Australian Government
Department of Health
Therapeutic Goods Administration

Worksharing on medicines evaluation: the ACSS experience

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10th Asia Regulatory Virtual Conference, 3 Nov 2020

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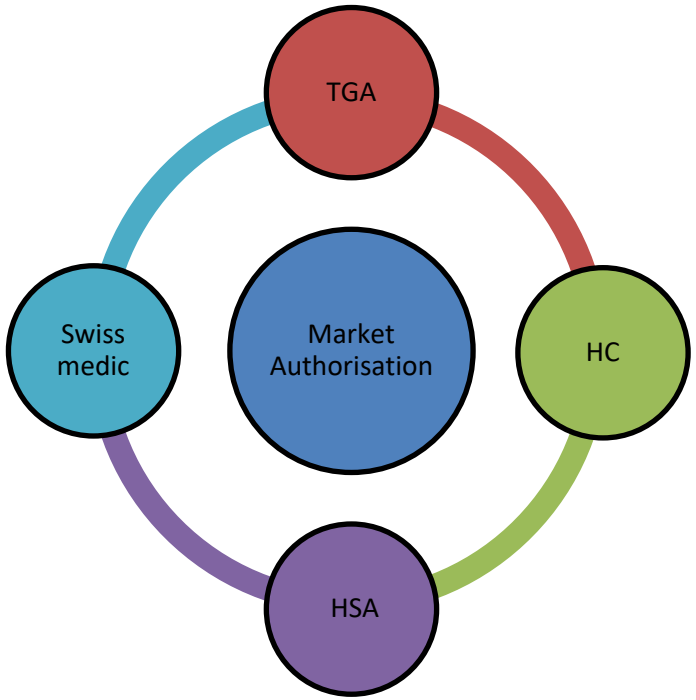

- **Regulatory collaboration between:**
  - ✓ Therapeutic Goods Administration (TGA)
  - ✓ Health Canada (HC)
  - ✓ Singapore Health Sciences Authority (HSA)
  - ✓ Swiss Therapeutic Products Agency (Swissmedic)
- **Including worksharing on market authorisation:**
  - Generic medicines
  - New Chemical Entities (New prescription medicines)

  ….. and Complementary Health product ingredients
- Supported by confidentiality agreements and MOUs
- Work-sharing on the evaluations but with **sovereign decisions by each country on market authorization**

Breaking news: the UK joins from 1 Jan 2021

- As a leading regulator, the MHRA will bring **additional expertise and resources** into the Consortium
- And the Consortium will be renamed **"ACCESS"**
- Will enable Access to take on **a greater number of work-shared applications**, including COVID products
- Sponsors will benefit from having their **products considered simultaneously for market authorisation** in Australia, Canada, Singapore, Switzerland and UK
- Access countries now represent a combined market of around **145 million people**

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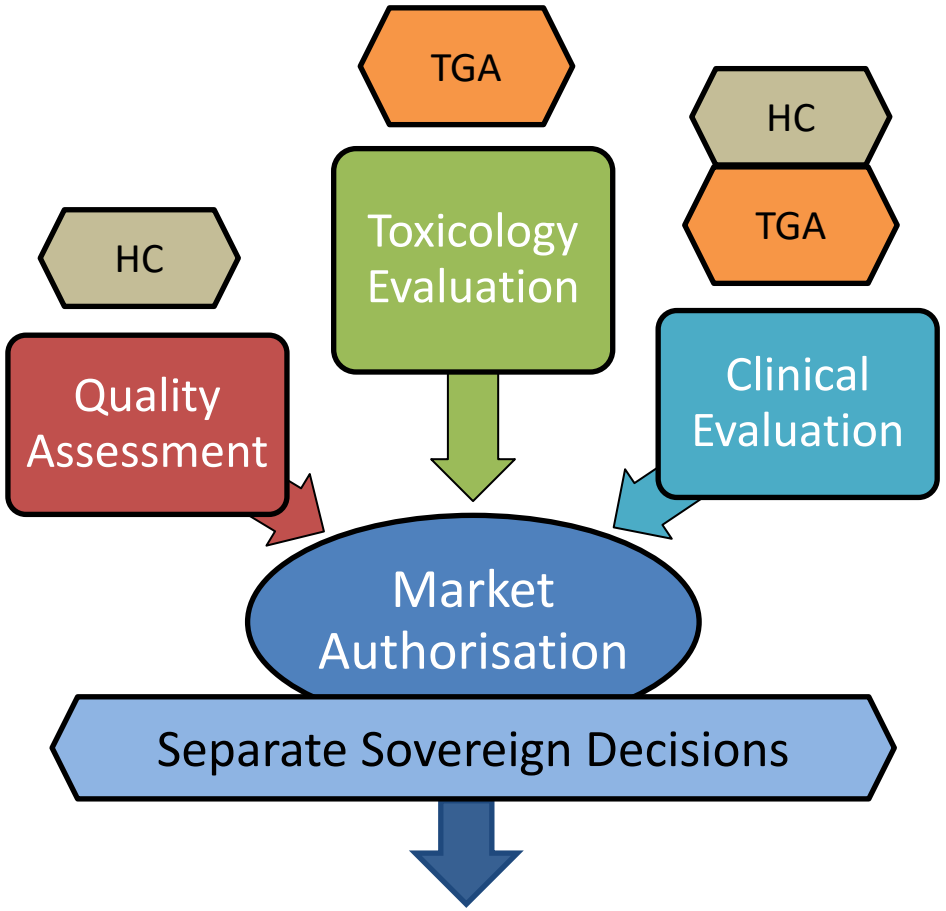
Australia - Canada NCE pilot



Information sharing was the first step

- Understand review frameworks for each regulator (both internal processes and the pathways)
- Conduct retrospective analysis of decisions made by each regulator on the same medicine

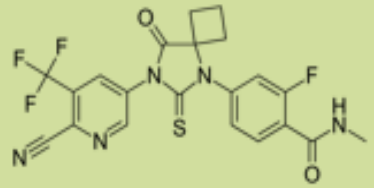
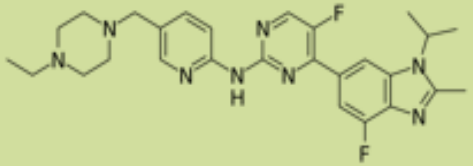
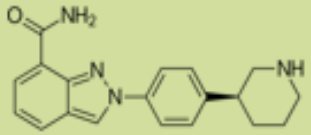
Confidence building prelude to worksharing

- Sharing of all pre-clinical and clinical evaluation reports
- Parallel reflection on evaluations and evaluator exchanges

Followed by a pilot

- Across 3 evaluation areas – clinical, non-clinical & quality
- HC and TGA - Parallel clinical evaluation or only one partner
- ***Work-sharing*** = division of evaluation of dossier modules between jurisdictions

Initial collaboration was between Australia and Canada

Submission	Indication (abbreviated)	Module 3 Quality	Module 4 Non-clinical	Module 5 Clinical	Status
apalutamide (ERYLAND) *Janssen-Cilag* 	prostate cancer				**approved** Jul 2018
abemaciclib (VERZENIO) *Eli Lilly* 	breast cancer				**approved** Apr 2019
niraparib (ZEJULA) *Takeda / Tesaro* 	ovarian, fallopian, peritoneal cancer				**approved** Jun 2019

Switzerland and Singapore now actively worksharing too

- **Seven new molecular entity medicines have been approved so far** following ACSS worksharing evaluation

- As of October 2020, a further:
  - ✓ **five** submissions are currently under evaluation, plus
  - ✓ **eight** submissions are under consideration for work-sharing

- **Names and broad indications of medicines under evaluation** will be made public from 1 January 2021
  - Canada already publishes some information

Submission	Indication	Module 3 Quality	Module 4 Non-clinical	Module 5 Clinical	Approval
ERLEADA (apalutamide)	Prostate cancer			 	July 2018
VERZENIO (abemaciclib)	Breast cancer				April 2019
ZEJULA (niraparib)	Ovarian cancer				June 2019
XOFLUZA (baloxavir marboxil)	Anti-viral (influenza)				Feb 2020
NUBEQA (darolutamide)	Prostate cancer				Feb 2020
VYNDAQEL (tafamidis)	Cardiomyopathy			 	March 2020
SARCLISA (isatuximab)	Multiple myeloma				Apr 2020

Encouraging the right applications for worksharing

- First three medicines were “agency identified”… now mainly **sponsor-nominated medicines**
- **Governance arrangements** were codified to build confidence and transparency
  - Assign lead coordinating regulator to manage across jurisdictions and sponsor communication.
  - SharePoint platform for secure communications and sharing of information
  - Establish leads for other dossier components e.g. BE, RMP, PopPK, clinical pharmacology, impurities
  - Flexible in use of external committee advice
- **EOI form, Q&As, Guidance for Industry** documents published:
  - Lead time of 3–6 months for planning then file within 2 weeks in each country
  - Identical dossiers across jurisdictions (except country-specific aspects)
  - Same registration pathway across jurisdictions (standard or priority for all)
  - Multi-way teleconferences include regulators and local sponsors
- **Independent decision-making** by each jurisdiction
- The ACSS partners - not sponsors - **decide which applications to worksharing** on

Generics – a slow start but some momentum now ?

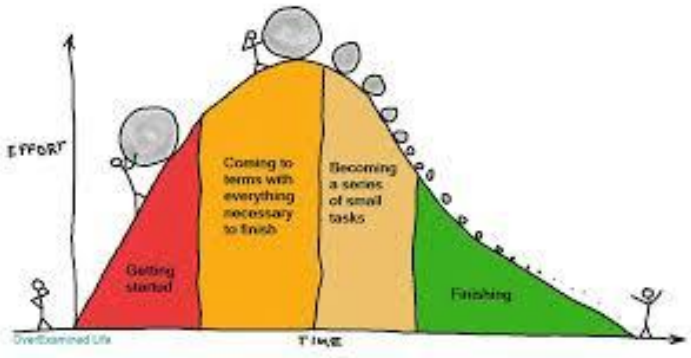
- **First promoted in 2013-14 – <u>before</u> NCE worksharing** – thought to be simpler
  - **Different approach used** – similar to the EU Decentralised Procedure
  - one regulator as Reference Agency reviewed all of the dossier except Module 1
- **Everolimus approved April 2017** – TGA reference agency, Canada and Swissmedic collaborators
- **Pasaconazole February 2020** – Canada reference agency, TGA and Singapore collaborators
- **Fulvestrant approved May 2020** – Singapore reference agency, TGA collaborator
- A **fourth generic is currently under consideration** for worksharing

Challenges: *Choice of reference products*
Differing patent expiration dates / sponsor arrangements between countries

Challenges with worksharing

- **Alignment of submission timeframes** can be difficult
- Increased **coordination effort** with applications across time zones
- Accommodating **specific national regulatory requirements** and differences between technical guidelines
- **Shorter evaluation timeframes** to accommodate peer review
- **Different risk/benefit analysis** or data interpretation/emphasis between regulators
- Different **administrative processes** between regulators – decision making process, advisory committees, transparency
- Challenges with **parallel HTA/ payer assessment**

Saving in work only now starting to exceed the investment of additional effort !



So, do the benefits outweigh challenges? Yes !

- **Reduced duplication of effort** leading to more efficient review
- Sharing of resources **eases internal resource pressure**
- Potential for **greater alignment of regulatory decisions**
- **Internationally showcases expertise** across evaluation areas
- Greater exposure to **emerging global trends and learnings**
- Greater technical discussion of issues **could make the final decision more robust**
- Greater **transparency of regulatory decisions** for industry
- **Earlier patient access to medicines** in several countries

Encouraged us to take part in additional collaborations e.g. US FDA Oncology

Will worksharing become the normal review approach for medium-sized regulators ?

Industry

- Simultaneous market authorisation in all participating jurisdictions
- Bespoke pathway with transparency and predictable time frames
- Reduced regulatory burden with global dossiers

Regulators

- Improved efficacy with potential to reduce regulatory effort
- Best of both worlds - Sovereign decisions and harmonisation
- Better decision through collaboration

More information

- https://www.tga.gov.au/australia-canada-singapore-switzerland-united-kingdom-access-consortium
- https://www.tga.gov.au/acss-nas-work-sharing-initiative
  - Expression of interest form with information on sharing of the evaluation reports
  - Information on the drafting of AusPARs following the release of the decision)
  - Q&A for sponsors
  - Guidelines for Industry

- Considering extending work-share arrangements to submissions for:
  - Extension of indications
  - Vaccines

- ACCESS is still interested in more expressions of interest from sponsors !!!