Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

TGA Prescription Medicines

Streamlined Submissions Process Newsletter

June 2012

The TGA—Safeguarding public health through the effective and timely regulation of therapeutic goods

Introduction

The TGA Prescription Medicines Streamlined Submissions Process Newsletter [formerly the *Prescription medicine BPR update* (*BPR update)]* reports on progress of the streamlined submission process.

In this edition:

Contact the Prescription medicine SSP team
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606
Telephone—02 6232 8444
Fax—02 6232 8140
streamlinedsubmission@tga.gov.au
(for current PPFs and submissions under streamlined process)
www.tga.gov.au

1—Impact of high application volume on TGA timelines

The first half of 2012 has seen a higher than usual number of applications submitted to the TGA. As an example, in January, April and June the TGA received 40 or more presubmission planning forms (PPFs). This consistently higher than usual volume of applications is stretching TGA resources and we anticipate that this will impact on application processing timelines. The TGA will continue to inform sponsors of any changes to milestone dates in the streamlined submission process letters.

2—Streamlined submission process

2.1 Summary of progress to date

The following is a summary of key statistics from applications lodged under the streamlined submission process since the end of the transition period. Due to the expansion and complexity of the summary statistics table, TGA will provide future progress to date of the streamlined submission process in a graph format only.

Number of applications

	Dec 2011	Jan 2012	Feb 2012	Mar 2012	Apr 2012	May 2012	Jun 2012
Number of PPFs lodged	22	46	35	26	40	32	48
Number not effective, deferred or withdrawn (%)	5 (23)	3 (6.5)	1 (2.9)	3 (11.5)	1 (2.5)	0 (0)	TBA
Number of subsequent submissions lodged	17	43	34	23	39	TBA	TBA
Number not effective, deferred or withdrawn (%)	4 (24)	0 (0)	0 (0)	1 (4.3)	TBA	TBA	TBA

Application types

	Dec 2011	Jan 2012	Feb 2012	Mar 2012	Apr 2012	May 2012	Jun 2012
A: NCE	2	8	2	2	1	6	6
B: New combination	1	1	1	2	0	1	3
C: Extension of indications	2	3	4	0	6	2	7
D: New generic	11	16	11	15	13	14	14
F: Major variation	1	3	2	1	3	4	4
G,H: Minor variation	0	3	1	1	1	1	2
J: Changes to PI	5	12	2	5	16	4	12
Total	22	46	35	26	40	32	48

2.2 Workflow analysis

The following is a summary of the number of calendar days taken to process specific types of applications from lodgement to decision of a submission. The data compares the quarterly average duration before and after the introduction of the streamlined submission process.

Workflow analysis before and after the streamlined submission process										
Application type	**Days elapsed from acceptance to decision**									
	Pre streamlined submission process					**Streamlined submission process**				
Period when decision finalised	Oct-Dec 2010	Jan-Mar 2011	Apr-Jun 2011	Jul-Sep 2011	Oct-Dec 2011	Oct-Dec 2010	Jan-Mar 2011	Apr-Jun 2011	Jul-Sep 2011	Oct-Dec 2011	Jan-Mar 2012
New Generic – type D											
Average Calendar Days	425	412	399	409	395	-	-	-	-	196	231
Average Work days	227	212	216	213	213	-	-	-	-	123	137
New Chemical Entities											
Average Calendar Days	379	467	443	457	395	-	-	-	-	-	326
Average Work days	190	237	228	237	225	-	-	-	-	-	204
Extension of Indication – type C											
Average Calendar Days	404	348	423	398	333	-	-	-	-	279	201
Average Work days	236	209	258	215	210	-	-	-	-	100	117
Major Variation – type F											
Average Calendar Days	274	393	345	394	355	-	-	-	-	-	246
Average Work days	168	207	199	211	204	-	-	-	-	-	140

2.3 Pre-submission planning form—common issues

The following information draws on common issues identified with pre-submission planning forms (PPF) lodged to date under the streamlined submission process. This information applies to all applications lodged under the streamlined submission process.

Pre-submission planning form—regulatory requirements		
Deficiency	**TGA requirement**	**TGA workflow impact**
Section 1.7 - GMP license or clearance scheduled to expire	It is a TGA requirement that for all manufacturers and finished product testing facilities involved in the active ingredient and/or product manufacture the sponsor must provide GMP licences or clearances with validity for at least 6 months after the scheduled full submission date. If, the GMP licences or clearances are due to expire in this period of time then the Certification Tracking Number for the renewal application lodged with the Office of Manufacturing Quality (OMQ) must be provided in Module 1.7.3 of the PPF. For more info: · Module 1.7 of *CTD- Module 1 Administrative Information and Prescribing Information for Australia* · Appendix C of *Information for sponsors completing a pre-submission planning form*	The TGA uses manufacturing licences (for Australian manufacturing sites) and good manufacturing practice (GMP) clearances (for overseas sites) to establish whether the manufacturing/processing standards are acceptable. Without valid manufacturing licences or GMP clearances, the TGA cannot evaluate the submission.
Section 1.6 – Drug Master File (DMF)	If the pre-submission form indicates that the submission will be making a reference to a Drug Master File then it is a TGA requirement that the Drug Master File number is provided in Section 1.6 of the PPF and the DMF is supplied both electronically and in hard copy prior to the submission dossier. For more info: · Attachment A of *Transitional Mandatory Guidelines for an Effective Submission* · Module 1.6 of *CTD- Module 1 Administrative Information and Prescribing Information for Australia* · Appendix 11 of the *Australian Regulatory Guidelines for Prescription Medicines*	The TGA requires that relevant DMF copies and details are provided with the PPF to enable access to information regarding the active substance at the time of submission. Without this information the TGA is unable to access essential information and evaluate the submission.

Pre-submission planning form—regulatory requirements		
Deficiency	**TGA requirement**	**TGA workflow impact**
Part 2 – Details of submission	The TGA is aware that there remain different understandings across industry regarding the TGA requirements to determine the scope and scale of an evaluation. The TGA would like to confirm that to ensure a PPF is accepted the requirements, instructions and explanations in the current (March 2011) PPF form and *Information for sponsors completing a pre-submission planning form* published on the TGA website is to be adhered to. Any alterations to the requirements will be only through the modification of the PPF form and associated publications. *For further questions contact the case management team:* — streamlinedsubmission@tga.gov.au	TGA requires the necessary information to arrange appropriate resourcing for the processing and evaluation of an application, including where relevant, the contracting of external evaluators. The information provided in the PPF allows the TGA to commit to timeframes for the evaluation of the application.

2.4 Streamlined submission process – first review

The TGA is currently conducting a review of the performance of the streamlined submission process with a view to introduce process improvements to address issues identified during the first 18 months of operation of the new process. The initial stages of the review will focus on milestones 5 to 8. The TGA has engaged with the Industry Working Group on the proposed refinements, and a very productive meeting of this group was held on 29 May 2012. The TGA is now following up on those discussions and developing process improvement options.

2.5 Meeting milestones

The streamlined submission process is based on a series of key dates and milestones, some of which involve the TGA providing certain information to sponsors, such as the planning letter at milestone 1 or the notification letter at milestone 2.

From May 2011 to December 2011, the TGA was not able to consistently meet the milestone dates associated with milestones 1 – 3. A number of reasons can be provided, such as

- resource challenges posed by the double-processing of applications under the previous process and the streamlined submission process,
- insufficient evaluation resources available to assess submissions; and
- additional workloads associated with the 48 hour 'grace period' that applied during the 12 month transition period.

The TGA has been taking action to address this issue, including procuring additional external evaluation resources to assist with clearing the backlog and assessing procedural options to improve our ability to meet these milestones. A key strategy has been to establish the case

management function, which was implemented in December 2011. The TGA announced this development in the December 2011 BPR Update.

These actions are having an impact. 84% of the planning letters for the combined December 2011/January 2012 batch were provided to sponsors within 3 days of the milestone 1 date. Given that this relates to 68 applications received in this batch and covers the TGA shutdown period and summer vacations for staff, this is an impressive achievement.

It can now be reported that from the February batch onwards, the TGA its meeting the milestone dates of the SSP in the majority of cases. Exceptions to this are when there are regulatory complex issues associated with a particular active ingredient or the PPF and supporting documentation or the submission dossier provided by the sponsor has been of poor quality requiring additional resources to identify and document the deficiencies.

2.6 Milestone dates

The TGA has received feedback via the IWG that sponsors require more clarity around the way that milestone dates are calculated in the SSP. The table below describes the standard business rules that are applied to submissions that are complete and of sufficient quality to facilitate their processing. It must be noted that for submissions that are complete but that suffer from data quality issues, the milestone dates will be adjusted to reflect the additional effort required by TGA evaluators and delegates. Sponsors are notified of these milestone dates that apply to their application via the planning and notification letters.

Milestone	Event description	Business rule for determining date
	Application processing commences on PPFs received in previous month	First working day(WD) of the month
	Assessment of PPF and supporting documents by evaluators	
	Organisation of external evaluation resources	
	Sponsor liaison and collation of information by case managers	
MS1	Planning letter due to be sent to the sponsor	15th of the next month or previous WD
	Submission dossier due to be provided to the TGA (*types A,B,C)	7th* and 14th of the month after MS1 or previous WDs
	Processing and logging of submission dossier by TGA Records Management	
	Administrative processing of submission	
	Assessment of dossier by evaluators	
	Sponsor liaison and collation of information by case managers	
MS2	Notification letter due to be sent to sponsors	Last WD of the month after MS1
	1st round evaluation due to commence	Next WD after MS2
	1st round evaluation and s.31 questions due for completion	Last WD three (regular) or four (large or complex) months after MS2
	Collation of information by case managers	

Milestone	Event description	Business rule for determining date
MS3	Consolidated s.31 questions and Module 3 evaluation report due to be sent to sponsor	Last WD of the month after previous date
MS4	s.31 response to be provided to the TGA by the sponsor	Next WD 30 or 60 days after MS3
	Logging of s.31 responses by TGA Records Management	
	2nd round evaluation due to commence	Next WD after MS4
	Collation of information by case managers	
MS5	2nd round evaluation reports to be sent to sponsor	Last WD of the month, a month after MS4
	Sponsor response to evaluation reports to be provided to the TGA	2 weeks after MS5
	Delegate's overview due to be sent to sponsor	PRE-SET DATE (must be at least 4 weeks after MS5)
	Pre-ACPM response	PRE-SET DATE
	Proposed ACPM Meeting	PRE-SET DATE
MS6	ACPM Outcomes	PRE-SET DATE
MS7	Delegate's decision letter due to be sent to sponsor	Last WD of the month of the ACPM Meeting
MS8	Administrative and registration activities complete	Last WD of the month after MS7

3—Risk management plans

To improve accessibility to information within the SSP the TGA is undertaking a pilot to provide final Risk Management Plan (RMP) evaluation reports at milestone 3.

The TGA will begin to progressively provide final RMP evaluation reports at milestone 3 with the consolidated section 31 request. This is a pilot exercise aimed at improving access to information. The standard RMP S31 question accompanying final RMP evaluation reports at milestone 3 will be as follows: *"Please provide information that is relevant and necessary to address the recommendations made in the RMP evaluation report."*

Sponsors should continue to be aware that safety considerations may be raised by the nonclinical and clinical evaluators through:

- the consolidated section 31 request; and/or
- the nonclinical and clinical evaluation reports respectively (when these reports are made available).

It is important to ensure that the information provided in response to these include a consideration of the relevance for the RMP, and any specific information needed to address this issue in the RMP. For any safety considerations so raised, please provide information that is relevant and necessary to address the issue in the RMP.

4—Fee arrangements

4.1 Online invoice generation for application fee payments through the streamlined submission process

Applicants are advised that the electronic Business Services (eBS) portal has been enhanced to automatically generate an invoice for an application fee after lodgement of a PPF.

As detailed in the July 2011 BPR Update, new fee arrangements for submissions lodged under the streamlined submission process commenced in July 2011. The new fee arrangements resulted from amendments to the Therapeutic Good Regulations 1990. Due to the changes in the legislation, there was a need to develop and implement enhancements to the TGA's eBS. **These changes are complete and applicants can now generate electronic invoices for application fees upon lodgement of their PPF.**

4.2 Transition to electronic invoicing of application fee

The TGA reminds applicants that an application fee is due and payable upon lodgement of the PPF. Please refer to the Summary of fees and charges to determine the relevant application fee for the application submitted. Paragraph 23(2)(a) of the *Therapeutic Goods Act 1989* (the Act) states than an application is not effective unless the application fee has been paid.

Applicants should continue to submit their payment directly to the TGA finance area using one of the prescribed payment methods and quoting the invoice number (e.g. ONLxxxxxx).

4.3 Payment of the evaluation fee

When the TGA accepts an application for evaluation, the applicant will be sent a notification letter as confirmation. The notification letter will specify the type of evaluation and the evaluation fee. Under section 24A of the Act, the evaluation fee is due and payable on the day the applicant is notified of the amount of the evaluation fee.

Under paragraph 24(2)(a) of the Act, an application lapses two months after the day on which the evaluation fee became due and payable (i.e., when the applicant was notified of the fee). The Act does not contain any provisions to grant extensions to applicants that fail to pay within this time. Payments can be made directly to the TGA finance area using one of the prescribed payment methods quoting the submission number (e.g. PM-2012-xxxxx-x) and Client I.D. or, upon being invoiced by the TGA.

4.4 Identification of the application to which the payment relates

It is the responsibility of the applicant to correctly identify the application to which the payment relates including payments made via EFTPOS. Identification of the application can occur through reference of the submission number (e.g. PM-xxxx-xxxx-x) or the invoice number (INV xxxxx, ONLxxxxxx).

5—Expert advisory committees

5.1 Implementation of Streamlined Submission Process changes

The ACPM meeting agendas now comprise almost entirely of SSP applications. The SSP business rules therefore apply to the relevant processes. This includes the timeline for the delivery of the ACPM outcomes. Work is currently underway to implement changes for alignment of the Pharmaceutical Subcommittee (PSC).

In addition, the TGA has taken the opportunity to streamline the outcomes notification process with the aim of delivering the full set of ACPM outcomes (extracted recommendation + minute) by the agreed milestone end date. This change adds significant value for sponsors as it modifies the previous process which involved the TGA delivering the extracted minute following the subsequent ACPM meeting (2 months after meeting where the application was discussed).

Please note that the alignment of Milestone 6 with the SSP will also provide predictable timeframes. The attached table illustrates the challenge in migrating from the previous "5 working day rule" for ACPM recommendations, in contrast to the "15th of the month rule" for the full outcome statement to be drafted, approved, ratified and delivered.

To implement these changes the TGA will advise each sponsor involved in the specific meeting about the new rules and will continue to do so for the remainder of 2012. We will also use this newsletter to advise all sponsors within the industry.

In addition, it is critical that sponsors fully comply with the requirements for their pre ACPM response. Unfortunately not all sponsors comply and this generates preventable delays and administrative burdens for the process.

ACPM outcome* delivery dates – impact of new business rules

ACPM meeting date		Previous 5 working day rule PART OUTCOME ONLY	Streamlined submission process
			15 month rule FULL OUTCOMES
285	3/08/2012	Fri 10 Aug	Wed 15 Aug
286	5/10/2012	Fri 12 Oct	Mon 15 Aug
287	7/12/2012	Fri 14 Dec	Fri 14 Dec
288	1/02/2013	Fri 8 Feb	Fri 15 Feb
289	5/04/2013	Fri 12 Apr	Mon 15 Apr
290	7/06/2013	Fri 14 Jun	Fri 14 Jun
291	2/08/2013	Fri 9 Aug	Thu 15 Aug

*Outcome = recommendation and full minute.

5.2 Pilot of new process and possible efficiencies within the Milestone 6

The TGA has initiated a pilot to test the feasibility and the impact of changes within milestone 6 to reduce the time required to complete this milestone.

The scope of the pilot involved:

- one week delay in due date for the delegates overview
- subsequent one week delay in the due date for the sponsors pre-ACPM response to the Delegates Overview.

Note that the one week delay does not impact on the scheduled ACPM meeting for the application and the sponsor has the same allocation of time to respond to the Delegates Overview.

All sponsors that have an application impacted by this pilot will receive communication from the Secretariat about the proposed changes to the process.

The TGA looks forward to advising sponsors of the outcomes for this pilot and confirmation of any new business rules under the SSP.

6—How does the TGA allocate submissions to ACPM meetings?

During the pre-submission phase, the TGA identifies the evaluation resources required for the submission. The evaluation plan and milestone dates for the submission are generated based on the business rules of the SSP, the size and complexity of the submission and the sponsors request for 30 or 60 days to respond to questions asked by the TGA after the first round evaluation. If the PPF is complete and effective, these dates are advised in the planning letter sent at milestone 1 (MS1).

Prior to the March 2012 batch of submissions, if an external evaluator was required, an extra month was added to the evaluation phase to allow this resource to be secured. Improvements to external evaluator procurement practices have now made this unnecessary and the extra month is no longer added. In the rare cases where an external evaluator can not be secured to evaluate a submission within the standard time frames, the TGA will work closely with the sponsor to develop an evaluation plan.

Milestone dates up to Milestone 5 (MS5) are generated according to standard business rules that apply to all submissions, as described in SSP guidance documents. After Milestone 5, there is a 2 week period for sponsors to notify the TGA of any error of omissions in the final evaluation reports relating to their submission. The next step in the SSP is the Delegate's Overview/ delegate's request for ACPM advice. This document is the Delegate's summary of the outcomes of the evaluation reports as well as the response by the sponsor to those reports.

The deadline for the Delegate's Overview to be completed and provided to the sponsor and the ACPM is determined by the ACPM Meeting Date. ACPM Meeting Dates are ratified 12-18 months in advance, as shown in Table 1.

Therefore the ACPM Meeting Date applicable to a particular submission is determined by identifying the next Delegate's Overview date after the deadline for sponsors to notify the TGA of any error of omissions in the final evaluation reports, as shown in Table 2.

If Milestone 5 falls on 30 November 2012, the deadline for sponsors to notify the TGA of any errors or omissions in the final evaluation reports is Friday 14 December and the Delegate's Overview for the February 2013 ACPM meeting is due on Monday 17 December. If there are no errors or omissions reported by the sponsor, no amendments are required to the Delegate's Overview so it may be dispatched on Monday 17 December and the submission may proceed to the February 2013 ACPM meeting. However if there is a response from the sponsor to MS5 evaluation reports, there will not be sufficient time to review and incorporate this response into the Delegate Overview by the deadline of 17 December 2012 and the submission will revert to the April 2013 ACPM meeting. Similarly, when Milestone 5 falls on 31 January 2013, the application may go to the April 2013 of June 2103 ACPM meeting depending on whether the sponsor provides a response to the evaluation reports which need to be incorporated into the Delegate's overview.

Table 1. Ratified ACPM meeting dates and associated deadlines

Meeting No.	Deadline for Delegate's Overview	Sponsor pre-ACPM response due	ACPM meeting date	ACPM outcomes (Milestone 6)
2012/4 (285)	27 June 2012	11 July 2012	**3 August 2012**	15 August 2012
2012/5 (286)	28 August 2012	11 September 2012	**5 October 2012**	15 October 2012
2012/6 (287)	31 October 2012	14 November 2012	**7 December 2012**	14 December 2012
2013/1 (288)	17 December 2012	8 January 2013	**1 February 2013**	15 February 2013
2013/2 (289)	22 February 2013	8 March 2013	**5 April 2013**	15 April 2013
2013/3 (290)	1 May 2013	15 May 2013	**7 June 2013**	14 June 2013
2013/4 (291)	26 June 2013	10 July 2013	**2 August 2013**	15 August 2013
2013/5 (292)	27 August 2013	10 September 2013	**4 October 2013**	15 October 2013
2013/6 (293)	30 October 2013	13 November 2013	**6 December 2013**	13 December 2013
2013/7 (294)	23 December 2013	14 January 2014	**7 February 2014**	14 February 2014

Table 2. Milestone 5 and next possible Delegate's overview date

Milestone 5 evaluation reports (last working day of the month)	Deadline for sponsor response to evaluation reports (2 weeks after MS5)	Next possible delegates Overview Date (>2 weeks after MS5)	ACPM Meeting Date
30 April 2012	14 May 2012	27 June 2012	**3 August 2012**
31 May 2012	14 June 2012	27 June 2012	**3 August 2012**
29 June 2012	13 July 2012	28 August 2012	**5 October 2012**
31 July 2012	14 August 2012	28 August 2012	**5 October 2012**
31 August 2012	14 September 2013	31 October 2012	**7 December 2012**
28 September 2013	12 October 2012	31 October 2012	**7 December 2012**
31 October 2012	14 November 2012	17 December 2012	**1 February 2013**
30 November 2012*	14 December 2012*	17 December 2012* or 22 February 2013*	**1 February 2013* or 5 April 2013***
10 January 2013	24 January 2013	22 February 2013	**5 April 2013**
31 January 2013	14 February 2013	22 February 2013 or 1 May 2013	**5 April 2013 or 7 June 2013**
28 February 2013	14 March 2013	1 May 2013	**7 June 2013**
29 March 2013	12 April 2013	1 May 2013	**7 June 2013**
30 April 2013	14 May 2013	26 June 2013	**2 August 2013**
31 May 2013	14 June 2013	26 June 2013	**2 August 2013**
28 June 2013	12 July 2013	27 August 2013	**4 October 2013**
31 July 2013	14 August 2013	27 August 2013	**4 October 2013**
30 August 2013	13 September 2013	30 October 2013	**6 December 2013**
30 September 2013	14 October 2013	30 October 2013	**6 December 2013**
31 October 2013	14 November 2013	23 December 2013	**7 February 2014**