

OND Reorganization and the New Drugs Regulatory Program Modernization

FDA Small Business Regulatory Education for Industry (REdI)

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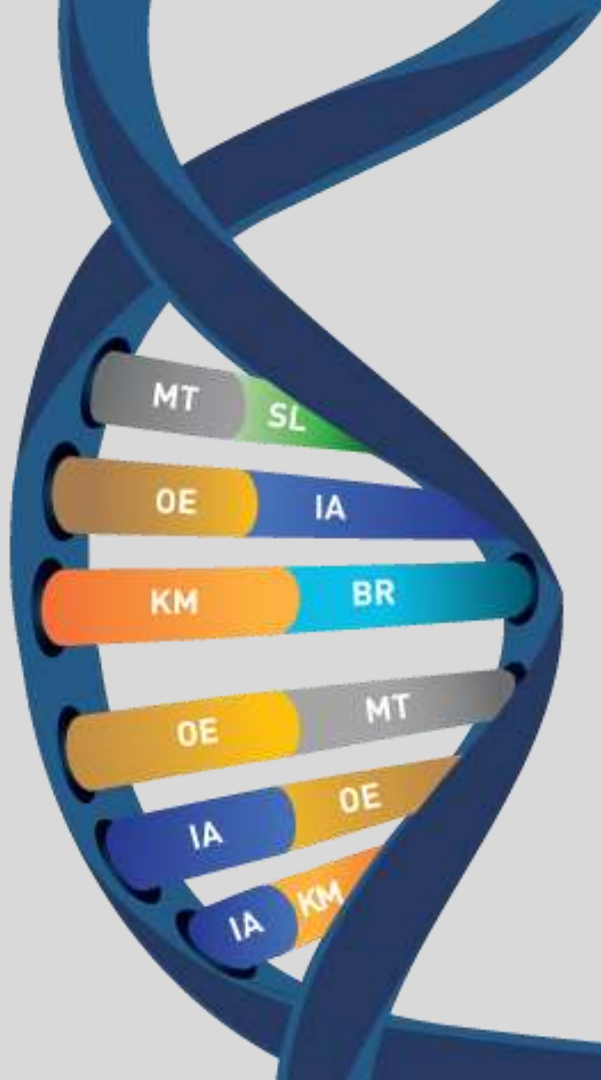
Kevin Bugin

Deputy Director of Operations (Acting)

Office of New Drugs

Center for Drug Evaluation and Research

U.S. Food and Drug Administration



The DNA of Modernization

-  **SL** Scientific Leadership
-  **IA** Integrated Assessment
-  **BR** Benefit-Risk Monitoring
-  **MT** Managing Talent
-  **OE** Operational Excellence
-  **KM** Knowledge Management

Learning Objectives

- Review Impetus for NDRP Modernization and OND Reorganization
- Review NDRP Modernization Objectives
- Review Structure of reorganized OND
- Share updates on ongoing NDRP Modernization Initiatives

Review Impetus for NDRP Modernization and OND Reorganization

Mission and Vision

CDER's Mission:

“Protect and promote public health by helping to ensure that human drugs are safe and effective for their intended use, that they meet established quality standards, and that they are available to patients.”

OND's Mission:

“To maintain and advance our global leadership in ensuring that safe and effective drugs and biologics are available to the American people.”

Modernization Vision:

“To advance our leadership in the science and regulation of New Drugs.”

OND's "Standing" and Reputation

- Shared *global* view that **CDER/OND is the leader and sets the standard** for regulatory management of drug development and review
- **What makes us the global leader?**
 - Our **independence** – rigorous focus on evidence, science, and not on external pressures
 - The **outstanding scientific and regulatory expertise** of our staff
 - Our **experience** in doing our regulatory work – evaluating and applying our learnings from past programs to current programs
 - Our **interdisciplinary approach** – leveraging expertise across disciplines, divisions, offices and centers
 - The **leadership** in our divisions and offices
 - That we are **mission-driven**: our deeply held view that we are “front line” in protecting and improving the health of the American public

What's Changing in the Landscape?



- **Rapidly evolving science** – knowledge of genetics and genomics applied to discovery, increasing identification of molecular defects and drivers, changing disease definitions – new areas of focus
- Increased number of programs for **rare diseases, disease subtypes, late/resistant disease** and decreasing number of programs of broad-based therapies for chronic common diseases (driven by science and by the marketplace)
- New **drug platforms**: increase in cell-based, gene-directed therapies, siRNA, ASOs, bi-specifics, ADCs, and others – making previously undruggable targets druggable
- **Changing clinical trial enterprise**: decentralized trials, remote monitoring, master protocols, adaptive designs, proposed Bayesian designs/analyses, externally controlled studies in small population diseases
- **Advances in bioinformatics** – analytic tools, AI/ML, management of huge databases, standardization of data structures across organizations

What's Changing in the Landscape? (cont.)

- Advances in developing massive clinical health databases / networks, and push to increase use of **RWD/RWE**, increased focus on pragmatic trials
- Increased sophistication of digital devices with more focus on **Digital Health Tool use in endpoints**
- Rising expectations for larger patient role in decision-making and increased patient-relevant information in labels (**Patient Focused Drug Development**)
- Expectation that FDA will address **public health emergencies**
- Expecting OND to address rising drug costs through **a focus on access**

Responding to the Challenges



- **Assuring our organization can respond to the many changes and challenges**
 - Evolving science, changing focus of drug development, new drug platforms, new data sources, changes in the drug trial enterprise, new study design approaches, new drug development tools
 - Changing demands and expectations from stakeholders: industry, patient groups, academics, Congress
- **In essence...**
 - Continuing the rigorous, independent, evidence-based, mission-driven approach that is fundamental to our success – yet preparing for and appropriately responding to the changing drug development and regulatory environment, and changing demands and expectations

New Drugs Regulatory Program and OND



- The New Drug Regulatory Program (NDRP) modernization – started 2 years ago - encompasses all disciplines involved in drug review – OND, OCP, OB, OSE, OPQ
 - **But, OND is at the “center” of the NDRP**
- NDRP has launched many workstreams that have already – and will increasingly – impact how OND works
- The changes in our organization with restructuring – standing up a number of new clinical offices and infrastructure offices (and new groups within offices) also impacts how we do our work

Review NDRP Modernization Objectives

NDRP Modernization: Strategic Objectives



Objectives

Guiding principles for modernizing the new drugs regulatory program

Scientific Leadership

We will grow our scientific expertise and clarify pathways to regulatory approval.

- Expanding the armamentarium to address unmet medical needs is an important part of our public health mission.
- Towards that end, we will proactively collaborate with academic medical scientists and patient/disease advocates, evaluate scientific gaps, and strategically foster drug development.

Integrated Assessment

We will critically, collaboratively and consistently assess whether information in submissions meets statutory and regulatory requirements.

- We will take a new approach to document our assessments, developing a more integrated, cross-disciplinary document to foster collaboration and reduce redundant information.
- Our assessments will be rigorous, risk-based, and clinically relevant; focus on the key issues; and incorporate the patient perspective.

Benefit-Risk Monitoring

We will establish a unified post-market safety surveillance framework.

- To effectively protect the American public, we will systematically monitor the benefits and risks of approved drugs across their lifecycles.

Managing Talent

We will attract, develop, and retain outstanding people.

- We will use 21st Century Cures Act authorities to recruit and retain technical, scientific and professional experts, and eliminate our backlog of vacant positions.

Operational Excellence

We will have a dedicated focus on operational excellence.

- We will enhance our ability to address OND's large volume workload through greater process standardization and better defined roles and responsibilities.
- This will improve operational efficiency and enable our scientists to focus on science, not ancillary tasks.

Knowledge Management

We will facilitate knowledge management.

- Vast and diverse information is submitted to and generated by the New Drugs Regulatory Program.
- We will make it easy for our staff to find and use scientific and regulatory precedents.
- This will reduce manual work time, increase the speed and efficiency of submission assessment, and increase the consistency and predictability of regulatory decision-making.

Reorganization supports our strategic objectives



Strategic Objectives

Scientific leadership

Integrated Assessment

Benefit-Risk Monitoring

Managing Talent

Operational Excellence

Knowledge Management

The reorganization will enable:

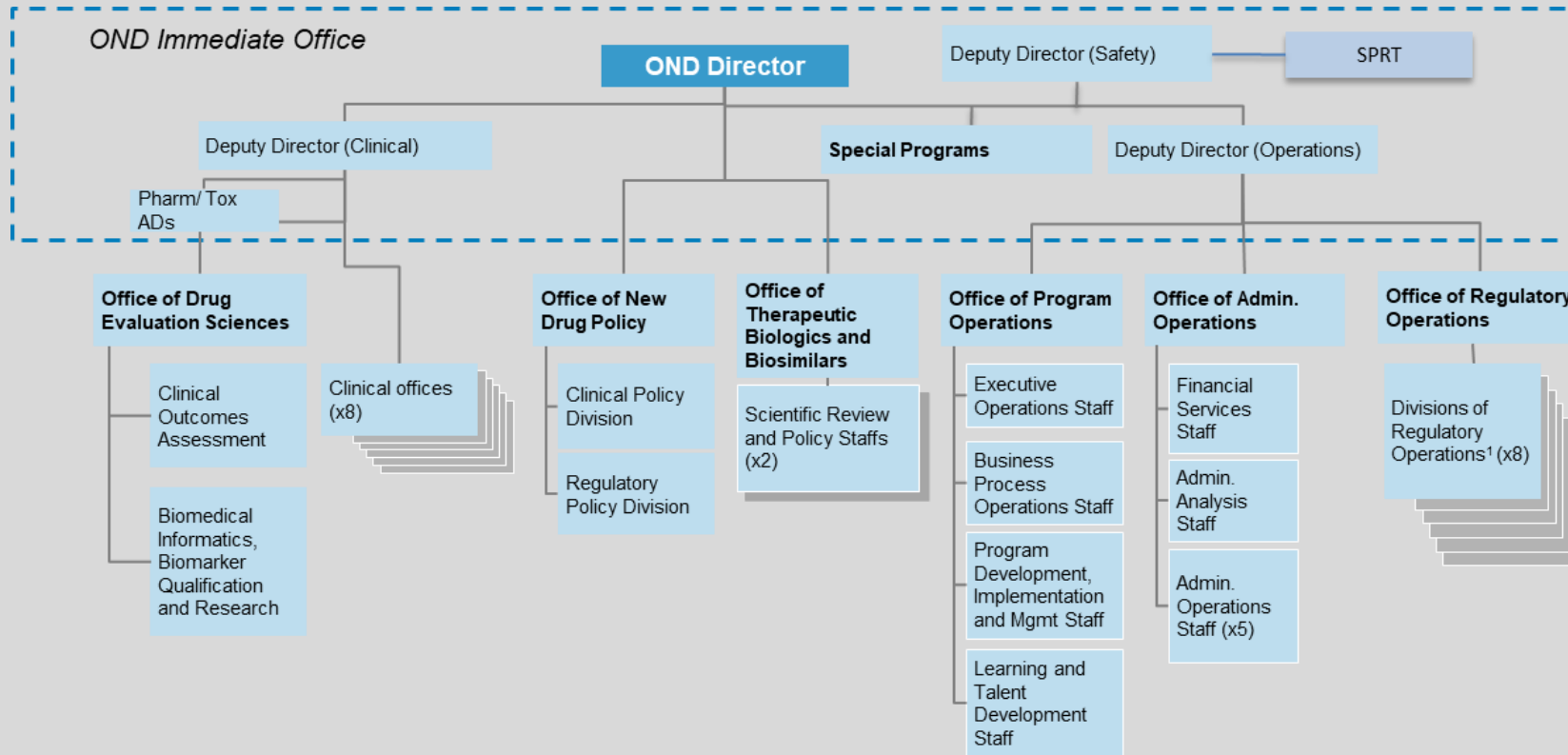
- Therapeutically focused divisions to be aligned to the products we regulate
- Cross-divisional interactions brought together by organizing offices in (“disease clusters”) based on evolving science, drug discovery, and development
- Enhanced career paths within the non-clinical divisions (i.e., pharm/tox, regulatory operations, and administrative)
- New roles that modernize and strengthen our work
- Organizational commitment to strengthening overall program operations (OPO) and the science behind drug evaluation (ODES)
- More balanced leadership span of control to help spread the large work volume and afford leaders more time to invest in developing colleagues
- Regulatory Operations and Pharm/Tox organized into their own divisions while maintaining alignment with clinical structure

Review Structure of Reorganized OND

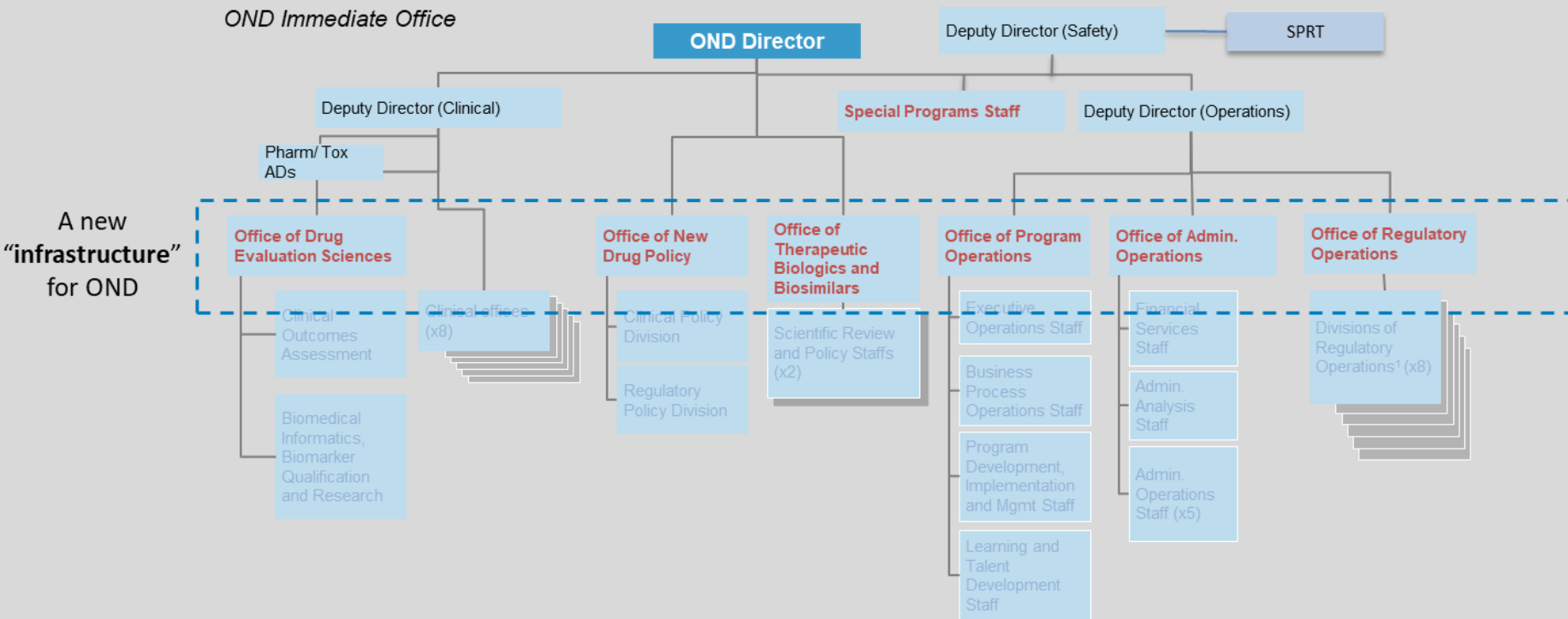
A New Organizational Structure

- The OND reorganization was implemented starting in mid-2019 and finalized in March 2020
 - Kudos to the Special Programs– that orchestrated a seamless transition
- The final (and largest) phase of the re-organization was implemented – at the same time as our “virtual” work started due to COVID-19
- Many new divisional and office leaders selected
- Many senior OND leaders have yet to meet with their organizations “face to face” (other than virtually)
- A challenging situation – limiting the social interactions which are often the “glue” that helps hold an organization together

OND Structure Post-reorganization



OND Structure Post-reorganization

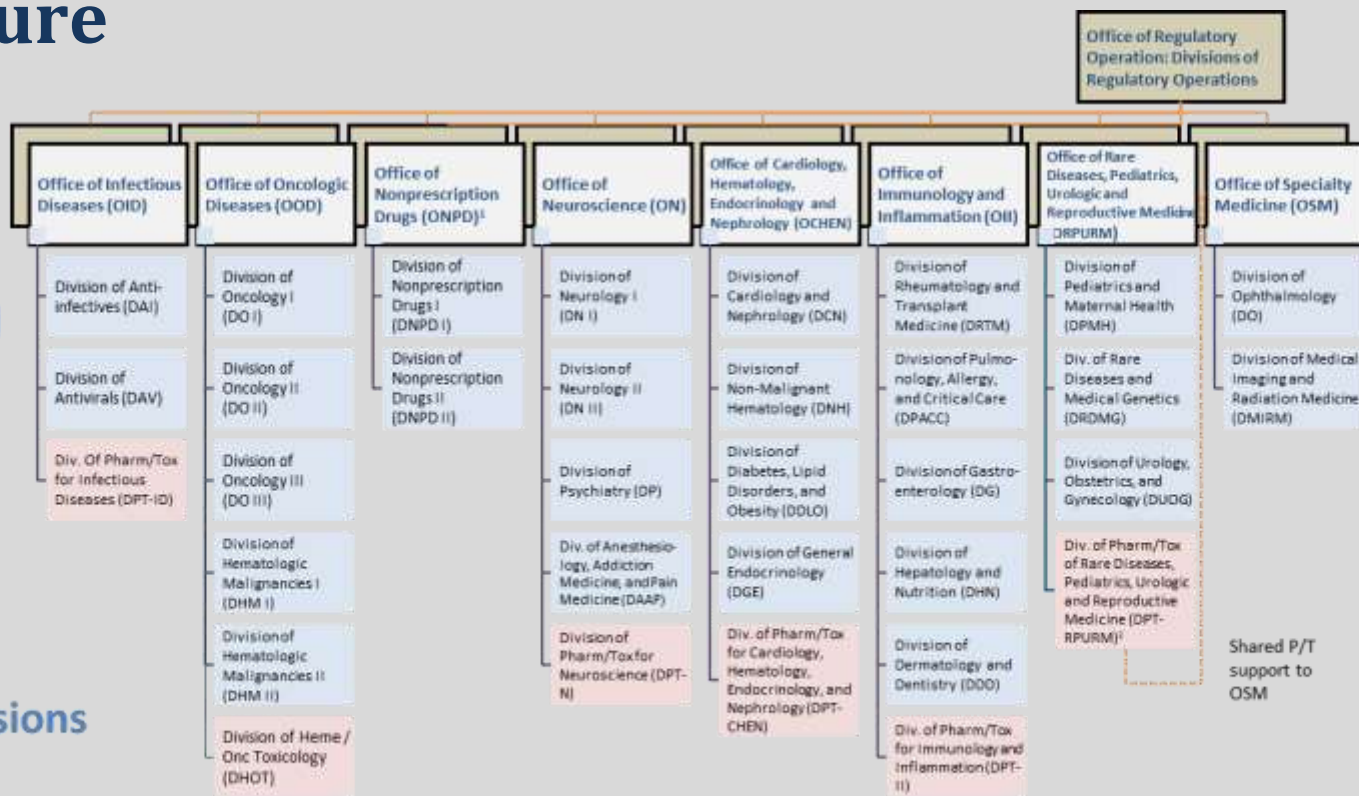


OND: Reorganized Clinical, Reg Ops, and Pharm/Tox Structure

8 offices

27 clinical divisions

6 P/T divisions



¹ ONPD P/T staff in the ONPD IO given the small current size of P/T staff.

² Single P/T division with staff supporting both ORPURM and OSM; PT DD will have dotted line reporting to ORPURM and OSM for P/T issues, and solid line to ORPURM Office Director for PMAP, etc.

Knowledge Check

FDA's OND Reorganization was intended to create more specialized and therapeutically aligned structures?

1. True
2. False

Updates on Ongoing NDRP Modernization Initiatives

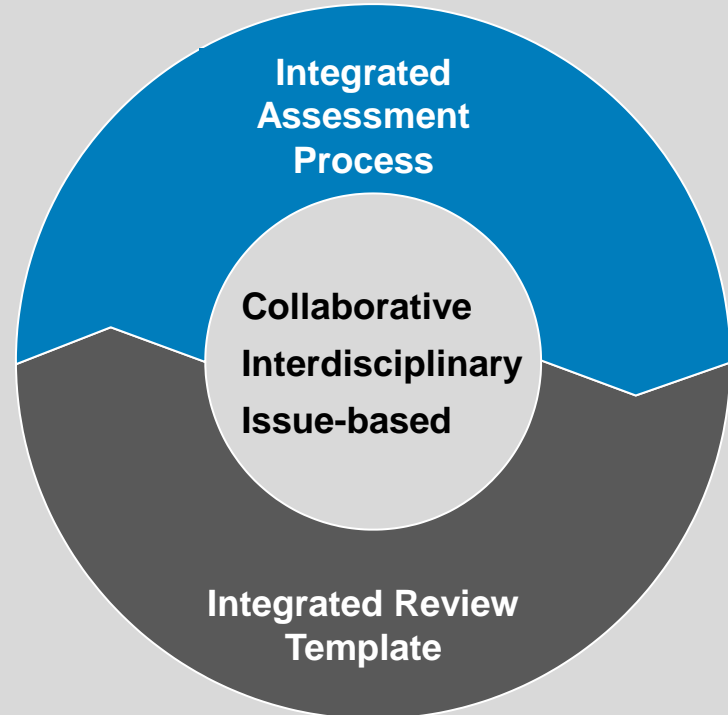
Integrated Assessment of Marketing Applications

Prior approaches to marketing application reviews...

- Disciplines work in silos leading to redundant work
- Reviews centered by disciplines rather than by review issues
- Review issues not discussed and tracked as early as possible
- Signatories not involved early enough
- Insufficient time for critical thinking
- RPMs not optimally utilized as regulatory experts or considered integral to review team
- Experts not part of review team



...to the Integrated Assessment



IND Review Management

Identified challenges for 30 Day Safety and Protocols & Amendment reviews

Variable practices (e.g., timelines, meetings, level of documentation) across divisions

Inconsistent and redundant documentation (e.g., Clinical summarizes Nonclinical Pharmacology/Toxicology findings, more than one discipline summarizes the protocol)

Unclear expectations regarding timelines (e.g., when to share potential hold issues, when to complete primary reviews)

Sponsors **may not receive comments in time** to influence study design



Objectives of the IND Workstream

Templates that are **issue-based**, foster **interdisciplinary collaboration**, **reduce redundancy** and low-value work, and enable better **knowledge management**

Procedures that **standardize** the review process, clearly **define roles and responsibilities** and improve our ability to provide **high-quality feedback** to sponsors in a **timely manner**

An approach to **categorize** incoming protocols and amendments and identify the protocols that should follow the **high priority process** developed

Ultimately, our goal is to more effectively identify and influence protocols that may have a significant impact on public health, and to do so in the most scientifically rigorous and efficient way possible

Postmarket Safety

- CDER has a demonstrated track record of excellence and innovation in postmarketing safety for decades, and we are excited to build on that existing legacy.
- Postmarket Safety is continuously evolving
- To help meet this challenge, CDER is establishing multi-disciplinary Drug Safety Teams that are accountable for the safety of a portfolio of drugs
- Teams will proactively design safety strategies for individual drugs and portfolios as a whole
- We want it to be easier for safety staff to use their time well, and to know where to get help when there is a disconnect or miscommunication across offices

Advisory Committees

- A well-planned and well-conducted Advisory Committee (AC) meeting is an incredibly important tool in new drug review
- ACs and AC Meetings have challenges
 - Burdensome to plan
 - Roles and responsibilities are unclear
 - Hard to find experts and harder to clear them
- We established a workstream to develop
 - Clear policies for when an AC meeting is appropriate
 - Approaches to enhance our recruitment and retention of outstanding advisory committee experts
 - A toolkit with useful, easily accessible information that helps clarify roles and responsibilities in the planning process
- Future projects include streamlined briefing documents, tools to support the identification and screening of experts, and resources to help FDA staff prepare for presentations and discussions on the day of AC meetings

Nexus for New Drug Review

- CDER's existing IT systems to support new drug review were designed at a time when records and paper-based documentation were the primary concern
- To capitalize on greater electronic data, information, and workflows, CDER is working to implement all new drug review process into CDER's Nexus system
- CDER Nexus will enable the new drugs program to continue to modernize operations, more easily implement new PDUFA mandates or programs, and adapt to changes in the new drug review landscape.
- CDER's new drug review programs, which cross multiple offices, will also benefit from the shared support of common, intra-center processes, documentation/records, workflows, and informatics.
- Better use of data. Better automation in our work. Better flexibility. Better access to new tools.

Knowledge Management

- Knowledge Management is a process of effectively gathering, sharing and utilizing institutional knowledge
- More than ever before we need to enable retrieval of our current and past decisions and precedents
- We launched a KM Workstream to operationalize and support knowledge management development and data governance across NDRP
- We are currently prioritizing enabling greater consistency of data capture and integration of knowledge across NDRP through data governance, standardized and structured review templates, workflow enabled processes and information technology tools as Nexus rolls out
- We aspire to create a collaborative knowledge sharing and a learning culture

Knowledge Check

The Integrated Assessment of Marketing Applications was intended to shift multidisciplinary review practices to:

1. Individually driven, siloed review approaches
2. More collaborative, interdisciplinary approaches
3. Combined assessments, but relatively individual

Summary

- The NDRP Modernization and OND Reorganization were intended to address the evolving nature of drug development
- The modernization of the NDRP is guided by six strategic objectives
- OND's new structure is more functionally and therapeutically aligned
- The NDRP Modernization has several ongoing initiatives

Questions



