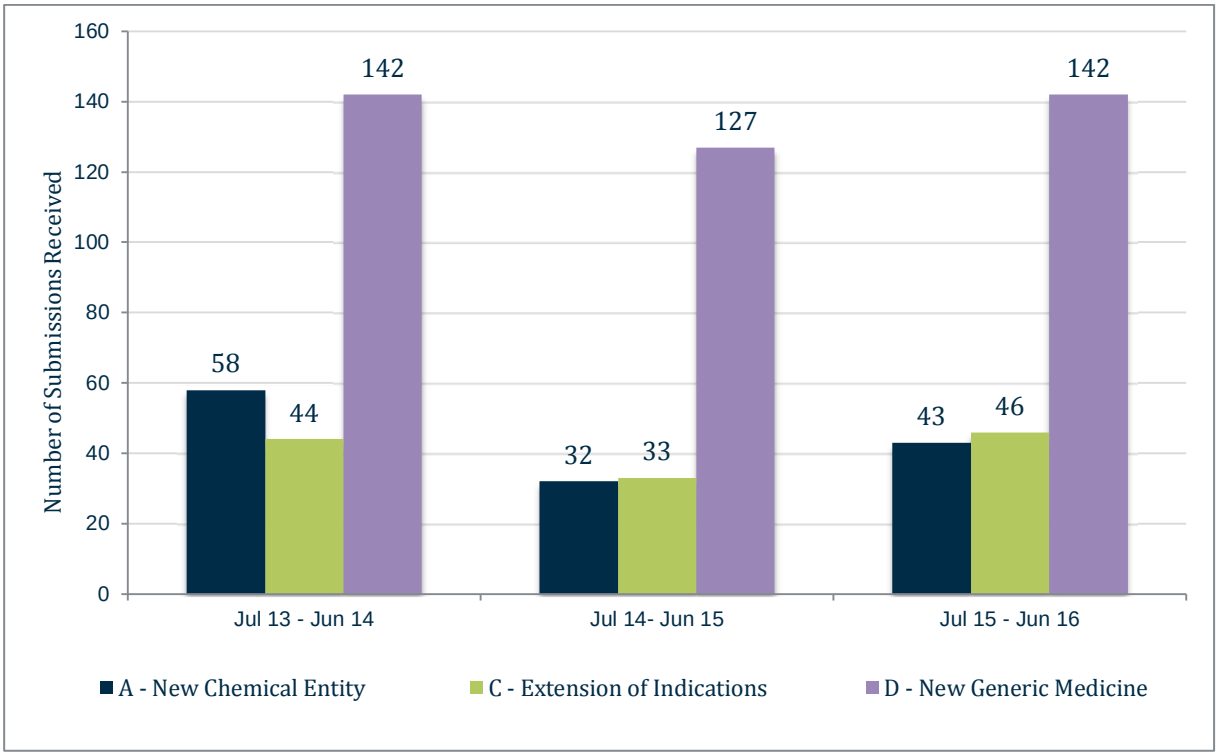



**Figure 2 Mean approval times 2013-14 to 2015-16**

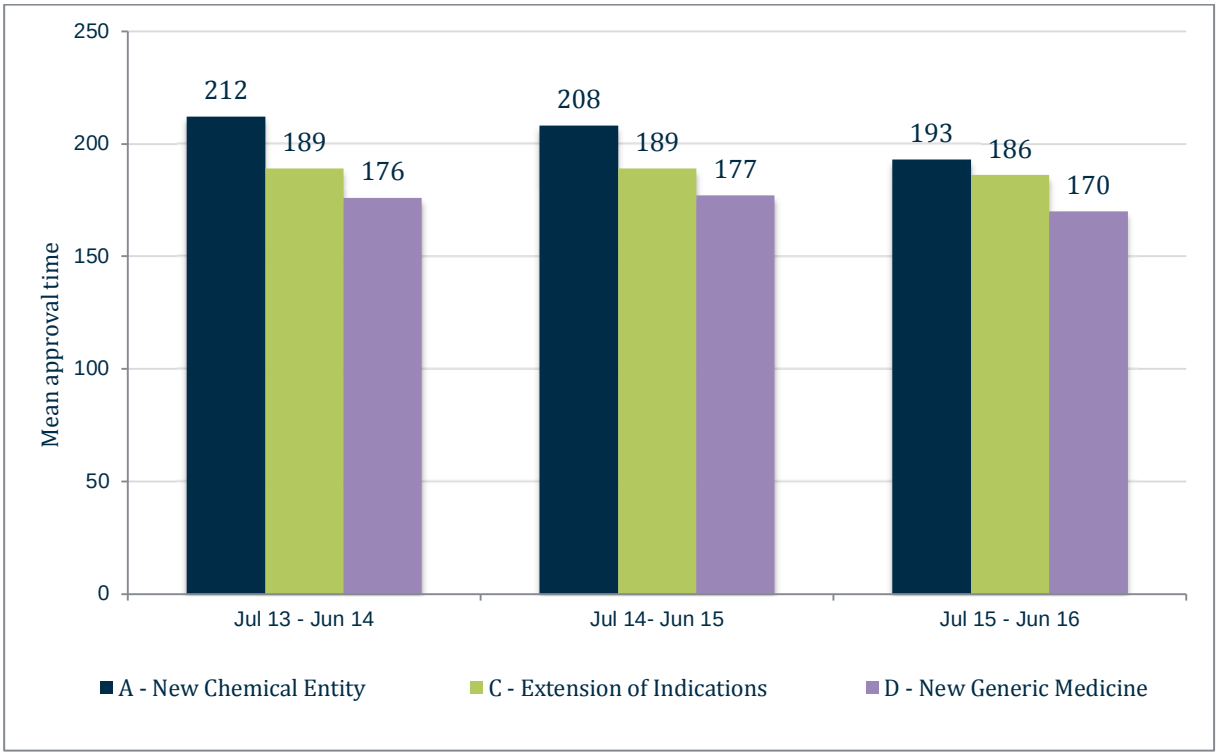
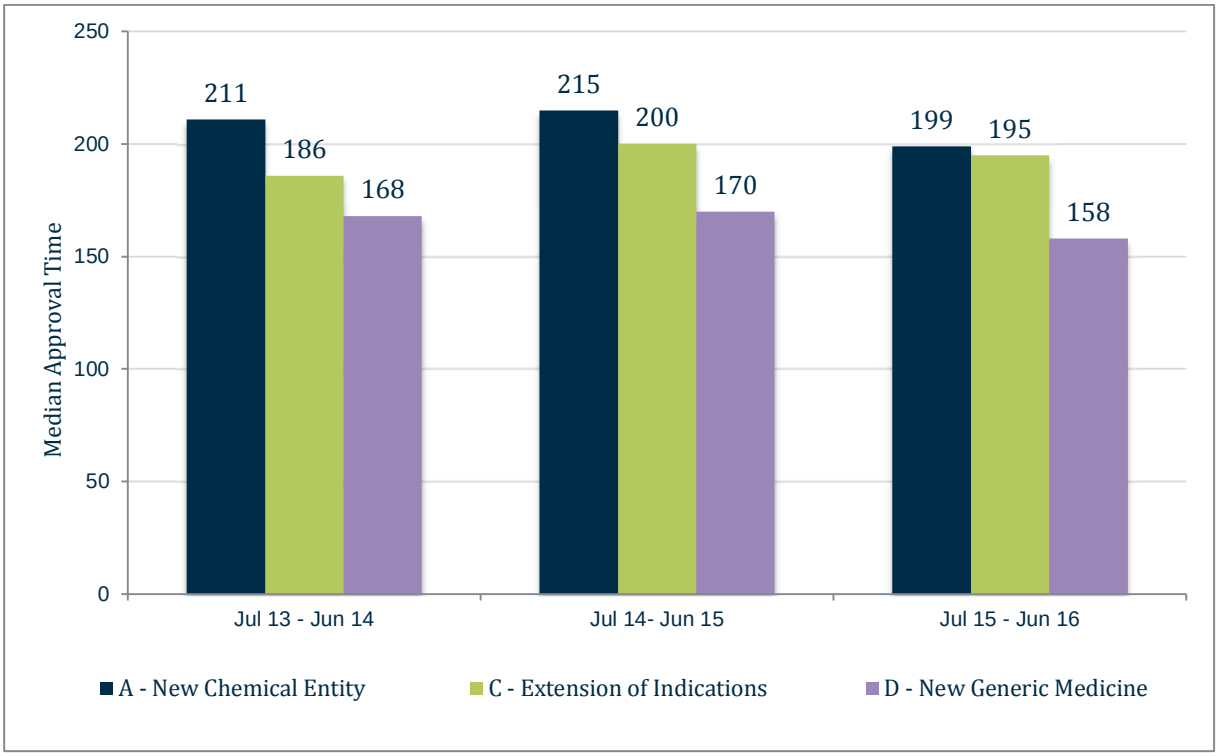


**Figure 3 Median approval times 2013-14 to 2015-16**




## 1.2. Submission outcomes

**Table 3 Number of completed prescription medicine submissions by type and outcome for July 2015 to June 2016**

| Submission Type | Approved | Withdrawn | Rejected | Total |
|---|---|---|---|---|
| A: New chemical entity | 38 | 4 | 1 | 43 |
| B: New fixed-dose combination | 7 | 0 | 0 | 7 |
| C: Extension of indication | 44 | 2 | 0 | 46 |
| D: New generic medicine | 123 | 16 | 3 | 142 |
| E: Additional trade name (ATN) (Category 1) | 38 | 2 | 0 | 40 |
| E: ATN | 32 | 0 | 0 | 32 |
| F: Major variation | 40 | 5 | 1 | 46 |
| G: Minor variation | 2 | 1 | 0 | 3 |
| H: Minor variation (Category 1) | 3 | 0 | 0 | 3 |
| H: Minor variation (Category 3) | 1,276 | 9 | 0 | 1,285 |
| J: Changes to Product Information | 81 | 4 | 0 | 85 |
| Total | 1,684 | 43 | 5 | 1,732 |

## 1.3. Other applications

In addition to the application types discussed above, we also process numerous other application types. These applications are assessed in accordance with a risk-based approach, for example, some requests are categorised as 'self-assessable' and do not usually involve the evaluation of scientific data. Some applications are received because the sponsors are obliged to inform the TGA of new information related to the safety of their products. Other applications involve editorial corrections to the register entry or the associated product information document. The number of such applications is presented below.

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, the TGA may grant an 'exemption' from a particular standard for a product. The number of such applications approved and rejected is also included in the following table.

**Table 4 Number of other prescription medicine applications**

| | 2013-14 | 2014-15 | 2015-16 |
|---|---|---|---|
| | Jul-Jun | Jul-Jun | Jul-Jun |
| Safety related request | 734 | 750 | 781 |
| Self-assessable request | 1,274 | 1,229 | 1,404 |
| Minor editorial change to product information | 530 | 553 | 481 |
| Correction of error | 219 | 163 | 123 |
| Total | 2,757 | 2,695 | 2,789 |
| Exemptions to comply with a standard | | | |
| Approved | | 80[a] | 88 |
| Rejected | | 0[a] | 0 |
| Total | | 80[a] | 88 |

[a] Data collection commenced January 2015.

## 1.4. Orphan drug designations

'Orphan drugs' are often developed to treat small and very specific patient populations who suffer from rare diseases and conditions. The application and evaluation fees for orphan drugs can be waived to help reduce their development costs and facilitate their access to the Australian marketplace. A medicine needs to be designated by the TGA as an orphan drug before an application can be accepted to register it on the Australian Register of Therapeutic Goods (ARTG). The designation process involves a review of whether the drug meets the established criteria which are underpinned by legislation.

The quality, efficacy and safety of orphan drugs are assessed at the same standard as for other registered prescription medicines.

**Table 5 Number of orphan drug designations**

| | 2013-14 | 2014-15 | 2015-16 |
|---|---|---|---|
| | Jul-Jun | Jul-Jun | Jul-Jun |
| Number of designations | 21 | 20 | 22 |

# 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 low risk, N5 and C4 are highest risk). The OTC application categorisation framework outlined below defines the different OTC medicine application levels and the key application criteria.

**Table 6 Categorisation of OTC medicine applications**

| 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:<br>· requires supporting safety and/or efficacy (clinical/toxicological) data or a justification for not providing such data; and/or<br>· requires a higher level of assessment due to the umbrella branding segment of the product name; and/or<br>· 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. |
| 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.<br>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. |

## 2.1. Approval times

Approval time is defined as the number of working days from the acceptance of the application until formal notification of decision. Approval time excludes time where we were unable to progress the application until the sponsor provided additional information unless otherwise specified.

We aim to have 80% of applications completed within target timeframes. Target timeframes for processing of applications are a result of new OTC pre-market business processes and are subject to ongoing review.

**Table 7 Median approval time for OTC medicine applications**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New medicine applications (days) | | |
| N1 | 29 | 14 |
| N2 | 26 | 26 |
| N3 | 43 | 90 |
| N4 | 119 | 89 |
| N5 | 137 | 151 |
| Change applications (days) | | |
| C1 | 7 | 5 |
| C2 | 11 | 8 |
| C3 | 51 | 31 |
| C4 | 44 | 110 |

**Table 8 OTC medicine approval time against target time by application category for July 2015 to June 2016**

| Application type | Number completed | Range | Mean | Median | Target time (days) | % within target |
|---|---|---|---|---|---|---|
| New medicines | | | | | | |
| N1 | 79 | 1-37 | 14 | 14 | 45 | 100 |
| N2 | 3 | 25-41 | 31 | 26 | 55[a] | 100 |
| N3 | 25 | 30-145 | 76 | 90 | 150 | 100 |
| N4 | 50 | 10-158 | 88 | 89 | 170 | 100 |
| N5 | 6 | 40-278 | 143 | 151 | 210 | 83 |
| Change applications | | | | | | |
| C1 | 618 | 0-53 | 6 | 5 | 20 | 97 |
| C2 | 309 | 0-74 | 18 | 8 | 64 | 99 |
| C3 | 4 | 19-69 | 37 | 31 | 120 | 100 |
| C4 | 12 | 60-122 | 100 | 110 | 170 | 100 |

[a] Target time for N2 applications was reduced from 75 to 55 days commencing 1 November 2015.

**Table 9 Percentage of OTC medicine applications processed within target time**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New medicine applications (%) | | |
| N1 | 96 | 100 |
| N2 | 100 | 100 |
| N3 | 100 | 100 |
| N4 | 100 | 100 |
| N5 | 100 | 83[a] |
| Change applications (%) | | |
| C1 | 93 | 97 |
| C2 | 99 | 99 |
| C3 | 80 | 100 |
| C4 | 100 | 100 |

[a] Of the six N5 applications completed in the 2015-16 period, one was not completed within the target timeframe. This application required referral to the Advisory Committee on Non-prescription Medicines (ACNM), which typically extends the evaluation process by 3-6 months.

## 2.2. Applications

### 2.1.1. New OTC medicine applications

**Table 10 Applications received for new OTC medicines and changes to existing medicines**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New medicine applications | | |
| N1 | 144 | 75 |
| N2 | 9 | 13 |
| N3 | 49 | 30 |
| N4 | 58 | 45 |
| N5 | 14 | 14 |
| Total | 274 | 177 |
| Change applications | | |
| C1 | 545 | 632 |
| C2 | 261 | 312 |
| C3 | 4 | 8 |
| C4 | 17 | 1 |
| Total | 827 | 953 |

### 2.1.2. Completed applications

**Table 11 New OTC medicine applications completed and outcomes**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| N1 | | |
| Approved | 162 | 79 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 9 | 0 |
| Returned/failed screening | 1 | 1 |
| Total | 172 | 80 |
| N2 | | |
| Approved | 9 | 3 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 0 | 0 |
| Returned/failed screening | 0 | 5 |
| Total | 9 | 8 |
| N3 | | |
| Approved | 27 | 25 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 1 | 7 |
| Returned/failed screening | 9 | 7 |
| Total | 37 | 39 |
| N4 | | |
| Approved | 56 | 50 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 6 | 0 |
| Returned/failed screening | 11 | 5 |
| Total | 73 | 55 |
| N5 | | |
| Approved | 15 | 6 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 0 | 1 |
| Returned/failed screening | 9 | 5 |
| Total | 24 | 12 |

**Table 12 OTC change applications completed and outcomes**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| C1 | | |
| Approved | 522 | 618 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 7 | 15 |
| Returned/failed screening | 0 | 0 |
| Total | 529 | 633 |
| C2 | | |
| Approved | 255 | 309 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 10 | 3 |
| Returned/failed screening | 5 | 0 |
| Total | 270 | 312 |
| C3 | | |
| Approved | 5 | 4 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 0 | 0 |
| Returned/failed screening | 0 | 0 |
| Total | 5 | 4 |
| C4 | | |
| Approved | 5 | 12 |
| Rejected | 0 | 0 |
| Withdrawn by sponsor | 0 | 0 |
| Returned/failed screening | 0 | 0 |
| Total | 5 | 12 |

# 3. Complementary medicines

## 3.1. Registered complementary medicines

Registered complementary medicines are considered to be of relatively higher risk than listed medicines based on their ingredients or the indications for the medicine. These medicines are fully evaluated by the TGA for quality, safety and efficacy prior to being accepted on the ARTG.

**Table 13 Registered complementary medicine applications by outcome**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New medicines | | |
| Approved | 4 | 2 |
| Rejected | 1 | 0 |
| Withdrawn | 0 | 1 |
| Returned/failed screening | 0 | 0 |
| Total new applications completed | 5 | 3 |
| Variations | | |
| Approved | 28 | 27 |
| Rejected | 1 | 0 |
| Withdrawn | 1 | 3 |
| Returned/failed screening | 0 | 0 |
| Total variations completed | 30 | 30 |
| Application for consent to import, supply or export goods under section 14/14A of the Act[a] | | |
| Approved | 0[b] | 1 |
| Rejected | 0[b] | 0 |
| Total applications completed | 0[b] | 1 |

[a] Applications can be made for consent to import, supply or export goods under section 14/14A of the *Therapeutic Goods Act 1989.*

[b] Data collection commenced January 2015.

## 3.2. New ingredients permitted for use in listed medicines

**Table 14 New listed medicine ingredient applications by outcome**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Approved | 5 | 18[a] |
| Rejected | 1 | 0 |
| Withdrawn | 0 | 0 |
| Returned/failed screening | 0 | 2 |
| Total completed | 6 | 20 |

[a] This includes 10 ingredients that were permitted as per the Therapeutic Goods (Listing) Notice 2015 (No. 4) following TGA initiated assessments.

## 3.3. Listed medicines

**Table 15 New listed medicines**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New listed medicines | 1,879 | 1,644 |

**Table 16 Listed medicine variations under section 9D of the *Therapeutic Goods Act 1989***

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Approved | 56[a] | 102 |
| Rejected | 3[a] | 16 |
| Total | 59[a] | 118 |

[a] Data collection commenced January 2015.

Section 9D of the *Therapeutic Goods Act 1989* provides for variations to be made to an entry on the ARTG in a set of limited and prescribed circumstances. These circumstances include where information included on the ARTG is incomplete or incorrect.

**Table 17 Listed medicine applications under section 14/14A of the *Therapeutic Goods Act 1989***

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Exemption granted | 2[a] | 7 |
| Rejected | 1[a] | 4 |
| Total | 3[a] | 11 |

[a] Data collection commenced January 2015.

Sponsors can apply for certain exemptions under Section 14 of the *Therapeutic Goods Act 1989*. Applications seek consent to import, export or supply a complementary medicine that does not comply with the applicable standards.

## 3.4. Listed medicine reviews

### 3.4.1. Investigations

Investigations include complaints and referrals from internal and external stakeholders and screening of recently listed medicines on the ARTG, but can also include products not listed on the ARTG. All investigations are assessed and triaged based on a risk management approach to provide the greatest overall benefit for the Australian public. Investigations may be completed through a number of mechanisms, such as initiating a targeted review or referral to another area of the TGA.

**Table 18 Listed medicine investigations undertaken and outcomes**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Initiated investigations | 86 | 114 |
| Completed investigations | | |
| Medicines prioritised for targeted review | 24[a] | 69 |
| Referred to another TGA area or government organisation | 5[a] | 14 |
| No further action taken | 24[a] | 32 |
| Total completed investigations | 99[a] | 115 |

[a] Data collection against categories commenced January 2015. There were a total of 46 completed investigations for the period Jul-Dec 2014.

The outcome 'no further action taken' includes examples where the investigation was resolved by other means such as the product has been or is currently under review; the complaint was not justified and did not warrant further action; or advice was provided to the complainant.

### 3.4.2. Compliance reviews

Listed medicines are not evaluated by the TGA before they are included on the ARTG. However, a proportion is reviewed to check their compliance against relevant regulatory requirements. Compliance reviews may only review selected listing requirements.

Medicines may be randomly selected or targeted for a review. Medicines are randomly selected for review by a computer, based on a mathematical model. Targeted reviews can originate from a number of signals and are initiated following an investigation.

A compliance review will result in one of the following outcomes:

- no compliance breaches are identified, the review is concluded and the medicine remains on the ARTG
- compliance breaches are identified for the selected listing requirements
- the review is not completed as the sponsor has cancelled the medicine
- the review is closed due to the unavailability of information in determining its compliance status.

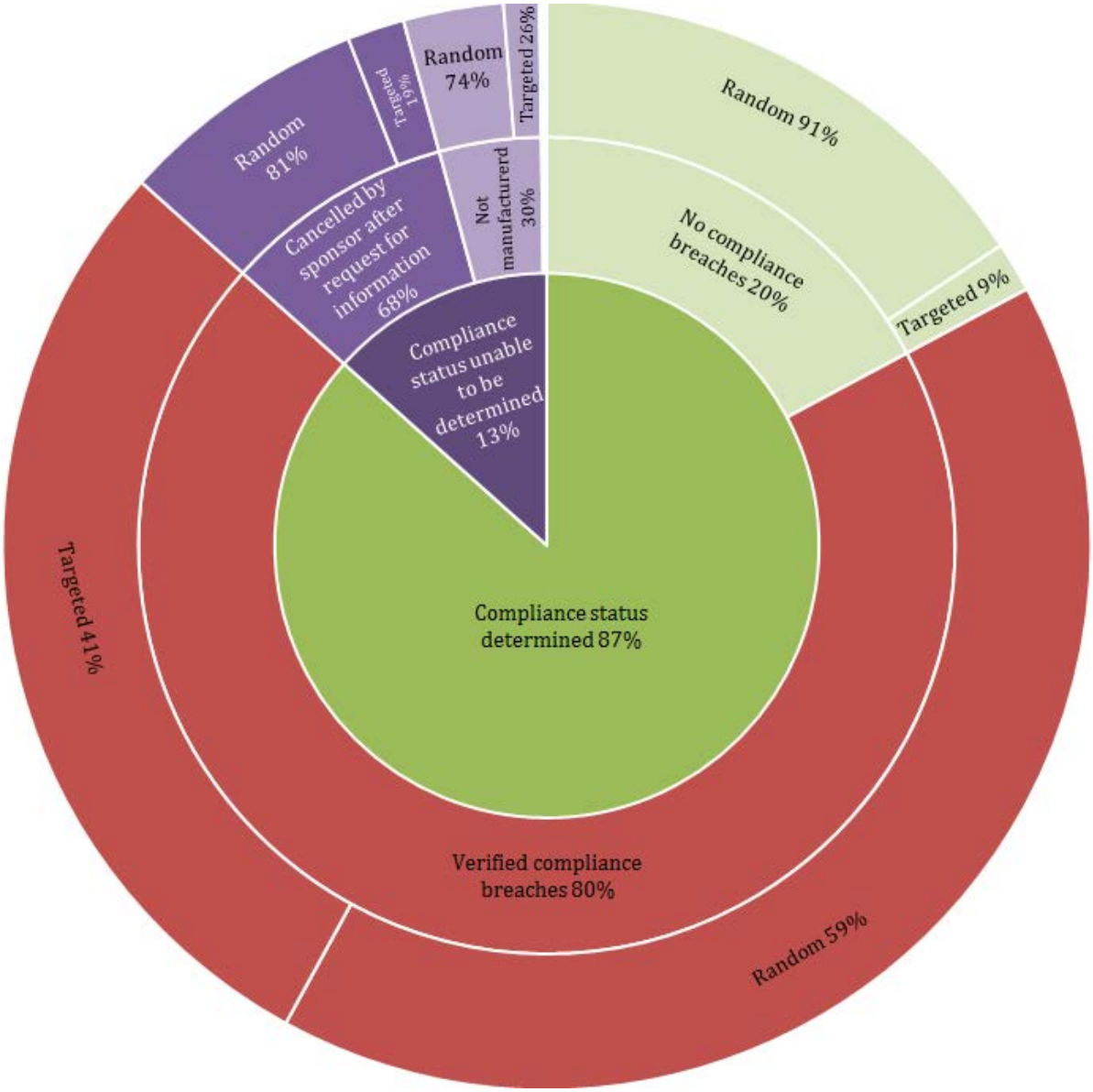
**Table 19 Listed medicine reviews by type**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Initiated reviews | | |
| Targeted reviews | 41 | 173 |
| Random reviews | 89 | 340 |
| Total | 130 | 513 |
| Reviews on hand | 188 | 151 |
| Completed reviews | | |
| Targeted reviews | 156 | 158 |
| Random reviews | 56 | 315 |
| Total | 212 | 473 |

**Table 20 Completed listed medicine reviews by outcome**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Compliance status determined | | |
| Medicines with no compliance breaches | 43 | 81 |
| Medicines with verified compliance breaches | 118 | 327 |
| Sub-total | 161 | 408 |
| Compliance status unable to be determined | | |
| Medicines cancelled by sponsors after request for information | 31 | 43 |
| Medicines not yet manufactured | 18 | 19 |
| Other | 2 | 1 |
| Sub-total | 51 | 63 |
| Product not a therapeutic good | 0 | 2 |
| Total completed | 212 | 473 |

**Figure 4 Outcomes of compliance reviews by reason for initiation**




In this period, we have more than doubled the number of compliance reviews completed compared to the previous period. We have also performed a higher proportion of random reviews to better inform our targeted compliance program. Of the reviews where we were able to determine a compliance status, 80% had verified compliance breaches, which is a higher rate of non-compliance than the previous period (73%).

**Table 21 Types of listed medicine compliance issues identified**

Of the completed compliance reviews, the following are the types of issues identified in those medicines where a compliance breach was verified. Individual medicines may have multiple issues.

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Information provided in ARTG entry | 9 | 53 |
| Manufacturing, quality and/or formulation | 15 | 63 |
| Labelling and/or advertising | 60 | 215 |
| Evidence | 42 | 210 |
| Safety | 0 | 13 |
| Other | 44 | 8 |

**Figure 5 Types of compliance issues identified by reason for initiation**

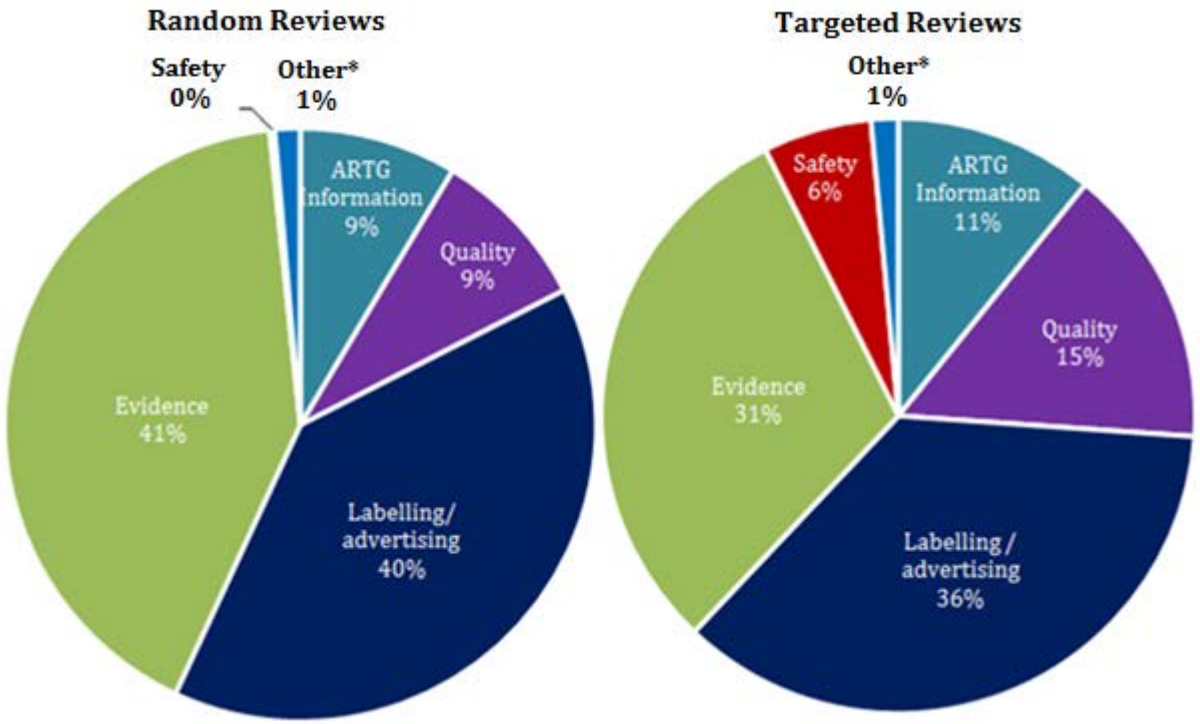



Figure 2 shows the types of compliance issues that are identified through reviews which are either randomly selected or targeted for a particular issue.

'Other' compliance issues may include the sponsor failing to comply with a condition that the medicine is subject to or not responding to a formal request for information.

For both random and targeted reviews, the most common compliance issues have consistently been labelling/ advertising and evidence issues. In this period, evidence and labelling/advertising issues were comparable for targeted reviews, whereas last period there were a significantly higher proportion of labelling/advertising issues. This is likely the result of a number of targeted compliance projects that we have undertaken during this period that focussed on evidence issues identified during our random review program.

**Table 22 Actions taken following listed medicine reviews**

| | |
|---|---|
| Actions following a Request for Information | |
| Medicines found to be compliant and review concluded | 81 |
| Medicines cancelled by the TGA without a proposal to cancel notice | 0 |
| Proposal to cancel notice sent by the TGA | 327 |
| Total | 408 |
| Actions following Proposal to Cancel notice | |
| Medicines cancelled by the TGA | 44 |
| Medicines cancelled by sponsors after being notified of compliance breaches | 76 |
| Reviews concluded after compliance breaches were addressed | 207 |
| Sub-total | 327 |

The figures provided under 'Actions following Proposal to Cancel notice' are a sub-set of the figure provided under 'Actions following a Request for Information'.

**Figure 6 Outcomes of completed compliance reviews**

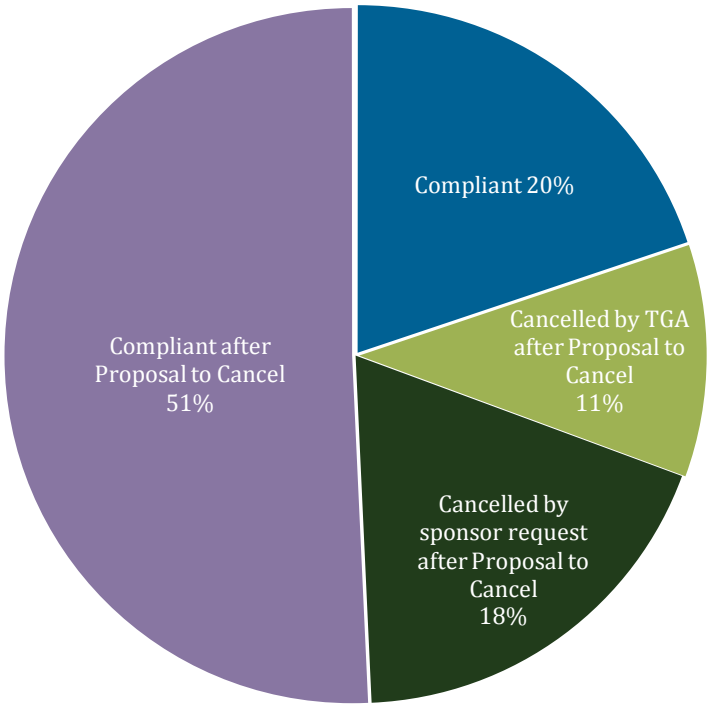



Figure 3 shows that a significant proportion of listed medicine reviews are concluded after the sponsor has adequately addressed the compliance breaches identified by us. Under the *Therapeutic Goods Act 1989* sponsors are given an opportunity to respond to issues raised during a compliance review. This high proportion also shows that industry is willing to work with us to ensure the supply of listed medicines on the ARTG is compliant.

# 4. Biologicals

The *Australian Regulatory Guidelines for Biologicals* define the different Biological classes.

## 4.1. Inclusion of biologicals

**Table 23 Applications for biologicals received and on hand**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Applications received | | |
| Technical Master File (TMF) new | 0 | 2 |
| TMF annual updates | 8 | 6 |
| TMF variations | 7 | 9 |
| TMF notifications | 8 | 7 |
| Plasma Master File annual updates | 16 | 15 |
| Biological Class 2 – new applications | 1 | 2 |
| Biological Class 3 – new applications | 0 | 2 |
| Biological Class 2 – variations | 5 | 26 |
| Biological Class 3 – variations | 2 | 2 |
| Total received | 47 | 71 |
| Applications on hand | | |
| TMF new | 3 | 2 |
| TMF annual updates | 6 | 4 |
| TMF variations | 0 | 2 |
| TMF notifications | 2 | 0 |
| Plasma Master File annual updates | 15 | 3 |
| Biological Class 2 – new applications | 5 | 3 |
| Biological Class 3 – new applications | 2 | 4 |
| Biological Class 2 – variations | 1 | 7 |
| Biological Class 3 – variations | 5 | 1 |
| Total on hand | 39 | 26 |

**Table 24 Completed applications for Biologicals**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Technical Master File (TMF) new | 1 | 2 |
| TMF annual updates | 4 | 5 |
| TMF variations | 6 | 7 |
| TMF notifications | 5 | 7 |
| Plasma Master File annual updates | 17 | 14 |
| Biological Class 2 – new applications | 15 | 4 |
| Biological Class 3 – new applications | 4 | 0 |
| Biological Class 2 – variations | 1 | 21 |
| Biological Class 3 – variations | 4 | 5 |
| Total completed | 57 | 65 |

# 5. Medicine and vaccine adverse event reports

## 5.1. Adverse medicine and vaccine reaction notifications

**Table 25 Source of notifications of medicine and vaccine adverse reaction**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Reports with clear causality by reporter | | |
| Hospitals | 2,402 | 2,194 |
| Companies | 8,946 | 8,776 |
| General practitioners | 745 | 644 |
| Specialists | 228 | 221 |
| Pharmacists | 1,232 | 883[a] |
| Members of the public (consumers) | 550 | 813 |
| Nurses, dentists, complementary healthcare practitioners | 224 | 214 |
| State/Territory Health departments | 2,560 | 2,619 |
| Reports withdrawn, or rejected, or without clear causality | | |
| | 1,770 | 1,269 |
| Total received | 18,657 | 17,633 |
| Mean number of reports received weekly | 359 | 339 |
| Vaccine reports included in above table | 3,259 | 3,361 |

[a] Pharmacist reporting classifications changed between the two reporting periods and some non-community pharmacist reports are now included in the other categories.

# 6. Medical devices

The regulatory framework for medical devices spans the life cycle for these products, including:

- **Conformity assessment:** Is the systematic examination by the manufacturer to determine that a medical device is safe and performs as intended and, therefore, conforms to the Essential Requirements. Certification of the manufacturer's conformity assessment procedure may (and in some cases must) be undertaken by the TGA, or we may recognise conformity assessment certification from European notified bodies.
- **Inclusion on the ARTG:** Medical devices cannot be imported, supplied in, or exported from Australia unless they are included on the ARTG (unless a valid exemption applies)[1]. A sponsor can apply to include a medical device on the ARTG if the device complies with the Essential Principles and appropriate conformity assessment procedures have been applied to the device (typically demonstrated through conformity assessment certification).
- **Post-market monitoring:** Once a medical device has been included on the ARTG the device must continue to meet all the regulatory, safety and performance requirements and standards that were required for the approval.

## 6.1. Conformity assessment

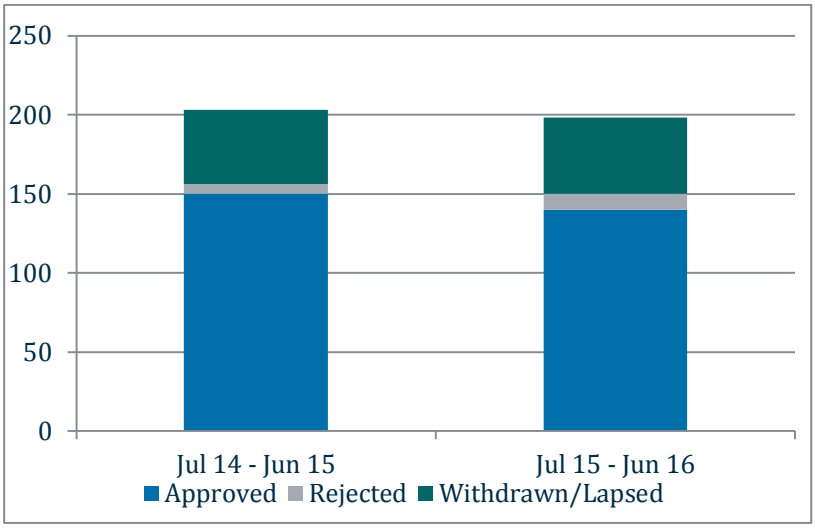
### 6.1.1. Applications

**Table 26 Number of conformity assessment applications (medical devices including In-Vitro Diagnostics (IVDs))**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Applications received | 193 | 257 |
| Applications on hand | 238 | 178 |
| Applications completed | 208 | 186 |

### 6.1.2. Outcomes

**Figure 7 Outcomes of conformity assessment applications**




[1] Exemptions include custom made medical devices, importation of samples, etc.

### 6.1.3. Processing times

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

Processing time is defined as the number of working days from the acceptance of the application until formal notification of decision. Under the *Therapeutic Goods Regulations 1990*, working days exclude public holidays and weekends. Processing time excludes time where we were unable to progress the application until the sponsor provided additional information unless otherwise specified.

**Table 27 Percentage of applications completed within target processing time**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New devices | 100% | 100% |
| Mean TGA processing times (days) | 130 | 133 |
| Median TGA processing times (days) | 161 | 178 |
| Changes or recertification | 100% | 100% |
| Mean TGA processing times (days) | 84 | 93 |
| Median TGA processing times (days) | 51 | 71 |

## 6.2. Inclusion of medical devices (including IVDs)

### 6.2.1. Applications

**Table 28 Applications for inclusion – medical devices (including IVDs)**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Class 1 medical devices[a] | | |
| Applications received | 2,503 | 2,685 |
| Applications completed | 2,497 | 2,690 |
| Class 1 measuring medical devices | | |
| Applications received | 74 | 48 |
| Applications completed | 74 | 48 |
| Applications on hand[b] | 4 | 2 |
| Class 1 sterile medical devices | | |
| Applications received | 249 | 257 |
| Applications completed | 265 | 253 |
| Applications on hand[b] | 7 | 11 |
| Class IIa medical devices | | |
| Applications received | 1,284 | 1,178 |
| Applications completed | 1,382 | 1,206 |
| Applications on hand[b] | 85 | 58 |

| | 2014-15 | 2015-16 |
|---|---|---|
| Class IIb medical devices | | |
| Applications received | 768 | 654 |
| Applications completed | 760 | 716 |
| Applications on hand[b] | 61 | 40 |
| Class III medical devices | | |
| Applications received | 425 | 344 |
| Applications completed | 372 | 249 |
| Applications on hand[b] | 260 | 313 |
| Class III Joint Reclassification medical devices[c] | | |
| Applications received | 637 | 0 |
| Applications completed | 364 | 355 |
| Applications on hand[b] | 538 | 294 |
| Active Implantable Medical Devices (AIMD) | | |
| Applications received | 51 | 49 |
| Applications completed | 46 | 19 |
| Applications on hand[b] | 51 | 62 |
| Class 1 IVDs[d] | | |
| Applications received | 156 | 92 |
| Applications completed | 158 | 112 |
| Applications on hand[b] | 7 | 1 |
| Class 2 IVDs | | |
| Applications received | 246 | 104 |
| Applications completed | 227 | 148 |
| Applications on hand[b] | 30 | 10 |
| Class 3 IVDs | | |
| Applications received | 223 | 65 |
| Applications completed | 183 | 131 |
| Applications on hand[b] | 22 | 11 |
| Class 4 IVDs | | |
| Applications received | 57 | 25 |
| Applications completed | 55 | 29 |
| Applications on hand[b] | 0 | 0 |

[a] Class I medical devices are automatically included (i.e. these applications are complete within 24 hours), there are no applications for this classification of device 'on hand'. Differences in the number received and finalised relate to those applications received on the last day of the reporting period.

[b] Applications on hand – figures shown are correct as of the date when the data was extracted. There may also be delays between the date of the decision and the time when the system is updated due to administrative and/or technological processes.

[c] The transition period for joint reclassification finished on 30 June 2015. A large number of applications were received at the end of this transition period, late in the January to June 2015 reporting period. As the transition period has now finished Class III joint reclassification applications will be rolled into the general Class III applications in future reports.

[d] The number of applications for Class 1 IVD includes auto-included devices and devices selected for audit.

### 6.2.2 Outcomes

Class I automatically included medical devices are not counted in the outcomes for inclusion applications as these applications cannot be rejected.

**Table 29 Outcomes of medical device applications by classification**

| | Number of applications | | | | | |
|---|---|---|---|---|---|---|
| | 2014-15 | | | 2015-16 | | |
| **Device Classification** | **Approved/ Accepted** | **Rejected/ Lapsed** | **Withdrawn** | **Approved/ Accepted** | **Rejected/ Lapsed** | **Withdrawn** |
| Class 1 | 2,497 | 0 | 0 | 2,690 | 0 | 0 |
| Class 1 Measurement | 59 | 2 | 13 | 47 | 0 | 1 |
| Class 1 Sterile | 246 | 3 | 12 | 234 | 0 | 19 |
| Class IIa | 1,285 | 11 | 67 | 1,132 | 2 | 72 |
| Class IIb | 701 | 5 | 38 | 679 | 1 | 36 |
| Class III | 267 | 41 | 15 | 207 | 12 | 30 |
| Class III Reclassification | 344 | 1 | 44 | 278 | 7 | 70 |
| AIMD | 27 | 1 | 0 | 17 | 0 | 2 |
| Class 1 IVD | 148 | 0 | 1 | 112 | 0 | 0 |
| Class 2 IVD | 204 | 1 | 17 | 136 | 3 | 9 |
| Class 3 IVD | 144 | 2 | 21 | 123 | 1 | 7 |
| Class 4 IVD | 53 | 0 | 2 | 28 | 0 | 1 |

### 6.2.3. Processing times

The agreed target time for level 1 application audits is 30 TGA work days and for level 2 application audits is 60 TGA work days (reflected in 'TGA days'). This does not include the period we are waiting for information or payment of fees (reflected in 'sponsor days').

**Table 30 Processing times for medical device application audits (including IVDs)**

| | 2014-15 | | | 2015-16 | | |
|---|---|---|---|---|---|---|
| | **Number of applications** | **Sponsor days** | **TGA days[b]** | **Number of applications** | **Sponsor days** | **TGA days[b]** |
| **Mean Processing Time** | | | | | | |
| Medical devices | | | | | | |
| Applications completed without audit | 2,183[a] | | | 2,112[a] | | |
| Non-compulsory audit[c] | 258 | 30 | 49 | 497 | 30 | 43 |
| Level 1 compulsory audit | 23 | 17 | 15 | 32 | 27 | 26 |
| Level 2 compulsory audit | 289 | 51 | 111 | 205 | 55 | 161 |
| IVDs | | | | | | |
| Applications completed without audit | 299[a] | | | 148[a] | | |
| IVD non-compulsory audit | 10 | 47 | 43 | 17 | 41 | 65 |
| IVD compulsory audit | 149 | 25 | 29 | 159 | 26 | 45 |
| **Median Processing Time** | | | | | | |
| Medical devices | | | | | | |
| Applications completed without audit | 2,183[a] | | | 2,112[a] | | |
| Non-compulsory audit[c] | 258 | 23 | 29 | 497 | 21 | 21 |
| Level 1 compulsory audit | 23 | 16 | 11 | 32 | 23 | 9 |
| Level 2 compulsory audit | 289 | 36 | 97 | 205 | 49 | 158 |
| IVDs | | | | | | |
| Applications completed without audit | 299[a] | | | 148[a] | | |
| IVD non-compulsory audit | 10 | 44 | 23 | 17 | 33 | 58 |
| IVD compulsory audit | 149 | 22 | 25 | 159 | 21 | 41 |

[a] Auto-included applications for Class I and Class 1 IVD are complete within 24 hours, and not included in the figures above.

[b] TGA time starts when the application is selected for audit, and it does not include public holidays and weekends, and the time when we wait for information or payment from the sponsor.

[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 (EC) certificates issued by certain notified bodies (for details see https://www.tga.gov.au/increased-application-audit-requirements-some-medical-devices-applications).

## 6.3. Post-market monitoring

### 6.3.1. Automatically included entries

As Class I medical devices are automatically included without review by the TGA, post-market regulatory reviews are undertaken to ensure Class I devices are correctly included. This includes restricted word reviews, where applications for Class I devices are identified by the use of specific words indicative of risk or issues relating to the inclusion of the device, and targeted reviews that are initiated on a case by case basis (targeted reviews are conducted in relation to devices of any Class).

**Table 31 Restricted word and targeted Class I medical device reviews**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Restricted word reviews | | |
| Reviews completed | 7 | 0 |
| Reviews commenced | 4 | 1 |
| Reviews on hand | 0 | 1 |
| Targeted reviews | | |
| Reviews completed | 157 | 104 |
| Reviews commenced | 79 | 83 |
| Reviews on hand | 117 | 164 |

### 6.3.2. Post-market reviews

The TGA also undertakes a range of post market reviews for devices above Class I.

**Table 32 Medical device targeted reviews**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Post market reviews | | |
| Reviews commenced – number of ARTG entries | 98 | 80 |
| Reviews completed – number of ARTG entries | 119 | 83 |
| Reviews on hand – number of ARTG entries | 183 | 163 |

### 6.3.3. Medical device incident reports

Processing time is defined as the number of working days from the receipt of the notification until the incident has been investigated and resolved. Under the *Therapeutic Goods Regulations 1990*, working days exclude public holidays and weekends.

The target timeframe for processing of medical device incident reports is 90 working days.

**Table 33 Number of medical device incident reports and processing times**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Reports received | 3,237 | 3,841 |
| Reports completed | 4,140 | 3,608 |
| Reports still in progress | 324 | 207 |
| Processing time | | |
| Mean TGA processing time (days) | N/A | 14 |
| Median TGA processing time (days) | N/A | 1 |
| Percentage processed within target timeframe | N/A | 100% |

**Table 34 Medical device incident report outcomes[a]**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Reviewed and used for trend analysis purposes | 3,049 | 2,988 |
| Reviewed, no further action required | 1,081 | 330 |
| Product recall | 62 | 40 |
| Recall for product correction | 18 | 19 |
| Hazard alert | 60 | 25 |
| Product notification | 1 | 1 |
| Safety alert | 19 | 9 |
| Product enhancement/improvement notice | 2 | 0 |
| Instructions for use amended | 26 | 3 |
| Referral for post-market review | 75 | 23 |
| Referral to TGA Office of Manufacturing Quality | 1 | 5 |
| Refer to another TGA Office | 55 | 46 |
| Company warned | 2 | 0 |
| Product suspended from ARTG | 0 | 0 |
| Product cancelled from ARTG | 6 | 4 |
| Manufacturing process improvements | 30 | 10 |
| Quality system process improvements | 11 | 1 |
| Maintenance carried out by the hospital | 0 | 0 |
| Change to design | 14 | 13 |
| Not device related | 7 | 9 |
| Other | 163 | 39 |

[a] Outcomes are not mutually exclusive.

# 7. Exports

Processing time is defined as the number of working days from the acceptance of the application, including payment, until formal notification of decision. Under the *Therapeutic Goods Regulations 1990*, working days exclude public holidays and weekends. Processing time excludes time where we were unable to progress the application until the sponsor provided additional information unless otherwise specified.

## 7.1. Export only medicines

The target timeframe for processing of export only medicine applications and variations is 31 working days.

**Table 35 Approval times for export only medicines**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New applications | | |
| Mean TGA processing time (days) | 20.5 | 21 |
| Median TGA processing time (days) | 20 | 20 |
| Percentage processed within target processing time | 100% | 98% |
| Variations | | |
| Mean TGA processing time (days) | 12.5 | 18 |
| Median TGA processing time (days) | 12 | 16 |
| Percentage processed within target processing time | 99% | 100% |

**Table 36 Applications for new and variations to export only medicines**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Applications received | 214 | 241 |
| Applications awaiting response from sponsor | 23 | 20 |
| Applications completed | | |
| Approved | 100[a] | 221 |
| Withdrawn | 2[a] | 10 |
| Total completed | 102[a] | 231 |

[a] Data collection commenced January 2015.

## 7.2. Export certifications for medicines

The target processing time for applications for an export certificate for a medicine is 15 working days.

**Table 37 Export certification applications and processing times**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Applications received | 2,190 | 2,124 |
| Applications completed | | |
| Approved | 2,179 | 2,127 |
| Withdrawn | 4 | 18 |
| Total completed | 2,183 | 2,145 |
| Processing times | | |
| Mean TGA processing time (days) | 12.5 | 12.1 |
| Median TGA processing time (days) | 12 | 12 |
| Percentage processed within target time[a] | 98% | 98% |

[a] We aim to have 100% of applications processed within the target timeframe.

## 7.3. Export certification assessment for medical devices

The target processing time for applications for an export certificate for a medical device is 5 working days.

**Table 38 Medical device applications and processing times for export certification assessments**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Applications received | 580 | 496 |
| Applications completed | | |
| Export certificates issued | 582 | 483 |
| Applications withdrawn | 13 | 3 |
| Total completed | 595 | 486 |
| Processing time | | |
| Mean TGA processing time (days) | 3 | 4 |
| Median TGA processing time (days) | 3 | 5 |
| Percentage processed within target time[a] | 95% | 96% |

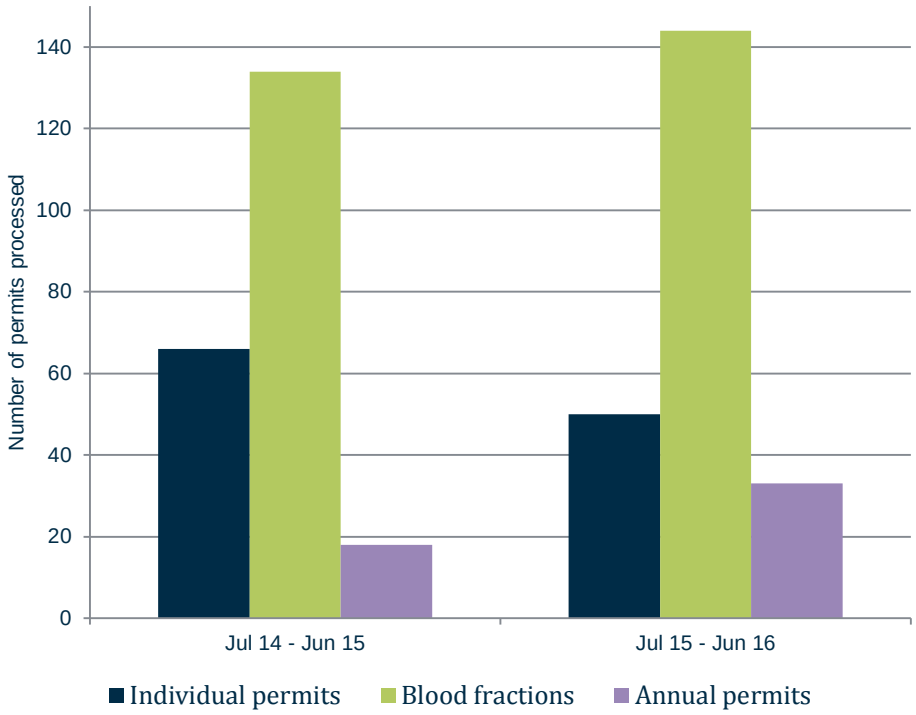
[a] We aim to have at least 90% of applications processed within the target timeframe.

## 7.4. Blood permits for export

The TGA issues permits to export human blood and its fractions (products derived from human blood) on receiving written applications from medical professionals, hospitals and bone banks. Most often these professionals or health organisations approach the Australian Red Cross which then applies for the permit on their behalf. Very rarely an individual citizen may also apply with reference to his/her requirement, for example, a patient travelling overseas with Biostate ® injections, which is a blood fraction and requires a permit to take it out of Australia.

In addition to issuing individual permits, the TGA also issues annual permits. Applications for these permits are submitted by commercial (pharmaceutical companies) or government organisations (such as the Australian Defence Force). The permits cover one year's worth of anticipated export supplies for these organisations.

**Figure 8 Number of blood permits processed**



# 8. Access to unapproved therapeutic goods

## 8.1. Special access scheme

The Special Access Scheme (SAS) provides for the import and/or supply of an unapproved therapeutic good for a single patient, on a case by case basis. Patients are grouped into two categories under the scheme:

- Category A: persons who are seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment. In this case prescribers are required to *notify* the TGA of the use.
- Category B: all other patients. In this case prescribers are required to *apply* to the TGA for the use.

**Table 39 SAS medicine notifications and applications**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Category A notifications | | |
| Total Category A notifications | 37,860 | 38,806 |
| Category B applications | | |
| Approved | 21,207 | 19,307 |
| Cancelled | 500 | 312 |
| Rejected | 61 | 51 |
| Pending at end of reporting period | 117 | 443 |
| Total Category B applications | 21,885 | 20,113 |

**Table 40 SAS device notifications and applications**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Category A notifications | | |
| Total Category A notifications | 3,456 | 3,922 |
| | | |
| Approved | 2,071 | 2,081 |
| Cancelled | 175 | 116 |
| Rejected | 27 | 20 |
| Pending at end of reporting period | 22 | 16 |
| Total Category B applications | 2,295 | 2,233 |

**Table 41 SAS biological notifications and applications**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Category A notifications | | |
| Total Category A notifications | 115 | 44 |
| Category B applications | | |
| Approved | 2,442 | 3,171 |
| Cancelled | 0 | 25 |
| Rejected | 1 | 0 |
| Pending at end of reporting period | 22 | 35 |
| Total Category B applications | 2,465 | 3,231 |

## 8.2. Clinical trials

Clinical trial notifications (CTNs) provide access to unapproved therapeutic goods where patients are participating in a clinical trial. Unapproved therapeutic goods can include biologicals, devices or medicines or a combination of any of the three types of goods.

The CTN scheme transitioned from a paper-based submission form to an online submission on 1 July 2015.

The online CTN system is capable of enhanced, automated reporting that provides further granularity and accuracy that was not previously possible with the paper-based system. Where the data collection between the paper-based and the online system are capable of being compared, the comparative data is supplied.

**Table 42 Number of notifications for new clinical trials involving unapproved therapeutic goods received by therapeutic good type**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Medicine | 506 | 458 |
| Device | 140 | 155 |
| Biological | 8 | 21 |
| Medicine and device | 347 | 288 |
| Device and biological | 1 | 6 |
| Medicine and biological | 0 | 14 |
| Medicine, device and biological | N/A[a] | 7 |
| Total | 1,002 | 949 |

Device includes both medical device and therapeutic device category.

[a] Not Available. This information was not previously reported under the paper-based CTN system.

**Table 43 Number of phases in new clinical trial notifications involving unapproved therapeutic goods received**

| | 2015-16 |
|---|---|
| | Jul-Jun |
| Clinical trial type | |
| Phase 1 | 205 |
| Phase 2 | 217 |
| Phase 3 | 301 |
| Phase 4 | 146 |
| Bioavailability/equivalence | 39 |
| None specified | 134 |

The new, online system is capable of enhanced reporting due to the additional capability of capturing multi-phase trials, which was not previously possible with the paper-based system.

**Table 44 Number of notifications for new clinical trials and variations to previously notified clinical trials, including non-fee attracting variations, involving unapproved therapeutic goods received by therapeutic good type**

| | 2015-16 |
|---|---|
| | Jul-Jun |
| Medicine | 1,090 |
| Device | 249 |
| Biological | 31 |
| Medicine and device | 1,072 |
| Device and biological | 20 |
| Medicine and biological | 37 |
| Medicine, device and biological | 27 |
| Total | 2,526 |

A variation may include any change to a previously notified clinical trial such as an additional site, change to a therapeutic good, or change in principal investigator etc.

Device includes both medical device and therapeutic device category.

The new, online system captures the actual number of notifications received for new clinical trials and requests to change significant details to clinical trials already notified (such as changes in the principal investigator, HREC and site address) which was not previously possible with the paper-based system. Furthermore, the new reporting system does not count variations that are made to a notified CTN that are of an editorial nature (e.g., fixing a typographical error) and counts the number of notifications and not the number of variations made within each notification.

**Table 45 Number of phases in new clinical trials and variations to previously notified clinical trials involving unapproved therapeutic goods received**

| | 2015-16 |
|---|---|
| | Jul-Jun |
| Phase 1 | 415 |
| Phase 2 | 598 |
| Phase 3 | 1,177 |
| Phase 4 | 274 |
| Bioavailability/equivalence | 46 |
| None specified | 217 |

A variation may include any change to a previously notified clinical trial such as an additional site, change to a therapeutic good, or change in principal investigator.

## 8.3. Authorised prescribers

The Authorised Prescriber Scheme allows approved medical practitioners authority to prescribe a specified unapproved therapeutic good(s) to patients who are identified by their medical condition. If a medical practitioner becomes an Authorised Prescriber they may prescribe the product to patients in their immediate care, within the indication specified, without seeking further approval from the TGA.

**Table 46 Authorised prescriber approvals for medicines and medical devices**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Number of approvals for medicines | 680 | 661 |
| Number of approvals for medical devices | 273 | 238 |

# 9. Medicines and biologicals manufacturing

## 9.1. Manufacturing licences issued to Australian manufacturers

**Table 47 Status of manufacturing licence applications**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New licences granted | 19 | 15 |
| Withdrawn application | 56 | 11 |
| Revoked licences – at request of licence holder | 28 | 42 |
| Revoked licences – TGA | 0 | 0 |
| Suspended – at request of licence holder | 0 | 3 |
| Suspended – TGA | 0 | 0 |

As at 30 June 2016, there were 248 Australian companies holding manufacturing licences covering 384 sites.

**Table 48 Outcomes of inspections of Australian manufacturers**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Inspections conducted | 198 | 220 |
| Satisfactory compliance (of completed inspections) | 92% | 81% |
| Marginal compliance (of completed inspections) | 8% | 18% |
| Unacceptable (of completed inspections) | 0% | 1% |
| In Progress[a] | N/A | 15% |
| Processing time | | |
| Initial inspections conducted within 3 months of application | 88% | 68% |
| Re-inspections conducted within 6 months of due date | 36% | 54% |

[a] Previous reports excluded inspections that had been conducted during the reporting period but had not yet been closed out. To ensure we report on all activities conducted by the TGA, the report for the current reporting period has been adjusted.

Applicants sometimes submit applications for Good Manufacturing Practice (GMP) licences before completing all of their systems and processes, resulting in requests to delay the initial inspection. It is therefore common for initial applications to be conducted later than the target of 3 months.

## 9.2. Approval (certification) of overseas manufacturers

**Table 49 Manufacturing certification application by status**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| New applications received | 94 | 38 |
| Re-inspection applications | 152 | 52 |
| Applications completed | | |
| Certified | 115 | 44 |
| Rejected | 137 | 28 |
| Total completed | 252 | 72 |

As at 30 June 2016, there were 374 overseas manufacturers covering 387 manufacturing sites that are subject to TGA inspection and approximately 2,200 overseas manufacturing sites that rely on evidence from recognised regulators.

**Table 50 Outcomes of inspections of overseas manufacturers**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Inspections conducted | 133 | 76[a] |
| Satisfactory compliance (of completed inspections) | 90% | 95% |
| Marginal compliance (of completed inspections) | 9% | 4% |
| Unacceptable (of completed inspections) | 1% | 1% |
| In Progress[b] | N/A | 18% |
| Processing time | | |
| Initial certification inspections conducted within 6 months of application | 63% | 40% |
| Certification re-inspections conducted within 6 months of due date | 59% | 75% |

[a] In 2014-15 we conducted a higher than usual number of overseas inspections to clear a backlog of overdue inspections. We have cleared this backlog so 2015-16 reflects business as usual.

[b] Previous reports excluded inspections that had been conducted during the reporting period but had not yet been closed out. To ensure we report on all activities conducted by the TGA, the report for the current reporting period has been adjusted.

Applicants sometimes submit applications for GMP certification before completing all of their systems and processes, resulting in requests to delay the initial inspection. It is therefore common for initial applications to be conducted later than the target of 6 months.

## 9.3. Good Manufacturing Practice (GMP) clearances

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

**Table 51 GMP clearance application status**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Applications received | 4,048 | 5,657 |
| Applications completed | | |
| Approved | 4,447 | 5,132 |
| Rejected | 315 | 263 |
| Total completed | 4,762 | 5,395 |

# 10. Recalls

## 10.1. Medicine recalls

**Table 52 Medicine recalls by reason for recall**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Adverse reactions | 2 | 0 |
| Foreign matter | 6 | 5 |
| Illegal supply | 0 | 1 |
| Impurity and degradation | 7 | 6 |
| Labelling and packaging | 13 | 18 |
| Micro-organisms | 2 | 4 |
| pH | 2 | 0 |
| Potency | 2 | 5 |
| Sterility | 2 | 1 |
| Other[a] | 9 | 17 |
| Total | 45 | 57 |

[a] 'Other' includes dissolution, physical defects, observed differences, variable content, diagnostic inaccuracy and wrong product.

## 10.2. Medical device recalls

**Table 53 Medical device (including IVDs) recalls by reason for recall**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Adverse incidents | 4 | 6 |
| Diagnostic inaccuracy | 71 | 82 |
| Electrical defect | 41 | 49 |
| Illegal supply | 1 | 0 |
| Labelling and packaging | 99 | 119 |
| Mechanical and physical defects | 193 | 173 |
| Software defects | 114 | 135 |
| Sterility | 9 | 3 |
| Other[a] | 45 | 44 |
| Total | 577 | 611 |

[a] 'Other' includes bioavailability, disintegration/dissolution, microbial contamination, variable content, foreign matter, impurity, wrong product, therapeutic inefficiency and observed differences.

## 10.3. Biological recalls

**Table 54 Biological recalls**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul-Jun | Jul-Jun |
| Recalls to hospital level | 0 | 0 |

# 11. Laboratory testing

The Laboratories Branch conducts post-market monitoring and compliance testing, investigations and reviews, as well as market authorisation assessment of therapeutic goods.

The Laboratories Branch identifies and prioritises therapeutic goods for testing to fulfil the regulatory compliance and monitoring requirements of the TGA, and the transparency and accountability requirements of government. The testing program also provides flexibility and capacity to provide testing for investigations into problem reports, complaints and urgent public health concerns.

The Laboratories Branch uses a risk management approach, which is consistent with *ISO 31000: Risk Management principals and guidelines,* to identify products with a higher risk of not complying with the required quality standards. This risk based, targeted approach to testing is reflected in the failure rates reported in Table 55.

**Table 55 Samples and products tested by type of therapeutic good and percentage which failed**

| | | 2014-15 | 2015-16 |
|---|---|---|---|
| | | Jul-Jun | Jul-Jun |
| Prescription medicines | Total | 861 | 941 |
| | % fail | 0.7 | 0.5 |
| OTC medicines | Total | 42 | 47 |
| | % fail | 31.0 | 19.1 |
| Complementary medicines | Total | 156 | 108 |
| | % fail | 21.2 | 20.4 |
| Medical devices | Total | 117 | 114 |
| | % fail | 14.5 | 29.8 |
| Contract[a] | Total | 83 | 19 |
| | % fail | 8.4 | 36.8 |
| Unregistered[b] | Total | 277 | 467 |
| | % fail | 66.1 | 76.2 |
| Total samples[c] | | 1,992 | 2,202 |
| Total samples (excluding AHQ samples) | | 1,536 | 1,696 |
| Percentage fail | | 16.9% | 25.5% |
| Total number of products tested[d] | | 756 | 761 |

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

[b] 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.

[c] Includes accreditation, harmonisation and quality control (AHQ) samples.

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

**Table 56 Samples that failed laboratory testing by reason for July 2015 to June 2016**

| | Medical devices | OTC medicines | Prescription medicines | Unregistered products | Complementary medicines | Total |
|---|---|---|---|---|---|---|
| Contamination | 5 | 0 | 0 | 0 | 2 | 7 |
| Formulation | 6 | 3 | 4 | 346 | 15 | 374 |
| Label and packaging deficiencies | 11 | 6 | 0 | 0 | 4 | 21 |
| Performance | 6 | 0 | 0 | 0 | 1 | 7 |
| Physical or mechanical properties | 6 | 0 | 1 | 0 | 0 | 7 |
| Unregistered | 0 | 0 | 0 | 10 | 0 | 10 |
| Total | 34 | 9 | 5 | 356 | 22 | 426 |

**Table 57 Batch release and export certification**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul–Jun | Jul-Jun |
| Batch release[a] | 394 | 401 |
| Export certification[b] | 14 | 59 |

[a] Evaluation of batch release documentation for vaccines, biotechnology and blood products.

[b] Certification of biological products being exported from Australian manufacturers to overseas markets.

The Laboratories Branch provides World Health Organization-approved certificates for batches of biological products to be exported by Australian manufacturers to overseas markets. The number of certificates provided by the Laboratories Branch therefore depends on the number of requests received.

**Table 58 Target timeframes in working days for laboratory testing by priority and testing type**

| Priority of testing | Biochemical/ chemical testing | Microbiological testing | Medical device testing |
|---|---|---|---|
| Urgent | 20 (95% of target times to be met) | 40 (95% of target times to be met) | 20 (95% of target times to be met) |
| Priority | 40 (80% of target times to be met) | 50 (80% of target times to be met) | 40 (80% of target times to be met) |
| Routine | 50 | 50 | 50 |

Testing on products linked to potential public safety concerns are assigned to the 'Urgent' testing category. Urgent testing may impact on the timeframes for priority and routing testing.

Priority is given to testing of products with the highest risk of a quality deficiency.

Compliance against these timeframes is outlined in Table 59.

**Table 59 Compliance with testing timeframes for July 2015 to June 2016**

| | Priority | Total | Percentage |
|---|---|---|---|
| Medical devices | Routine | 83 | 71% |
| | Priority | 26 | 96% |
| | Urgent | 5 | 100% |
| OTC medicines | Routine | 32 | 38% |
| | Priority | 10 | 100% |
| | Urgent | 5 | 100% |
| Prescription medicines | Routine | 170 | 65% |
| | Priority | 13 | 46% |
| | Urgent | 8 | 100% |
| Complementary medicines | Routine | 88 | 72% |
| | Priority | 19 | 100% |
| | Urgent | 1 | 100% |
| Unregistered products | Routine | 82 | 1% |
| | Priority | 375 | 86% |
| | Urgent | 7 | 100% |

Low numbers of samples within categories may affect compliance percentages.

Samples involving complex biological assays are excluded from the target turnaround timeframes.

# 12. Regulatory compliance

Using signals from numerous sources as intelligence, the TGA Regulatory Investigations and Enforcement Unit conducts compliance and enforcement activities against a risk based compliance framework. Using principles of responsive regulation, a range of tools are utilised including encouragement and guidance to comply, restrictions or warnings, suspensions or sanctions and cancellations. At the apex, activities including investigations into illegal import or manufacture of unapproved and counterfeit therapeutic goods can result in criminal or civil court action. All compliance activities have the intended purpose of protecting public health.

**Table 60 Regulatory compliance investigations by final action taken**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul–Jun | Jul-Jun |
| Investigation in progress | 241 | 361 |
| Completed investigations | | |
| Warned | 689 | 946 |
| No offence detected | 141 | 185 |
| Goods released under Personal Import Scheme | 74 | 519 |
| Referred to another agency or department outside Health | 9 | 28 |
| Referred to another branch within the TGA | 4 | 10 |
| Filed for intelligence purposes | 0 | 55 |
| Finalised in a linked file | 0 | 11 |
| Import treated as abandoned goods by Customs | 0 | 3 |
| Recall of goods | 0 | 2 |
| Matters referred to the Commonwealth Director of Public Prosecutions | 1 | 1 |
| Total completed | 918 | 1,760 |

**Table 61 Types of products investigated[a]**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul–Jun | Jul-Jun |
| Complementary medicines | 486 | 463 |
| Prescription medicines | 860 | 1,802 |
| Medical devices | 156 | 98 |
| Homoeopathic medicines | 4 | 4 |
| OTC medicines | 86 | 45 |
| Biological products | 30 | 48 |
| Other | 31 | 66 |
| Total | 1,653 | 2,526 |

[a] Regulatory compliance investigations may include more than one type of product.

**Table 62 Regulatory compliance investigations by special interest categories**

| | 2014-15 | 2015-16 |
|---|---|---|
| | Jul–Jun | Jul-Jun |
| Unapproved product | 1,404 | 2,110 |
| Counterfeit product | 232 | 320 |
| Parallel import/export | 1 | 9 |
| Manufacture without licence | 0 | 1 |
| Advertising offence | 3 | 17 |
| Traditional Chinese medicines | 1 | 7 |
| Other[a] | 4 | 7 |
| Total | 1,645 | 2,471 |

[a] Products that fall outside the remit of the *Therapeutic Goods Act 1989,* for example food products.

**Table 63 Investigations by complainant type and state/territory for July 2015 to June 2016**

| Origin | ACT | NSW | NT | QLD | SA | VIC | WA | Other[a] | Total |
|---|---|---|---|---|---|---|---|---|---|
| Complaints resolution | 0 | 11 | 0 | 1 | 0 | 1 | 0 | 1 | 14 |
| Customs | 0 | 943 | 9 | 90 | 5 | 339 | 95 | 2 | 1,483 |
| External agency | 3 | 3 | 0 | 9 | 1 | 0 | 0 | 5 | 21 |
| General public | 1 | 29 | 0 | 5 | 1 | 10 | 1 | 83 | 130 |
| Patient/ practitioner | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 4 |
| Sponsor/client | 0 | 12 | 0 | 0 | 0 | 9 | 0 | 8 | 29 |
| TGA internal | 21 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 21 |
| Total | 25 | 998 | 9 | 107 | 8 | 359 | 96 | 100 | 1,702 |

[a] Other includes investigations of reports from Tasmania and anonymous (unknown) origin.

# Version history

| Version | Description of change | Author | Effective date |
|---|---|---|---|
| V1.0 | Original publication | Reporting and Collaboration Services | September 2016 |

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Reference/Publication #R16/578869