Health Canada Santé Canada

Canada

International Work Sharing

CAPRA Education Day

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Outline

- What is it?
- Why are we doing it?
- Why is it important?
- What we have done?
- The future

What is International Work-Sharing?

- It is exactly what the name says:
  - The work that we do to review drug submissions is shared between different regulators.

- We can share the work for each submission:
  - We'll review this part of the submission and you review the other part.

- We can share the work across multiple submissions:
  - We'll review this submission and you review the next one.

Why are we work-sharing?

- So we can do more with our existing resources:
  - More efficient review
  - Reduce duplication of effort across jurisdictions
- To promote convergence and harmonisation of Regulatory requirements:
  - Foster commonality in review approach and data requirements
  - Share best practices
- To reduce the regulatory burden for sponsors:
  - Filing of the same submission content in multiple jurisdictions
  - Simultaneous review with the sending of a common list of questions and the filing of common responses
- Faster access to drug products – Earlier authorisation

International Work-Sharing at Health Canada

- Why is it important to Health Canada now and in the future?
- Continuing globalisation of the pharmaceutical industry
- Ever increasing overall cost of pharmaceuticals in our health care system
  - Pressure to reduce prices
- Less regulatory burden and a more efficient regulatory process
  - Contributes to earlier/greater access to drugs for Canadians

- Initiative under the “Regulatory Review of Drugs and Devices”
  - Strengthening our international partnerships in submission review
  - Enabling a prompt authorisation of the drug product to allow Canadians to have faster access to the medicines they need.

International Work-Sharing at Health Canada

Expanded collaboration with health partners

- Alignment of the Health Technology Assessment (CADTH) Review with Health Canada Review
- Implementing a Mechanism for Early Parallel Scientific Advice
- Use of Foreign Reviews/Decisions
- **International Collaboration and Work Sharing in Reviews**

More timely access to drugs and devices

- Expansion of Priority Review Pathways
- Improving Access to Biosimilars and Biologics
- Improving Access to Generic Drugs
- Building Better Access to Digital Health Technologies
- Pre-Submission Scientific Advice for Medical Devices
- Special Access Programme (SAP) Renewal

Enhanced Use of real world evidence

- Leveraging Data for Assessing Drug Safety and Effectiveness
- Strengthening the use of real world evidence and regulations for medical devices

Modern and flexible operations

Updated System Infrastructure

Appropriate cost recovery framework

Public Release of Clinical Information

What have we been doing?

- Testing it out:
  - We have two work sharing trials:
    - GMWST – Generic Medicines Work Sharing Trial
    - NCEWST – New Chemical Entities Work Sharing Trial
      - Small molecules and Biologics

- Our work-sharing partners:

Australian Government
Department of Health
Therapeutic Goods Administration

Health Canada Santé Canada

HSA Health Sciences Authority

swissmedic

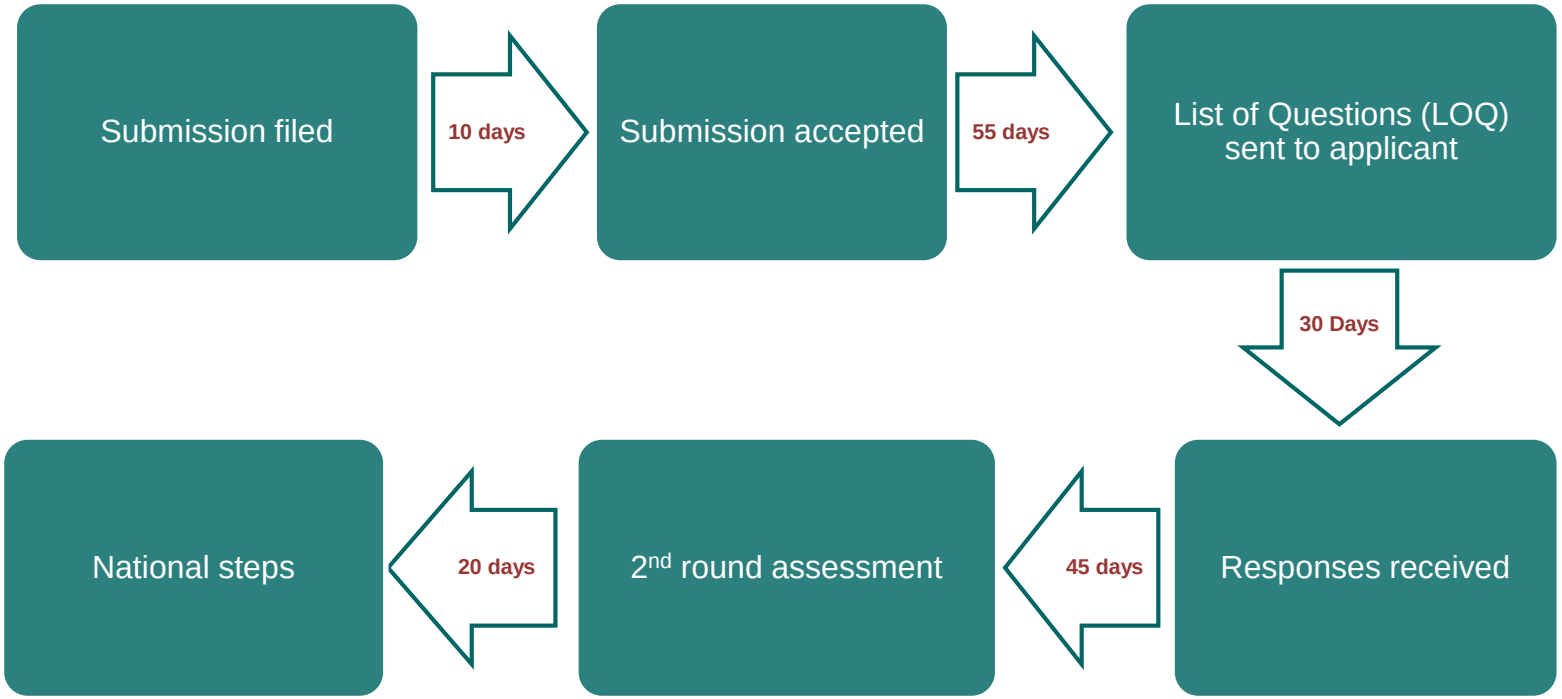
  - The ACSS Consortium - Australia, Canada, Singapore and Switzerland
    - 'Like-minded' regulatory authorities with smaller markets
    - Promote greater regulatory collaboration and alignment of regulatory requirements.
    - Goal is to maximise international cooperation, reduce duplication, and increase each agency's capacity to ensure consumers have timely access to high quality, safe and effective therapeutic products.

Generics – GMWST – The first Trial

- The “we review this one, you review the next one” model
  - The sharing takes place over time and the review of multiple submissions.
- One agency does a complete review of a particular submission and the other regulators do a ‘peer’ review.
- Each agency des there own review of the regional information such as labelling
- Each agency makes their own decision based upon their national context.
- Modelled after EU Decentralised Procedure with a Reference Regulatory Agency (RRA) and Concerned Regulatory Agencies (CRAs)

Generics – GMWST – The Plan

- Scope was limited to simple dosage forms (solutions and immediate release solid orals)
- Submission needed to be filed in at least 3 of the 4 ACSS countries
- Decision targeted for 5 months after acceptance to encourage applications

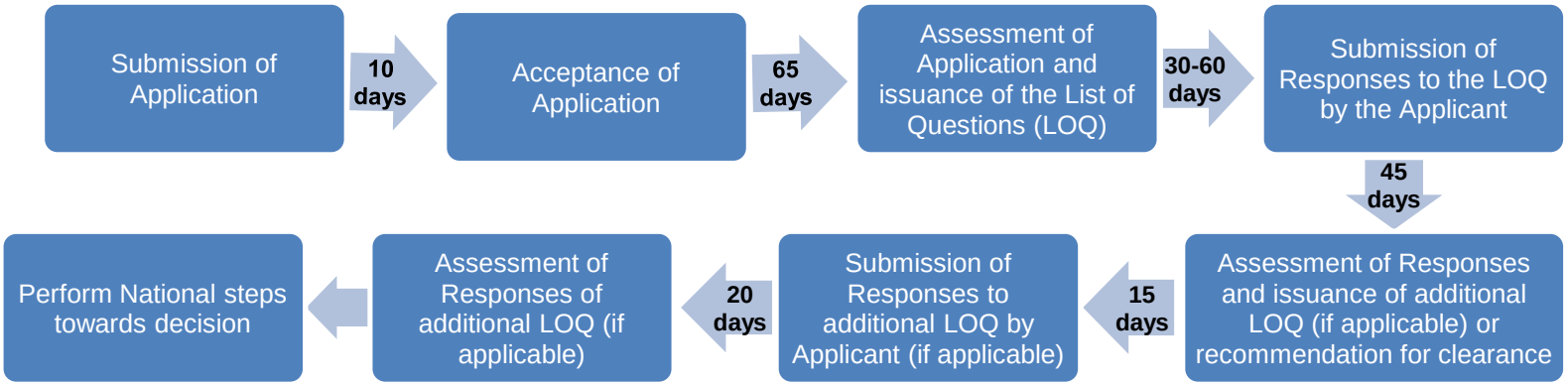


Generics – GMWST – The first submission

- The TGA did the primary review with HC and Swissmedic doing a ‘peer’ review.
  - The questions from all three agencies were put to the sponsor on time
  - Time for sponsor response was extended (HC issued a NON)
  - Second round of questions was needed
- Application was approved all three jurisdictions.
  - The time taken compared to the target timeframes was:
    - About the same in Australia
    - 4.5 months quicker in Canada
    - 7.5 months quicker in Switzerland

Generics – GMWST – The Future

- The scope for acceptable submissions has been widened:
  - From only immediate release oral solid and solution dosage forms to any possible generic products.
  - We will accept submission to only 2 of the 4 agencies
- Timelines amended to reflect experience



- 2 more submissions expected to be filed this year.

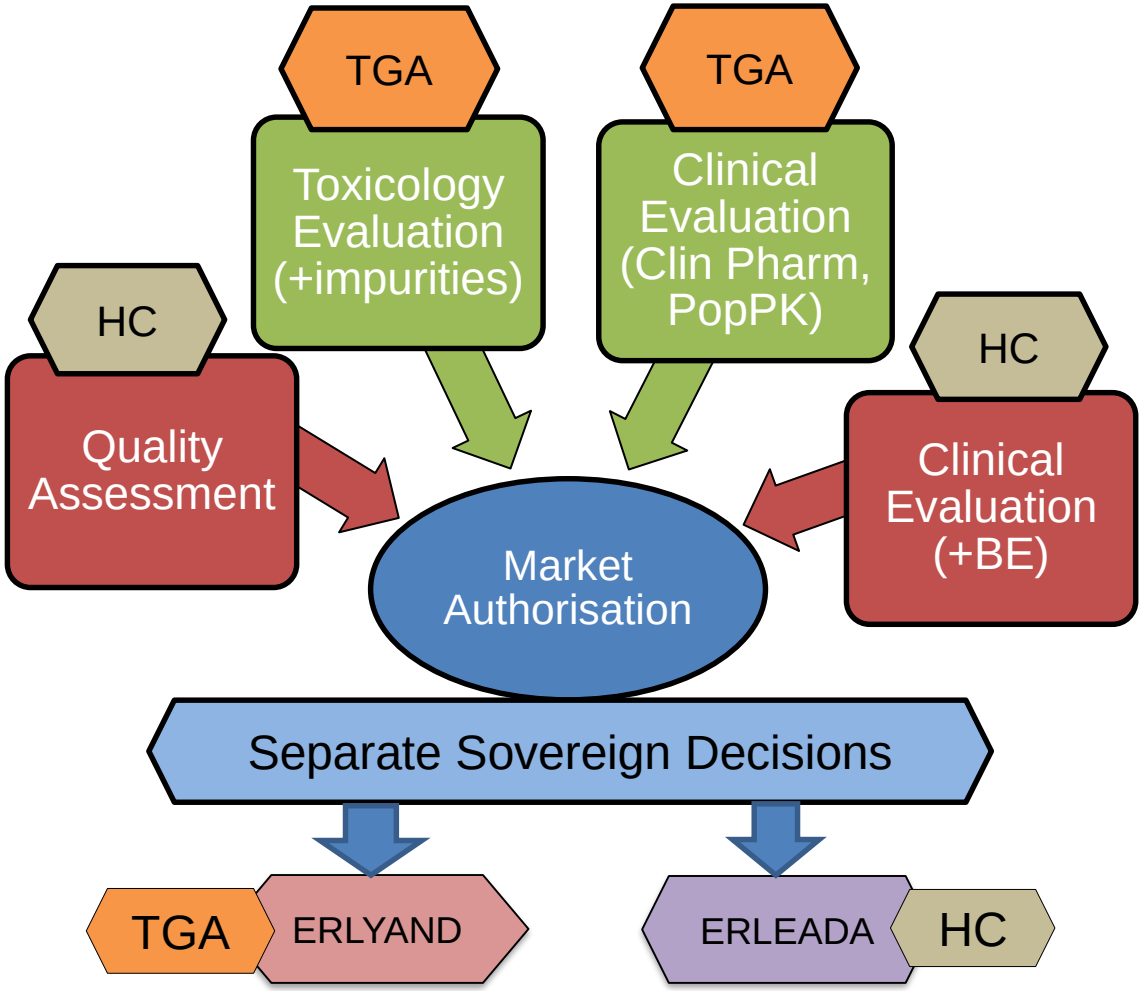
New Chemical Entities – NCEWST – The Plan

- This trial was to use the “we do this part you do that part’ approach
- Coordinated assessment of a single NCE application by Australia and Canada. Singapore and Switzerland participating as observers.
- This would provide a proof of concept for:
  - Division of labour
    - Each regulator evaluates their respective Module 1
    - Health Canada evaluates Module 3 (Quality)
    - TGA evaluates Module 4 (Toxicology)
    - Both regulators separately evaluate Module 5 (Clinical)
    - Each regulator reviews its own labelling
  - Common list of questions
    - Regulators to send a common list of questions after initial review
    - Common response to be filed in both jurisdictions within 30 days

New Chemical Entities – NCEWST – The First Submission

- The first submission was identified after it had been filed in both Australia and Canada
- Apalutamide (Erleada / Erlyand)
  - Priority review for both HC and TGA
    - Indicated for a type of prostate cancer with limited treatment options
  - Needed to modify the plan to accommodate timelines and processes for a priority review
- Questions sent to local sponsor office as needed during review
    - Similar to usual HC clarifax process
    - Cc'd other regulator and other local sponsor office
    - Sponsor filed responding eCTD sequence in both jurisdictions
- Division of labour went as planned
    - TGA – Partial clinical evaluation (clinical pharmacology, popPK) and Full toxicology assessment + impurities
    - HC – Full clinical & quality evaluation & BE studies
    - Integrated clinical evaluations between HC & TGA
      - During evaluation - multiple TCs between agencies to discuss issues, Q's & responses to Q's
    - Separate PI/PM negotiations with local sponsors
    - Sovereign Decisions for market approval

Apalutamide (Erleada/Erlyand)



NCEWST – First Submission - Results

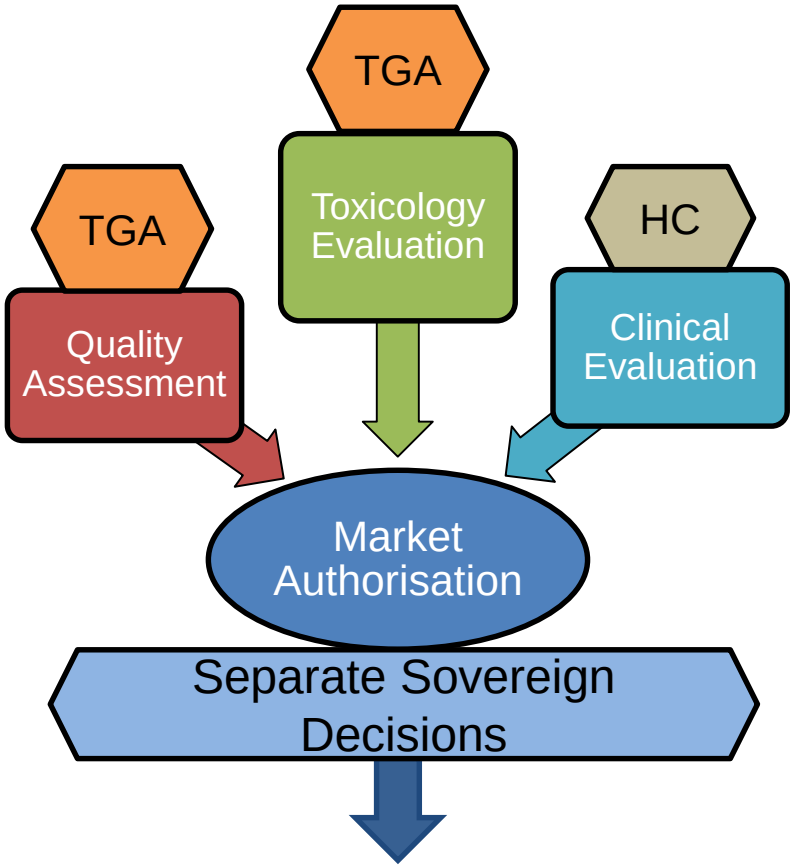
- First cycle approval in both Australia and Canada
- Reviews completed at same time in both countries
  - Met target in Canada
  - Early in Australia
- Process allowed for regional differences in health care context
  - Minor differences in approved indication
  - Other minor differences in Product Information

Lessons Learned

- Communication, communication, communication
- Creation of Expression of Interest Form
  - Including Summary of Differences
- Preparation of review plan
  - Granular division of labour
  - Milestones for sharing of draft reviews of each section
- Regular teleconferences (fortnightly)
  - Ensure on target
  - Adjust where needed
  - Discuss review issues

2nd Submission - Abemaciclib (Verzenio)

- Standard pathway for treatment of metastatic breast cancer
- Negotiated timelines/milestones with Eli-Lilly
  - Consolidated questions for Quality
  - Rolling questions for Clinical
- HC – Clinical evaluation
- TGA – Toxicology evaluation & quality assessment
- During evaluation - multiple TCs between agencies to discuss issues
- Separate PI/PM negotiations with local sponsors
- Sovereign Decisions for market approval.



NCEWST – The Future

- Expansion of work sharing to all ACSS members
- Expansion of scope
  - Now includes biologics
- Expansion of interest
  - More sponsors are participating
  - More submissions already in review

Process

-6 months

- Contact ACSS member with EOI in work sharing (https://www.tga.gov.au/acss-nce-work-sharing-pilot)
- Determine Regulatory pathway (priority, standard) & Lead regulator reaches out to nominated CRs to canvass opportunities

-6 to -3 months

- Establish pre-submission meetings (multi-way between regulators & affiliates)
- Clarify any differences in dossiers, synchronize submission dates
- Design bespoke pathway using available global resources – shared with Sponsor

submission

- Pre-screening & negotiations with sponsor regarding pathway design
- Sponsor communication plan developed (Sponsor and inter-jurisdictional)

Evaluation

- Share evaluation draft reports; Evaluators/Delegates discuss data & any issues; finalize reports

Sovereign decisions

- Simultaneous market authorization decisions across all participating jurisdictions
- National PI/PM negotiations & RMP

NCEWST – The submissions

Submission	Module 3 Quality	Module 4 Non-clinical	Module 5 Clinical	Status
apalutamide (ERLEADA) *Janssen-Cilag*				**completed**
abemaciclib (VERZENIO) *Eli Lilly*				**Completed**
Submitted - TPD				**near completion**
Submitted - TPD				In Review
Submitted - TPD				In Review
Coming - BGTD				Expected Soon
Coming - BGTD				Expected Soon

Note: There are 4 other work-sharing files that do not involve Health Canada

NCEWST – Successes and Challenges

- Successes
  - Work-sharing of priority review and others completed on target
  - Saving of resources by reducing duplication of effort across jurisdictions
  - Sharing of knowledge and review practices
- Challenges
  - Earlier identification of work sharing submissions
    - Identification pre-filing allows for better planning
  - Allowing for differences in review process timelines across regulators – while meeting/exceeding targets
    - E.g., staggered filing time due to differences in pre-acceptance processes (to allow for simultaneous first cycle review)
  - Development / Adaptation of external processes and procedures to Work-sharing
    - E.g., Procedures for eFiling of Expression of Interest
  - Development / Adaptation of internal processes and procedures to Work-sharing
    - Modified document templates (e.g. Clarifax)
    - Modified docuBridge procedures to include review documents generated during work-sharing

Links

- GMWST
  - https://www.canada.ca/en/health-canada/services/drugs-health-products/international-activities/notice-applicants-consortium-generic-medicines-work-sharing-trial.html
- NCEWST
  - https://www.canada.ca/en/health-canada/services/drugs-health-products/international-activities/notice-acss-new-chemical-entities-trial-phase-1.html
  - https://www.canada.ca/en/health-canada/services/drugs-health-products/international-activities/australia-canada-singapore-switzerland-consortium/new-chemical-entities-work-sharing-initiative-overview.html
- Apalutamide approval
  - https://www.canada.ca/en/health-canada/corporate/transparency/regulatory-transparency-and-openness/improving-review-drugs-devices/notice-erleada.html
- Verzenio approval
  - https://www.canada.ca/en/health-canada/news/2019/04/health-canada-approves-new-drug-to-treat-metastatic-breast-cancer-through-international-and-domestic-joint-reviews.html

Thank you

Australian Government
Department of Health
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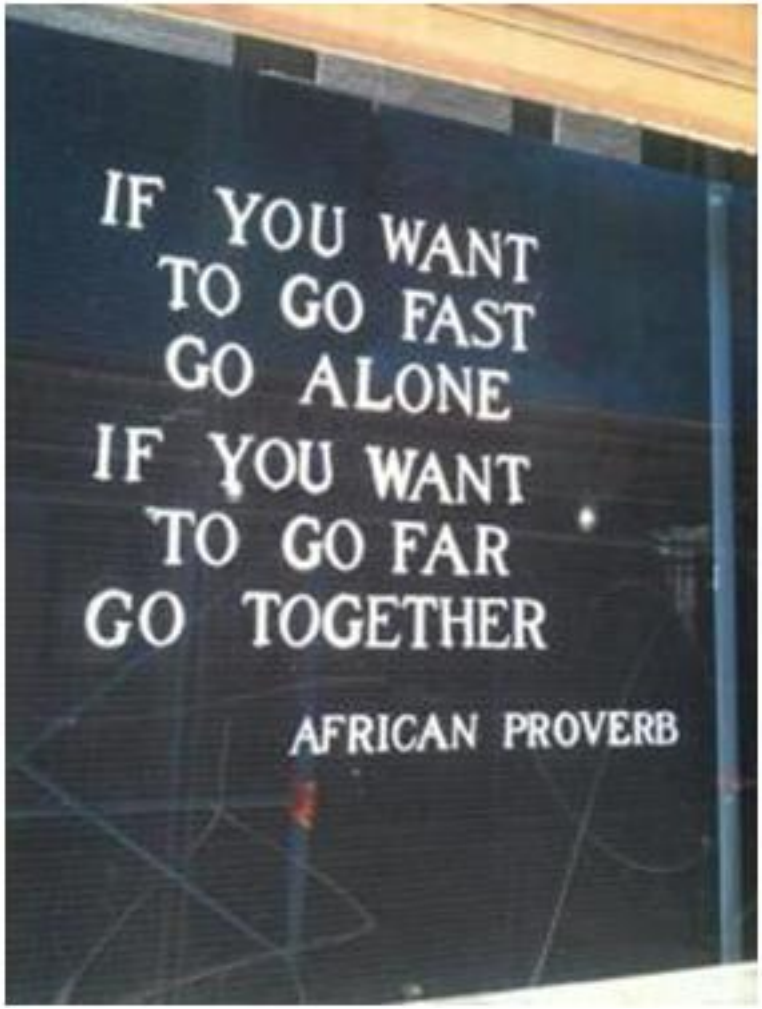

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