Australian Government
Department of Health
Therapeutic Goods Administration

Accelerated assessment of medical devices – Priority Review pathway

Implementation

Version 1.0, November 2016

TGA Health Safety Regulation

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Contents

Glossary of abbreviations

ARTG	Australian Register of Therapeutic Goods
FDA	Food and Drug Administration (US)
MMDR	Medicines and Medical Devices Review
MSAC	Medical Services Advisory Committee
NRA	National Regulatory Authority – currently the TGA in Australia
PLAC	Prostheses List Advisory Committee
TGA	Therapeutic Goods Administration

Introduction

This paper outlines the proposed approach for implementing an accelerated assessment pathway for medical devices, referred to in this paper as Priority Review. This pathway will continue to require medical devices to meet the essential principles, including clinical evidence requirements, while expediting assessment through administrative changes.

Implementation of Priority Review as an accelerated assessment pathway is in response to Recommendation 15 and Recommendation 19 of the March 2015 report of the Medicines and Medical Devices Review (MMDR).

> **Recommendation Fifteen**
> The Panel recommends that: […]
>
> 2. In order to provide timely access to devices that are safe, high quality and fit for purpose, there be multiple pathways to seek approval for the inclusion of other classes of medical device in the ARTG. Such pathways to provide for: […]
>
>   **Pathway Three: Expedited approval of medical devices in certain circumstances.**
>
> **Recommendation Nineteen**
> The Panel recommends that:
>
> 1. The Australian government develop transparent criteria under which application may be made for accelerated assessment of novel medical devices for inclusion in the ARTG.
> 2. In circumstances where accelerated assessment is granted, the Australian NRA have capacity to place conditions on the inclusion of the medical device in the ARTG.

The recommendations were accepted by Government, and announced by Minister Ley on 15 September 2016.

In the MMDR, the panel formed a view that an expedited pathway should be consistent with that adopted by comparable overseas NRAs for accelerated assessment of medical devices. This recommendation in principle is similar to the Priority Review pathway of the US FDA, in that "granting Priority Review status means that a marketing application that is determined to be appropriate for priority review is placed at the beginning of the appropriate review queue and receives additional review resources, as needed."[1]

The MMDR also proposed expedited pathways for medicines in certain circumstances.[2] For medicines this includes both 'provisional approval' and 'priority review' pathways. The medical device accelerated assessment pathway proposed by the MMDR is to be a 'priority review' pathway.

Current environment

This section identifies existing processes and developments in progress to provide a context for the proposed implementation of the Priority Review pathway.

[1] FDA, May 2013, Priority review of premarket submissions for devices, Guidance for Industry and FDA staff, FDA Maryland U.S.A
[2] MMDR Report, Recommendation 3, Pathway 3, and related recommendations 8 and 10.

Mechanisms in place to expedite assessment within the TGA

There are several ways TGA currently, or will soon, interact with sponsors prior to submitting applications that can expedite the assessment process. These are outlined below.

1. **Pre-submission meetings:** Pre-submission meetings for conformity assessment applications, where the TGA advises on the requirements, including for the clinical evidence. Because novel devices are likely to lack depth of clinical evidence and often do not have predicate devices, pre-submission meetings can help identify gaps in clinical evidence prior to submitting an application, thus helping to avoid extensive delays if the submission had proceeded with inadequate clinical evidence.

2. **Guidance documentation:** Providing guidance documents for preparing an application, especially for the collection and submission of clinical evidence[3]. Inadequate clinical evidence is a major reason for assessment delays and one of the reasons for rejecting applications. This is relevant for both conformity assessment applications and applications for inclusion of devices in the ARTG that are subject to audit.

3. **EU conformity assessment:** TGA often accepts conformity assessment certification issued by a notified body in the European Union (EU) as evidence of the application of the appropriate conformity assessment procedures for the majority of medical devices. This means TGA does not expect manufacturers with medical devices properly covered under EC Certificates to submit a conformity assessment application to the TGA (however some applications for ARTG inclusion are selected for audit). Thus duplication in conformity assessments is reduced.

Accelerated approval and assessment methods of the US FDA

The US FDA Pre-Market Approval (PMA) assessment procedure is for new devices for which there are no existing predicates and is considerably different to the TGA approval process. It is often considered more rigorous in its clinical data requirements, while having a lesser regard for approvals outside of the US.

The US FDA Priority Review Pathway was created in 2008 and is a "front of the queue" approval pathway for devices addressing life-threatening or irreversibly debilitating conditions, theoretically without changes to premarket clinical data requirements. Between 2008 and 2015 18 devices were approved using this pathway and it is likely that there have been less than 10 medical device applications per year for the pathway[4], although this may have been increasing in recent years. Importantly, this is very different to medicine expedited pathways, where hundreds of applications have been submitted[5].

In 2011 the US FDA piloted a process called the Innovation Pathway, which later developed into the Expedited Access Pathway (EAP) available in 2015[6]. These pathways were designed to expedite the **development, assessment and review** of novel medical devices addressing life-

[3] TGA, March 2016, *Consultation: Draft Clinical Evidence Guidelines-Medical Devices*, version 1.0, TGA, Canberra, available at https://www.tga.gov.au/node/714419.
[4] U.S. Government Accountability Office (GAO), February 2012, FDA has met most performance goals but device reviews are taking longer, Report to congressional requesters, GAO Washington DC U.S.A, 2012
[5] GAO, December 2015, *FDA expedites many applications, but data for post approval oversight need improvement,* Report to the Ranking Member, Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, House of Representatives, GAO, Washington DC U.S.A.
[6] FDA, April 2015, Expedited Access for Premarket Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions, Guidance for Industry and FDA staff, FDA Maryland U.S.A.

threatening or irreversibly debilitating conditions with a "whole of life" approach. In these pathways the US FDA interacts with sponsors early and throughout device development. In its first year the EAP received 29 applications (17 of which were accepted). The MMDR recommendations do not suggest that TGA should introduce the EAP model. It is possible that, as the Priority Review pathway is the only option open in Australia for faster evaluation and potentially inclusion on ARTG, applications which would in USA apply via the Expedited Access Pathway may, in Australia, be submitted via the Priority Review pathway. This would affect the number of requests for Priority Review.

Issues to consider

Public health: The TGA seeks to protect public health by ensuring that therapeutic goods available for supply in Australia, including medical devices, are safe and fit for their intended purpose. It is important that any proposed changes do not unacceptably undermine public health protections while making available necessary therapeutics to the Australian public in a timely fashion.

Industry development: The flexibility of Priority Review for novel devices would allow faster marketing of products. Time to market is critical to the success of many new products and has a major impact on the commercial viability of many new innovations.

Current environment

- Are there any other environmental issues that would inform or benefit the development of this proposal?
- Are there other issues to be considered in developing this proposal?

Principles and criteria

The TGA approach to implementing recommendations from the Medicines and Medical Devices Review (MMDR) aims to reduce duplication of processes to support the MMDR recommendations. As Priority Review pathways are recommended for both medicines and medical devices:

- a common suite of principles are proposed to apply, and
- eligibility criteria for Priority Review will be aligned to the extent appropriate given the differences between medicines and medical devices.

This section details the proposed principles and selection criteria for Priority Review.

Principles for Priority Review

TGA is applying the following principles to guide the development of the expedited pathways for medicines and medical devices:

1. Health professional and consumer confidence in TGA regulation of the safety, performance and quality of therapeutic goods must be maintained
2. TGA will provide clear guidance to enable the applicant to adhere to the designation and registration processes
3. Applicants will be responsible for providing TGA with all information necessary to get, and support, continued designation
4. Both TGA and the applicant will commit to open and timely communication to support expediting the application in the interest of public health benefit
5. There will be transparency of the criteria, and of designation and registration decisions
6. The designation and registration processes will be cost recovered
7. Appeal rights regarding the designation decision will exist
8. The designation and registration processes should not result in an unreasonable diversion of TGA resources from business as usual activities

Criteria for Priority Review

In response to Recommendation 19 of the MMDR, the proposed criteria for designation of medical device Priority Review have been developed with consideration of the US FDA's criteria for Priority Review. The US FDA criteria are provided for reference at Attachment A**.**

Medical devices may seek designation for Priority Review for conformity assessment and for applications for inclusion on the ARTG, and are required to meet ALL of the following criteria:

9. The medical device is intended for the prevention, diagnosis or treatment of a life threatening or seriously debilitating disease or condition; AND
10. The medical device addresses an unmet clinical need in Australian patients; AND
11. Meets at least one of the following:
    - the device represents a breakthrough technology with evidence of a major *clinical** advantage over existing technology, OR

- there is evidence that the device offers a major *clinical** advantage over existing alternatives included in the ARTG, OR
- In the case of in vitro devices (IVDs) ONLY, early availability in Australia will result in a major public health benefit.

* Engineering or pre- clinical evidence is insufficient on its own; there must be evidence of a major clinical advantage.

When applying for a Priority Review, a sponsor acknowledgement will be requested indicating that a full dossier is available to support conformity assessment or an ARTG inclusion application if the device is designated as eligible for Priority Review.

Principles and criteria

- Are the criteria appropriate to restrict acceptance for Priority Review to the truly new and novel devices for patients in immediate need? Noting that acceptance of a large number of applications would undermine the viability of Priority Review.
- Do the proposed criteria cover all issues which should be considered in assessing a medical device for Priority Review designation?
- What is your estimated likelihood of making an application for a medical device to have Priority Review designation?

Proposed implementation of Priority Review

This section outlines the proposed implementation of the Priority Review pathway for medical devices in response to Recommendation 15 of the MMDR, with discussion of:

- a process for applying for Priority Review:
  - sponsor alert to TGA
  - application for Priority Review designation
- management of applications for Priority Review designation,
- decision making process, and
- the Priority Review pathway for designated applications.

A flow chart for the proposed TGA implementation of the Priority Review business process is provided at Attachment B.

Applying for Priority Review

Sponsor alert

Prior to making an application for Priority Review the sponsor is requested to provide TGA with an alert of their intention to make a Priority Review application. The alert will be made via a dedicated form on the TGA website and include:

- a one page outline of the application e.g. nature of the technology, use of the device
- indicate if the application is for ARTG inclusion only, or with a view to the device being considered for reimbursement by the Prostheses List Advisory Committee (PLAC) and/or the Medical Services Advisory Committee (MSAC)
- estimated timeframe until the Priority Review application will be made

The sponsor alert will be a minimum of four (4) weeks prior to the planned application for Priority Review. This timeframe is to allow TGA to identify the relevant technical and clinical experts to facilitate the Priority Review.

Application for Priority Review designation

An application form and submission instructions will be provided through the TGA website.

Application by a sponsor for Priority Review will be treated as a priority.

We envision that the application will be a concise argument as to how the device meets the criteria. We expect a self-evident argument with overwhelming rational and clinical foundations for our decision to put the device in the accelerated assessment pathway *without* requiring further information from the sponsor (i.e. the application should stand-alone). This is not a conformity assessment dossier or information that would be required for an ARTG inclusion application.

The sponsor will indicate whether this is a new device or a new intended purpose for a currently included device, with expert opinion of the medical profession provided as to the novelty and patient need for the medical device and a summary of clinical evidence. Therefore the sponsor may attach brief (2-3 pages) support from relevant medical experts. Like the application itself,

support from relevant medical experts should be self-evident and provided without an accompanying dossier of information.

Sponsors will be requested to indicate if there is a related medicine Priority Review or Provisional Approval sought.

It will be possible for more than one device of the same type to be accepted into the Priority Review pathway at the same time.

Although not used as part of the application for ARTG inclusion (or conformity assessment if appropriate), the Priority Review application will include acknowledgement that an inclusion or conformity assessment application is ready to be submitted within three (3) months of receiving advice of designation for Priority Review.

It is expected that the sponsor of a medical device applying for Priority Review will want to seek ARTG inclusion as soon as possible if their application for Priority Review designation is accepted. A maximum of three (3) months will however apply, after which time the designation will lapse.

For those products seeking both regulatory approval and reimbursement, the sponsor should indicate whether they consent that all documents provided to us or developed during the TGA assessment can be shared with the relevant committee, currently the MSAC or PLAC.

Managing applications for Priority Review

It is proposed that there will be an alert to TGA by a sponsor as advance notice of the intention to seek Priority Review. The application will be submitted as detailed in the above section.

On receipt of an application for Priority Review designation:

- a Priority Review case co-ordinator will be assigned to co-ordinate and support the decision-maker process and communicate with the sponsor, and
- it is proposed that the Priority Review application will be published on the TGA website. A sample statement is provided below.

> Sponsor *(name)* requested Priority Review for (*name of product/technology).* The TGA decision will be advised by *(dd/mmm/yyyy calculated based on date of receipt and maximum timeframe).*

The designation decision will be informed by expert opinion of the medical profession (possibly including but not limited to members of the Advisory Committee on Medical Devices) as to the novelty, patient need and clinical advantage of the medical device.

Applications for Priority Review will be determined within six (6) weeks of acceptance and acknowledgement to the sponsor. Sponsors are encouraged to submit applications for conformity assessment or ARTG inclusion as soon as possible after designation advice is given.

Decision making and oversight

Due to the focus on clinical evidence and public health as part of the criteria for a medical device entering Priority Review, the decision on eligibility for the Priority Review pathway will be made by the Principal Medical Adviser.

In the event of an appeal against the decision of the decision-maker, the Deputy Chief Medical Officer, Department of Health will conduct an internal review of the decision. Existing appeal timeframes will apply.

The Advisory Committee on Medical Devices will be regularly informed of applications for Priority Review decisions.

It is proposed that Priority Review decisions will be published immediately following advice of designation (eligible or non-eligible) to the sponsor. Public release of information is made under the *Therapeutic Goods Act 1989* (the Act), Section 61(5A). A sample statement is provided:

> Sponsor (*name*) applied for Priority Review designation for (*name of technology*) to assist (*state the condition/illness/disease/public health reason*) patients. The application was found eligible for Priority Review *(brief statement of reason/criteria met)*.
>
> OR
>
> Sponsor (*name*) applied for Priority Review designation for (*name of technology*) to assist (*state the condition/illness/disease/public health reason*) patients. The application was found non-eligible for Priority Review due to (*brief statement of reason/criteria not met*).

It is proposed that a high-level statement will be included in TGA performance reporting providing details of common reasons why applications were approved or not.

Priority Review pathway for designated applications

- By gaining Priority Review designation, the sponsor's conformity assessment or ARTG inclusion (whatever is relevant) application will go to the front of the queue for all conformity assessments or ARTG inclusion audits deemed necessary. Current in-progress assessments will be reprioritised.
- Standard business as usual assessment requirements will be applied with no truncation or omission of assessment processes.
- A coordinating assessor will be assigned to the application to supervise timely assessment and suitable expertise assigned for the assessment of the application.
- The TGA aims to develop an application for inclusion checklist which will apply for priority review and routine applications. The checklist will be used to ensure that the application is complete and of good quality ie it includes unredacted copies of FDA and/or EC assessment reports to document overseas approval.
- Medical devices meeting the criteria for Priority Review are expected to be novel or new technology for which inclusion in the ARTG will stimulate a Level 2 audit if an application for the device is submitted with EC certification. This is to ensure that the device satisfies all the standard criteria for inclusion in the ARTG of a novel medical device and there is no difference in the risk/benefit analysis applied.
- As part of a Priority Review pathway the sponsor is also required to treat the ARTG inclusion (or conformity assessment) application as a priority. Current requests for information (e.g. under Section 41JA) generally provide twenty (20) working days to reply. It is proposed that if these timeframes are exceeded, the application's Priority Review status will be revoked and the application reallocated in the standard assessment pathway.
- Consideration of imposing additional conditions on ARTG inclusion for devices assessed using the Priority Review pathway will be consistent with the standard decision making process and, importantly, is expected to be consistent with similar decisions made following standard assessment pathways. It is in the interest of patients that novel devices are limited to:
  - use on the appropriate patient cohort,

  - use by appropriate medical practitioners,
  - used by clinicians provided with appropriate training, and
  - support for the device is easily available.

- When devices are included in the ARTG it will be noted that applications went through Priority Review. Additionally it is proposed that sponsors will provide for publication, consumer information about the product, such description, its use and benefits.
- Designation for Priority Review will be revoked if:
  - the conformity assessment or ARTG inclusion application (whatever is relevant) is not submitted to the TGA within three (3) months after the designation is granted;
  - the eligibility criteria for Priority Review are no longer met;
  - the information required by the TGA is not provided by the date specified in the request for information (e.g. Section 41JA); or
  - the application has been rejected or withdrawn from supply by a comparable overseas regulator and the reasons are deemed applicable to the Australian context.
- Post-market scrutiny will apply consistently as for any device assessed through the normal mechanism.

Implementation of Priority Review

- Is the proposed sponsor alert timeframe adequate for industry?
- Decisions will need to be made promptly, within six (6) weeks. Large submissions will undermine this, as will applications that are incomplete in meeting the criteria. Will applicants be able to present a succinct and compelling argument for Priority Review designation, independent of the full application process?
- In the proposed implementation it is expected that sponsors on receipt of designation advice will promptly submit their full application for conformity assessment or inclusion. Is this a reasonable expectation?
- It is proposed that priority review status will be revoked if timeframes for reply to request for information are not met. Is the existing practice of a twenty (20) working day timeframe appropriate?
- Is the proposed approach to publication of Priority Review applications and decisions appropriate?
- Is the proposal to publish medical device product information for consumers supported, and what extent of detail would consumers seek?
- Is the Priority Review pathway for designated applications adequately detailed? If not, which areas are unclear or require more detail?

TGA operational impacts

To operationalise the Priority Review application and designation pathway, TGA will:

- implement a Priority Review business process,
- develop supporting documentation,
- apply the Australian Government Cost Recovery Guidelines,
- incorporate the proposed implementation of Recommendations 15 and 19 of the MMDR for a Priority Review pathway into the TGA's functions by legislative amendment and regulations, and
- plan for a post-implementation review.

Implementing a Priority Review business process

Medical device Priority Review applications will be assigned a case co-ordinator to provide consistent communication and advice to the decision maker and applicant.

Assessment of an application for Priority Review will be treated as a priority and will include:

- identifying experts to provide advice on the application;
- researching the technology of the device and available alternative therapies;
- assessing the application against the criteria; and
- assessing the validity of core assertions in the application.

If an application for Priority Review is accepted, the business process for designated Priority Review applications (conformity assessment or ARTG inclusion applications) will require front of the queue prioritisation of the application during the standard assessment. This administrative change will be applied to expedite the conformity assessment or ARTG inclusion assessment.

The business process will include reprioritisation of in-progress assessments.

Develop supporting documentation

TGA will develop supporting documentation for the business process and to support sponsors. Documentation will include:

- application forms,
- guidance documents, including a comprehensive checklist, and
- internal standard operating procedures for receiving and processing applications

Cost recovery

Existing TGA operations (assessment and evaluation costs) are recovered as fees from applicants, while post-market monitoring and surveillance are recovered in the form of annual

charges. Cost recovery of the Priority Review pathway is proposed to be consistent with existing practice, as well as with the Australian Government Cost Recovery Guidelines[7].

The proposed front of queue administrative process for designated Priority Review applications (conformity assessment or ARTG inclusion applications, whatever is relevant) will require more resources during the premarket assessment process and will largely benefit sponsors of these devices (as well as patients wishing to access these devices). To recover the additional costs it is proposed to:

- Create a **Priority Review application fee** for assessing whether the device meets the Priority Review pathway criteria.
- Priority Review eligible devices will be assessed using standard assessment processes. Devices eligible for Priority Review will be of a novel nature and require either TGA conformity assessment application or a **Level 2 audit** for ARTG inclusion applications with EC Certificates. Standard assessment processes are performed on a cost recovery basis (application fees, conformity assessment fees or audit assessment fees).

The proposed Priority Review application fee based on cost recovery will also serve to discourage disingenuous applications.

Evaluation on whether fees and levies have achieved cost recovery should occur at regular intervals. Importantly these new fees will require changes to Regulations (see below).

Legislative and regulatory amendment

It is our intention to incorporate the criteria for the Priority Review pathway into the Therapeutic Goods (Medical Devices) Regulations 2002 (MD Regulations), as well as the associated additional fees.

The details of the criteria and pathway will be published in a guidance document, with the internal standard operating procedures published on the TGA website.

Legislative amendment will be required to enable regulations to establish the Priority Review pathway – to apply to both conformity assessment and ARTG inclusion application processes, including related fees.

MD Regulations are expected to be amended, outlining:

- Priority Review criteria
- Assessment process
- Related fees

A Cost Recovery Impact Statement (CRIS) will be required to support the fees arising from these changes.

Evaluation and Review

The Australian regulatory context is different from that of the USA, thus it is difficult to accurately anticipate the volume of Priority Review pathway applications that will be received.

[7] Department of Finance 2014, Australian government cost recovery guidelines, July 2014, Third edition, Department of Finance, Canberra.

It is proposed that a post-implementation review will be undertaken. The timeframe is yet to be determined. The review may include:

- Was the assessment faster in comparison to similar applications assessed through normal pathways? If not, why not? What further efficiencies can be built into the pathway?
- What devices were chosen and were these enthusiastically adopted by the proposed patient cohort? If not, why not? How can we better select effective devices for this pathway?
- What was the quality of the applications and what can we alter to gain better applications?
- How did this pathway affect TGA business as usual operations? Has this pathway been properly cost recovered?

TGA operational impacts

- Are there any gaps in the proposed implementation plan?
- What aspects of the proposed implementation would you suggest for inclusion in a post-implementation review?
- What timeframe would you suggest for the review – 1 year, 2 years or 3 years after commencement?

Attachments

Attachment A – US FDA criteria for Priority Review (for information)

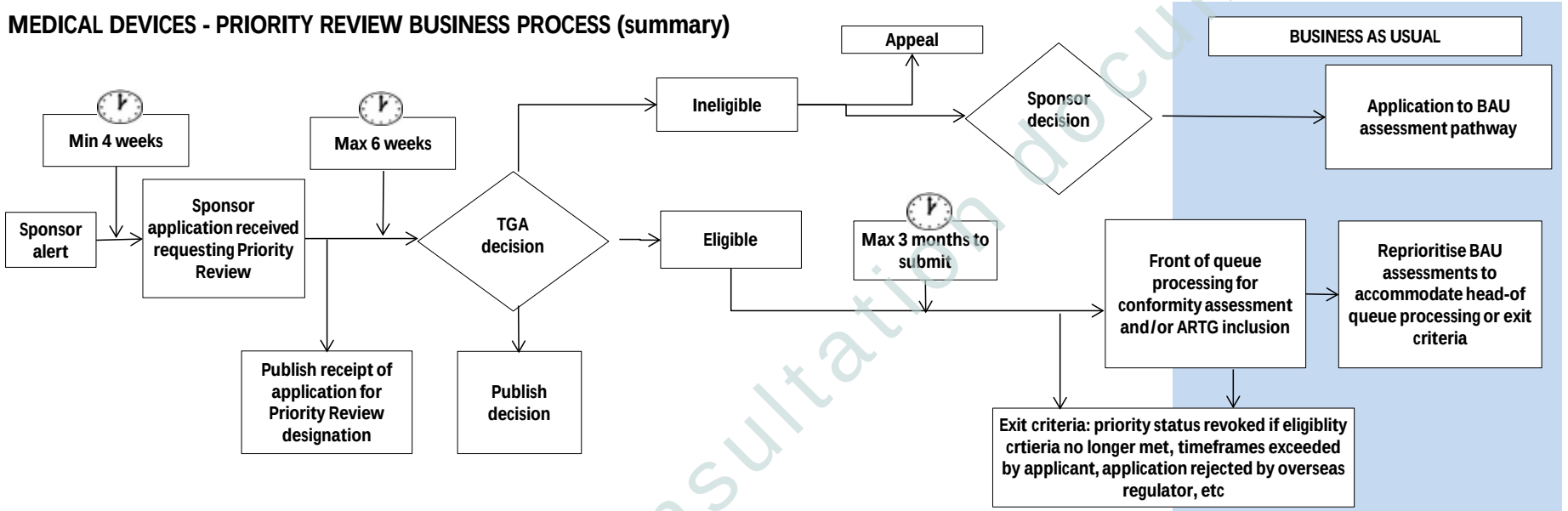
Extract from FDA 'Guidance for Industry and Food and Drug Administration Staff - Priority Review of Premarket Submissions for Devices', retrieved on 20/9/2016 from http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089643.htm#s3

III. Devices Appropriate for Priority Review

Using the criteria in section 515(d)(5) of the FD&C Act, FDA considers a device or a combination product containing a device,[3] appropriate for priority review if the device or combination product:

1. **is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition,** and
2. **meets at least one of the following:**
    a. **The device represents a breakthrough technology that provides a clinically meaningful advantage over existing technology.** Breakthrough technologies should be demonstrated to lead to a clinical improvement in the treatment or diagnosis of the life-threatening or irreversibly debilitating condition
    b. **No approved alternative treatment or means of diagnosis exists.**
    c. **The device offers significant, clinically meaningful advantages over existing approved alternatives.** The device should provide for a clinically important earlier or more accurate diagnosis or offer important therapeutic advantages in safety and/or effectiveness over existing alternatives. Such advantages may include demonstrated superiority over current treatments for effects on serious outcomes (e.g., morbidity), ability to provide clinical benefit for those patients unable to tolerate current treatments, or ability to provide a clinical benefit without the serious side effects associated with current treatments.]
    d. **The availability of the device is in the best interest of patients.** That is, the device provides a specific public health benefit, or meets the need of a well-defined patient population. This may also apply to a device that was designed or modified to address an unanticipated serious failure occurring in a critical component of an approved device for which there are no alternatives, or for which alternative treatment would entail substantial risk of morbidity for the patient.

Attachment B – Priority Review business process diagram



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