U.S. FOOD & DRUG ADMINISTRATION

International Regulatory Collaboration:
Project Orbis Update

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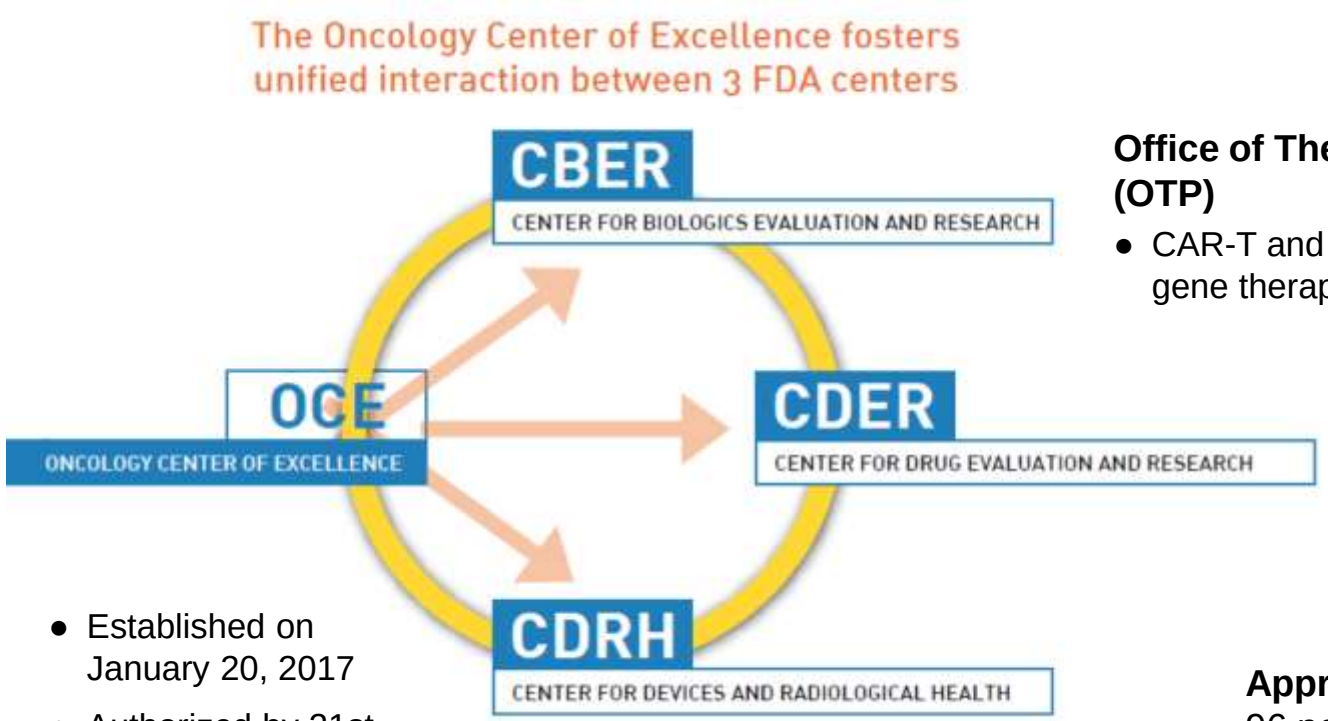
Presentation Outline

- Oncology Center of Excellence (OCE) and Global Collaboration
- Project Orbis Framework
- Project Orbis Update
- Challenges and Future Directions

FDA Oncology Center of Excellence (OCE)



Office of Therapeutic Products (OTP)

- CAR-T and other cellular therapies, gene therapy, therapeutic vaccines

Office of Oncologic Diseases (OOD)

- small molecule drugs, monoclonal antibodies, antibody-drug conjugates

- Established on January 20, 2017
- Authorized by 21st Century Cures Act: First FDA Inter-Center Institute

Office of In Vitro Diagnostics and Radiological Health

- diagnostic devices

Approvals Jan 2017 to Sep 2023:
96 new molecular entities (NME)
261 new indications
Average review time ~ 6 months

FDA Oncology Global Collaboration

- Began in October 2004 with European Medicines Agency (EMA)
- **Expanded Oncology Cluster to other Regulatory Authorities:**
  - January 2010: Health Canada (HC)
  - January 2014: Pharmaceuticals and Medical Devices Agency (PMDA) (Japan)
  - July 2014: Therapeutic Goods Administration (TGA) (Australia)
  - July 2016: Swissmedic (SMC) (Switzerland)
- **Project Orbis:** Collaborative Review Program
  - Launched in May 2019
  - Current participating countries (Project Orbis Partners): Australia, Brazil, Canada, Israel, Singapore, Switzerland, United Kingdom

Key Features of Project Orbis

- **Earlier submission of applications to Orbis countries**
  - within 1-2 months of FDA submission
- **Collaboration with other regulatory authorities**
  - Project Orbis teleconferences
  - Invitation to observe FDA standard processes and meetings
  - Assessment Aid document
    - **FDA:** formal review document
    - **Orbis countries:** core reference document

Key Features of Project Orbis

- **Leverages FDA staffing and expertise with application review**
  - **FDA Oncology Staff:** 280+ full-time (95 oncologists + 10 clinical analysts, 40 statisticians, 30 clinical pharmacologists, 35 nonclinical, 70 project managers)
  - **FDA Disease-Specific Teams**: ~ 18

Breast-Gynecologic (3)	Genitourinary (2)	Thoracic/Head-Neck (2)
Gastrointestinal (2)	Melanoma/Sarcoma	Pediatric/Neuro-oncology (2)
Leukemia/HSCT (3)	Lymphoma (2)	Myeloma

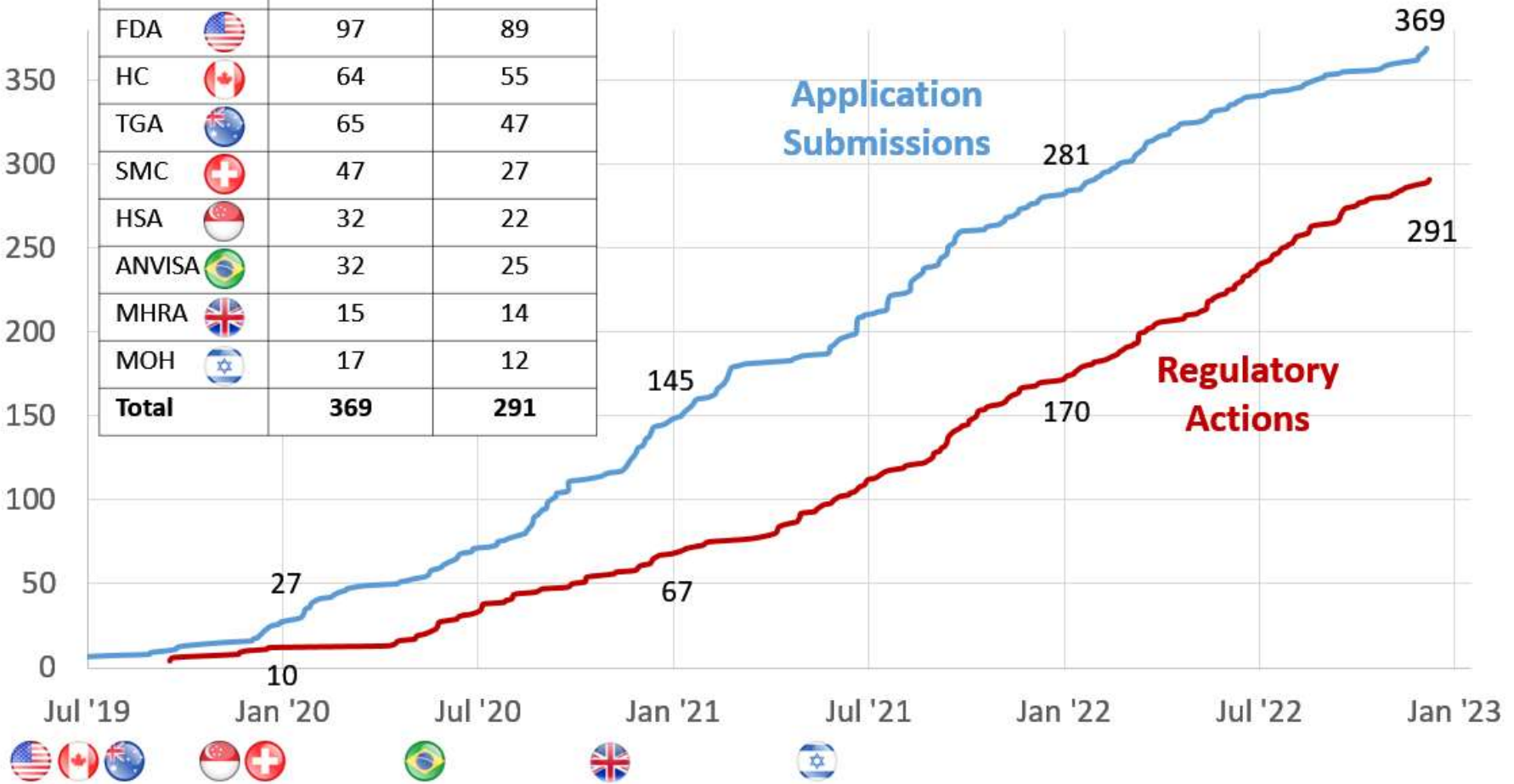
  - FDA review provides for independent multi-disciplinary assessment including full review of datasets.
- **Each country retains independent decision-making for each application**

Project Orbis Types

Orbis Type	Submission Timeline	Submission overlaps with FDA	Sharing of FDA reviews	Multi-country review meetings (POP TCONs)	POP Attendance at FDA review meetings	Concurrent review with FDA	Near concurrent action with FDA
Type A	≤ 1 month of FDA submission	Expected	Yes	Yes	Yes	Expected	Possible[1]
Type B	> 1 month of FDA submission	Expected	Yes	Yes	Yes	Possible	No
Type C	Any time after FDA submission	Permitted	Yes	No	Unlikely	Unlikely	No

Project Orbis: Dec 2022 Update

	Submitted	Action
FDA	97	89
HC	64	55
TGA	65	47
SMC	47	27
HSA	32	22
ANVISA	32	25
MHRA	15	14
MOH	17	12
Total	**369**	**291**



Project Orbis Highlights

- 80 unique “projects” in 3.5 years
  - 33% are NME NDAs (50% used PQAA) or Original BLAs
  - other applications: new indications (SE1), new dosage forms for pediatric population
- Median number of countries per application: 3
- ~ 40% of OOD NME/SE1 workload referred for Orbis
- Submission Gap to FDA: median 1.9 months
- Action Gap to FDA: median 5.8 months

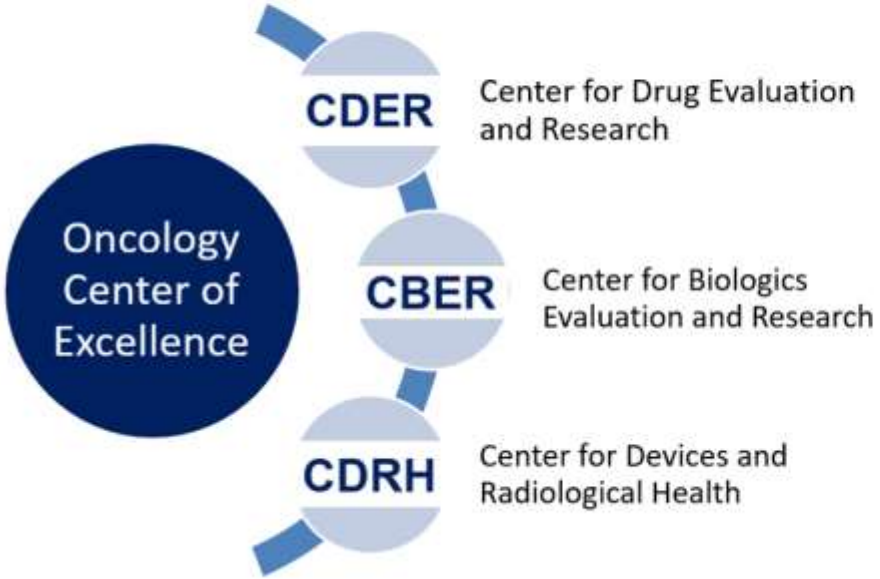
Challenges and Future Directions

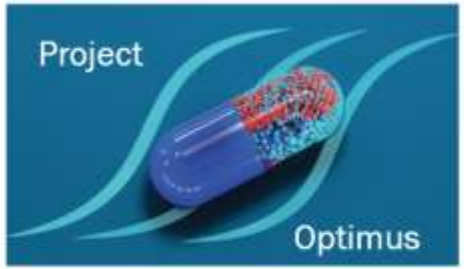
- **Logistical Challenges**
  - **Regulatory authorities**: review coordination and logistics (e.g., multiple time zones)
  - **Applicants/Sponsors**: concurrent submission and management of applications
- **Other Challenges:** expansion to other countries, translation requirements, operational considerations (e.g., review clock)
- **What's new in 2023?** EMA to participate as an observer

FDA Oncology Center of Excellence (OCE)

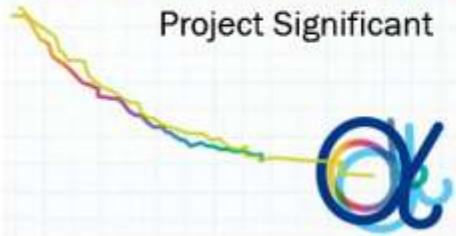
Mission

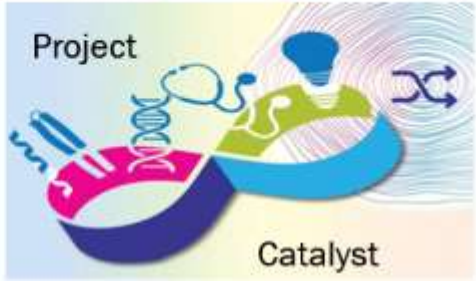
The mission of the OCE is to achieve patient-centered regulatory decision-making through innovation and collaboration.





Project
Renewal





Summary

- Oncology is a highly active area of drug development.
- Global collaboration between regulatory authorities facilitates drug application submission and review.
- Important role of engagement with key stakeholders including patient groups, academia, industry, and regulators