TGA collaboration and expediated regulatory pathways – Benefits, hints and challenges

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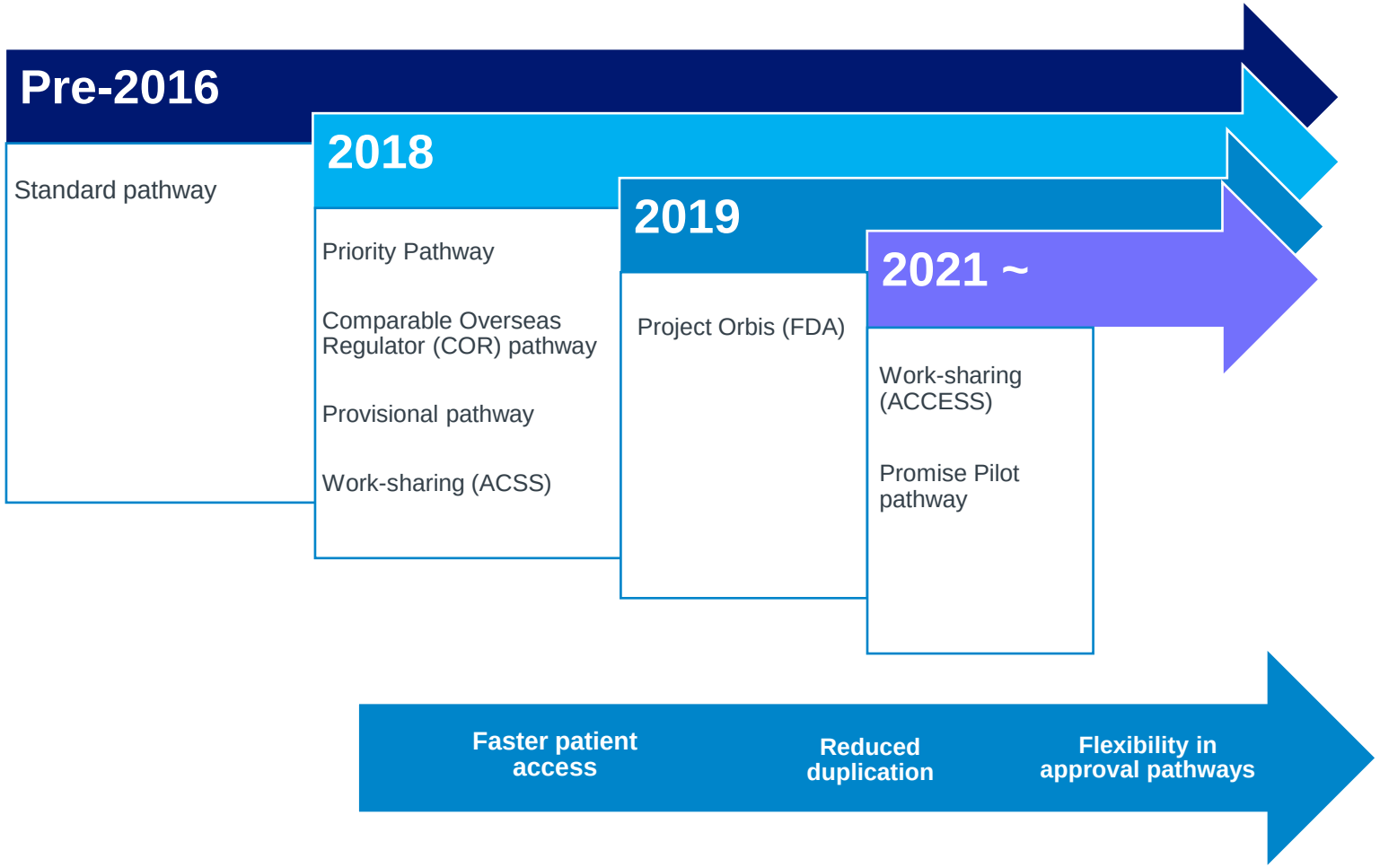
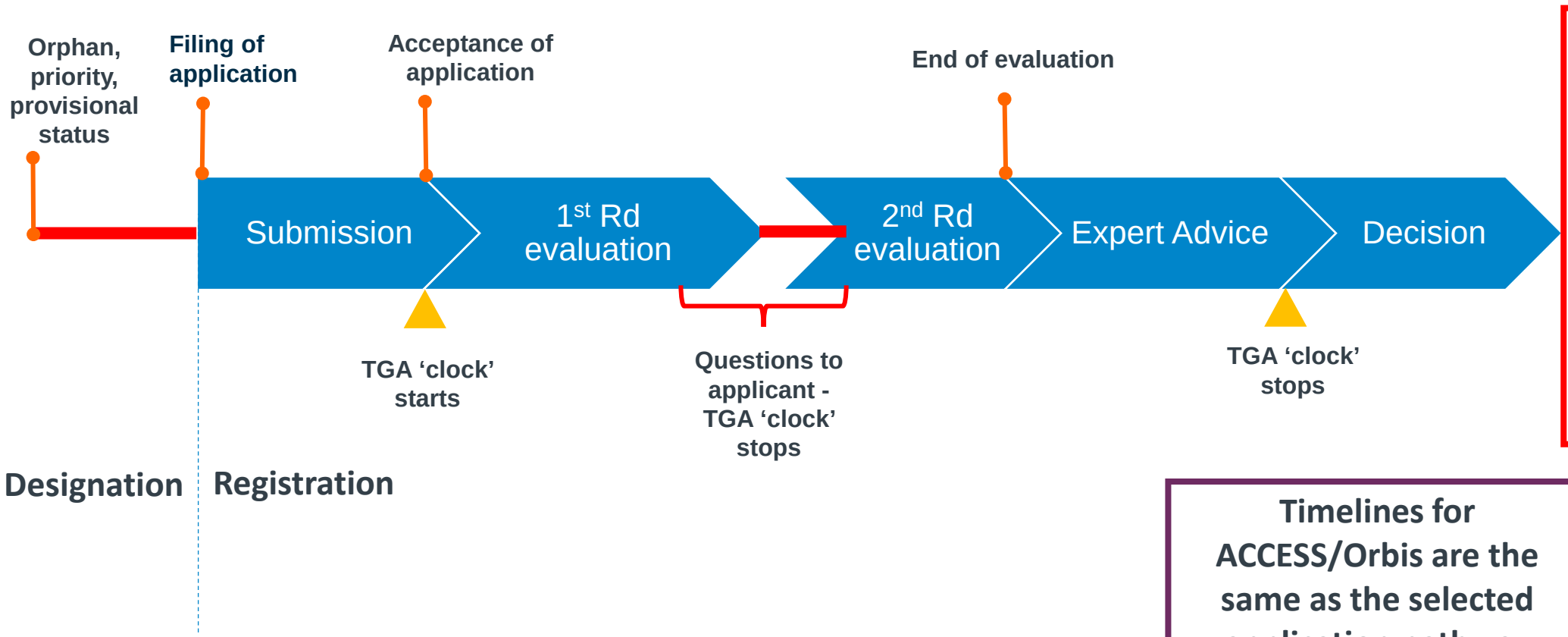
Overview

- Overview of TGA’s collaboration pathways and principles
- COR report-based process
- Access work-sharing
- Project Orbis
- Selecting the TGA collaboration pathways
- Further information

Regulation of prescription medicines in Australia



Snapshot: Designations and pathways



Timeframes
(TGA 'working days')

COR-A: 120*
COR-B: 175*
Priority: 150
Generic: 155
Standard: 220
Provisional: 220

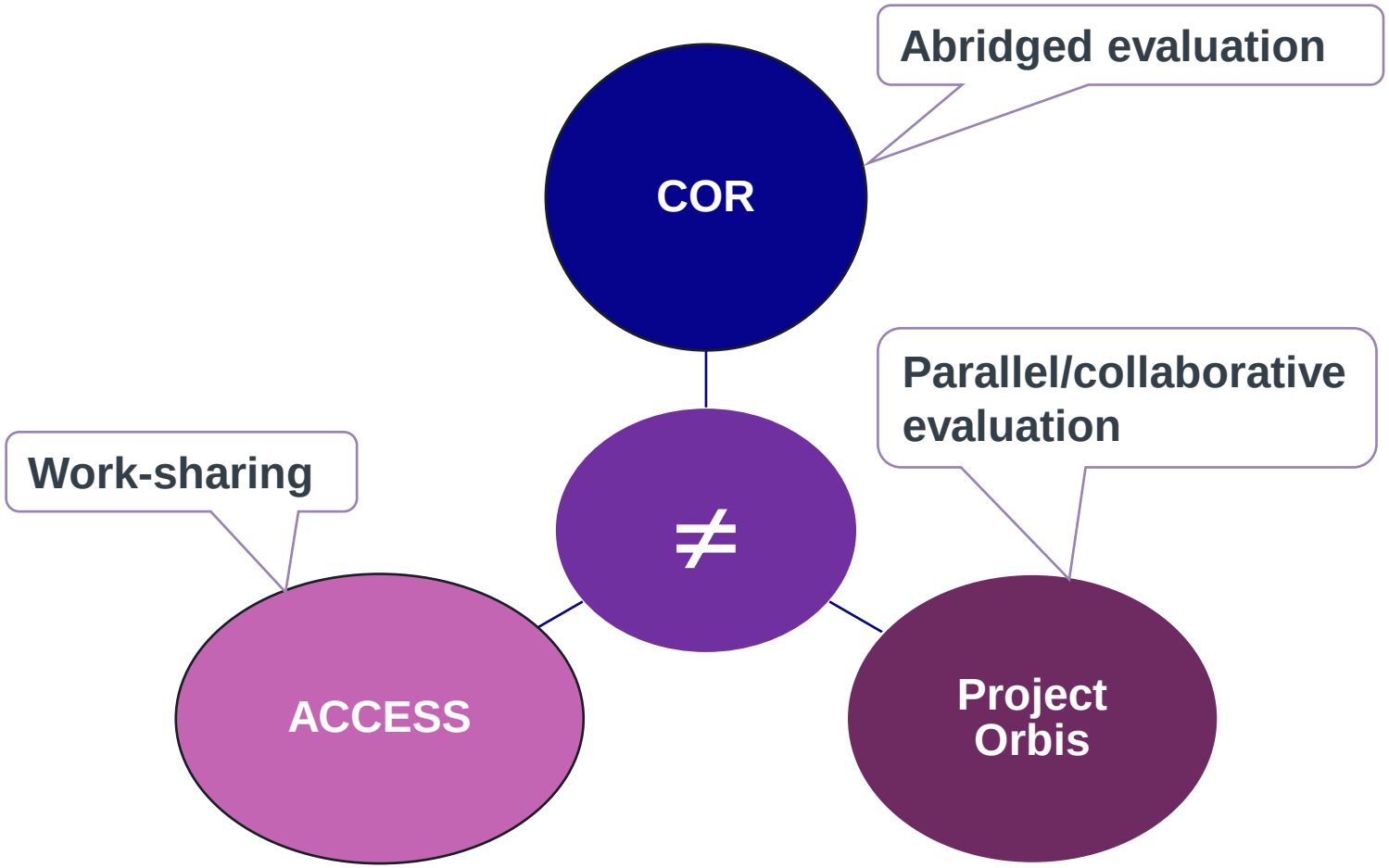
*Legislated timeframe

Timelines for ACCESS/Orbis are the same as the selected application pathway

TGA collaboration pathways

Key principles:

- TGA sovereignty over decision making
- Regulators we work with have similar vision and approaches to evaluation & decision-making
- Reliance provides flexibility to TGA/applicants and can be tailored to the needs of the regulatory system



Industry's support and adherence to these principles is vital to the success of these collaboration pathways

COR report-based process

- The TGA uses assessments from Comparable Overseas Regulators (CORs)

- Key features:
  - a list of countries and jurisdictions from whom TGA will accept reports (CORs)
  - transparent criteria and guidance for identifying CORs
  - a process for using overseas reports
  - Abridged evaluation instead of *de novo* evaluation with shorter legislative timeframes

Use of comparable overseas regulator reports

COR-A

- Approved overseas < 1 year
- Identical medicine and supply chain
- Identical dossier (except Module 1)
- Approval < 120 working days (legislated)

COR-B

- No approval timing restrictions
- Identical medicine and supply chain
- Certain additional data allowed (e.g. updated stability data)
- Approval < 175 working days (legislated)

Benefits for all

Industry

- Faster market access for new products
- Decreased workload through reduced number of RFI
- Leverage previous regulatory work

TGA

- Potential to reduce regulatory burden
- Best of both worlds – sovereign decisions and potential for greater international harmonisation
- Share expertise across regulators

COR report-based process

Pre-submission

- Applicants use ‘Criteria for acceptance of COR reports’ to determine if a particular report is suitable
- Applicant submits COR application with **unredacted COR report** and full dossier

Screening

- TGA confirms application is *effective* during preliminary screening
- Whether the application meets the conditions for COR criteria (e.g. conditions for 120 or 175 working days) will be advised before or at MS3

Evaluation

- TGA evaluation based on COR report(s) **AND** evaluation of data generated specifically for the Australian context
- TGA confirms that the submission is suitable for COR pathway, planning dates are updated accordingly

Access New Active Substance Work Sharing Initiative (NASWSI)

- The Access Consortium is a group of like-minded, medium sized regulatory authorities
- Formed in 2007 (“ACSS”), renamed to Access Consortium in October 2020*
- New Chemical Entity (NCE) or New Biological Entity (NBE) or new indication applications
- Access Consortium members include:
  - Australia – Therapeutic Goods Administration (TGA)
  - Canada – Health Canada
  - Singapore – Health Sciences Authority (HSA)
  - Switzerland – Swissmedic (SMC)
  - UK Medicines and Healthcare products Regulatory Agency (MHRA)

swissmedic

HSA Health Sciences Authority

Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Health Canada Santé Canada

Medicines & Healthcare products Regulatory Agency

ACCESS Goals and Mission

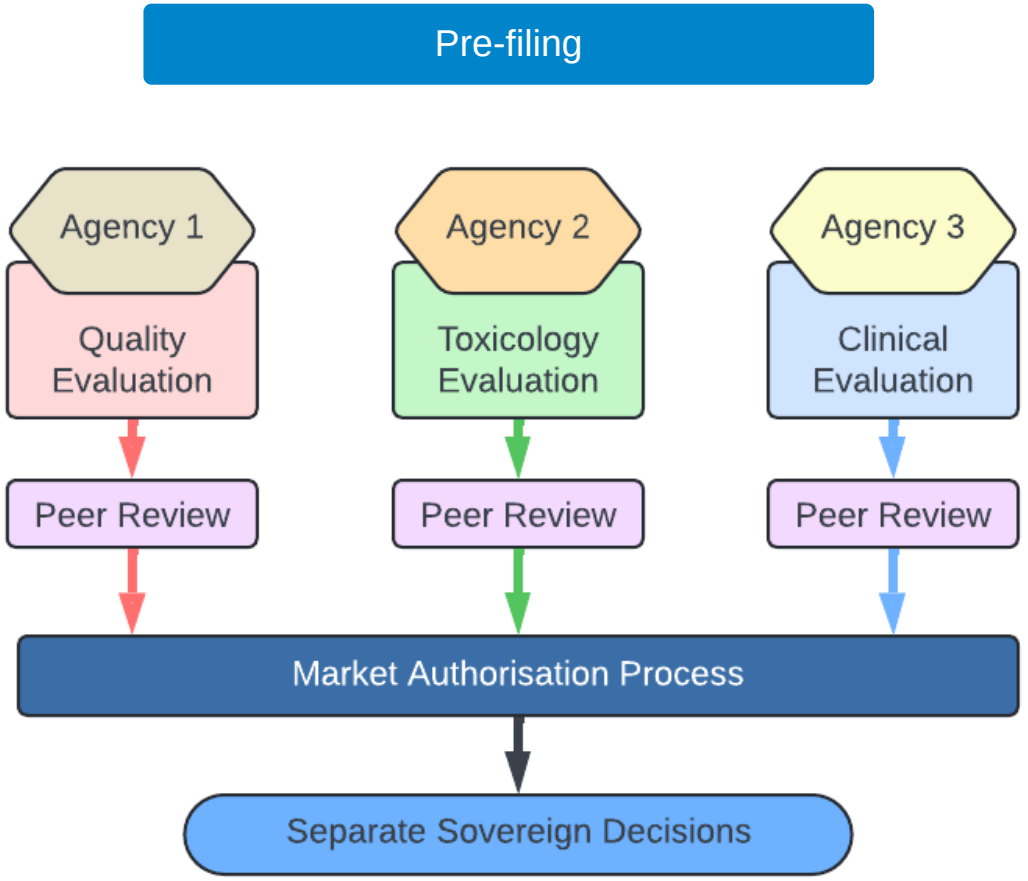
Access Consortium's goal is to:

- Maximise international cooperation
- Share knowledge
- Reduce duplication
- Provide consumers with timely access to high quality, safe and effective therapeutic products

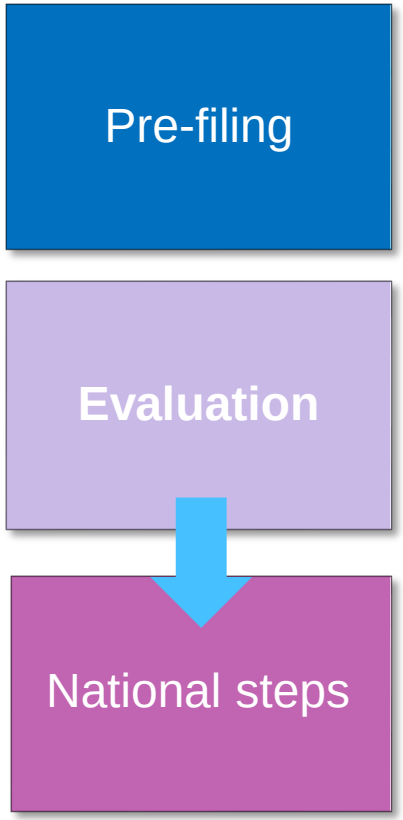
TGA retains **sovereignty** over decision making

ACCESS Workshare Process

- Expression of Interest (>3 months)
    - Company nominates participating countries
    - Proposed indication, application type, nominated S31 response time
    - Summary of differences between dossiers (if any)
    - Additional information may be requested including a list of clinical studies
- Agreement of partner regulators to participate
- Participating regulators to negotiate a division of labour and joint-review timeline, e.g.:
    - **Module 3** – Quality evaluation (± BE)
    - **Module 4** – Toxicology evaluation (+ impurities)
    - **Module 5** – Clinical evaluation (± popPK, clinical pharmacology)
    - All regulators peer review
- Evaluation plan tailored to each submission through negotiation



ACCESS work-sharing process



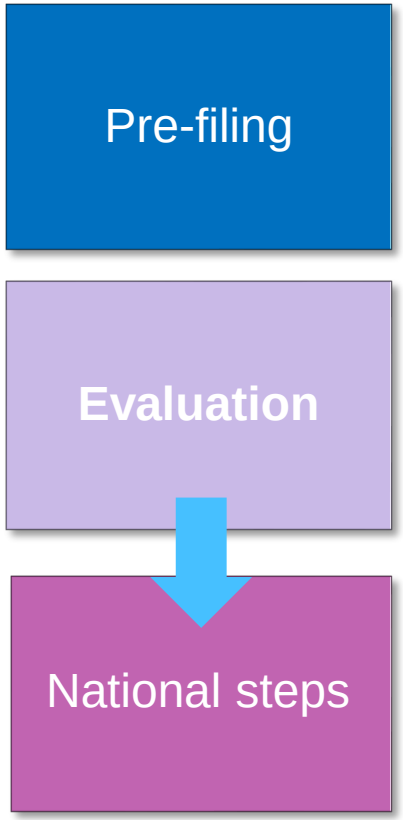
- Agencies evaluate their assigned module(s)
  and any country specific aspects:
  - Mod 1 (labels, GMP, RMP)
  - Mod 3 (TGOs, stability, container)
  - Mod 4 (pregnancy category)
  - Wording of indications

- Consolidated List of Questions (LoQ)*
  - Common questions
  - Country-specific questions

**Responses to reports/LoQs to be provided to each agency*

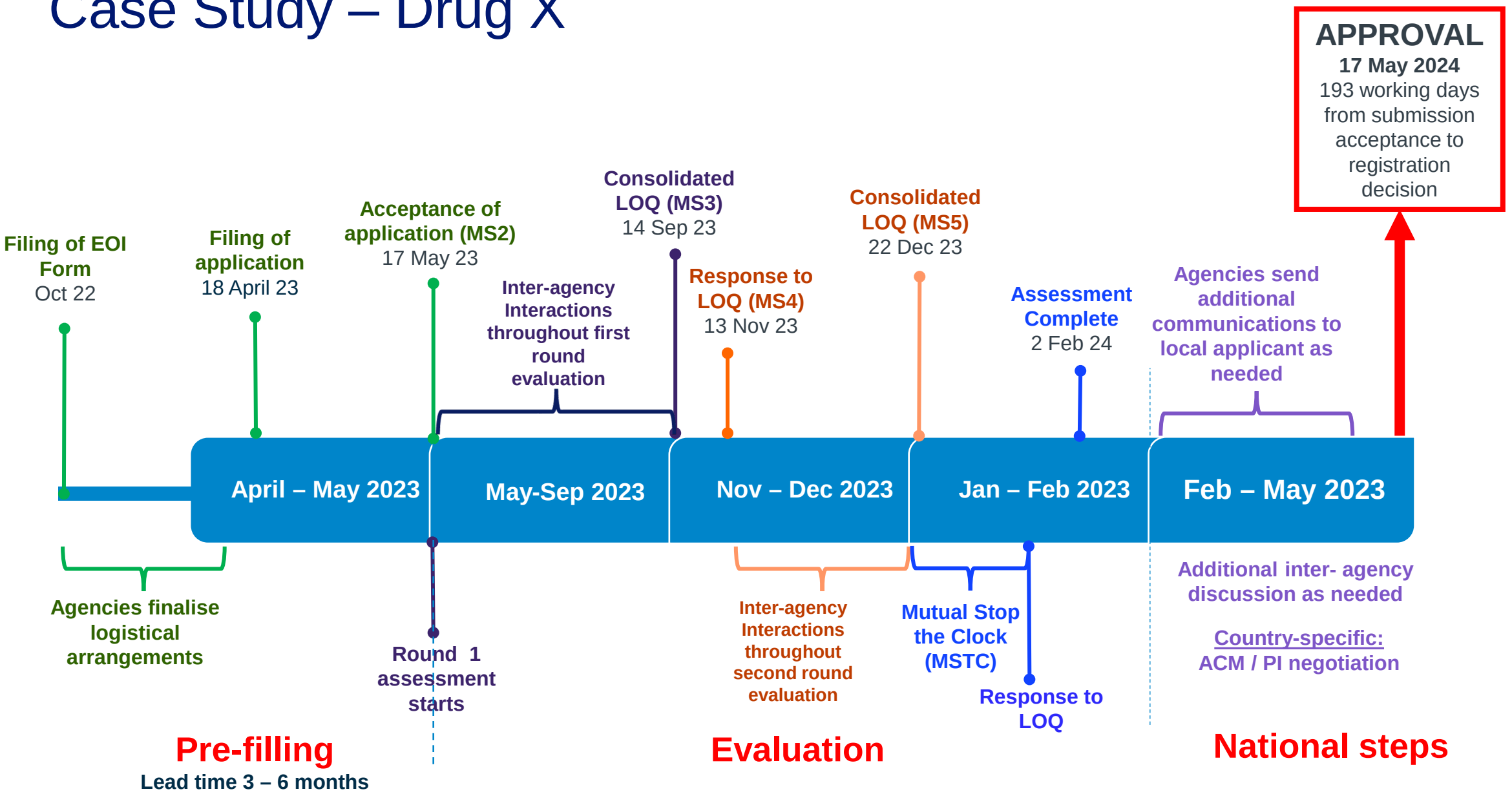
- Inter-agency interactions throughout the review (evaluator t/c)

ACCESS work-sharing process



- Work-sharing concludes at the end of the evaluation
- **National steps include:**
  - Expert advice
  - Wording of indications
  - Finalisation of product label
- Independent decision-making by each jurisdiction

Case Study – Drug X



Access Benefits and Challenges (TGA perspective)

Benefits

- Reduced duplication
  - Consolidated questions
- Collaborative approach during evaluation leading to more robust decisions
- Sharing global expertise and resources
- Increased market access
  - Better access to medicines for the Australian community and around the globe

Challenges

- Timing of EOI
  - At least 3 months before proposed filing date for standard work-sharing
  - At least 6 months before proposed filing date for Promise pilot work-sharing
- Screening – incomplete EOI / dossier
- Country-specific regulatory compliance – e.g. GMP, PI format etc
- Greater need to align TGA registration process with other activities – post-registration

ACCESS work-sharing – Hints and Tips

- **Advance Notice**: early interactions with regulators to assess whether work-sharing is a feasible option – e.g. pre-submission meeting
- **Timely submission**: prepare for submission to each regulator within 2- week window
- **Comprehensive data**
  - **Identical dossiers** across jurisdictions (noting country-specific aspects) – differences should be noted in EOI
  - Ensure that the dossier contains relevant complete and robust data
  - Structured format – follow the Common Technical Document (CTD) format
  - Clear and concise documentation
- **Regulatory compliance:** ensure GMP clearances are all in place (TGA-specific)

Note: Possibility of **near simultaneous access** to ACCESS markets **BUT** reimbursement not part of work-sharing

Project Orbis

- Initiative of the **FDA** (May 2019)

- Global collaborative review program for **oncology** drug applications
  - new drugs
  - new indications

- Clinical Criteria
  - Highly impact, clinically significant

- Should generally qualify for priority review in the US
  - Serious condition
  - Demonstrating potential significant improvement in safety or effectiveness

- Project Orbis Partners (POPs) include:

FDA	HSA Singapore
TGA	ANVISA
Health Canada	MHRA
Swissmedic	IMoH Israel

Concurrent evaluation by regulators, with **collaborative discussions** (Orbis Types A and B)

Project Orbis Collaboration Type

Orbis Type A

- Concurrent submission to participating regulators (within 1 month or so of FDA submission)
- Concurrent review and sharing of Assessment Aids
- Near simultaneous regulatory action
- Drug of “Clinical significance”*
- For TGA, generally reduced timeframes

**In general, the TGA will only consider applications of exceptional clinical significance*

Orbis Type B

- Application submission to participating agencies >1 month of FDA submission
- Overlapping review period
- Multi-country review meetings (POP TCONs)
- Regulatory action at the TGA is *unlikely* to occur immediately after FDA action
- Timeline follow the relevant TGA registration pathway

Orbis Type C

- FDA has already taken regulatory action
- FDA makes reports available to Project Orbis Partners (POPs)
- Interaction during review process *may* be limited
- Timeline follow the relevant TGA registration pathway

Allow for collaboration without concurrent review

Project Orbis – Hints and Tips

- **Early Engagement**: Early interactions with FDA and other participating regulatory agencies early in the process
- **Comprehensive Data:** Ensure that your application address Australian specific requirements, and include all necessary clinical trial data, safety and efficacy information, and other relevant information such as:

  Topline results
  FDA assessment aids (Orbis Type C)
  Sponsor Authorisation Letter (SAL)

- **Data Similarities & Differences:** Any differences should be clearly indicated in the application cover letter
- **Evaluation Timeline:** Submissions will follow the standard TGA timeline – companies should consider this when planning post-decision and reimbursement activities

Which TGA collaborative pathway is right for you?

COR report-based

- Submitting to TGA (only)
- Suitable for **all** therapeutic areas
- Applicants **must** provide reports to TGA that meet legislated criteria
- TGA conducts **abridged assessment** based on COR report(s) in lieu of *de novo* evaluation
- Reduced timeframes

Work-sharing

- Submitting to 2 or more to ACCESS agencies
- Suitable for **all** therapeutic areas
- Applicant(s) submit Expression of Interest
- Regulators **divide review of quality, safety and efficacy modules**
- Standard timeframes apply

Project Orbis

- Submitting to US FDA **and** TGA (& others)
- Oncology drugs **only**
- Suitable applications identified by FDA
- Regulators conduct **parallel, collaborative evaluation** and share information (Orbis Type A and B)
- Timeframes **may** be reduced (Orbis Type A)
- Timeline follow the relevant TGA registration pathway

Further Information

Prescription medicines registration process

- TGA guidance on the process and regulatory requirements COR report-based process
- TGA guidance on the COR report-based process

ACCESS work-sharing

- NASWSI TGA website
- NASWSI Operational Procedures (OP)

Project Orbis

- FDA Project Orbis website
- TGA Project Orbis website

Provisional Registration pathway

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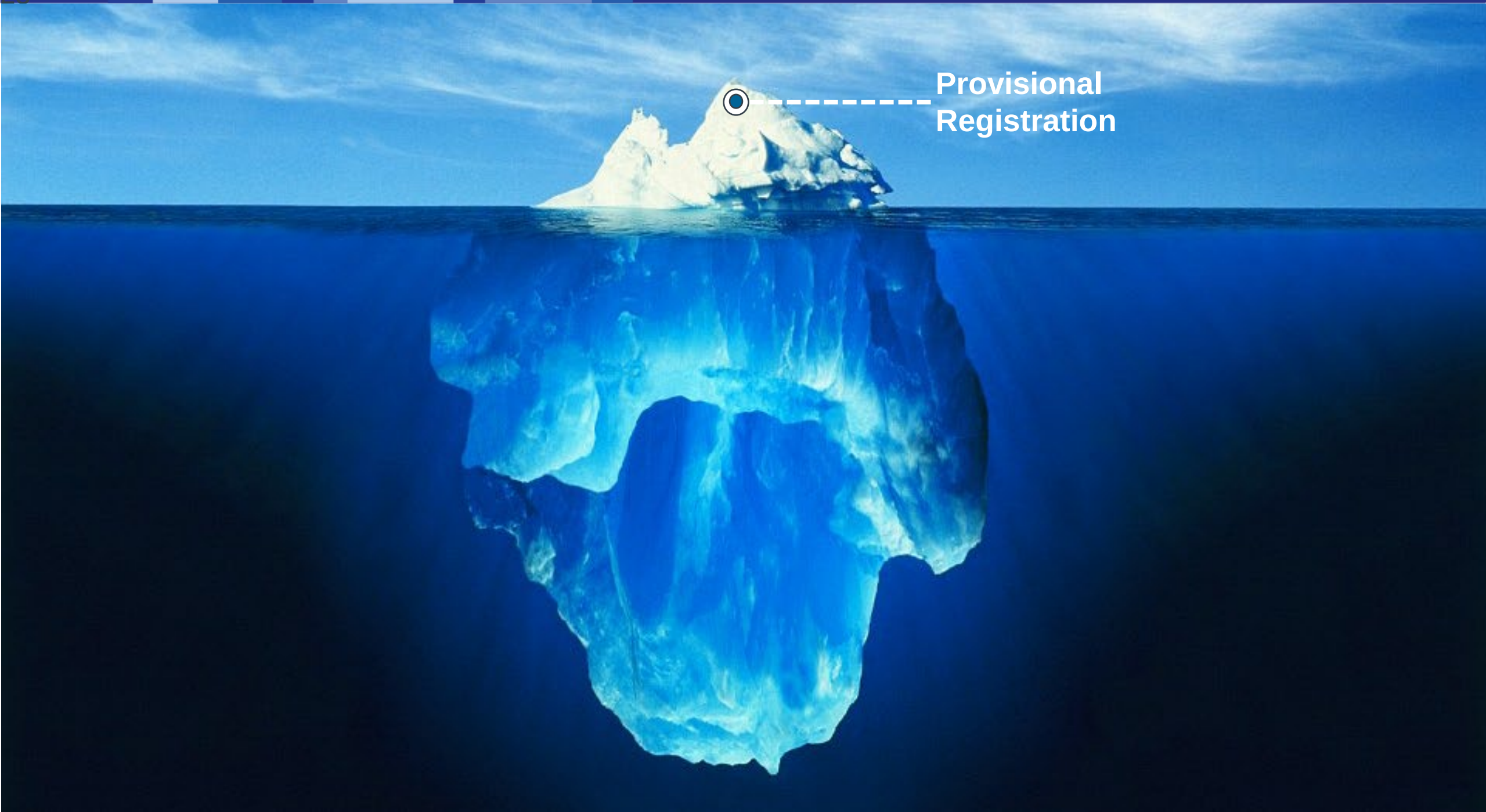

Provisional
Registration

Quiz time!

Scan the QR code with your device and select “Polls” to participate.

Role of the regulator – Therapeutic Goods Administration

Therapeutic Goods Act 1989

- Establishment and maintenance of a national system of controls relating to the **quality, safety, efficacy and timely availability of therapeutic goods.**

Provisional Registration pathway

- On the basis of preliminary clinical data, where the **benefit of early availability of the medicine** outweighs the risk that additional data are still required

Applying for provisional registration for a prescription medicine | Therapeutic Goods Administration (TGA)

Navigating the pathway

First step

Applying for a provisional determination

Assessment

- Granting of a provisional determination

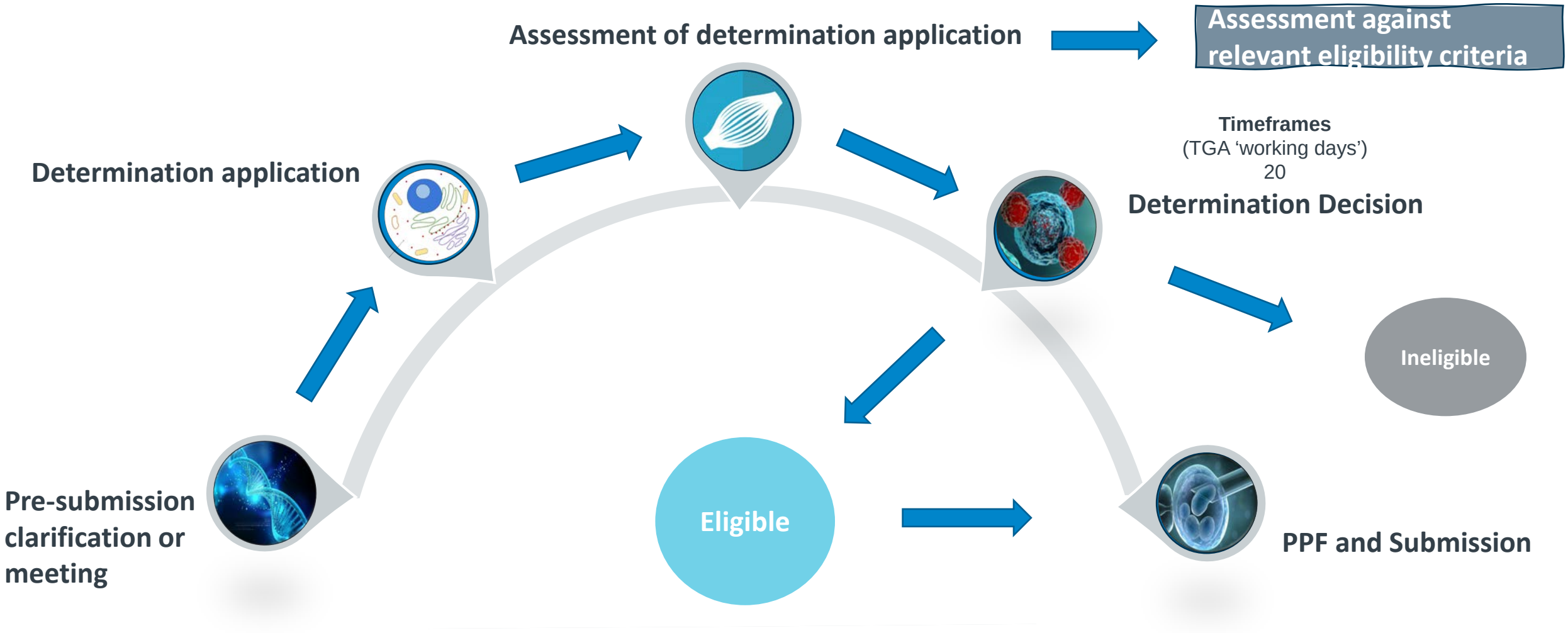
Submission

- Applying for Provisional Registration

Quiz time!

Scan the QR code with your device and select “Polls” to participate.

Provisional determination process



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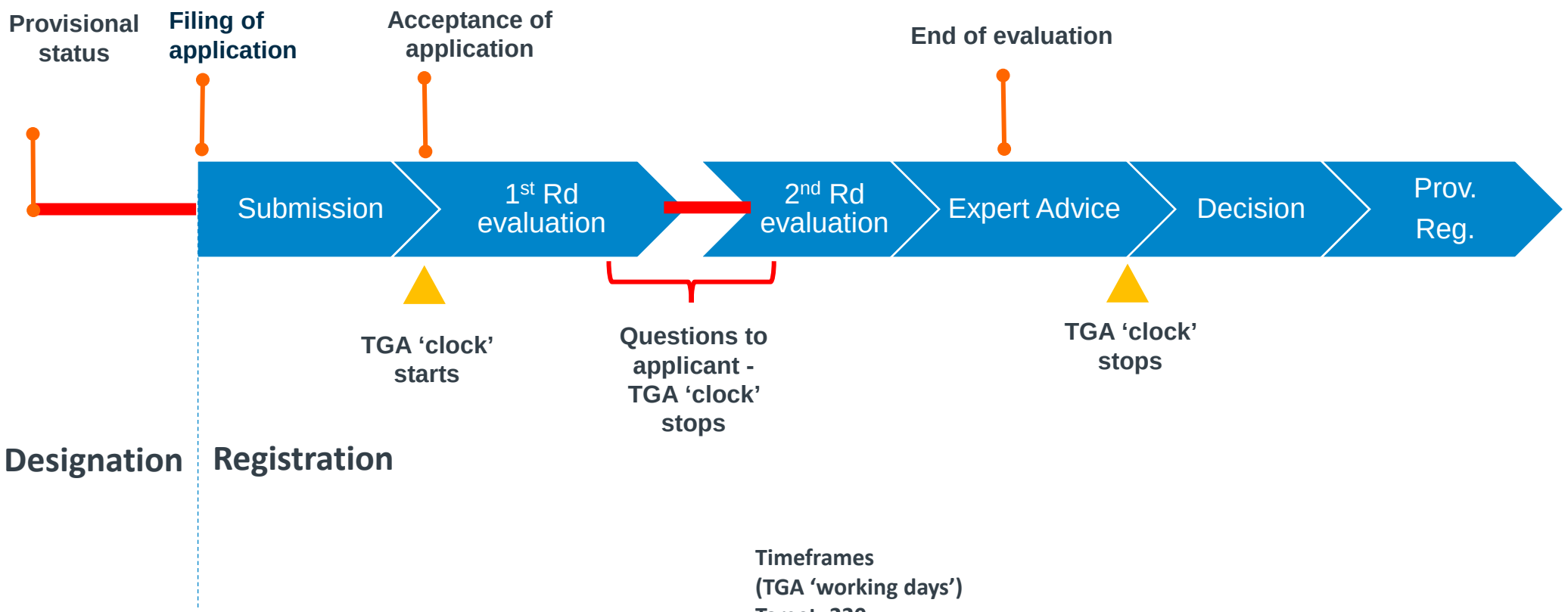
Provisional registration process



Timeframes
(TGA 'working days')
Target: 220
Statutory: 255

Provisional approval pathway | Therapeutic Goods Administration (TGA)

Quiz time!

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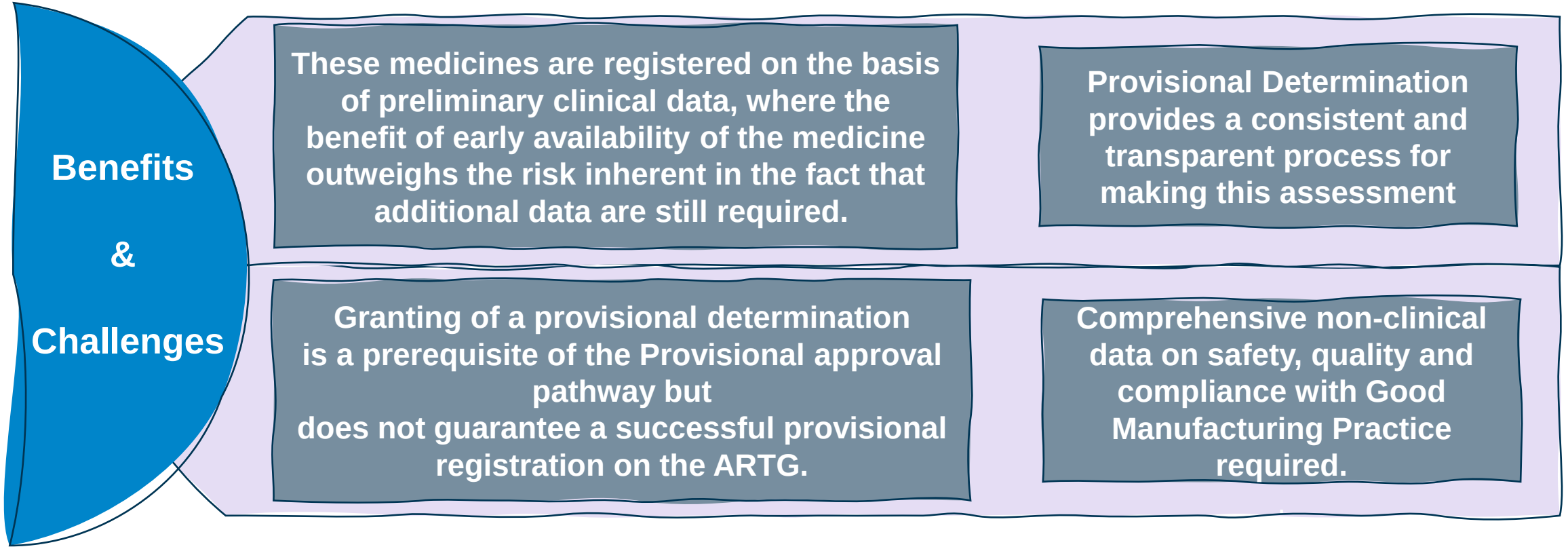
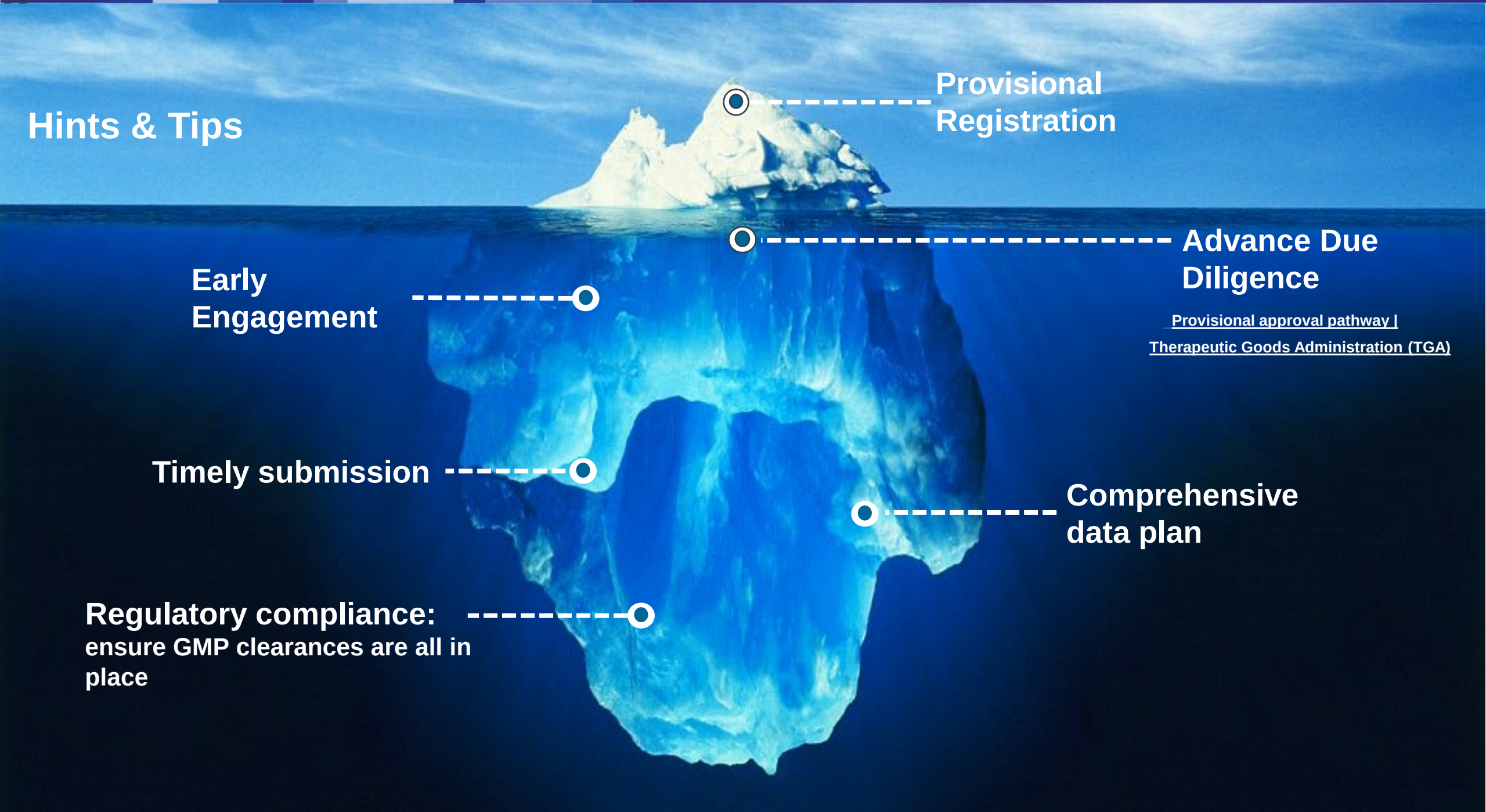
Benefits and Challenges



Provisional approval pathway | Therapeutic Goods Administration (TGA)

Hints & Tips


Provisional Registration
Advance Due Diligence
Early Engagement
Provisional approval pathway | Therapeutic Goods Administration (TGA)
Timely submission
Comprehensive data plan
Regulatory compliance:
ensure GMP clearances are all in place

Takeaway

Engage early, for a timely submission with a comprehensive data plan ensuring GMP clearances are in place.

Questions?

Scan the QR code with your device to submit a question.

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration