‘S’ is for sure

Type S submissions to convert provisional to full registration

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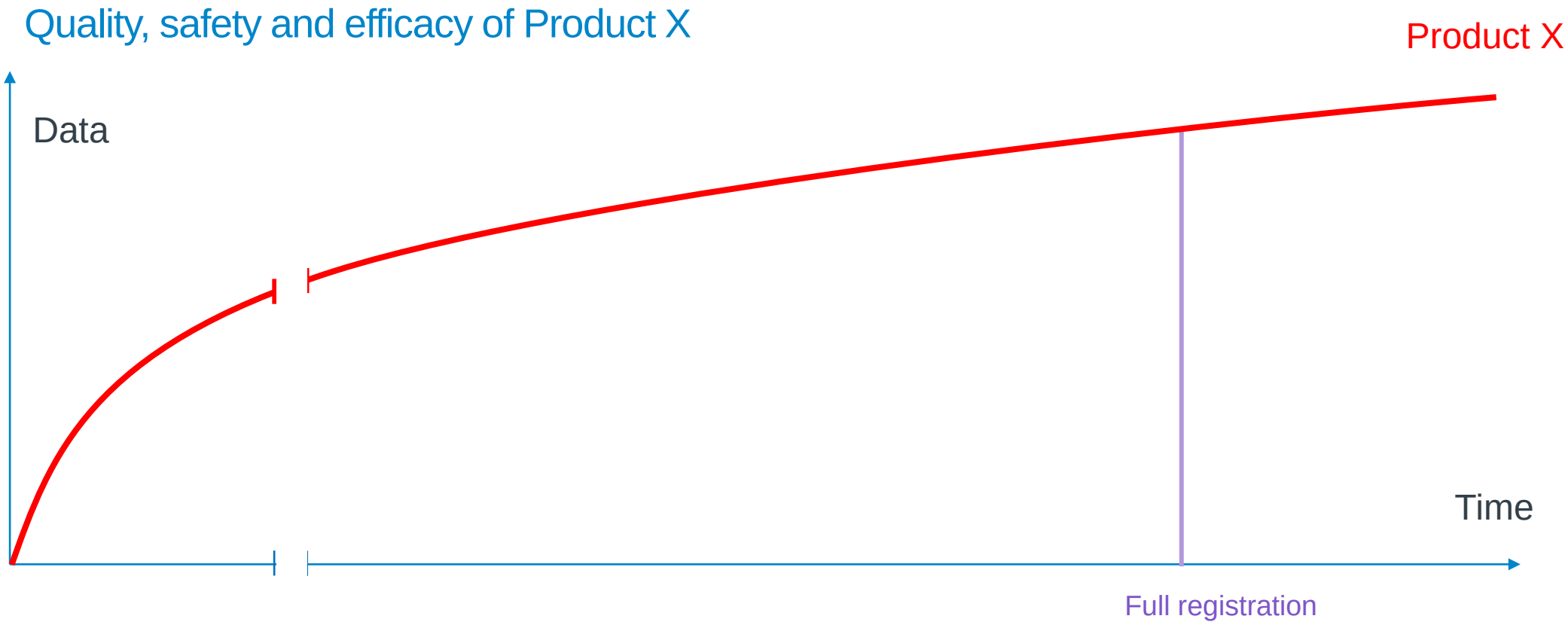
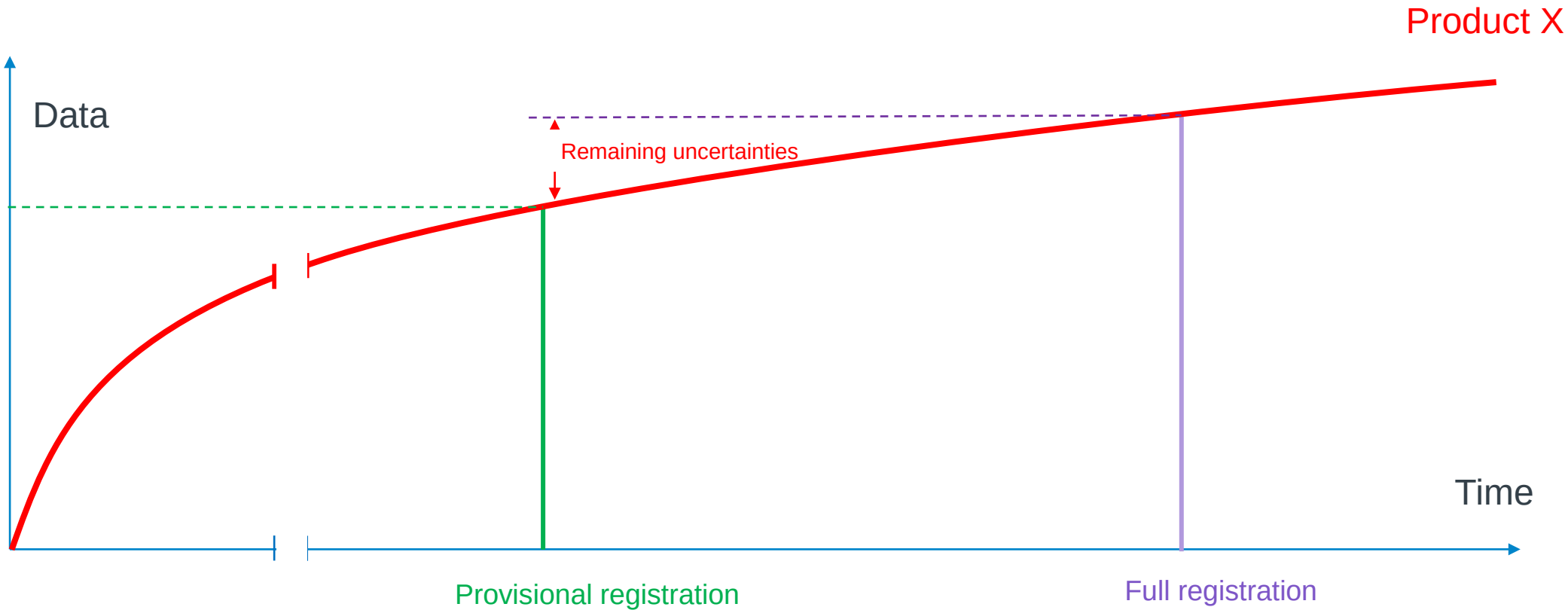
Data accumulates over time



Enter provisional



Therapeutic Goods Act 1989
https://www.legislation.gov.au/Details/C2021C00376

The Act says

The Secretary must consider

Full registration:

- whether the **quality**, **safety and efficacy** of the goods for the purposes for which they are to be used have been satisfactorily established

Provisional registration:

- whether, based on **preliminary clinical data**, the **safety and efficacy** of the medicine for the purposes for which it is to be used have been satisfactorily established; and
- whether the **quality** of the medicine for the purposes for which it is to be used has been satisfactorily established;
- whether…the Secretary is satisfied with the applicant's plan to submit comprehensive clinical data on the safety and efficacy of the medicine before the end of the 6 years that would start on the day that registration would commence;

Therapeutic Goods Act 1989
https://www.legislation.gov.au/Details/C2021C00376

The Act says

The Secretary must consider

EITHER

Full registration:

- whether the **quality**, **safety and efficacy** of the goods for the purposes for which they are to be used have been satisfactorily established

OR

Provisional registration:

- whether, based on **preliminary clinical data**, the **safety and efficacy** of the medicine for the purposes for which it is to be used have been satisfactorily established; and
- whether the **quality** of the medicine for the purposes for which it is to be used has been satisfactorily established;
- whether…the Secretary is satisfied with the applicant's plan to submit comprehensive clinical data on the safety and efficacy of the medicine before the end of the 6 years that would start on the day that registration would commence;

Built-in, transparent management of uncertainties

Requirement for a plan to obtain comprehensive data to address uncertainty.

The plan goes into the Australia-Specific Annex to the Risk Management Plan.
TGA assesses it before granting provisional determination/registration or extensions.

Automatic lapse at 2 years unless:

- Extended for 2 more years (type T)
- Converted to full (type S)

Type T applications must be lodged **a minimum of 6 months** prior to the lapse date.

Type T acts as a 2-yearly **checkpoint:**

- Is the plan going ok?

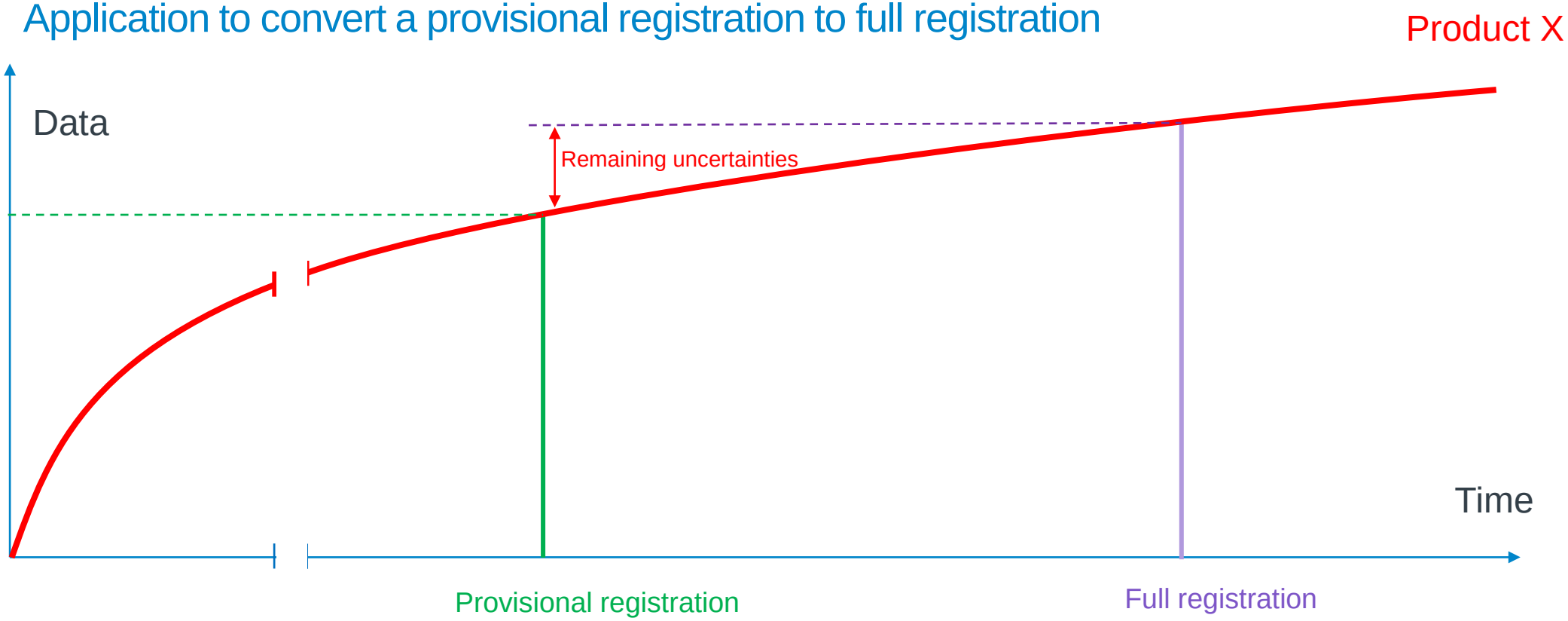
Also “anything else”

Maximum of 2 extensions (6 years total).

i.e. If approved, the 2 year extension applies from date that provisional registration would have lapsed, not from date of application.

Type S

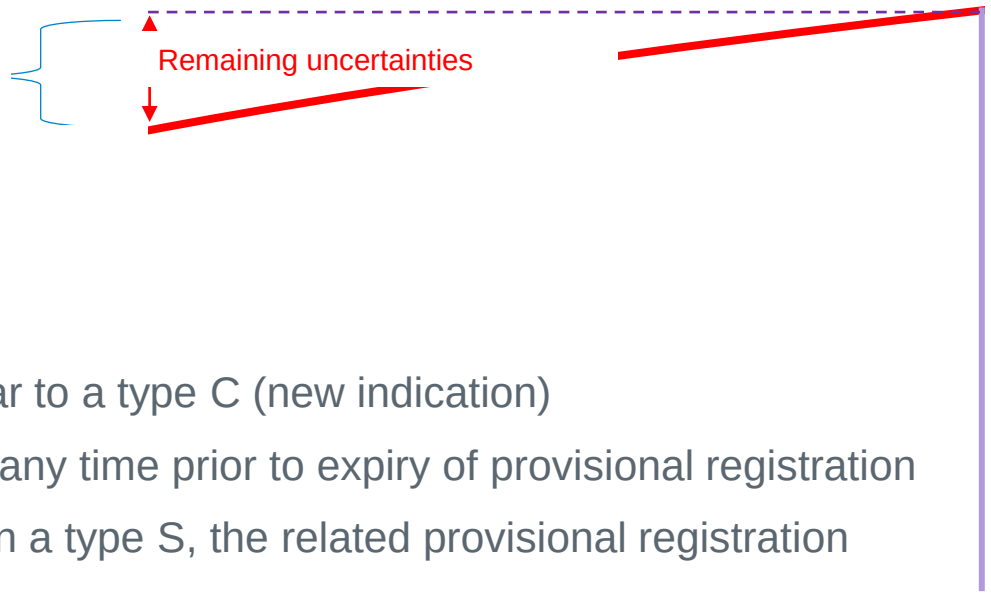
Application to convert a provisional registration to full registration



Type S

Application to convert a provisional registration to full registration

- Consists of the data gathered according to pla
rer
so
cli
“comprehensive
- The process is very similar to a type C (new indication)
- Type S can be submitted any time prior to expiry of provisional registration
- Until there is a decision on a type S, the related provisional registration continues



What content might be in a type S?

Limitations of provisional dataset	Possible uncertainties	Comprehensive data might include
• No internal comparator • Other statistical limitations	1. Was this a chance finding? 2. What would have happened in that group if you hadn't intervened? 3. Time-to-event endpoints (PFS, OS) can't be reliably interpreted.	1. Reproduction 2/3. Randomisation
• Small group size • Short duration of follow-up	4. Low precision estimates (effect size, durability) 5. Limited safety data (population, duration)	4&5. Additional patients/follow-up time

1 WHAT

2 WHEN

Tips for planning

FDA draft guidance on accelerated approvals and CT design in the oncology space:

https://www.fda.gov/news-events/press-announcements/fda-issues-draft-guidance-aimed-improving-oncology-clinical-trials-accelerated-approval

EMA reflection paper on single arm trials supporting regulatory decisions:

https://www.ema.europa.eu/en/establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing-authorisation

What if…?

Things can change

- Open communication is key
- Shared philosophy

Scenarios:

1. What if ‘confirmatory’ trial fails?

2. What if we get to six years and there is still meaningful uncertainty?

Provisional pathway in the COVID-19 pandemic

Dr Mohit Khera
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Department of Health and Aged Care, TGA

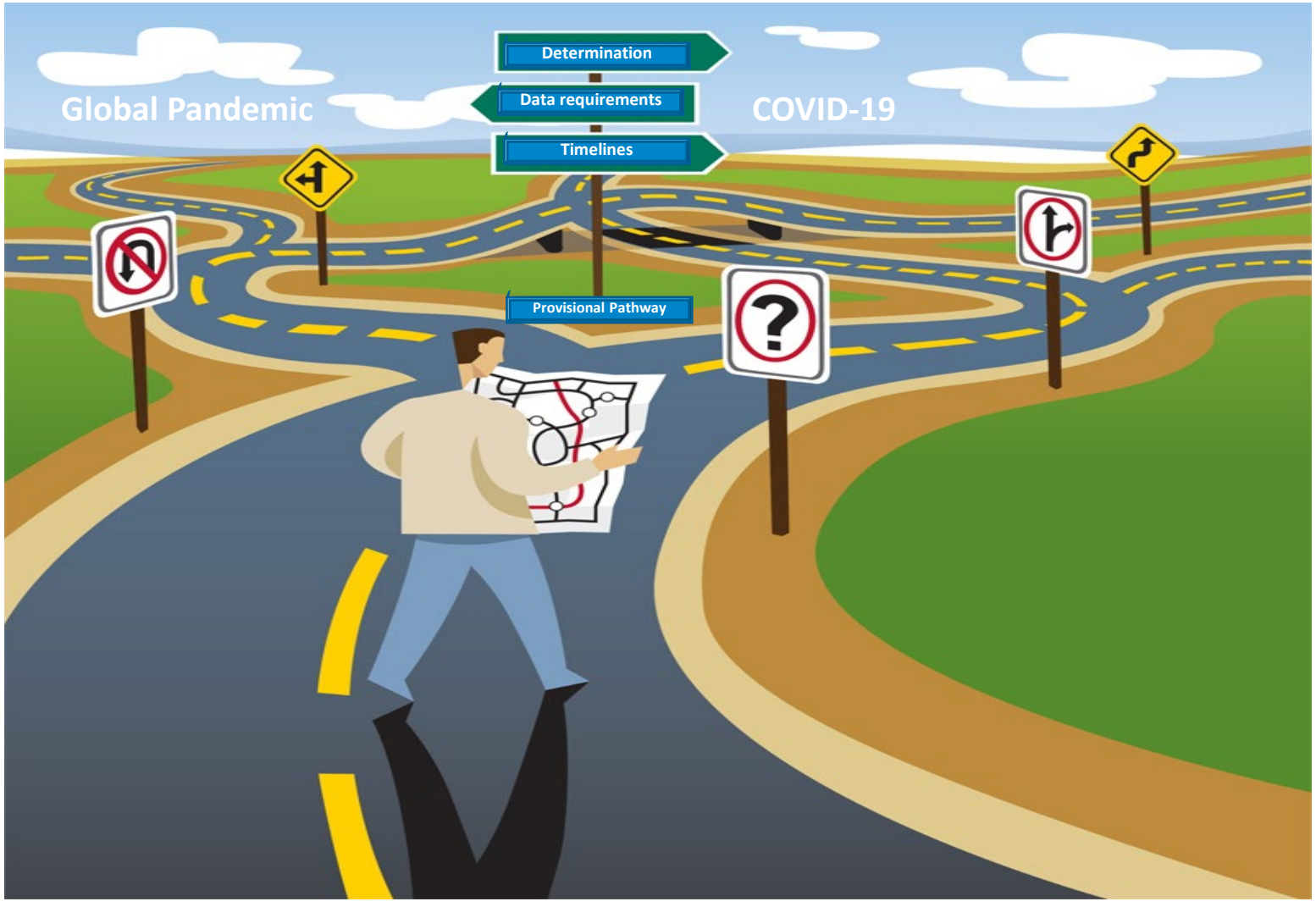
Role of the regulator – Therapeutic Goods Administration

- 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**

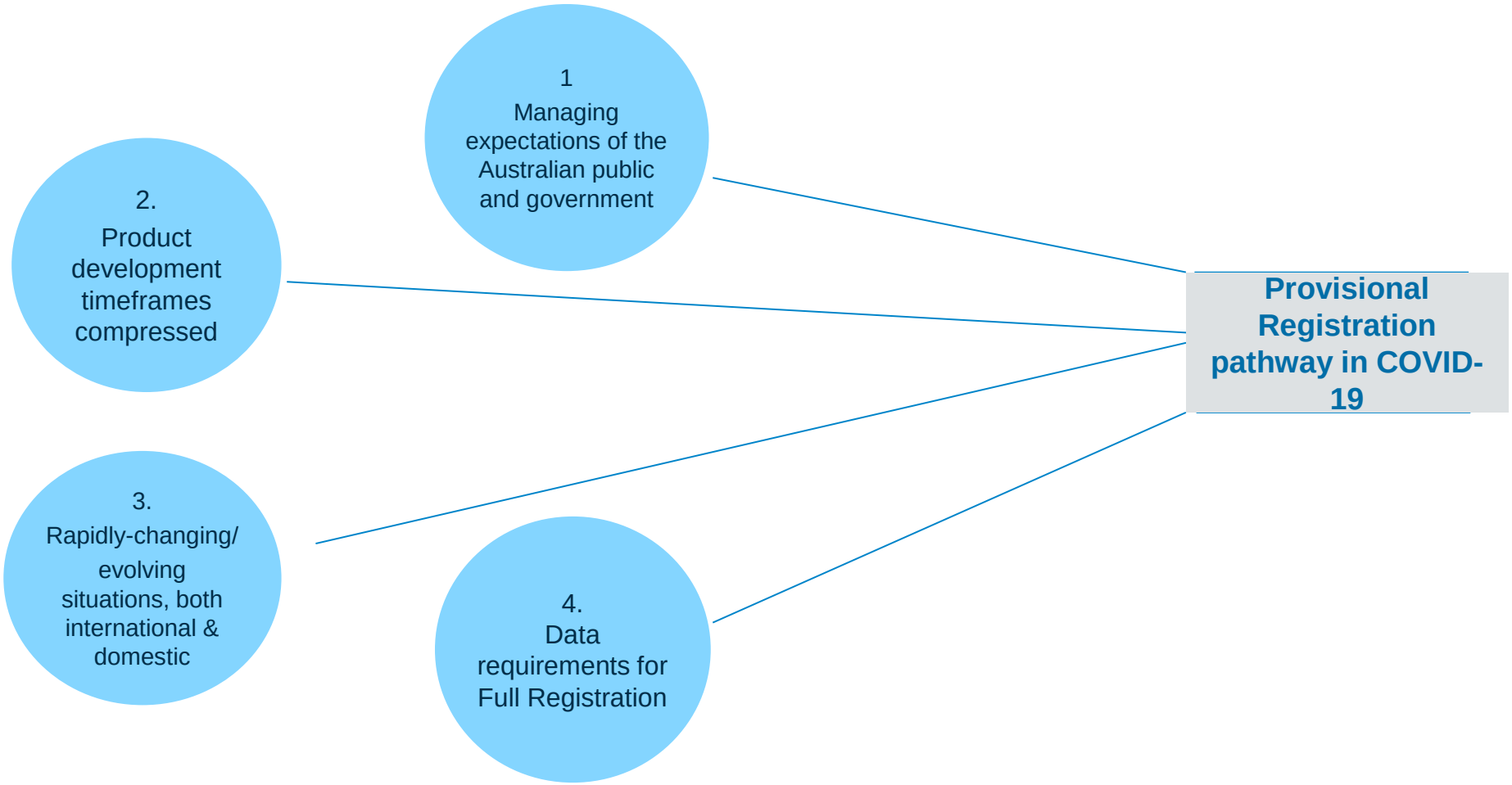
Regulation in a Pandemic: COVID-19

- 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

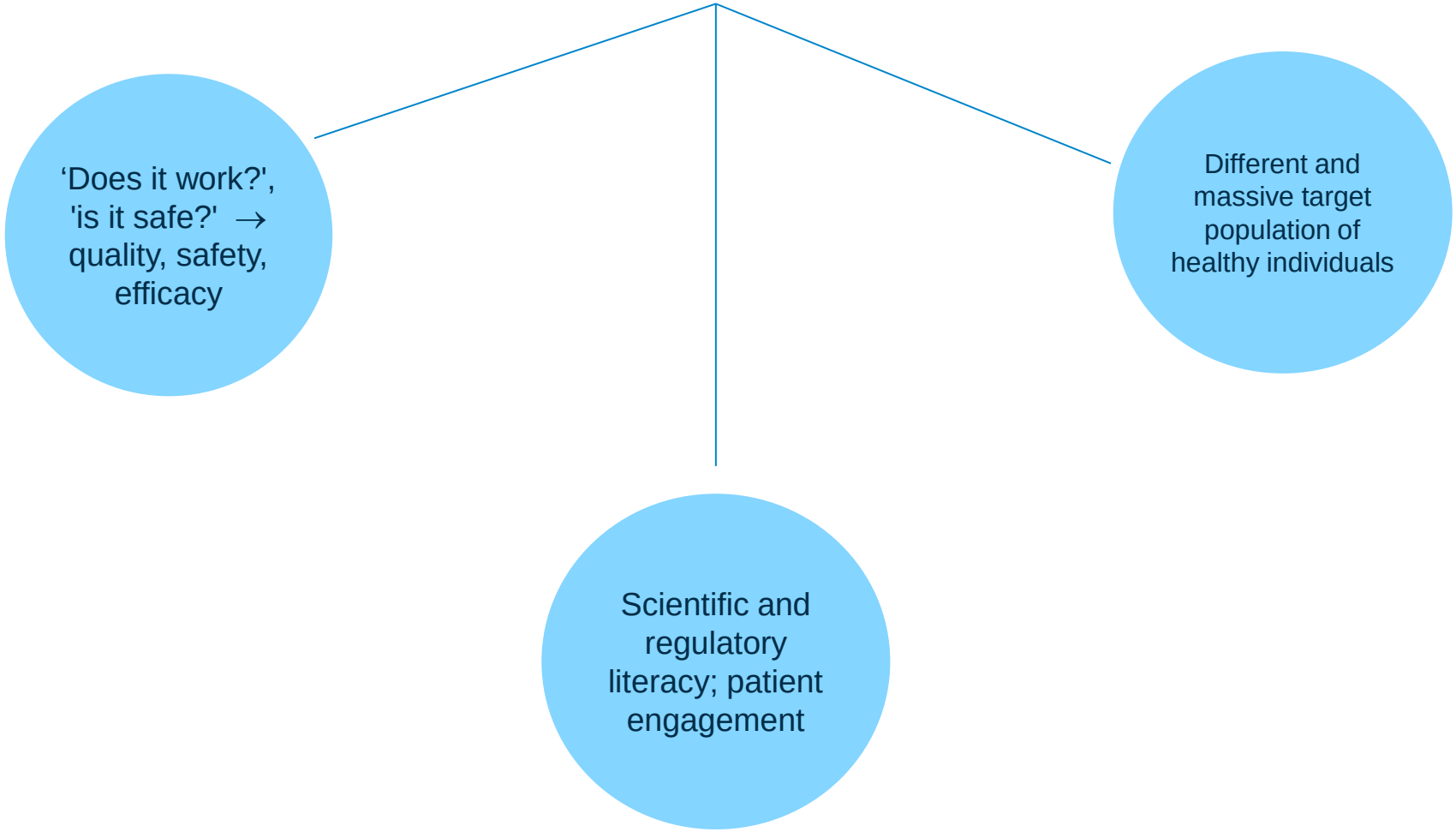
Fit for purpose – Emergency situation



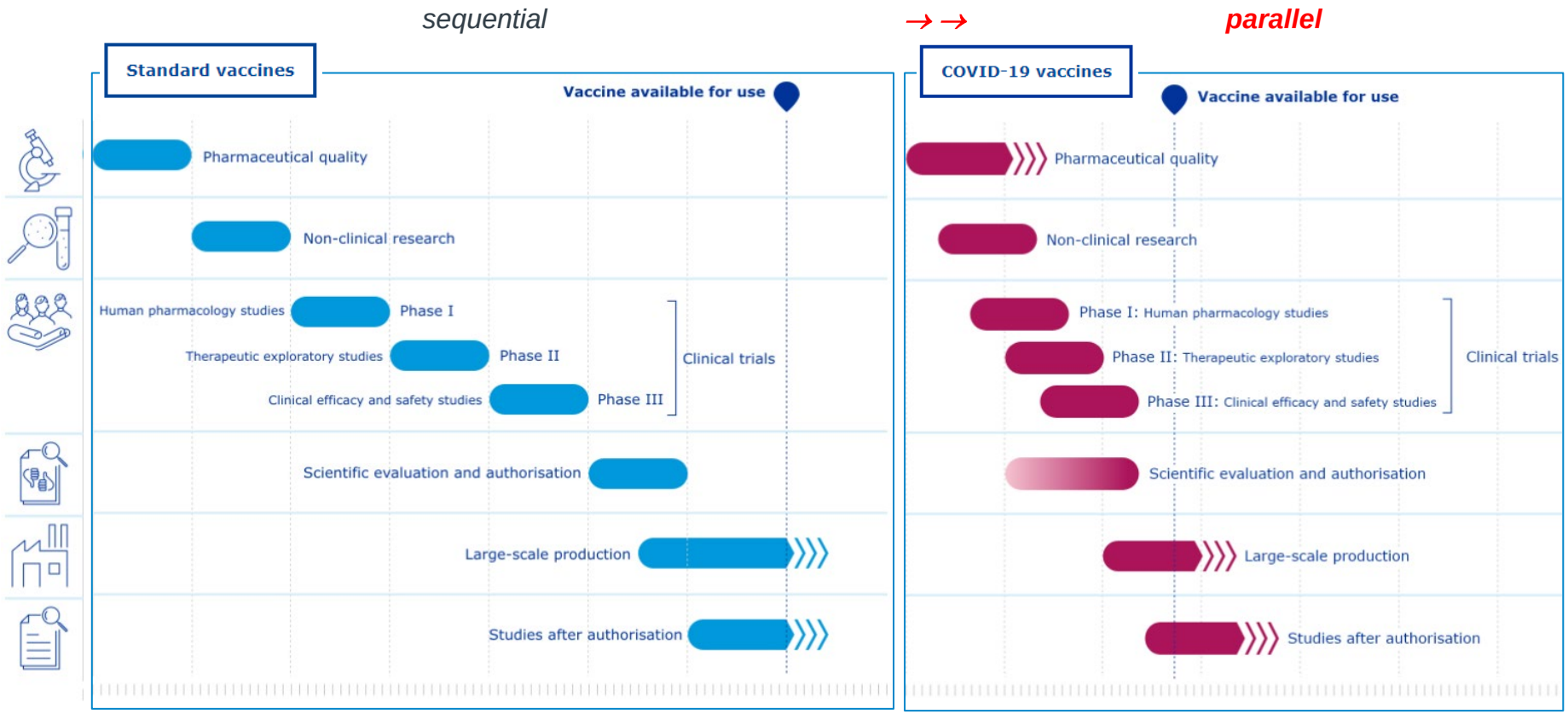
Challenges


1
Managing expectations of the Australian public and government
2.
Product development timeframes compressed
3.
Rapidly-changing/ evolving situations, both international & domestic
4.
Data requirements for Full Registration
Provisional Registration pathway in COVID-19

Managing expectations of the Australian public and government



Product development timeframes compressed



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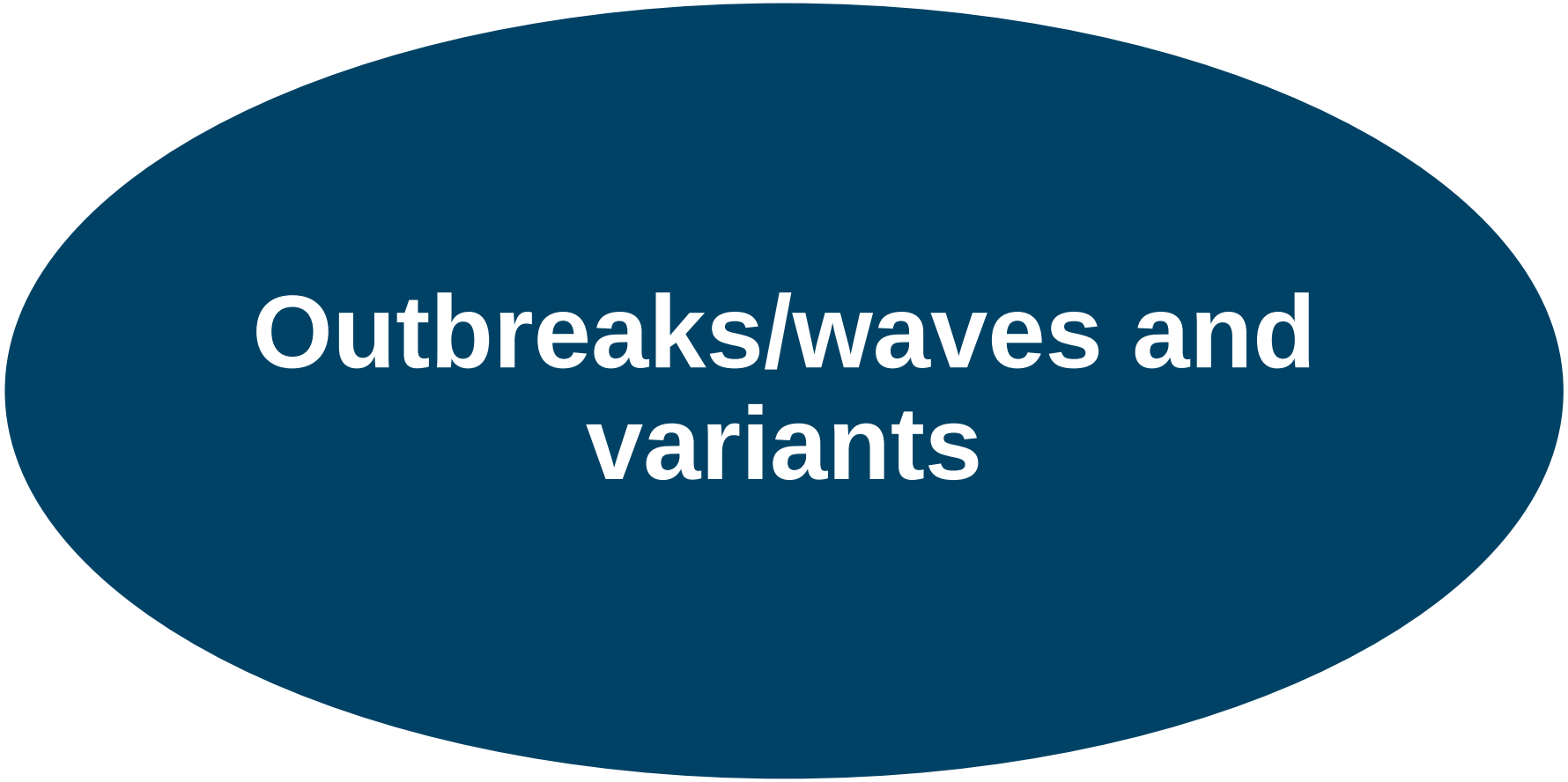
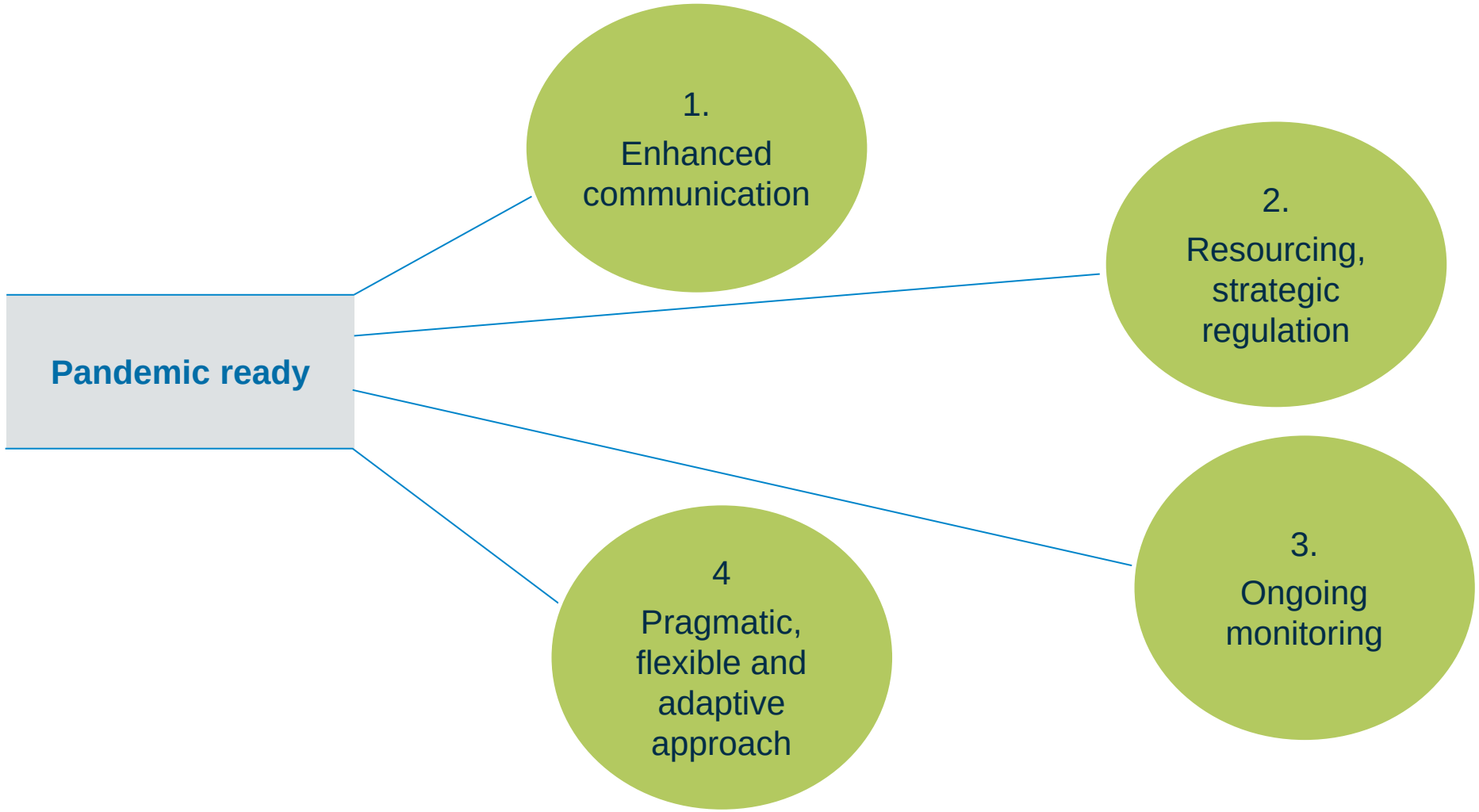
https://www.tga.gov.au/covid-19-vaccine-information-consumers-and-health-professionals#provisional

Provisional process in the COVID-19 situation

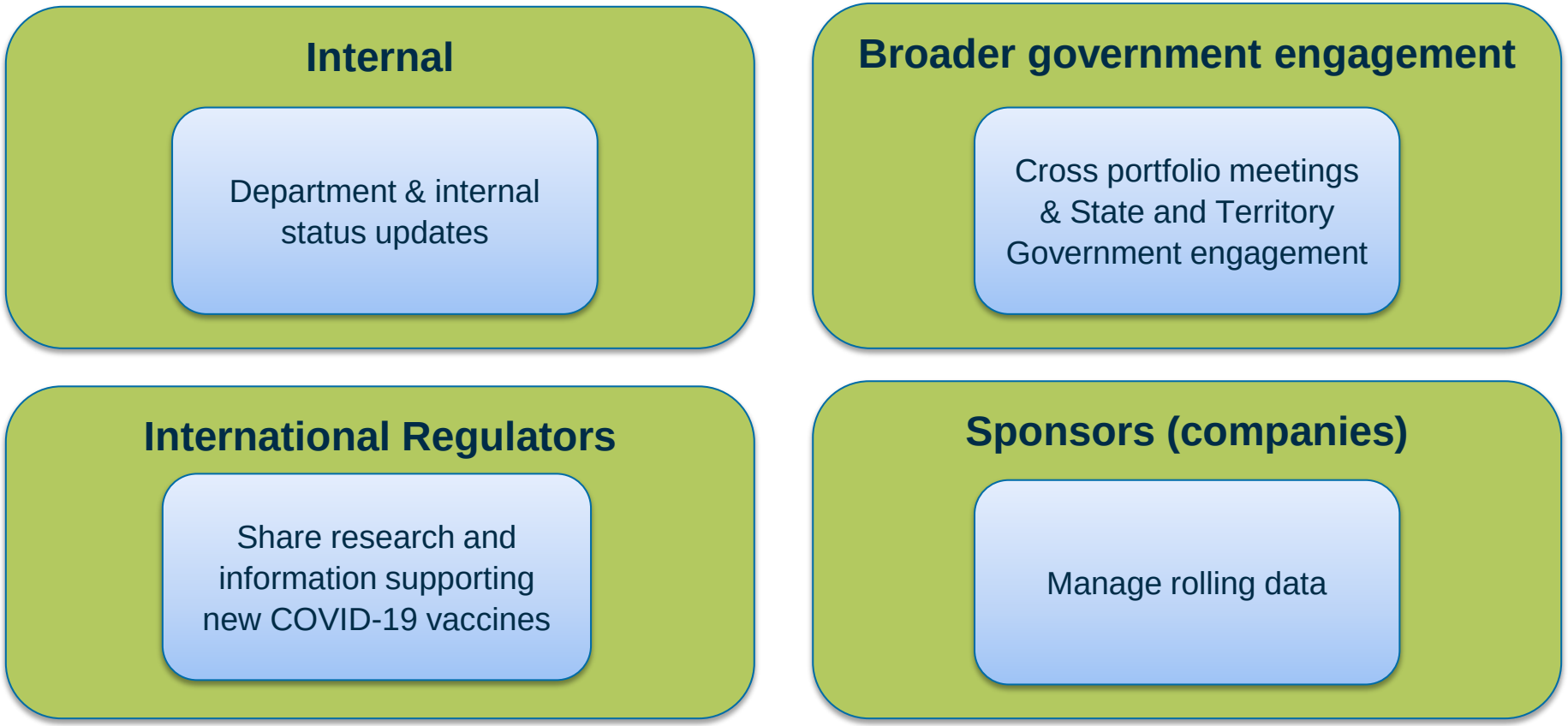
Rapidly-changing/evolving situations, both international & domestic



TGA strategies and response



Enhanced communication



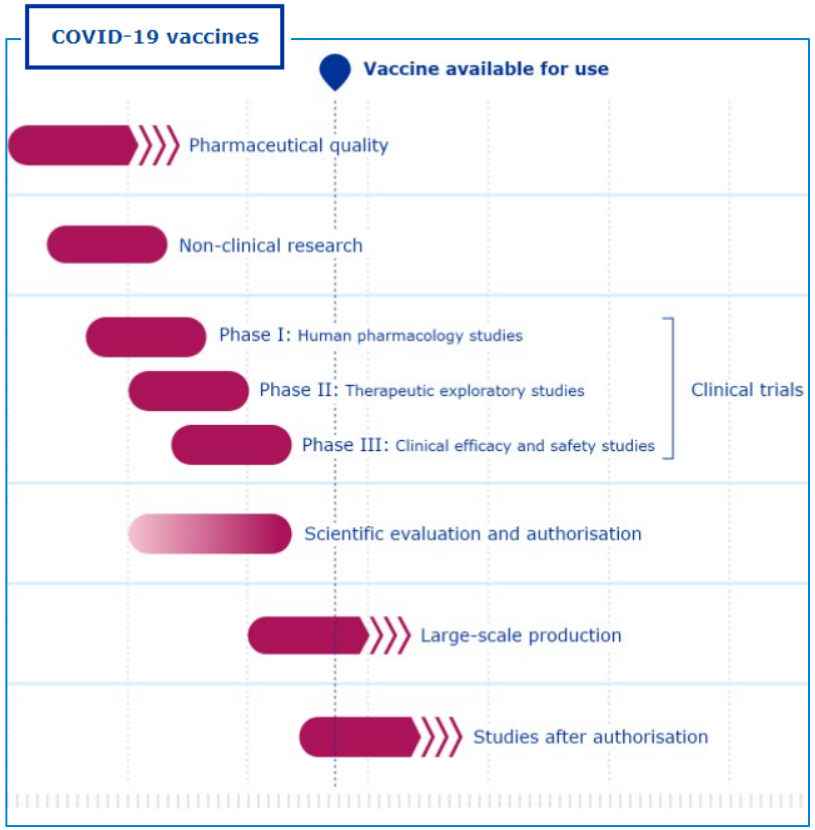
Resourcing, strategic regulation

- Additional layer of support to regulatory scientists/medical officers & Executive
- Liaison & coordination with internal/ external (companies, evaluators, broader Dept., Intl regulators)
- Communications, updates, queries (Minister, Senate Estimates, consumers)
- Strategic options, legislation (pathways, flexibilities in a pandemic)

Expedited evaluation process

Product development and regulatory evaluation timeframes compressed:

- Enhanced communication and planning:
  - weekly t/c with companies during evaluation
- Rolling data & 'informal' format
- Rapid and rolling review by evaluators:
  - highest priority work
  - additional hours
- Ad-hoc meetings of expert advisory committees
- International collaboration with other regulators



https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-development-evaluation-approval-monitoring
https://www.tga.gov.au/covid-19-vaccine-information-consumers-and-health-professionals#provisional

Provisional process in the COVID-19 situation

COVID-19 vaccine and treatments: Provisional registrations

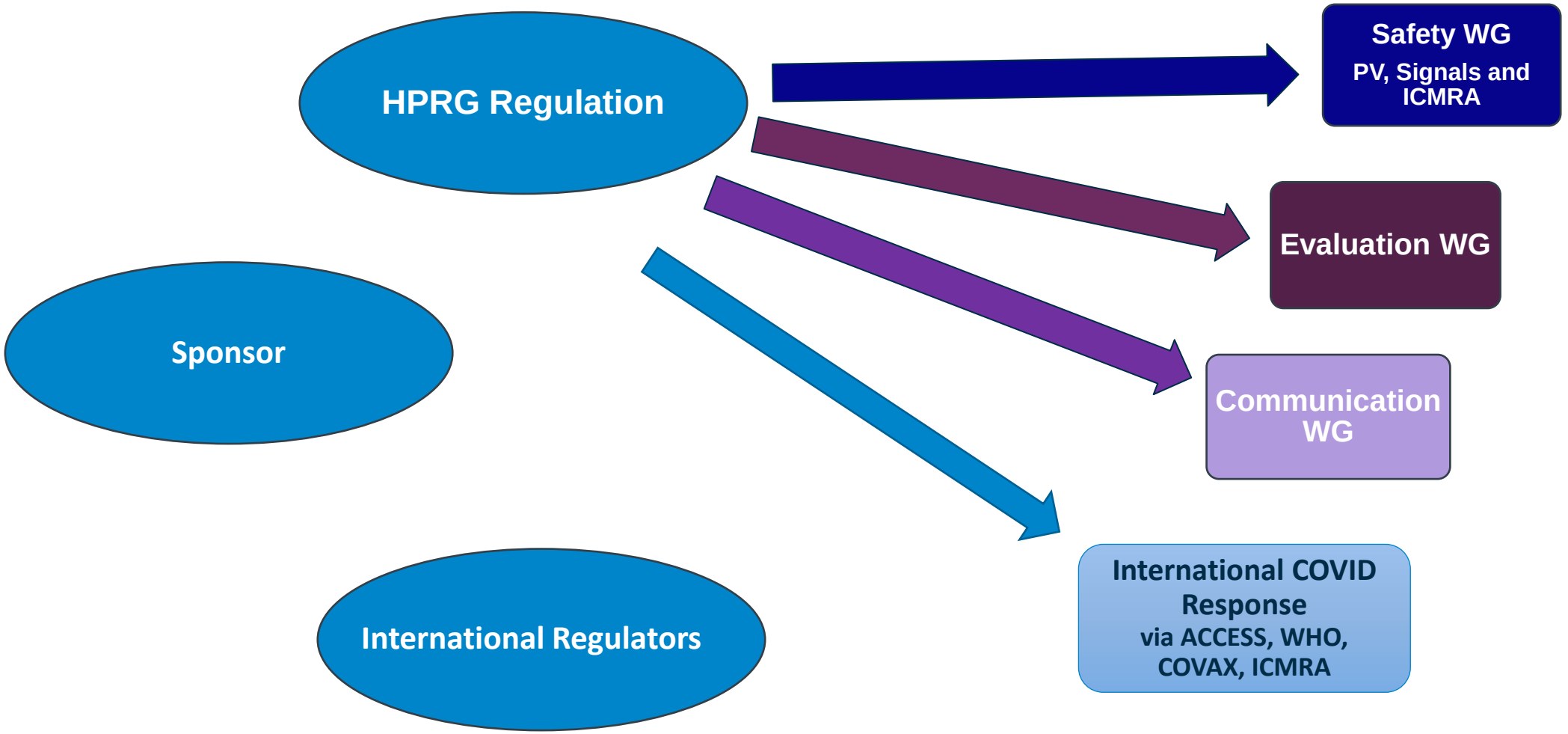
Before any COVID-19 vaccine is approved for use in Australia, it will be subject to the well-established and rigorous assessment and approval processes of the Therapeutic Goods Administration (TGA), part of the Department of Health.

COVID-19 vaccine: Provisional registrations | Therapeutic Goods Administration (TGA)

COVID-19 vaccines undergoing evaluation | Therapeutic Goods Administration (TGA)

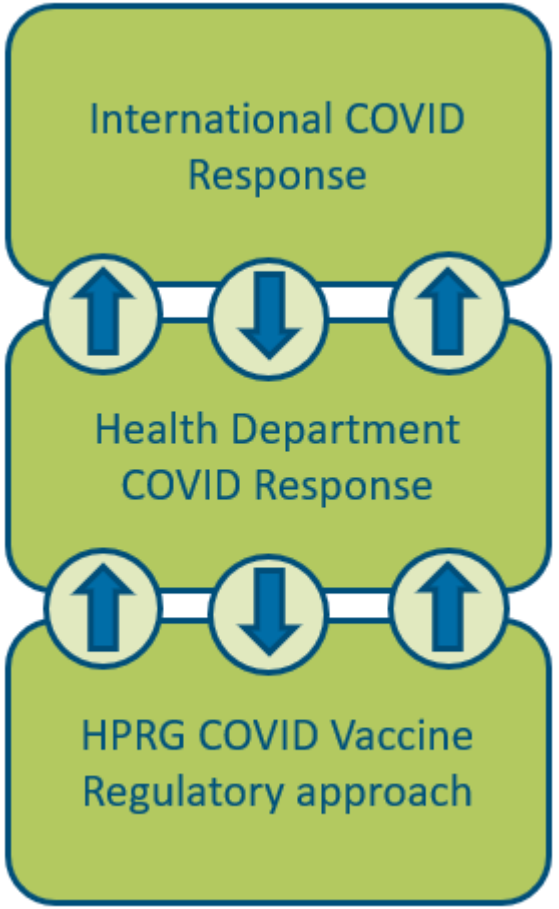
COVID-19 treatments: Provisional registrations | Therapeutic Goods Administration (TGA)

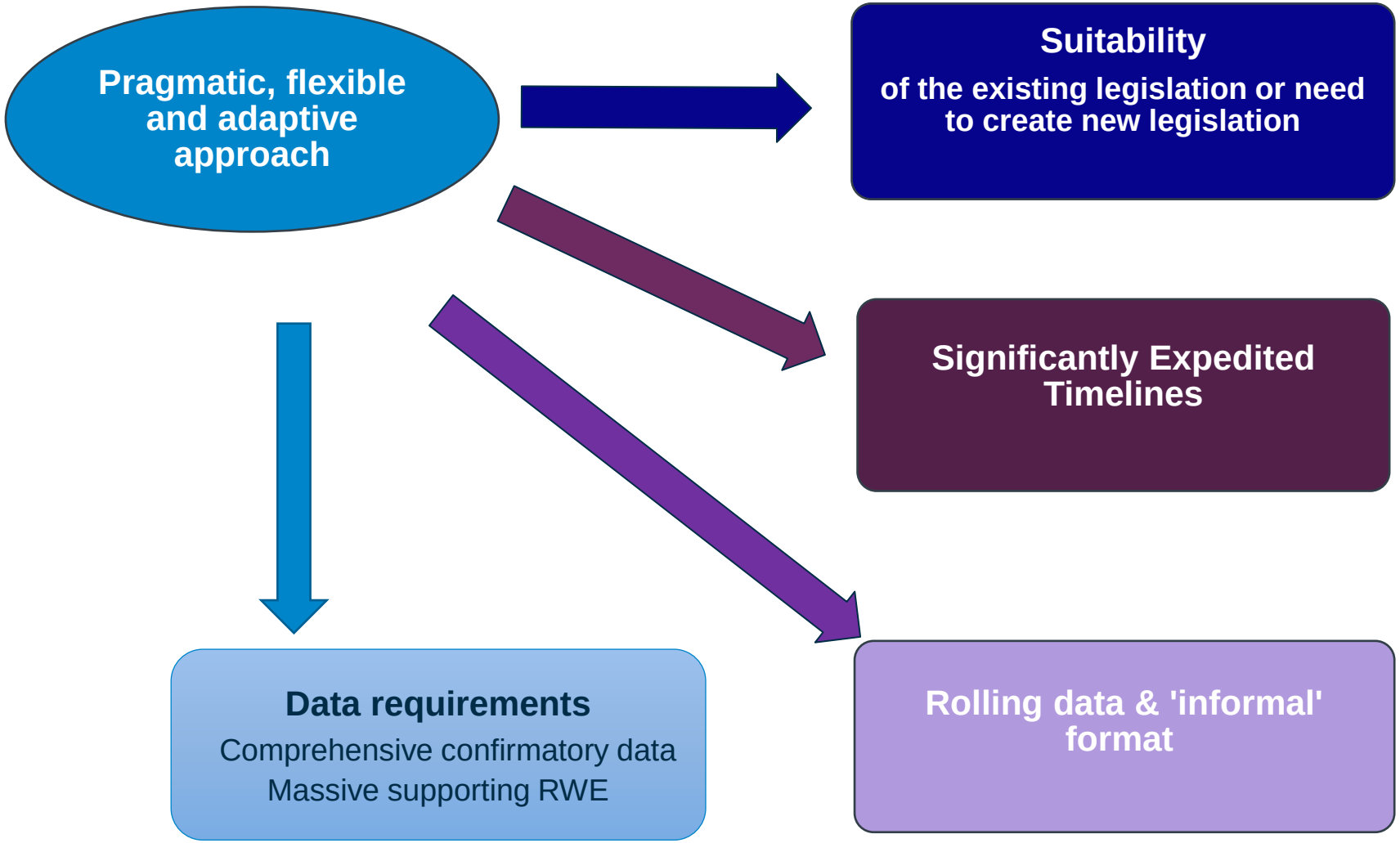
Ongoing monitoring



Global COVID response & interlinkages

- **TGA involvement with International COVID Response**
  - via WHO, COVAX, ICMRA & subgroups, ACCESS consortium
- **Health Department COVID response**
  - Multi-faceted - various programs mental health, immunisation, testing, Aged Care
  - National COVID vaccine strategy taskforce (5 teams)
  - ATAGI, OGTR, Communications
- **HPRG COVID regulatory approach**
  - Evaluation WG, Safety WG & Communications WG




Pragmatic, flexible and adaptive approach
Suitability
of the existing legislation or need to create new legislation
Significantly Expedited Timelines
Data requirements
Comprehensive confirmatory data
Massive supporting RWE
Rolling data & 'informal' format

Learnings- The Three “C” for S (Success)

Collaboration = Proactive

Communication = Open and enhanced

Confidence-building = gaining comfort/confidence in processes and regulatory framework

Australian Government

Department of Health

Therapeutic Goods Administration