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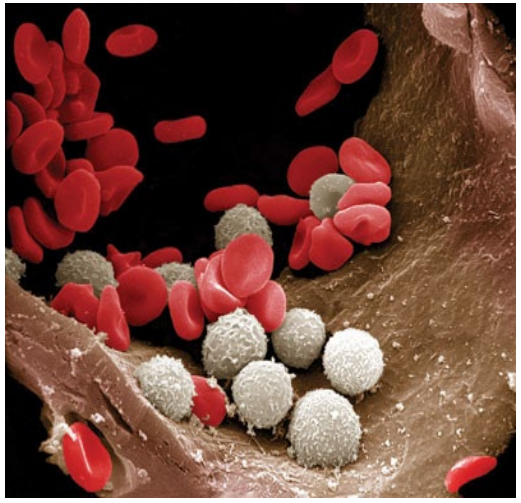
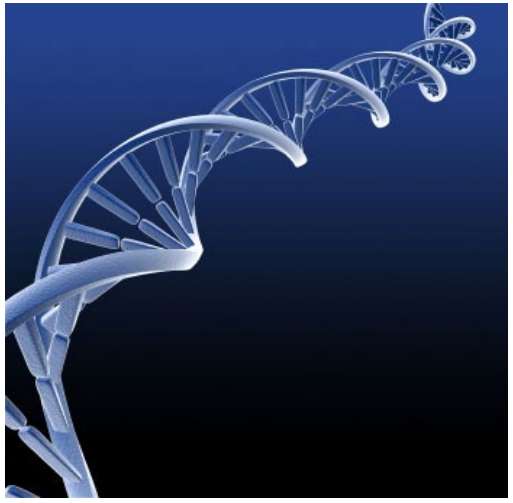
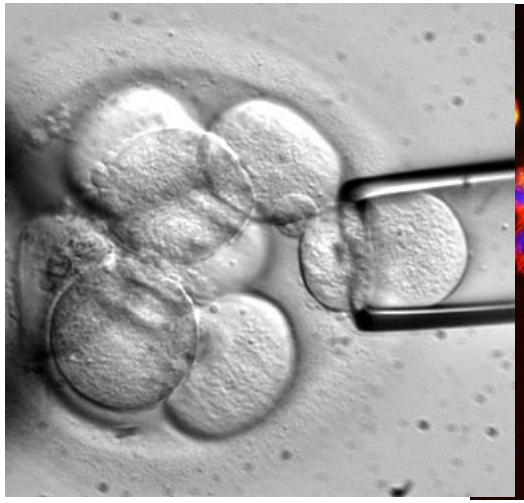
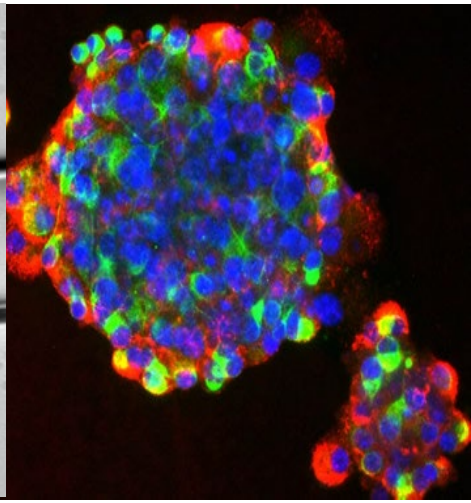
U.S. FOOD & DRUG ADMINISTRATION

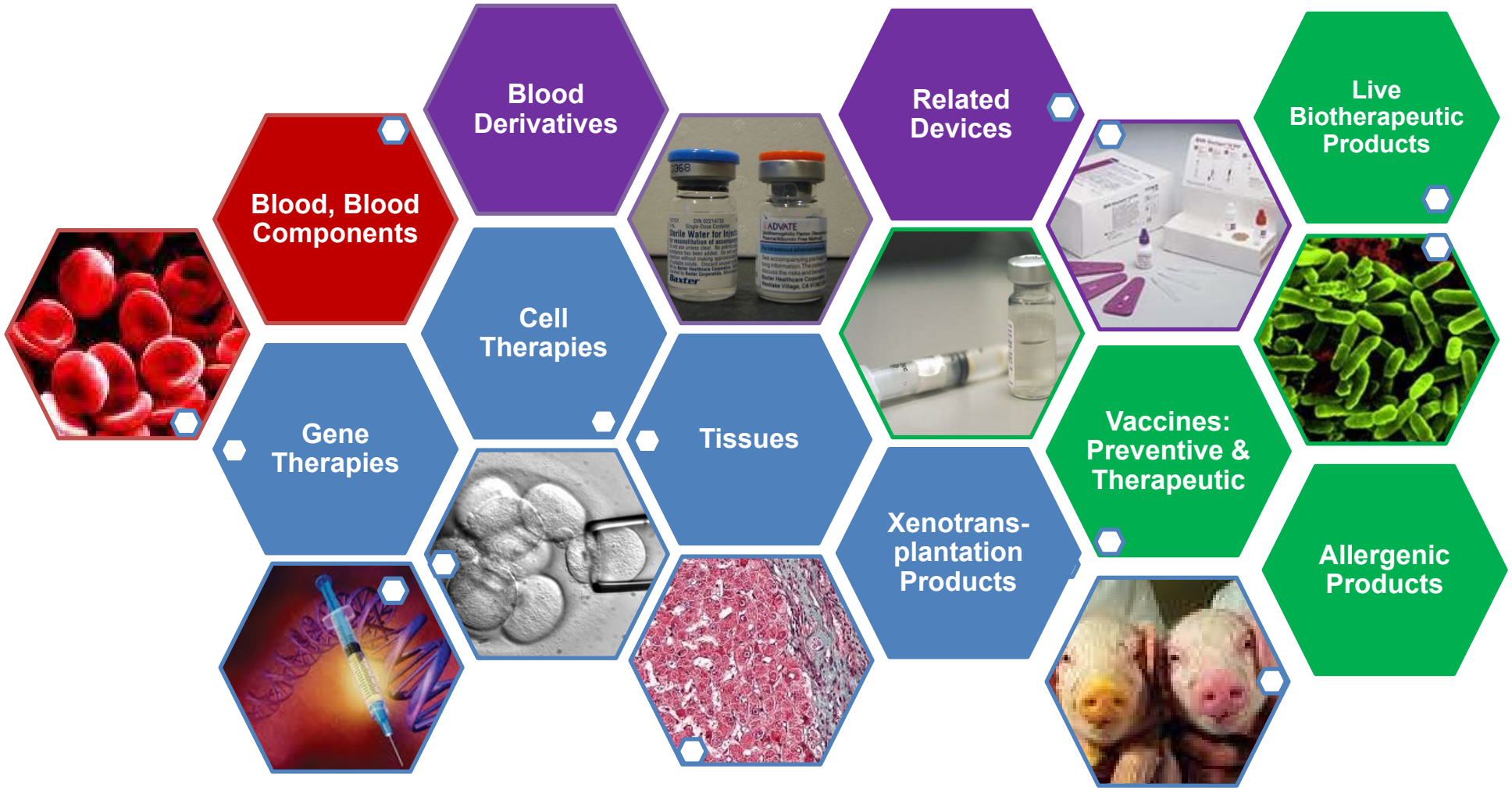
Center for Biologics Evaluation and Research, FDA

Overview of CBER Research

Tod Merkel, Ph.D.
OVRR, Associate Director for Research

CBER Regulates Complex Biological Products



CBER Strategic Plan Goals, 2021 – 2025

White Oak Campus Laboratories and Facilities

- 450,000 square feet for ~ 150 BSL-1 to BSL-3 laboratories and offices for ~ 450 research staff
- Core technologies:
  - Flow cytometry
  - Confocal microscopy
  - High-performance Integrated Virtual Environment (HI
  - Biotechnology core facility:
    - Oligonucleotide, siRNA, PNA, and peptide synthesis
    - Peptide sequencing, DNA sequencing, RNASeq
    - HPLC; capillary electrophoresis
    - Mass spectrometry and proteomics
- State-of-the-art vivarium
  - Imaging facility with MRI, digital X-ray, IVIS, ultrasound
  - Transgenic derivation facility

Funding

- CBER operating funds distributed to Offices (Congressional appropriations)
- Competitive FDA funding opportunities:
  - Office of Women's Health
  - Office of Minority Health
  - Nanotechnology CORE Grants
  - MCMi Challenge Grants
  - Chief Scientist Challenge Grants
- External sources
  - Interagency Agreements with other government units
  - Competitive grants, with CRADAs
  - Not applicable to all programs

CBER Laboratory Staffing

- Lab staff are a mix of permanent employees (FTEs), staff scientists, and temporary ORISE fellows, contracts
  - FTEs are assigned by Division/Office, based on program needs
  - FTE staff fellows (temporary) and staff scientists (permanent) are subordinate to PIs
  - Funding for ORISE fellows, ranging from post-bac to post-doc, comes from division/lab budget and external funds; subject to annual budgets

CBER's Researcher-Reviewers: The Approach to Regulating Biologics

- Investigator-initiated research
- Topics of research include:
  - Basic to targeted studies, related to regulated products
  - Studies that develop data and tools that support development of classes of products
  - Studies to fill knowledge gaps that inform policy development and regulatory decision-making
- CBER's research and review are integrated

CBER's Researcher-Reviewers: Role in Regulatory Review Teams

- Chemistry, manufacturing, and control (CMC) product reviewer:
  - Scientific rationale, data for proof-of-concept
  - Production techniques and resulting product
  - Quality control testing
  - Clinical assays

Other review team members:

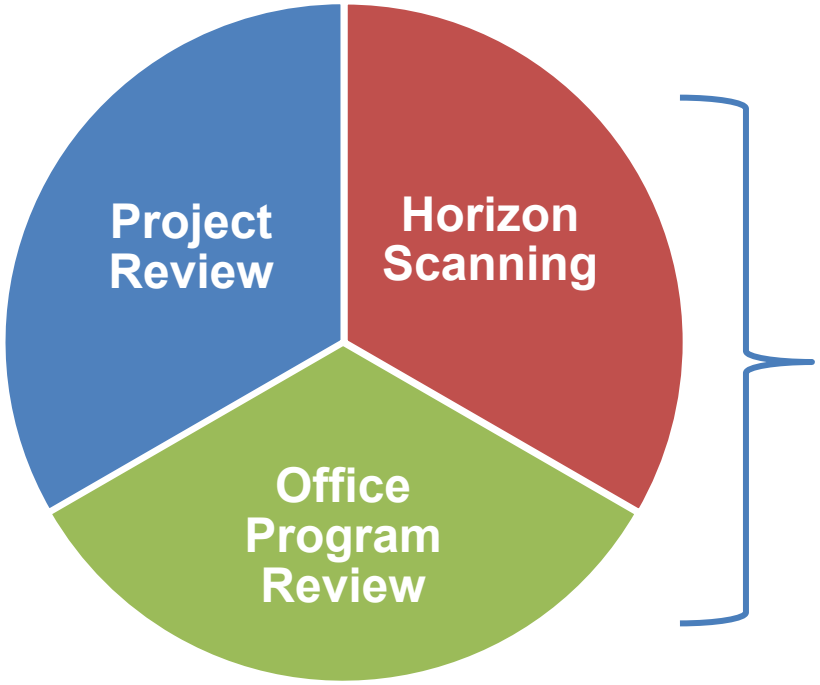
- Regulatory Project Manager: oversight
- Pharmacology/toxicology reviewer
- Clinical reviewer
- Statistical reviewer

Benefits of the CBER Research Program

- Develops knowledge and tools focused on supporting product development
- Ensures understanding state-of-the-art techniques that are the source of data in regulatory decisions
- Facilitates recruitment and retention of highly trained scientists
- Prepares for review of future innovative products and public health challenges

- Ensures efficient, effective, credible review and decisions based on sound science

CBER Research Evaluation Framework



Evaluation	Frequency	By Whom
Project Review	Annually	Lab/Branch Chiefs, Division, and Office Management
Office Review of Projects	New projects	Office staff & Center (RSC)
Horizon Scanning	Every 4 years	Office staff & Center (RSC)
Site Visits	*Every 4 years*	*External SME committee*

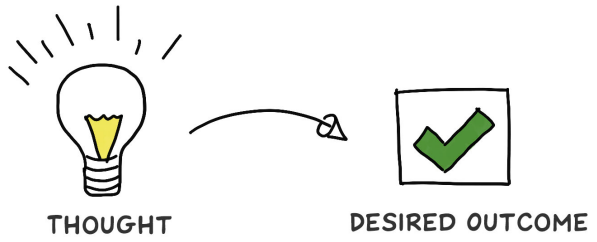
CBER Site Visits: Reviewers' Roles

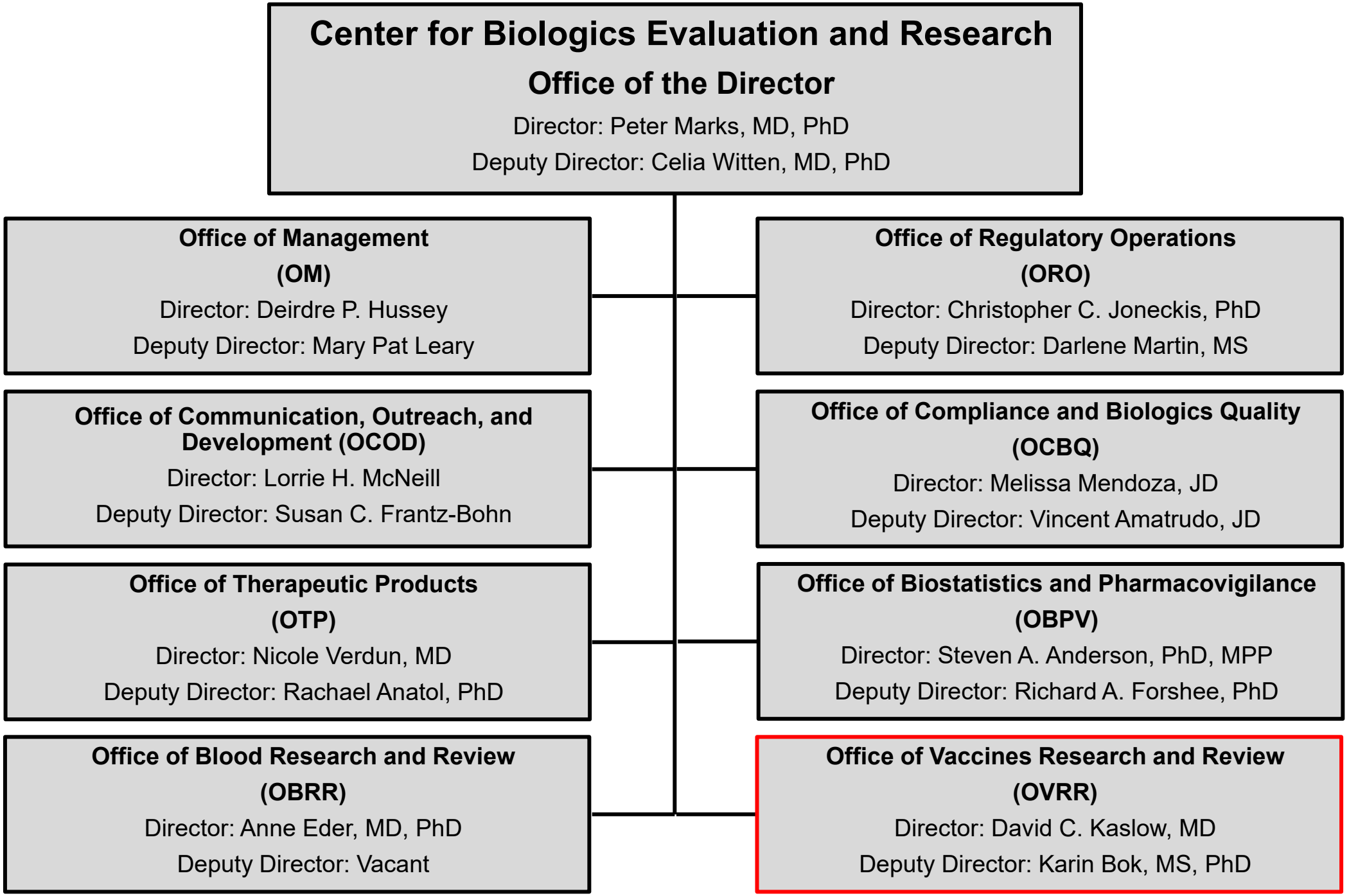
For each principal investigator's research program, site visit reviewers are asked to comment on:

- Quality and relevance of science
- Progress and productivity since last SV, in the context of the work's nature, resources, and regulatory assignments
  - *CBER researchers are regulators too*
- Future research directions
- Laboratory organization, program management, mentoring

CBER Site Visits: Outcomes

- Draft report will be reviewed by the Advisory Committee to:
  - Accept report as is
  - Amend report
  - Reject report and send back to Site Visit committee
- Report is final upon the Advisory Committee's approval
- Final report is used in many ways:
  - Internal review of individual scientists' progress
  - By PIs and staff, to improve research program
  - By management, to respond and consider resource allocation decisions (pending resource availability)




Center for Biologics Evaluation and Research
Office of the Director
Director: Peter Marks, MD, PhD
Deputy Director: Celia Witten, MD, PhD
Office of Management
(OM)
Director: Deirdre P. Hussey
Deputy Director: Mary Pat Leary
Office of Communication, Outreach, and Development (OCOD)
Director: Lorrie H. McNeill
Deputy Director: Susan C. Frantz-Bohn
Office of Therapeutic Products
(OTP)
Director: Nicole Verdun, MD
Deputy Director: Rachael Anatol, PhD
Office of Blood Research and Review
(OBRR)
Director: Anne Eder, MD, PhD
Deputy Director: Vacant
Office of Regulatory Operations
(ORO)
Director: Christopher C. Joneckis, PhD
Deputy Director: Darlene Martin, MS
Office of Compliance and Biologics Quality
(OCBQ)
Director: Melissa Mendoza, JD
Deputy Director: Vincent Amatrudo, JD
Office of Biostatistics and Pharmacovigilance
(OBPV)
Director: Steven A. Anderson, PhD, MPP
Deputy Director: Richard A. Forshee, PhD
Office of Vaccines Research and Review
(OVRR)
Director: David C. Kaslow, MD
Deputy Director: Karin Bok, MS, PhD

OVRR Regulates

- Vaccines
- Allergenic products
- Live biotherapeutic products (probiotics, FMT)
- Phage

OVRR Mission

- To protect and enhance public health by assuring the availability of safe and effective vaccines, allergenic extracts, and other related products

OVRR Core Activities

- **Review, evaluate, and take appropriate** actions on INDs, BLAs, amendments, and supplements for vaccines and related biological products and participation in inspections
- **Develop policies and procedures** governing the pre-market review of regulated products
- **Conduct research** related to the development, manufacture, and evaluation of vaccines and related products and to better understand pathological processes.

Importance of Research In Regulation of Vaccines and Related Products

Emphasis on Safety

- Products for mass use (often universal)
- Recipients are healthy individuals, often children

Keeping pace with technology

- New manufacturing technologies are rapidly evolving

High level of Scrutiny by Public

- Regulatory decisions must be based on science
- Increasing number of anti-vaccine organization and groups

Responding to Public Health Threats

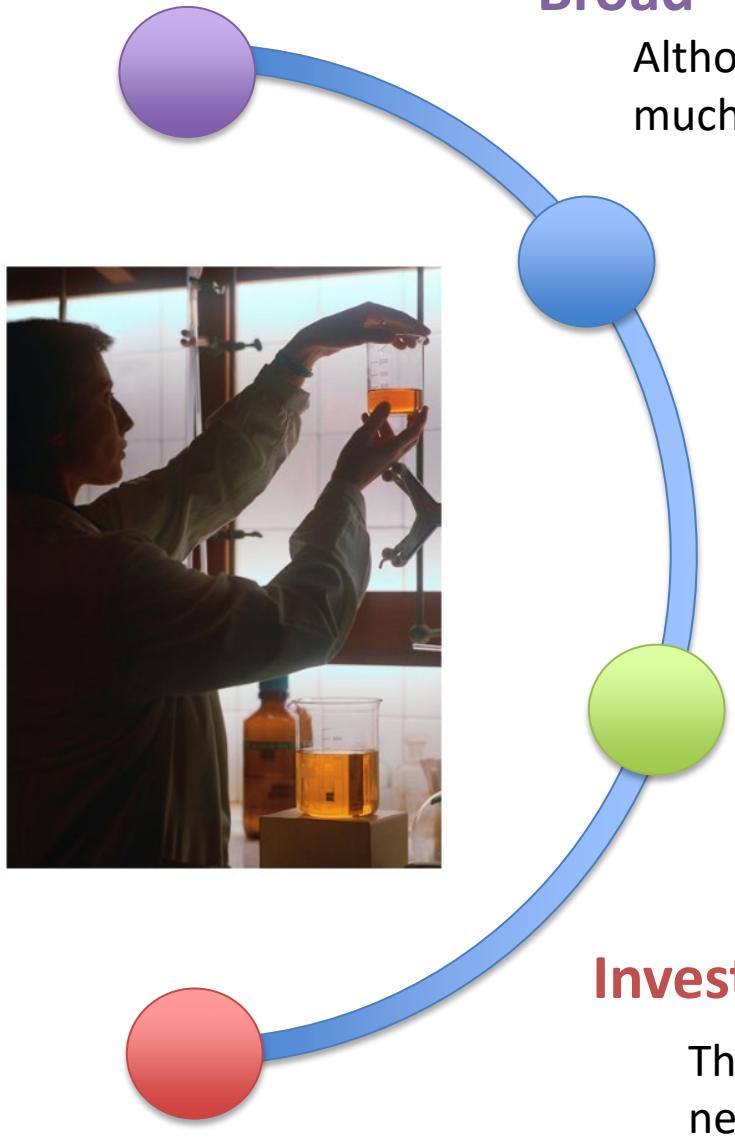
- Antibiotic resistance
- Clostridium difficile
- Emerging agents

Generating results and placing them in the public domain

- Our research benefits not just individual companies but the entire industry sector, and therefore the American consumers

Recruiting and retaining expert scientist to support Review

OVRR's Research Is



Broad

Although we can't cover everything, we need to cover as much as possible within the scope of our responsibilities

Collaborative

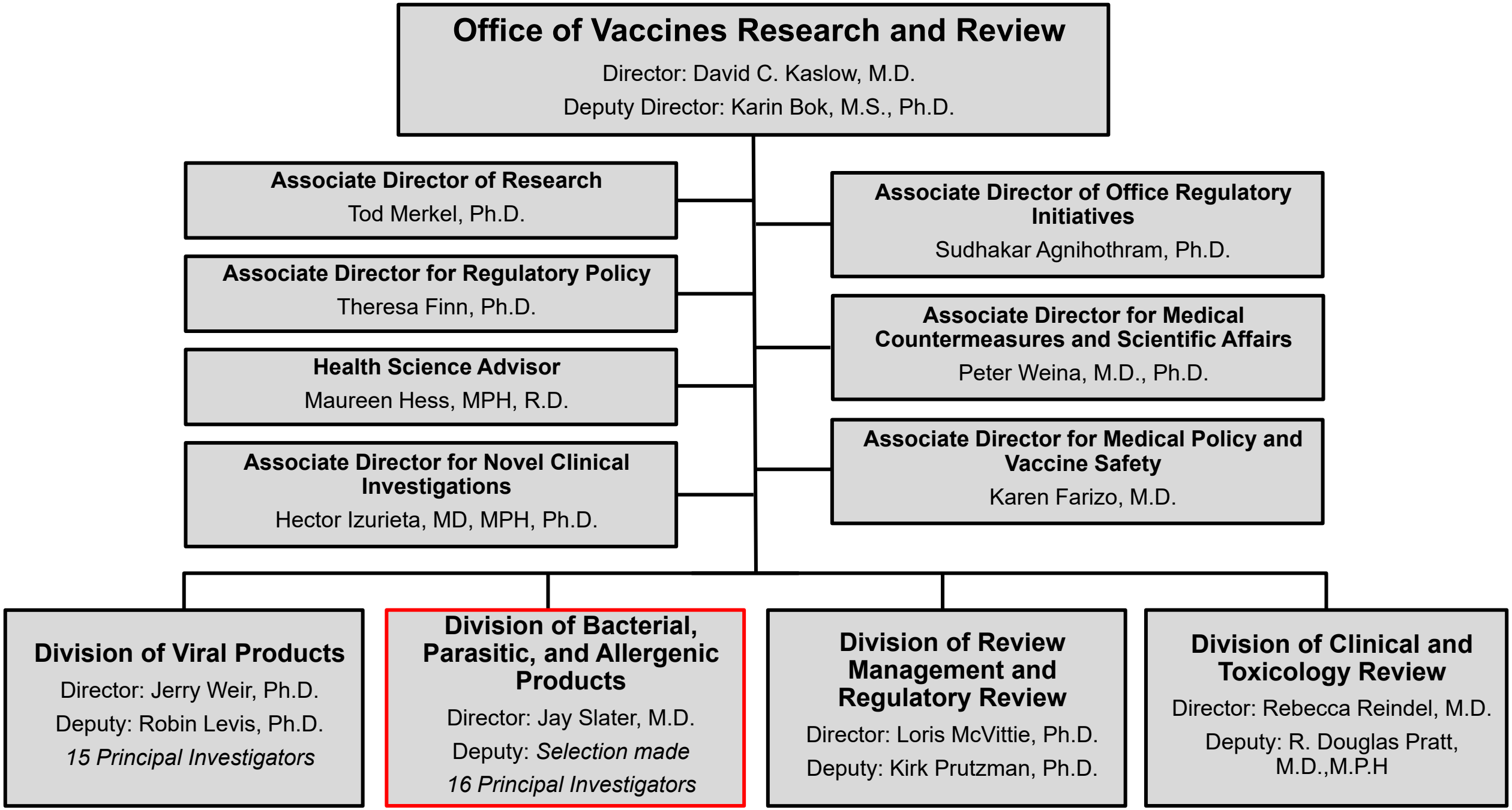
Collaboration with scientists around the country and the world allows us to leverage our investments in research

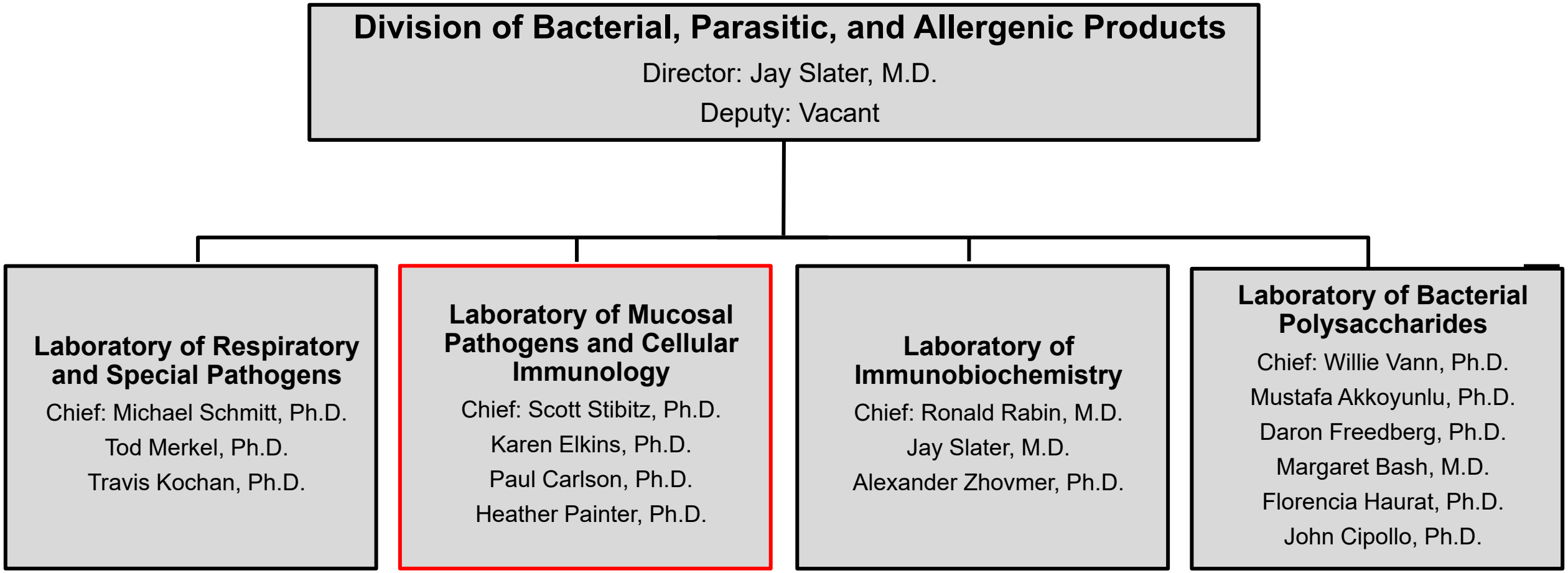
Excellent

- Our research is published and broadly cited and used
- Our research scientists are members of the broader scientific community, and many are well-known experts in their fields

Investigator-initiated and Flexible

This allows our researcher/reviewers to anticipate regulatory needs and proactively address important questions


Office of Vaccines Research and Review
Director: David C. Kaslow, M.D.
Deputy Director: Karin Bok, M.S., Ph.D.
Associate Director of Research
Tod Merkel, Ph.D.
Associate Director for Regulatory Policy
Theresa Finn, Ph.D.
Health Science Advisor
Maureen Hess, MPH, R.D.
Associate Director for Novel Clinical Investigations
Hector Izurieta, MD, MPH, Ph.D.
Associate Director of Office Regulatory Initiatives
Sudhakar Agnihothram, Ph.D.
Associate Director for Medical Countermeasures and Scientific Affairs
Peter Weina, M.D., Ph.D.
Associate Director for Medical Policy and Vaccine Safety
Karen Farizo, M.D.
Division of Viral Products
Director: Jerry Weir, Ph.D.
Deputy: Robin Levis, Ph.D.
15 Principal Investigators
Division of Bacterial, Parasitic, and Allergenic Products
Director: Jay Slater, M.D.
Deputy: Selection made
16 Principal Investigators
Division of Review Management and Regulatory Review
Director: Loris McVittie, Ph.D.
Deputy: Kirk Prutzman, Ph.D.
Division of Clinical and Toxicology Review
Director: Rebecca Reindel, M.D.
Deputy: R. Douglas Pratt, M.D.,M.P.H


Division of Bacterial, Parasitic, and Allergenic Products
Director: Jay Slater, M.D.
Deputy: Vacant
Laboratory of Respiratory and Special Pathogens
Chief: Michael Schmitt, Ph.D.
Tod Merkel, Ph.D.
Travis Kochan, Ph.D.
Laboratory of Mucosal Pathogens and Cellular Immunology
Chief: Scott Stibitz, Ph.D.
Karen Elkins, Ph.D.
Paul Carlson, Ph.D.
Heather Painter, Ph.D.
Laboratory of Immunobiochemistry
Chief: Ronald Rabin, M.D.
Jay Slater, M.D.
Alexander Zhovmer, Ph.D.
Laboratory of Bacterial Polysaccharides
Chief: Willie Vann, Ph.D.
Mustafa Akkoyunlu, Ph.D.
Daron Freedberg, Ph.D.
Margaret Bash, M.D.
Florencia Haurat, Ph.D.
John Cipollo, Ph.D.

DBPAP regulatory/research portfolio

Mucosal Pathogens and Cellular Immunology (LMPCI)

Non-invasive, toxin producers
- *Bacillus anthracis*
- *Bordetella pertussis*
- *Clostridium botulinum*
- *Clostridium tetani*
- *Corynebacterium diphtheriae*
- *Clostridioides difficile*

Invasive, protective responses to polysaccharides
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Streptococcus pneumoniae*

Intracellular
- *Francisella tularensis*
- *Mycobacterium tuberculosis*
- *Mycobacterium bovis*

Enteric
- *Campylobacter jejuni*
- *Salmonella Typhi*
- *Salmonella Typhimurium*
- *Shigella dysenteriae*

Parasite
- *Plasmodium spp*

Other/emerging
- *Staphylococcus aureus*
- Allergenic products
- Live biotherapeutic products (probiotics)
- Phage
- Microbiome-related products

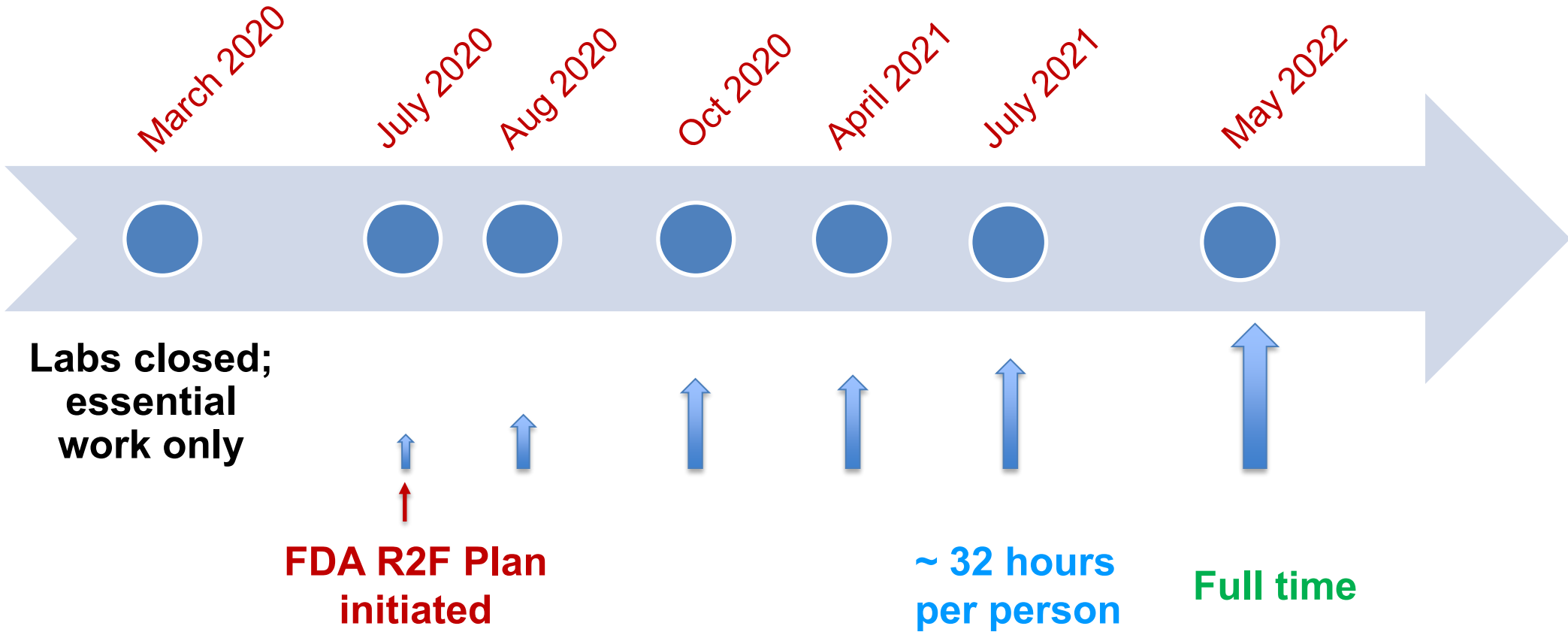
Thank you!

Site visit input ensures CBER maintains high quality research programs

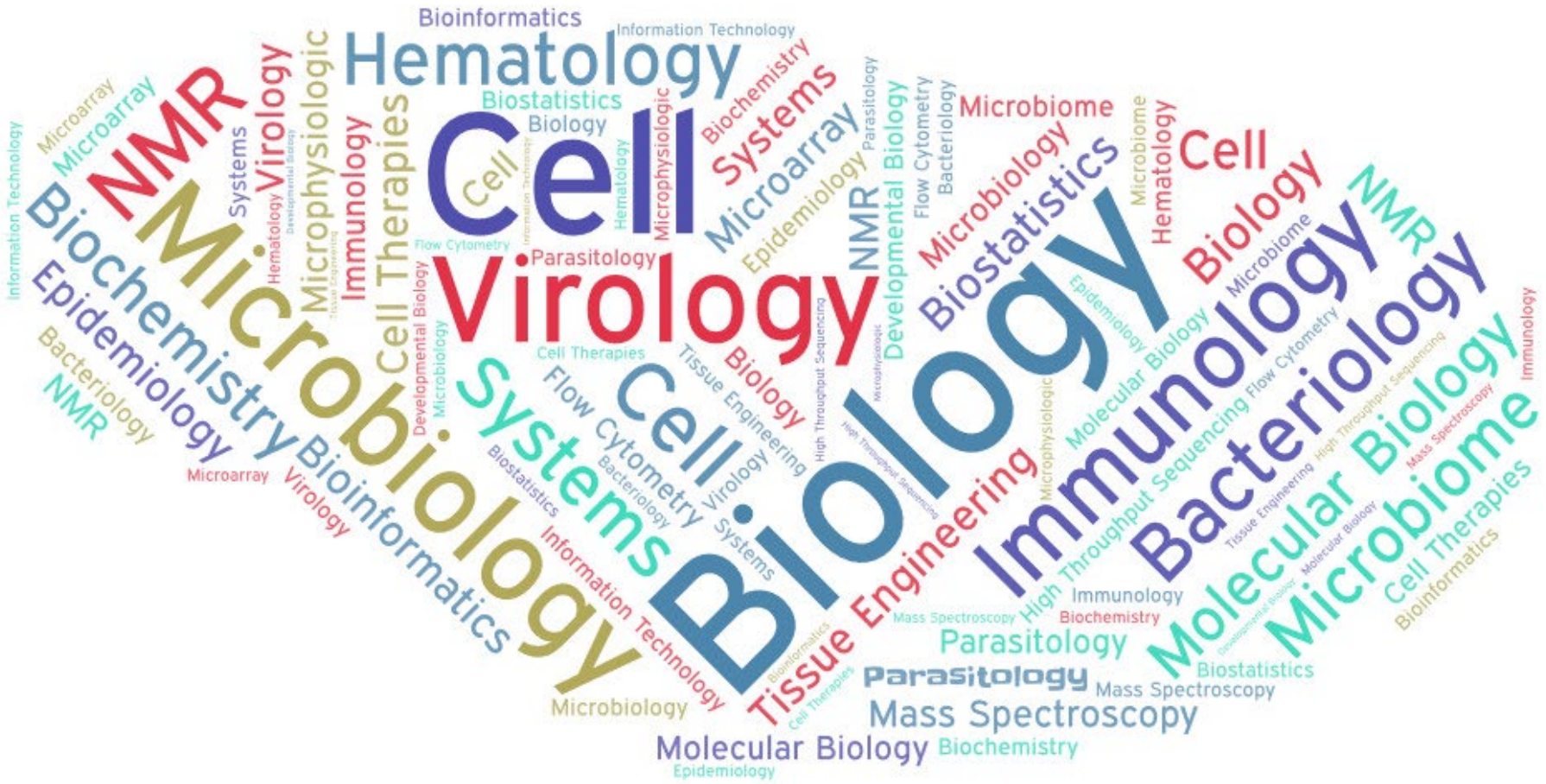
External review is critical to fulfilling CBER's regulatory mission!

COVID-19 Pandemic Impact on Laboratories

- *On-site work voluntary; FDA set policies on building occupancy*



CBER Scientific Expertise



CBER Research Annual Reporting: Programs and Projects

- Scientific rationale, background, expected outcome for investigator-initiated research
- Relevance to CBER/FDA goals and objectives
- Specific aims:
  - Experimental approach
  - Results and progress – previous year
  - Future plans – upcoming year
- Staff and budget
- Scientific and regulatory impact
- Accomplishments: publications, presentations, technology transfer