Public Stakeholder Meeting on Prescription Drug User Fee Act (PDUFA) Reauthorization

December 11, 2020

Dr. Theresa Mullin
Associate Director for Strategic Initiatives
Center for Drug Evaluation and Research
Food and Drug Administration

Outline for this meeting

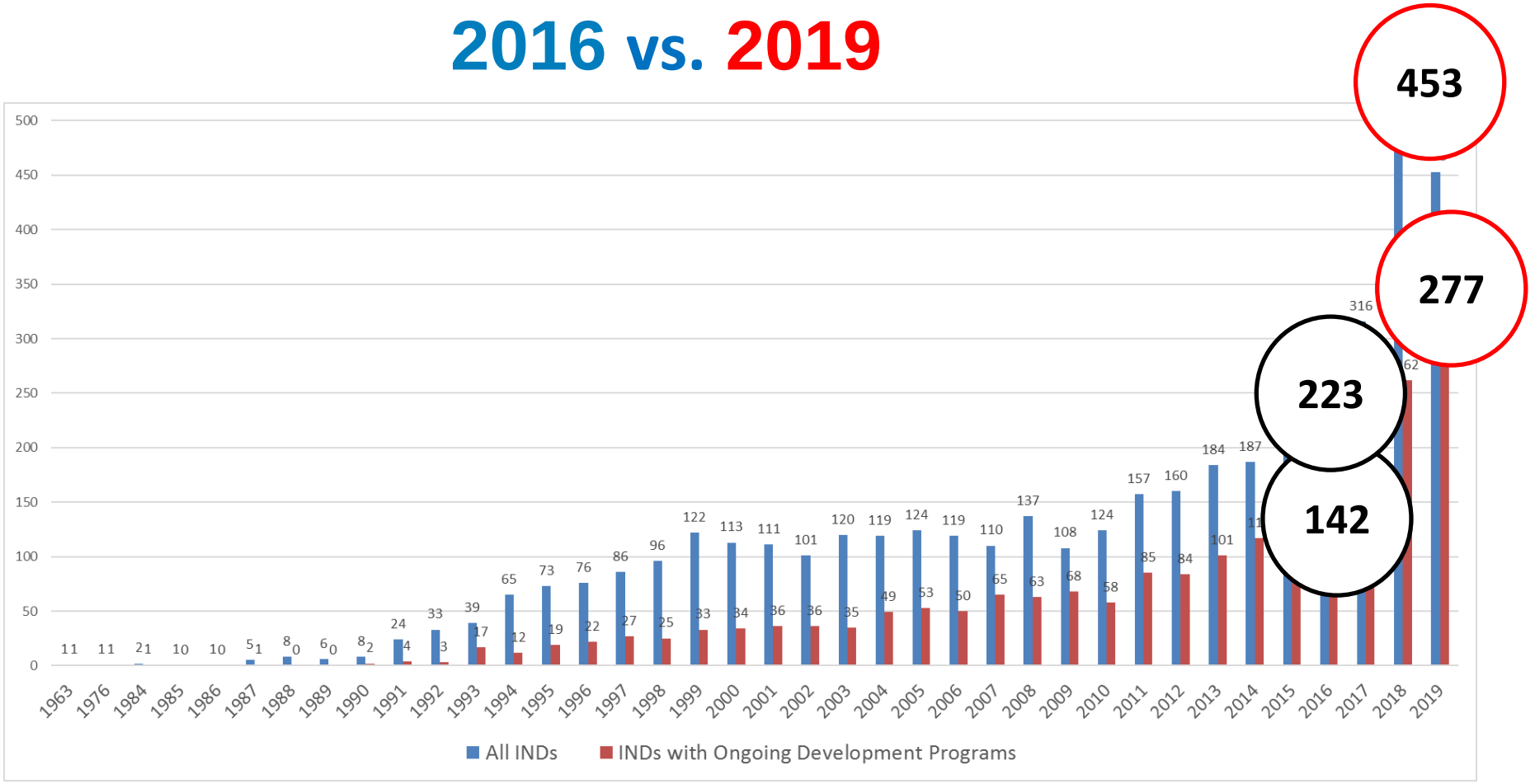
- Welcome and Roll Call
- Presentation Topics:
  - CBER cell and gene therapy review programs
  - PDUFA Financial Status Update
  - CDER recent work to modernize new drug review information infrastructure (knowledge management) and reviewer talent management Discussion
- Topics for upcoming meetings
- Recap and Closing

Cell and Gene Therapy
A Regulatory Perspective

PDUFA Briefing
December 11, 2020

Wilson W. Bryan, MD
Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)

All New OTAT Investigational New Drug Applications (INDs) and Investigational Device Exemptions (IDEs) 2016 vs. 2019



OTAT-Regulated Gene and Cell Therapies

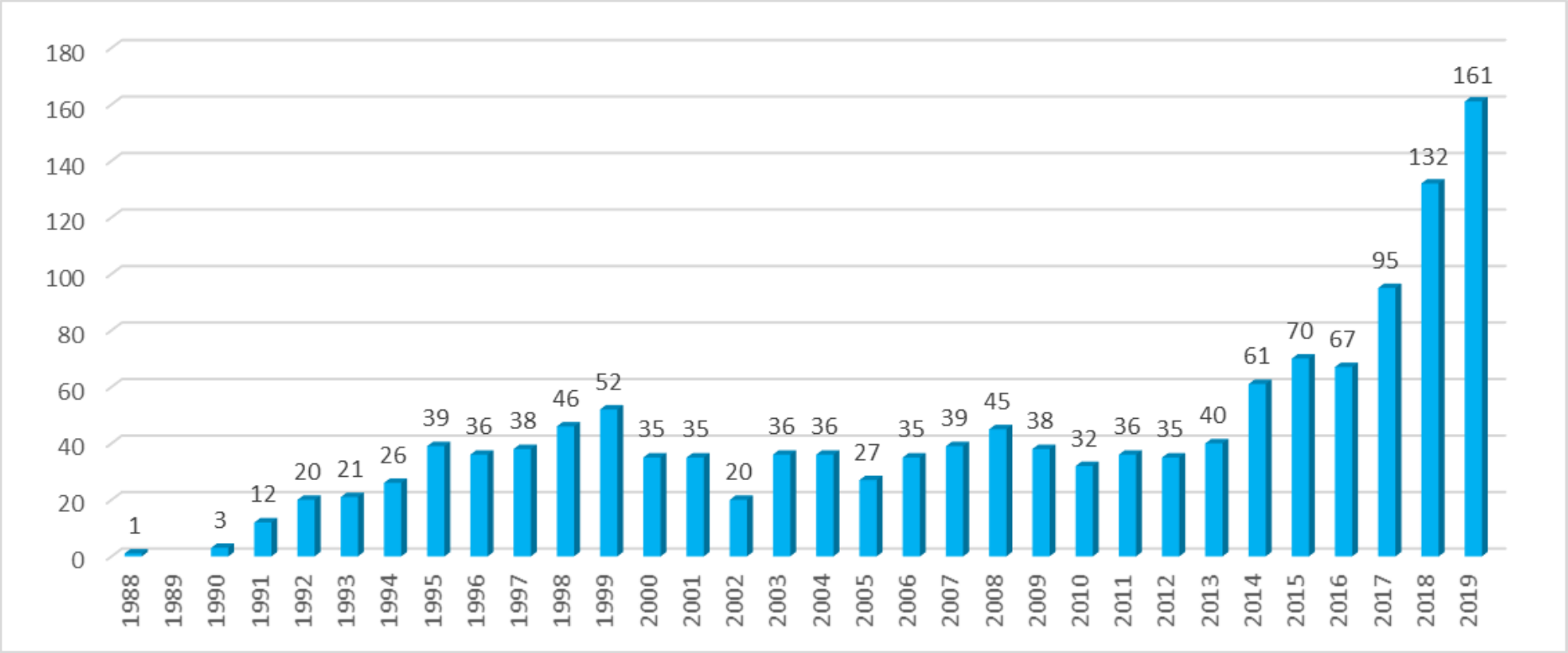
Gene Therapies

- Directly-administered Therapies
- Ex vivo Genetically-modified Cell Therapies
- Genome editing Therapies

Cell Therapies

- Structural functions
- Metabolic functions

INDs with gene therapy development programs



Gene Therapy: Scientific Advances

Human Genome Project

- Completed in October 2003
- 99% of human genes sequenced to 99% accuracy

Development of new vectors

- Adeno-associated virus (AAV)
- Lentivirus

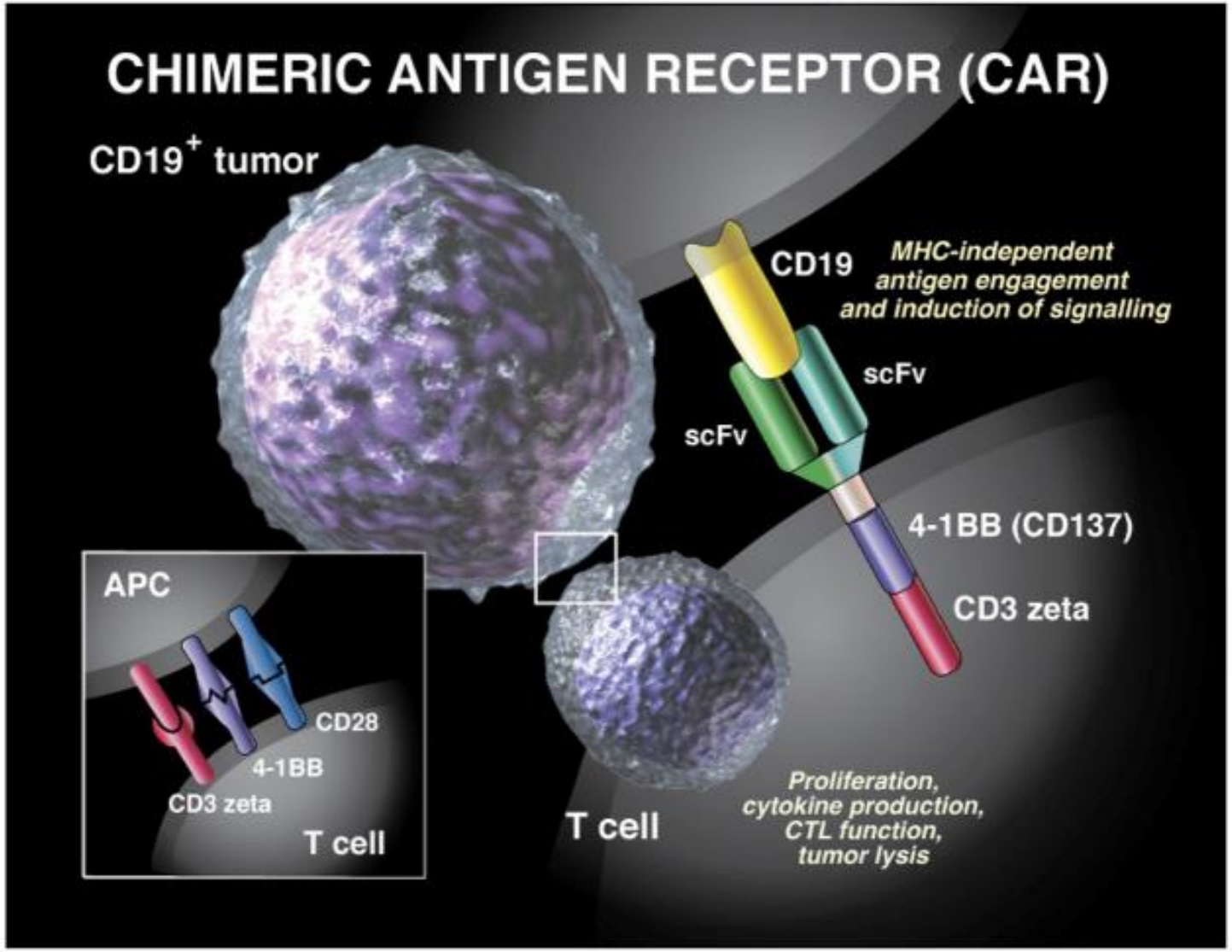
Genome editing

Gene Therapy Approved Products

- Zolgensma (onasemnogene abeparvovec-xioi): infantile spinal muscular atrophy (SMA)
- Luxturna (voretigene neparvovec-rzyl):
  RPE65 mutation-associated retinal dystrophy

- Oncology (Leukemia/Lymphoma)
  - Kymriah (tisagenlecleucel)
  - Yescarta (axicabtagene ciloleucel)
  - Tecartus (brexucabtagene autoleucel) – under accelerated approval

CAR T Cells: A Novel Way to Treat Cancer



Shannon L. Maude et al. Blood 2015

CTL, cytotoxic T lymphocyte; MHC, major histocompatibility complex

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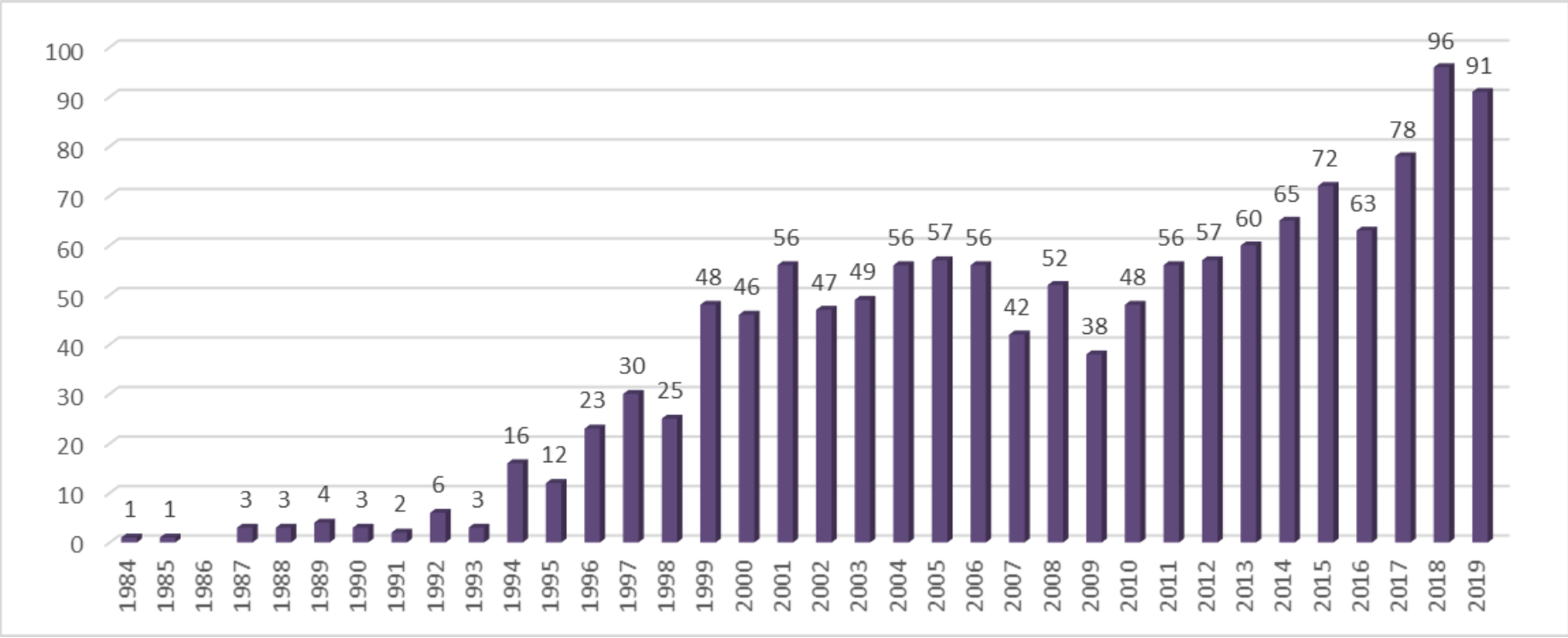
INDs with cell therapy development programs



Cellular Therapy Approved Products

- CARTICEL (Autologous Cultured Chondrocytes) (1997) for cartilaginous defects of the femoral condyle
- PROVENGE (sipuleucel-T) (2010) for asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer
- HPC (hematopoietic progenitor cells), Cord Blood licensed for unrelated donor hematopoietic progenitor cell transplantation procedures
- LAVIV (Azficel-T) (2011) for moderate to severe nasolabial fold wrinkles
- GINTUIT (Allogeneic Cultured Keratinocytes and Fibroblasts in bovine collagen) (2012) for topical treatment of mucogingival conditions
- MACI (Autologous Cultured Chondrocytes on porcine collagen membrane) (2016) for full-thickness cartilage defects of the knee

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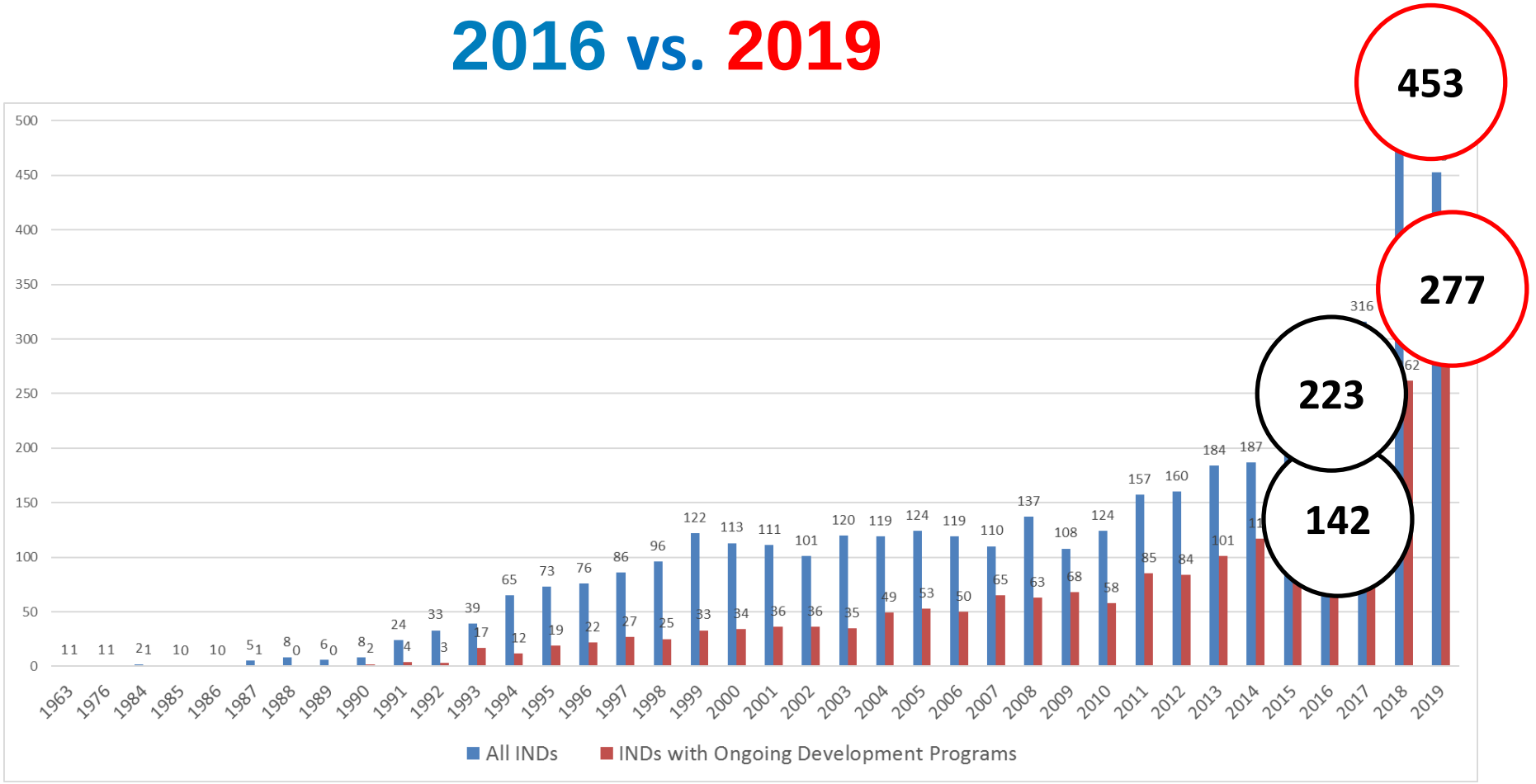
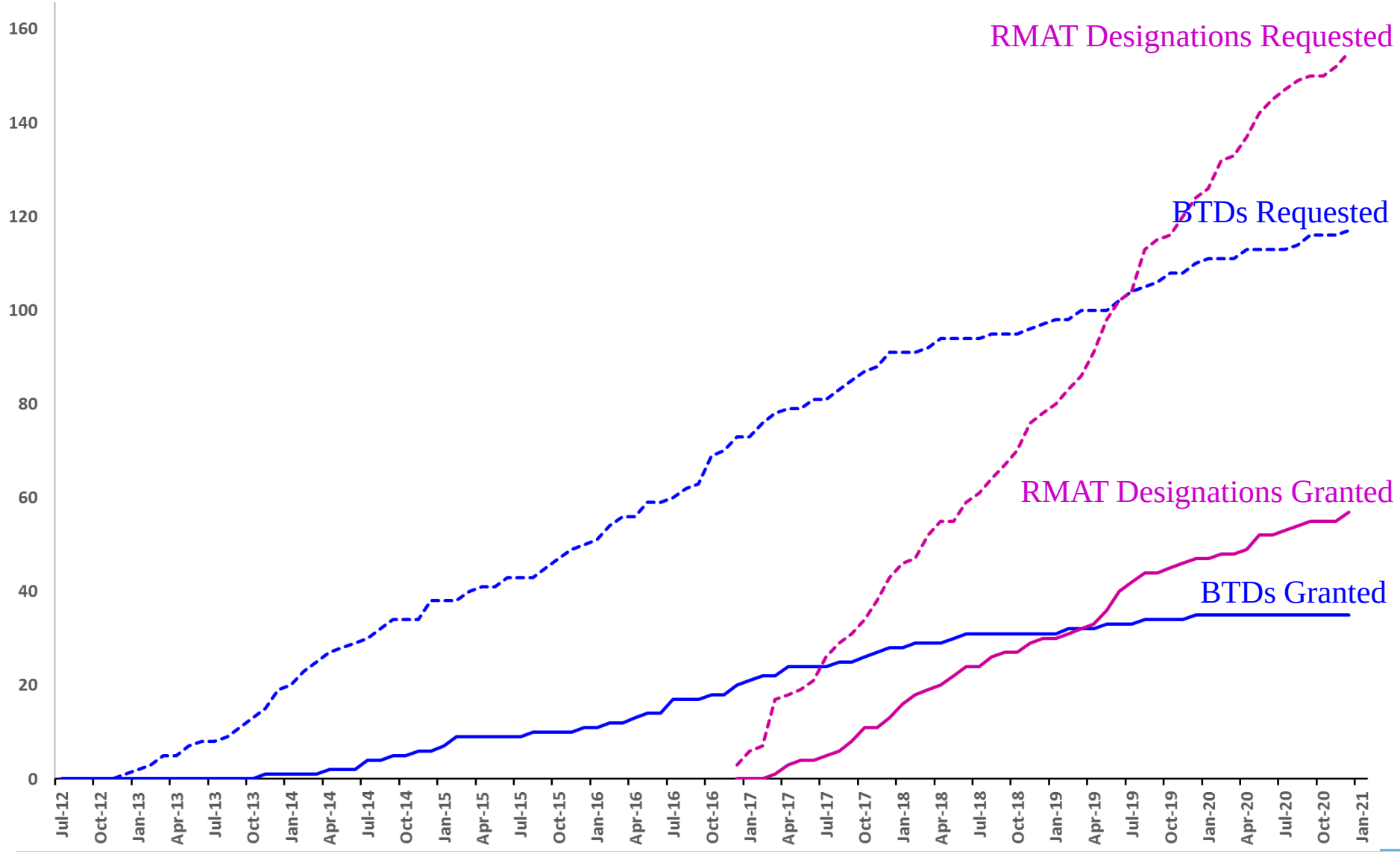
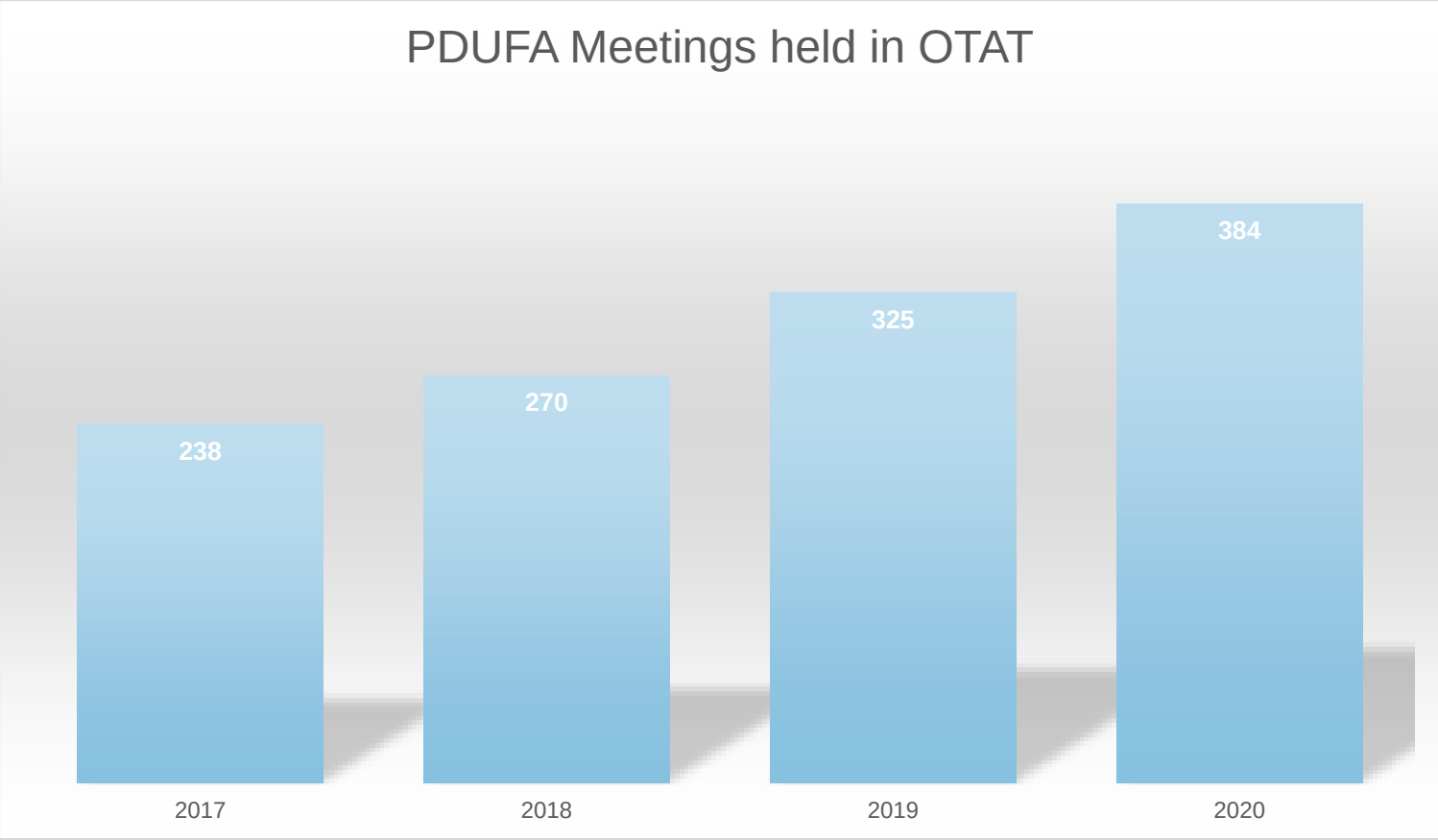


Cumulative Overview of BTD and RMAT Designation Requests (excludes withdrawn and pending requests)



OTAT Meetings with Sponsors



INitial Targeted Engagement for Regulatory Advice on CBER producTs

(previously known as pre-pre-IND interactions)

Gene Therapy Guidances (2020)

FINAL GUIDANCES

- Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)
- Testing of Retroviral Vector-Based Gene Therapy Products for Replication Competent Retrovirus (RCR) during Product Manufacture and Patient Follow-up
- Long Term Follow-Up After Administration of Human Gene Therapy Products
- Human Gene Therapy for Hemophilia
- Human Gene Therapy for Retinal Disorders
- Human Gene Therapy for Rare Diseases

DRAFT GUIDANCE

- Interpreting Sameness of Gene Therapy Products Under the Orphan Drug Regulations

Summary

- Scientific advances spur growth in research and development (R&D) of advanced therapies
- Growth in R&D for advanced therapies increases demand for OTAT advice
- OTAT staff are dedicated to advancing the development of cell and gene therapies

Acknowledgements

- Rachael Anatol, PhD
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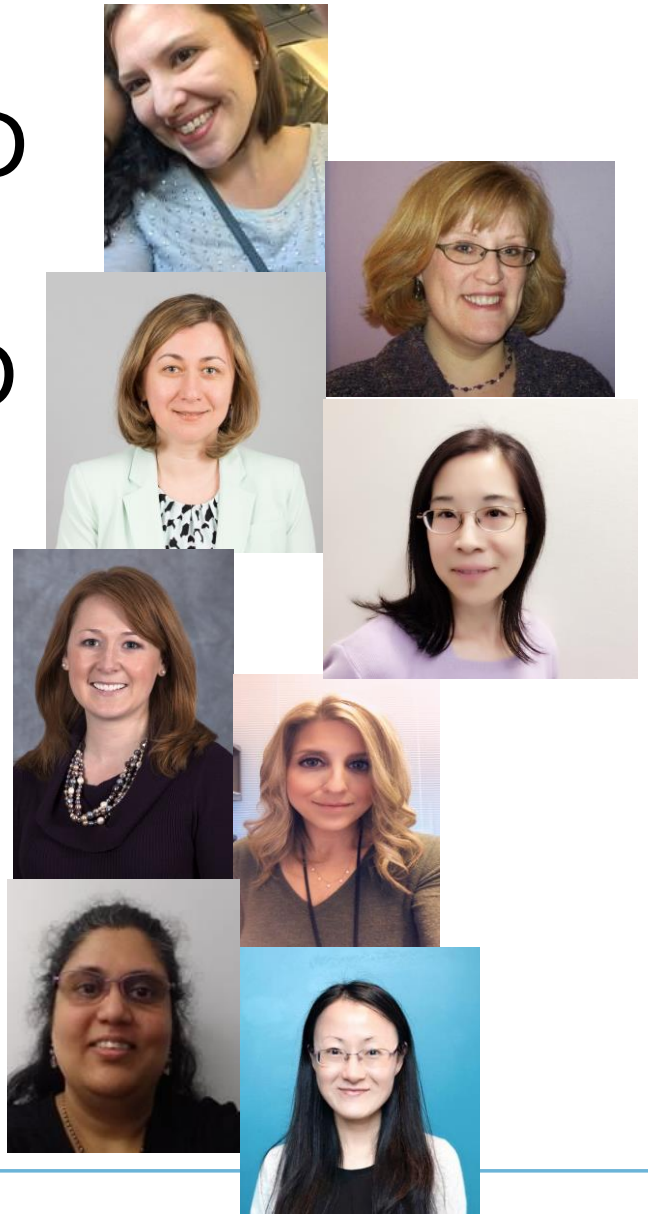

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Questions?

Cell and Gene Therapy
Resource Needs
&
CBER Modernization

Christopher Joneckis, Ph.D.
Associate Director For Review Management
December 11, 2020

Cell and Gene Therapy Resource Needs

December 11, 2020

Current Situation: Pace and complexity of growth forces CBER to play catch up

- The pipeline for cell and gene therapies has grown exponentially recently, and this trajectory promises to continue and lead to increases in meeting requests and regulatory submissions including BLAs.
- The complexity of applications continues to increase with genomic editing of cells, complex directly administered gene therapies, and combination products
- The COVID Public Health Emergency has also placed additional strain on the Cell and Gene Therapy Program and crosscutting indirect functions such as post-market surveillance
- We are meeting most PDUFA UF deadlines, but at the expense of staff working considerable overtime and facing significant burnout

*Excluding Expanded Access

FDA's Cell and Gene Therapy Program Goals for PDUFA VII

- Relieve the stress and strain on the Cell and Gene Therapy (CGT) program, right-sizing the baseline to get ahead of growth in the sector and ensure long-term sustainability through Resource Capacity Planning
- Add capacity to increase the average time spent on CGT submissions to account for novel development challenges, new regulatory requirements, and engagement with industry and stakeholders
- Appropriately resource all facets of the program, including indirect, such as policy and guidance, and support functions, and modernize information technology*
- Provide resources to support development of treatments for unmet medical needs and individualized therapies
- Make resources for the RMAT program permanent to support continued success of the program

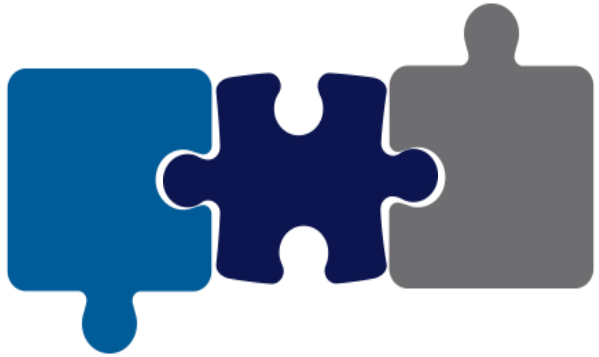
* will be discussed in Digital Health & Informatics subgroup

Detailed Resource Breakout

Assessing the near term needs of the Cell and Gene Therapy Program requires a holistic approach while leveraging current methodologies and best practices from FDA's Resource Capacity Planning capabilities

Indirect FTEs

- Indirect FTEs are tied to specific categories such as policy, communications, and science and research that scale in proportion to the amount of direct work
- Categories are based on benchmark values from established product classes with SME input



Program Support FTEs

- Overhead work, principally conducted through OCOD, OM, and in parts of OD vitally support all product classes
- While some of this work is fixed, a portion of their time scales with direct CGT work or increases in hiring of direct or indirect FTE

Direct FTEs

- Cross validated and tuned forecasts from the Capacity Planning Adjustment were paired with recent CATTS data to develop CGT specific task times for OTAT, OCBQ, and OBE
- Adjustments were made based on SME input to account for needed increases in time dedicated to each submission review. This accounts for the strain on current staff, which results in trade offs and prioritization

Ensure sufficient review capacity and time for expected volume

Current staffing in the Cell and Gene Therapy (CGT) program has **not kept up with growth in INDs** and **average time per submission is insufficient** to support needs for novel products

Current State Challenges

-IND and meeting volume has risen drastically in recent years without corresponding increases in staff

-CBER is starting to see corresponding increases in marketing applications, which are expected to accelerate in coming years

-The number of REMS for CGT products growing rapidly, with no dedicated REMS review staff

-Limited bandwidth prevents optimal use of advisory committees

-The percentage of meeting requests that receive a written response more than doubled between 2015 and 2019

Benefits of Additional Staffing

- Hire staff to support increased volume and increased time per submission
- Setting an appropriate baseline will support long term sustainability via the capacity planning adjustment
- Provide staff to support novel technologies and new regulatory elements, including REMS
- Proactively engage advisory committees for recommendations on emerging topics
- Support improved engagement with sponsors during the development lifecycle

Sustain the RMAT Program

21st Century Cures created the **Regenerative Medicine Advanced Therapies (RMAT)** Designation after PDUFA VI negotiations had concluded, but resources are needed to sustain workload beyond the current five year cycle.

Current State and Challenges:

21st Century Cures established the RMAT designation program for certain cell and gene therapies for serious conditions where there is unmet need

FDA invested carryover resources to rapidly scale up staffing to support the program, but cannot sustain funding for these staff beyond the current 5-year period

This investment has facilitated an extremely successful program, but creates significant risks for CBER if the funding is not made permanent

Benefits of Additional Funding:

- The RMAT program has been tremendously popular, with growth in both requests and designations outstripping OTAT's Breakthrough Designations

- Without funds to make the RMAT FTE permanent, CBER will have to prioritize funding for these already on board positions and scale back hiring for new vacancies in other areas

- Continued resourcing for this program is critical to build on early success

Prepare for increasing postmarket workload

As CGT products begin coming to market, they carry postmarket requirements to monitor safety and efficacy that are unique in CBER's portfolio of products and create new resource demands.

Current State and Challenges:

- CBER currently has 5 active REMS programs, expected to grow substantially PDUFA VII, however CBER has no dedicated REMS staff. Post-approval submissions will grow proportionally
- Recent guidance recommends long-term follow-up for gene therapy products, contributing in expected increase in post-market submissions
- Adverse event monitoring also trending upwards. Patient populations for some products, e.g., CAR-Ts for oncology, are significant in size and may see a larger volume of adverse events

Benefits of Additional Staffing:

- Robust monitoring of post-market safety and effectiveness is critical to FDA's public health mission and public confidence in regulated products
- Without additional resources, post-market safety work competes with pre-market review

Enhance outreach and guidance development efforts

A robust program for guidance development and stakeholder engagement is critical to engage on priorities such as individualized therapies and standardization

Current State and Challenges:

-CBER recognizes the critical role of guidance work to provide regulatory clarity, which has been welcomed by industry (e.g., Gene Therapy Guidances finalized January 2020)

-We also aim to engage stakeholders whenever possible, but are not always able to accept invitations to speak, etc… due to bandwidth constraints

-Additional advances in technology and growing potential for treatment of ultra rare diseases will require continued engagement and leadership from CBER

Benefits of Additional Staffing:

- Robust guidance development providing clarity for expectations and pathways
- Strong engagement with industry, patients, and other stakeholders to promote development
- Catalyze progress on individualized gene therapies
- Take more topics to the advisory committee for input from external experts

Ensure regulatory science program is sufficient to support novel technologies

CBER's Researcher-Reviewer model supports effective regulatory review of scientific products, and is not on track to keep pace with the explosion of new products

Current State and Challenges:

-FDA's cadre of experts, who both review CGT application and conduct applied research, facilitate the development of a wide variety of new and promising products and technologies

-The regulatory science portfolio for cell and gene therapy is small relative to expected growth in submissions

Benefits of Additional Staffing:

- Support evaluation of vectors for gene therapy for individualized gene therapies
- Bring scientific expertise to bear on engagement between CBER and innovators in support of scaling of manufacturing processes
- Ensure appropriate expertise for engagement in efforts related to standardization for CGT

CBER Modernization

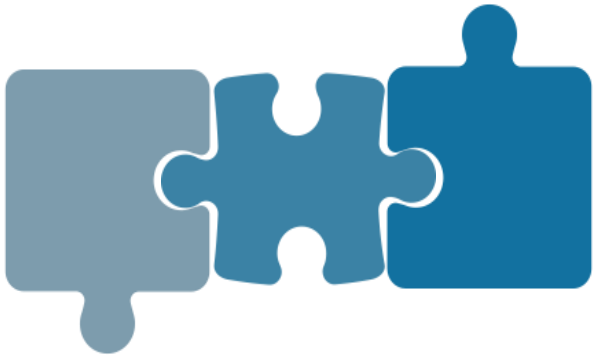
December 11, 2020

CBER Scope

- CBER has a mix of products, regulatory authorities, funding mechanisms, business, data, & IT needs.
- Most staff are not dedicated to one product.
- PDUFA is a significant part of the CBER world, but not its entire world
- Therefore, there is a need for agility and flexibility

Biologics (PDUFA)

- PDUFA defined biologics, devices & drugs
- Cell and GT, Vaccines, Phage, FMT



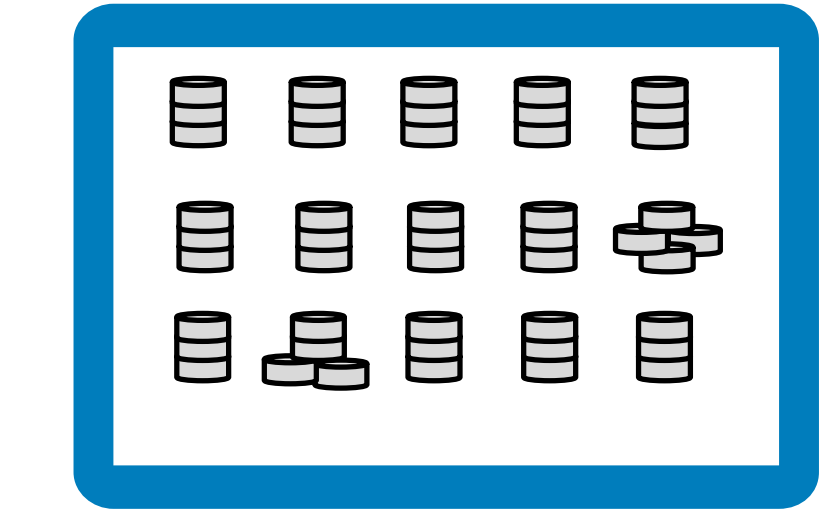
Devices (MDUFA)

- OBRR Diagnostic Test Kits
- OTAT Devices/ OVRR Devices
- Combination Products – device component

Biologics (non-PDUFA)

- Wide variety of biologics (e.g., blood, blood components, tissues) devices

Current CBER Information Technology Challenges



35 systems on 30+ tech stacks

80+ servers

60+ technologies

End of life technologies – over 20 legacy technologies contained in 35 systems

Increased **risk and security**

~$150k O&M costs per system per year

~250 change requests per year

~$17k per system change

Lengthy **delivery time**

Unmet business expectations

11 user interfaces

Challenges

- Can't easily provide staff (e.g., workload, workflow, data capture, data analysis).
  - Data requires extensive manual manipulation
- Difficult to support Cell and Gene Therapy growth, vaccines, business needs.
- Surge Capacity – Pandemic response – data collection and analysis
- Future regulatory submissions - incorporating novel data from a variety of sources (e.g., Real World Evidence, Digital Health information, adaptive clinical trials, bioinformatics, and other informatics)

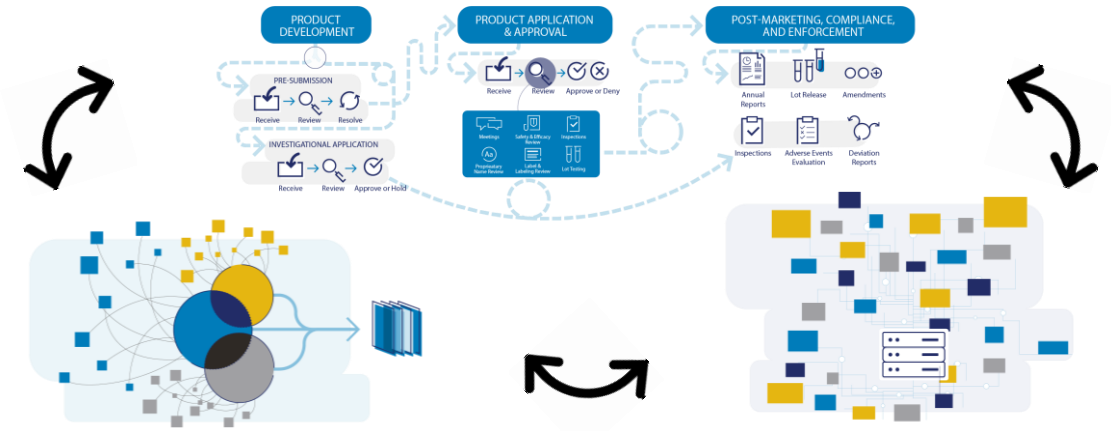
- **CBER needs to modernize its business, data and information technology to keep pace with these challenges**

Integrated Modernization

Address business, data, and technology challenges in a united fashion and take advantage of the interconnectedness and dependencies that exist between and among them

BUSINESS
Streamlined and harmonized business processes =
effective regulatory reviews | more time for other activities

GOVERNANCE



DATA
Less time looking for information =
more time for review

TECHNOLOGY
Less spending fixing aging systems = **more resources for implementing innovative technologies**

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Approach to CBER Modernization

Reusable Tools

Saving time and resources by using reusable code

Open Source Software

Leveraging technology best practices while making it easier to secure our systems and helping to mitigate risks

Automation

Reducing time spent on redundant tasks, minimizing errors and improving data quality

Cloud-ready

Preparing the Center to move to the cloud when it makes sense, avoiding additional cost incurred with a later migration to the Cloud

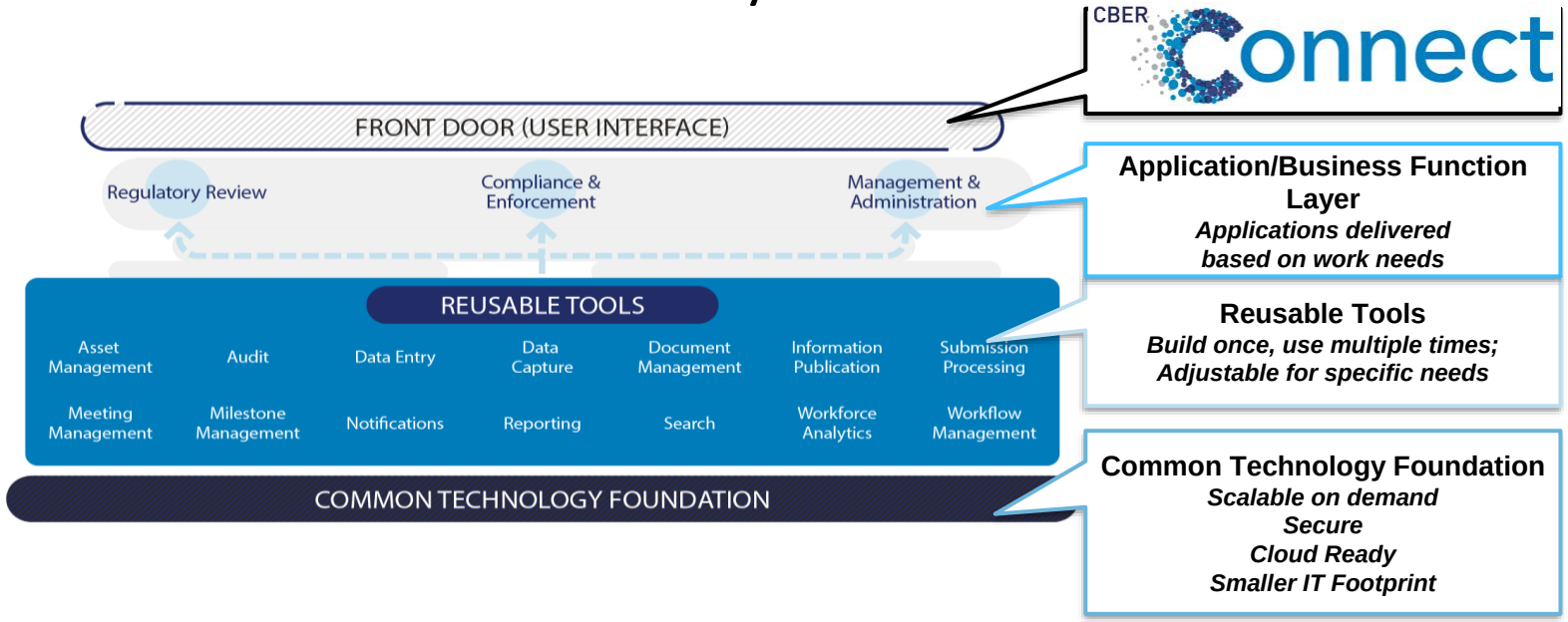
Enterprise Shared Services

Leverage FDA-wide or other Center solutions

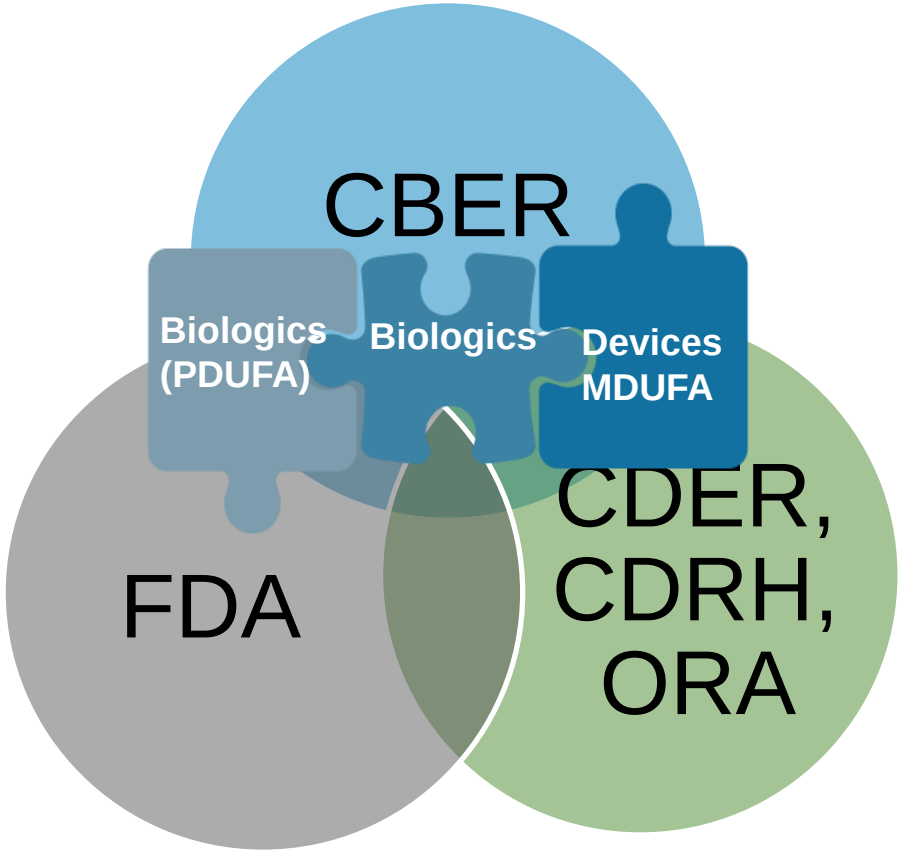
- Technology
- Governance
- Cost

CBER Modernization Progress

- Modernization Initiated 2019
- Development of IT platforms covering product lifecycle – better integration
- Increased agility and flexibility to accommodate wide variety of CBER products and regulatory pathways
- CTF will allow us to interact with various systems

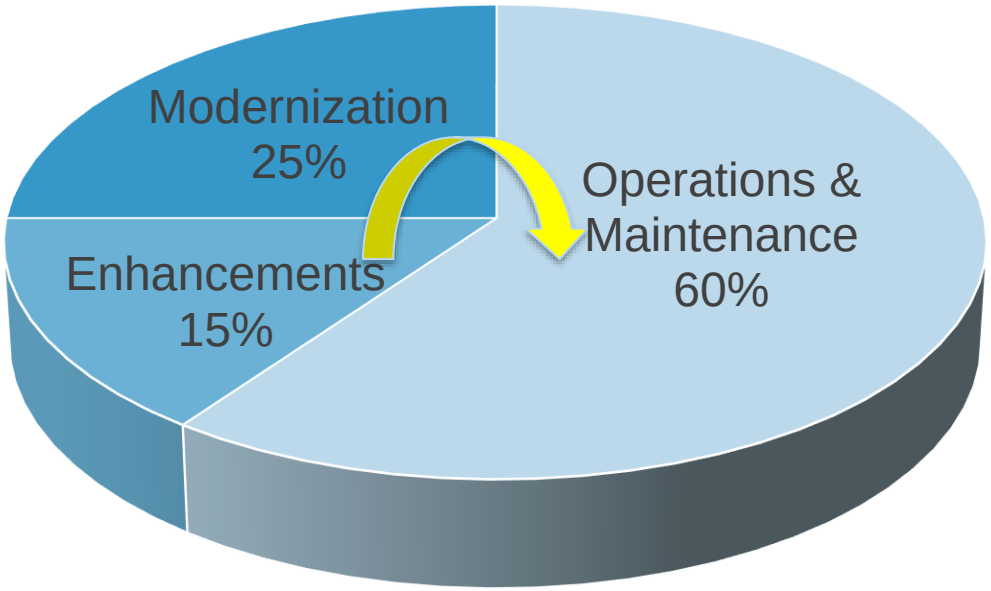


CBER Modernization - Leveraging



Evolution of CBER/ FDA IT

DISTRIBUTION OF CBER IT BUDGET 2018-2020



Accelerate Modernization

- CBER has maximized use of IT dollars
  - CBER staff assume development work
  - focus contractors on technology development

- Modernization takes additional resources
  - Resources for PDUFA products
  - Resources for non-PDUFA products

Benefits Of Modernization

- REDUCE RISK
- Enhance supports of cellular and gene therapy, vaccines and other complex biologics;
- Improved internal management leading to enhanced review efficiency, effectiveness and quality;
- Ability to accept, analyze and manage newer source of data in regulatory submissions;
- Improved knowledge management harmonizing with and leveraging knowledge management efforts;
- Facilitation of external interactions with developers, manufacturers, and patients – resulting in faster information exchange, data analysis, and dissemination of safety information; and
- Better consistency of advice and decisions to guide and foster new product development, review, and approval.

Questions?

Prescription Drug User Fee Act (PDUFA) Financial Status Update

Agenda

- Financial changes implemented in PDUFA VI
- Financial status of the program
- Resource Capacity Planning

Agenda

- **Financial changes implemented in PDUFA VI**
- Financial status of the program
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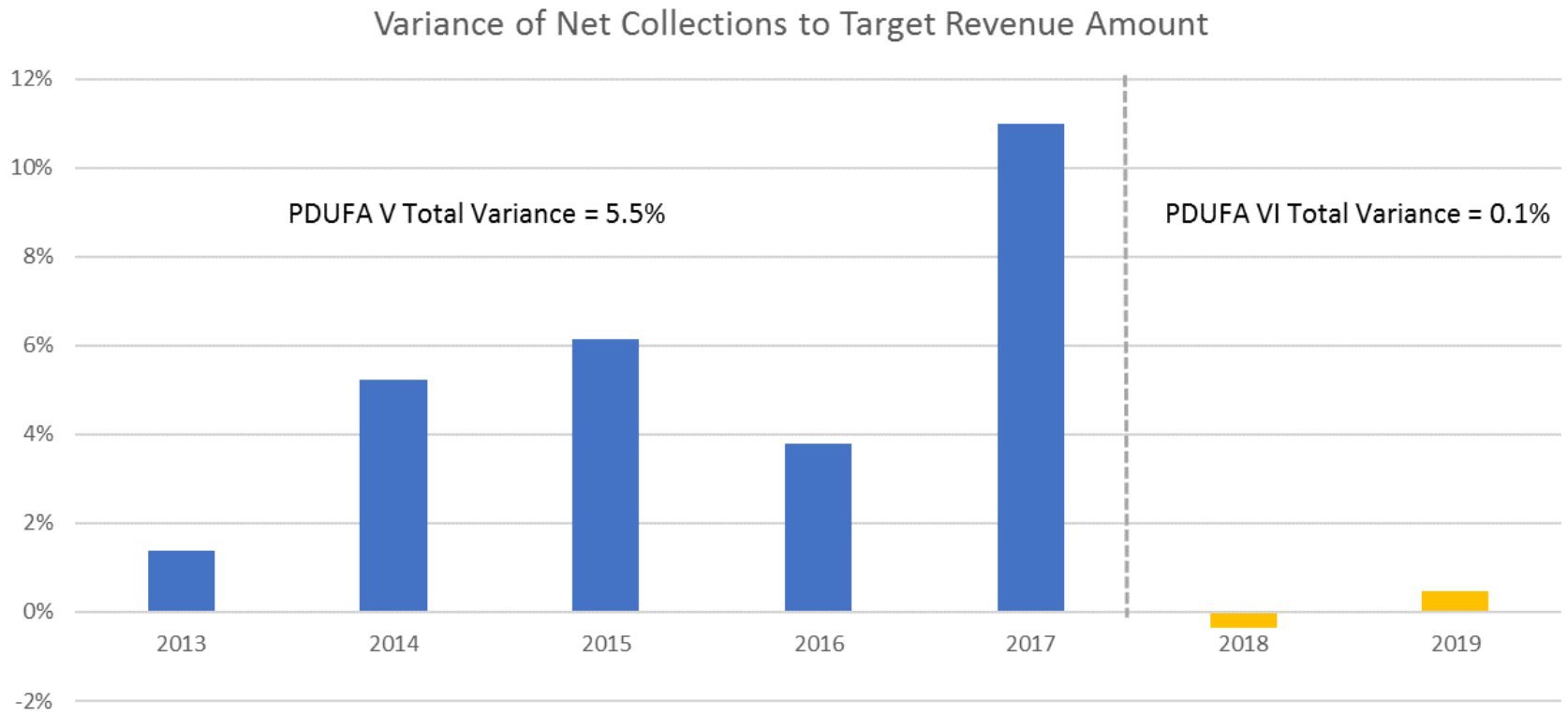
Significant financial changes were implemented in PDUFA VI

PDUFA VI represented significant changes to financial aspects with the following objectives:

- **Enhancing the predictability** of PDUFA funding levels and sponsor invoices
- **Minimizing inefficiency** by simplifying the administration of the program
- Improving FDA's ability to **manage program resources** and engage in **effective long-term planning**

Enhancing the predictability of PDUFA funding levels and sponsor invoices

- Increased reliability of program collections
  - Shifting fee allocation to more reliable fee types appears to have reduced variance of collections to target revenue

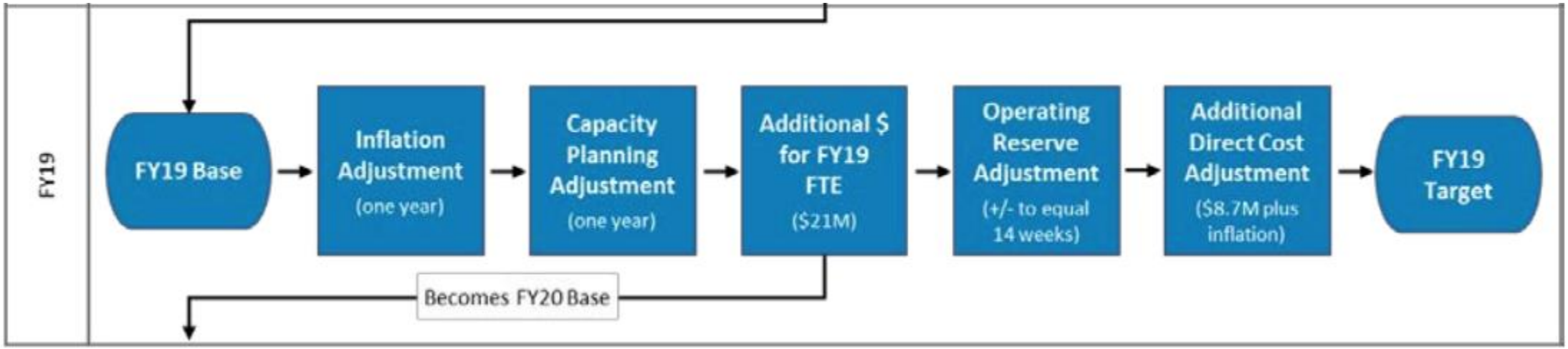


Minimizing inefficiency by simplifying the administration of the program

- Discontinued establishment fee
- Minimized multiple billing cycles
- Discontinued Fees-Exceed-the-Costs waiver

Improving FDA's ability to manage program resources and engage in effective long-term planning

- Replaced 5-year offset and final year adjustment provisions with Operating Reserve Adjustment
- Established forward-looking Capacity Planning Adjustment methodology to better enable ability for resources (full-time equivalents) to keep pace with review workload growth
- Created an annualized base revenue amount



FDA has faithfully delivered on all commitments in the financial aspects of PDUFA VI

Commitment	Status
Publish RCP/MTR implementation plan	Published on time
Staff an RCP team	Staff duties established in CDER, CBER, & HQ
3rd party study of new CPA published for public comment	Published ahead of schedule; new CPA established for FY21 fee-setting
Allocate CPA funds to org components engaged in direct review work and report in annual financial report	Reported in each annual financial report
3rd party evaluation of PDUFA program resource management in FY18	Published; FDA action plan initiated in response
Publish 5-year financial plan with annual updates	Published (FY19 delayed due to shutdown)
Convene public meeting to discuss program finances (starting in FY19)	FY19 & FY20 meetings hosted

Agenda

- Financial changes implemented in PDUFA VI
- **Financial status of the program**
- Resource Capacity Planning

Overview of the PDUFA Financial Plan

Budgetary Resources	FY 2018	FY 2019		FY 2020	FY 2021	FY 2022
	Actual	Estimate	Actual	Estimate	Estimate	Estimate
Target Revenue	**$911,346,000**	**$1,010,322,000**	**$1,010,322,000**	**$1,074,714,000**	**$1,121,803,000**	**$1,168,054,000**
Cash Collections	$908,077,723	$1,010,322,000	$1,015,152,012	$1,074,714,000	$1,121,803,000	$1,168,054,000
Recoveries	$13,149,599	$10,000,000	$12,857,171	$9,000,000	$9,000,000	$9,000,000
Carryover Available for Use, Beginning of Year	$232,969,623	$125,372,943†	$125,372,943	$136,237,817†	$133,219,097	$128,916,297
Total Budgetary Resources	**$1,154,196,945**	**$1,145,694,943**	**$1,153,382,126**	**$1,219,951,817**	**$1,264,022,097**	**$1,305,970,297**

User Fee Obligations	FY 2018	FY 2019		FY 2020	FY 2021	FY 2022
	Actual	Estimate	Actual	Estimate	Estimate	Estimate
Payroll & Operating						
CBER	$129,543,398	$133,147,244	$132,847,629	$135,357,938	$140,880,201	$146,587,238
CDER	$688,935,477	$641,479,230	$632,811,258	$680,411,849	$717,861,387	$754,552,492
CDRH	$786,091	$2,630,174	$1,501,379	$4,051,811	$4,184,089	$4,321,933
ORA	$7,733,467	$8,498,654	$7,443,695	$8,628,940	$8,880,776	$9,143,184
HQ	$54,211,488	$58,486,768	$55,910,342	$56,102,552	$59,097,922	$55,178,077
Total Rent	$49,964,883	$65,278,320	$52,437,964	$65,931,103	$66,590,414	$67,256,319
Total Shared Services	$130,936,781	$133,751,844	$134,192,042	$136,248,526	$137,611,011	$138,987,121
Total Obligations	**$1,062,111,583**	**$1,043,272,234**	**$1,017,144,309**	**$1,086,732,719**	**$1,135,105,800**	**$1,176,026,364**

Carryover	FY 2018	FY 2019		FY 2020	FY 2021	FY 2022
	Actual	Estimate	Actual	Estimate	Estimate	Estimate
Total Carryover, End of Year	$209,223,938	$186,273,705	$220,088,812	$217,070,092	$212,767,292	$213,794,928
Carryover Unavailable for Use, End of Year	($83,850,995)	($83,850,995)	($83,850,995)	($83,850,995)	($83,850,995)	($83,850,995)
Carryover Available for Use, End of Year	**$125,372,943**	**$102,422,710**	**$136,237,817**	**$133,219,097**	**$128,916,297**	**$129,943,933**

**Numbers rounded to nearest whole dollar*
Target Revenue has been rounded to the nearest thousand dollars
†Indicates an actual amount

Carryover Balance

- Available carryover decreased from beginning of FY18 to end of FY20 (est.) by $99.8M
- Ending balance in FY22 accounts for roughly 9.5 weeks of operating reserves

Impact of Fee Structure Change

Increase in efficiency and stability

- Elimination of burdensome fees and additional “cleanup” billing
- In FY19 FDA collected 100.49% of the planned target revenue
- Through the first two years of PDUFA VI, FDA has collected 100.08% of the total planned target revenue

Agenda

- Financial changes implemented in PDUFA VI
- Financial status of the program
- **Resource Capacity Planning**

RCP Commitments

- As part of PDUFA VI, BsUFA II, and GDUFA II, FDA committed to:
  - Modernize its activity-based **time reporting**
  - Building a **resource planning capability (RCP)**

- The capabilities would provide FDA with the tools to better understand its **future resource needs** and adjust internal operations to meet the expected workload

- There was a recognition that these two capabilities, when established, would provide FDA with the data to better inform a more optimal **Capacity Planning Adjustment (CPA)** for its user fee target revenue for **PDUFA and BsUFA**.

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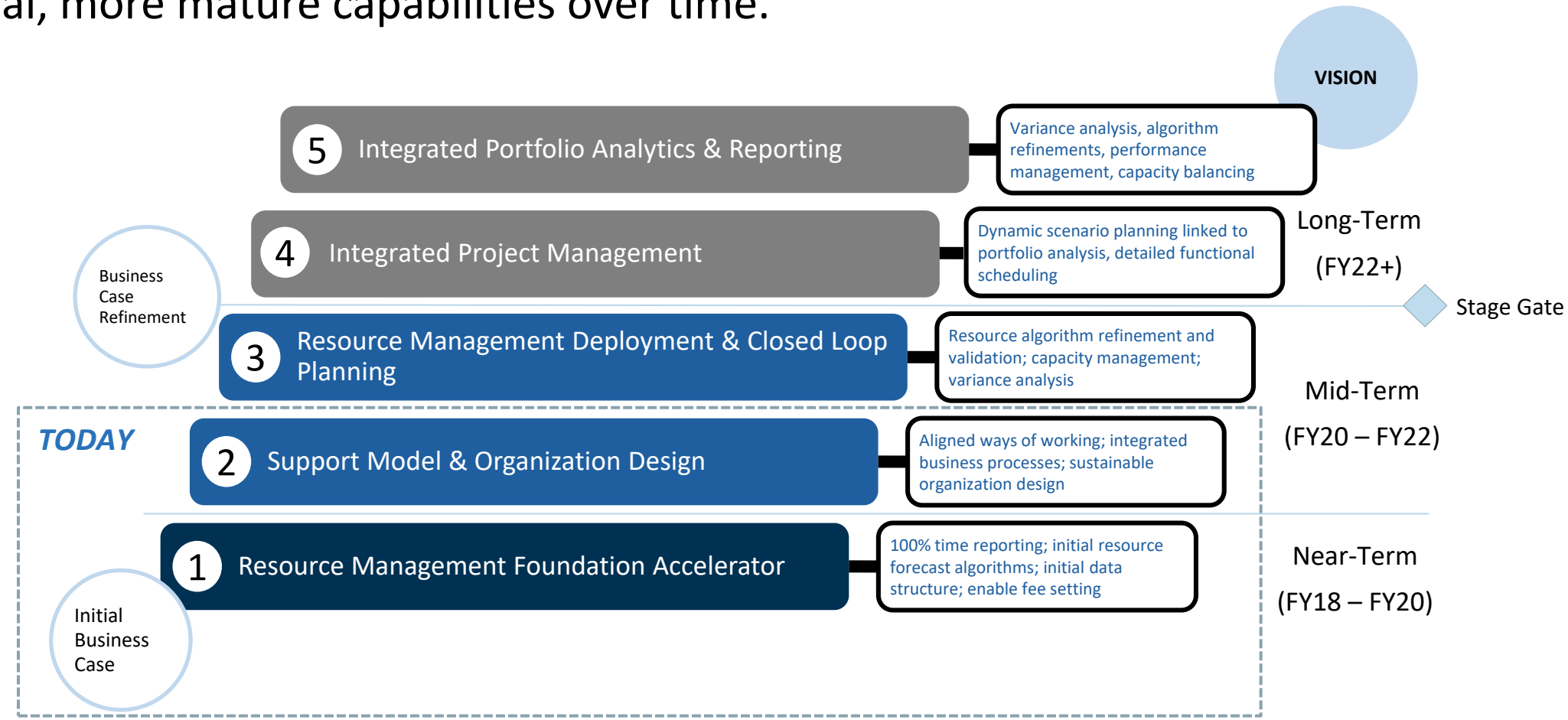
FDA's Journey to Excellence in Operations

FDA's vision will be achieved by first establishing a foundation and then building additional, more mature capabilities over time.



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What is Resource Capacity Planning?

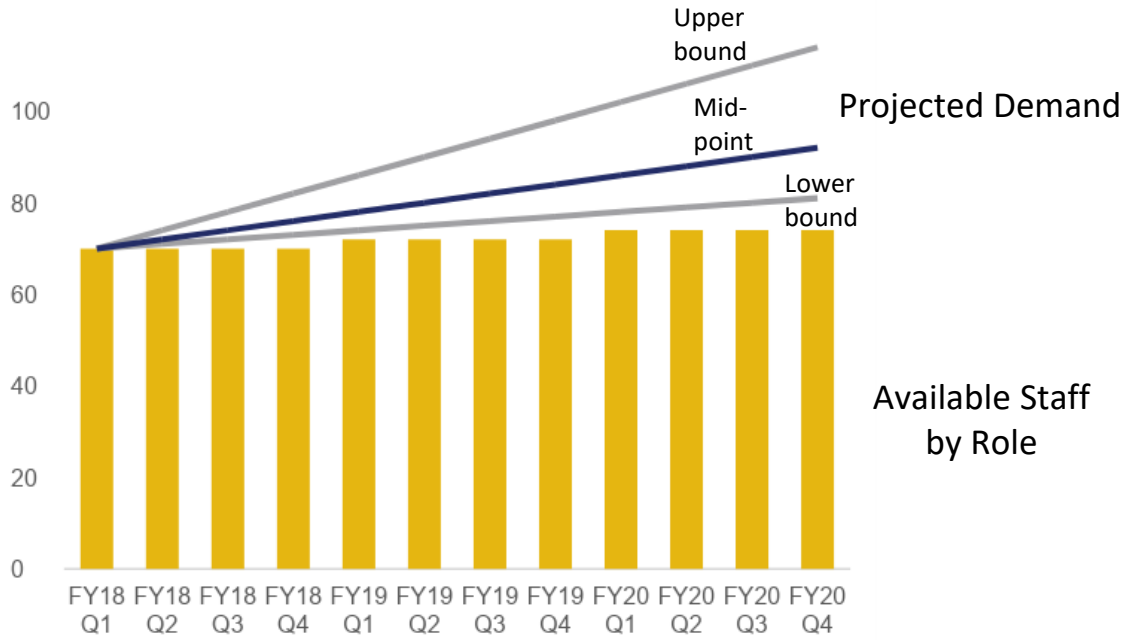
RCP allows FDA to identify the resources needed **before** they are needed

Modernized Time Reporting (MTR)
52-week time reporting to provide:
- Better measure of level of effort
- Better analysis of available hours

Workload Forecasting
Advanced analytics to forecast likely incoming work & productivity

Operational Data
HR Data (attrition, hiring times)
Financial Data

Resource Forecast



Applications of Resource Forecasts

Capacity Balancing
Identify ops to prioritize existing resources

Revenue Adjustment

Hiring Plans

Financial Forecasting

RCP near-term implementation timeline

Done

Build Foundational Capabilities

- Implement Time Reporting across CDER & CBER
- Develop the methodology for advanced resource capacity planning

Ongoing

Operationalize RCP Capabilities

- Ensure Time Reporting compliance & accuracy
- Operationalize predictive models and algorithm engines to produce resource forecasts

Next Steps

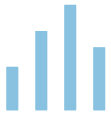
Develop Sustainable & Scalable IT & Support to Expand Capabilities

- Develop a technical infrastructure to enhance automation and replicability, of analysis and reporting
- Expand IT/RCP capabilities to other centers
- Build an enterprise-wide support model to sustain RCP capabilities

Program milestones to date

Established Time Reporting within CDER and CBER

- ~ 6,000+ employees recording time year-round within CDER & CBER
- Achieved at least 95% center-wide compliance
- Created interactive dashboard visualizations to enable leadership decision-making



Designed predictive models for incoming regulatory submissions

- Developed models to predict upcoming future submissions (IND, NDA, BLA, supplements) and industry meetings across CDER and CBER

Developed future-looking resource forecasts

- Created continuous forecast resource algorithms which utilize time reporting and historical submission data
- Developed resource algorithms across both CDER and CBER offices

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RCP capabilities will enhance the way FDA operates

Resource capacity planning is built on the data gathered through implementation of time reporting and sets the organization up for a more structured, data-driven approach to operational decisions.

Proactive Resource Planning

- Reprioritization of work and resources based on time reporting and utilization data
- Targeted hiring plans based on workload forecasts

Improved User Fee Setting Methodology

- Data driven target revenue adjustments based on predictive modeling of resources rather than historical averages of submission volume
- Ability to incorporate increases in submission complexity into the adjustment
- Future forecasts can provide foundational data for updating of the Five-year Financial Plan

Enhanced Management of Financial Resources

- Increased visibility into future resource needs to inform budget
- Tracking of forecasted financial needs versus actuals

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Improved user fee setting methodology

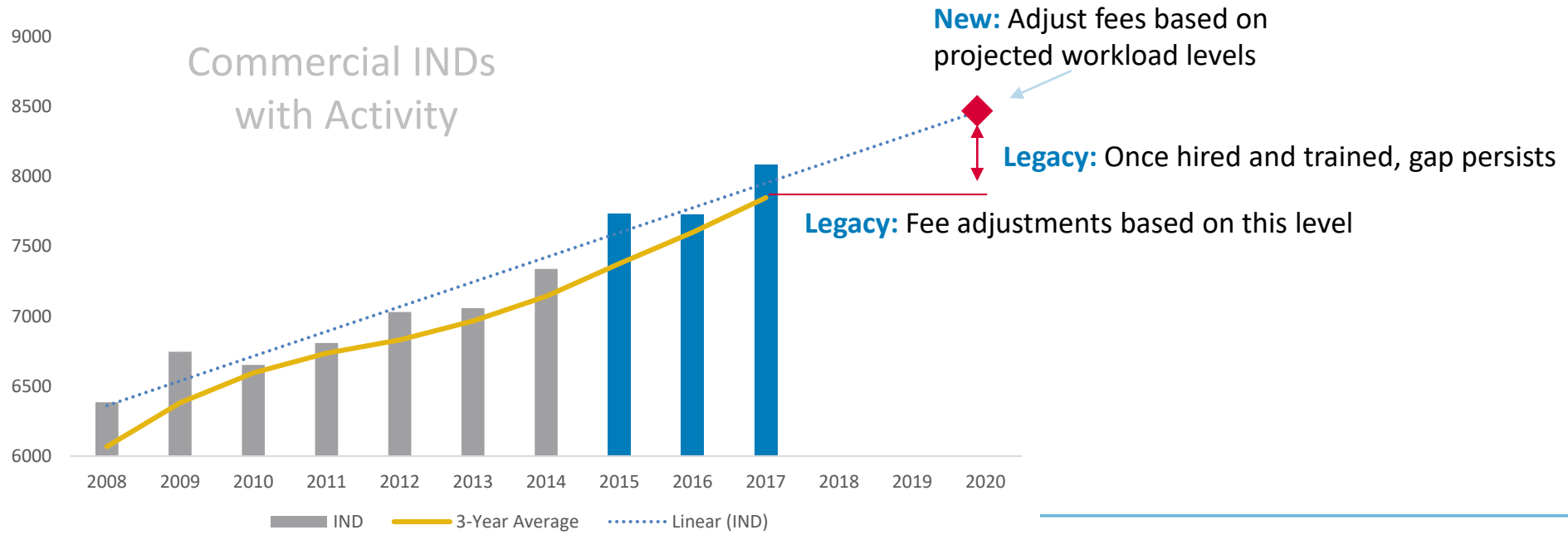
The new CPA improves upon the interim CPA by developing a forward-looking approach for the annual revenue setting.

Legacy adjustment:

- Lagging indicator using 3-year averages
- Compensates for increases occurring in the past
- Based on submission counts
- Timing compounded by hiring timeframes

New adjustment:

- Forward looking
- Compensates for likely increases
- Translates submission activity to likely resource demand
- Times resources to account for hiring and training timeframes



CPA adjustment approach

The adjustment accounts for expected direct review work – work driven directly by incoming volume of submissions.

1. Forecast Submission Volume

- Predictive models estimate the volume of direct review submissions

Includes:

- Commercial INDs/BPDs
- Original NDAs/BLAs
- Efficacy Supplements
- Labeling Supplements*
- Manufacturing Supplements
- Industry Meetings

2. Calculate Future Resource Forecast

- FTE** forecast algorithms informed by time reporting data
- These algorithms forecast the required FTE demand for direct review effort

3. Assess Feasibility of Acquiring Needed Resources

- Compare the forecast against capacity and adjust the forecast to ensure that an adjustment is made only for what is needed and what can realistically be utilized.

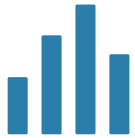
4. Convert Adjusted FTEs to Dollars

- Determined by FTE cost model
- The final feasible FTEs needed will be converted to a dollar amount and added to the inflation-adjusted annual target revenue

** New submission type included in adjustment*
*** Full-Time Equivalent*

Fully enabling RCP capabilities

The foundational RCP capabilities have been built, however development and identification of improvement opportunities continues.



Continually improve predictive models and resource algorithms

- Integrate additional data sources into the workload models for enhanced accuracy
- Ensure that time reporting compliance remains high and that activities are reported accurately
- Incorporate additional drivers of effort into resource forecasting algorithms

Build and maintain a technical environment to support RCP operationalization

- Create an environment to store foundational data in a centralized location
- Enable an advanced analytical capability to run predictive models and resource algorithms
- Provide visualization and reporting of RCP outputs to inform operational decision-making

Continue to incorporate RCP into FDA business processes and operations

- Integrate RCP outputs into FDA financial processes
- Hire required talent to support RCP capability at FDA
- Change its ways of working to support and maintain the RCP capability into the future

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Questions?

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New Drugs Regulatory Program Modernization

PDUFA VII Stakeholder Meeting
December 11, 2020

Kevin Bugin, PhD, MS, RAC
Director, Special Program Staff
Office of New Drugs
Center for Drug Evaluation and Research

William Lewallen
International Program Analyst
Office of the Center Director
Center for Drug Evaluation and Research

Agenda

NDRP Modernization Overview and Strategic Objectives

- Impetus, Vision, and Strategic Objectives

Integrated Assessment of Marketing Applications

- Patient Experience Data Table

Knowledge Management

- Internal Efforts to Identify Knowledge Management Priorities

Talent

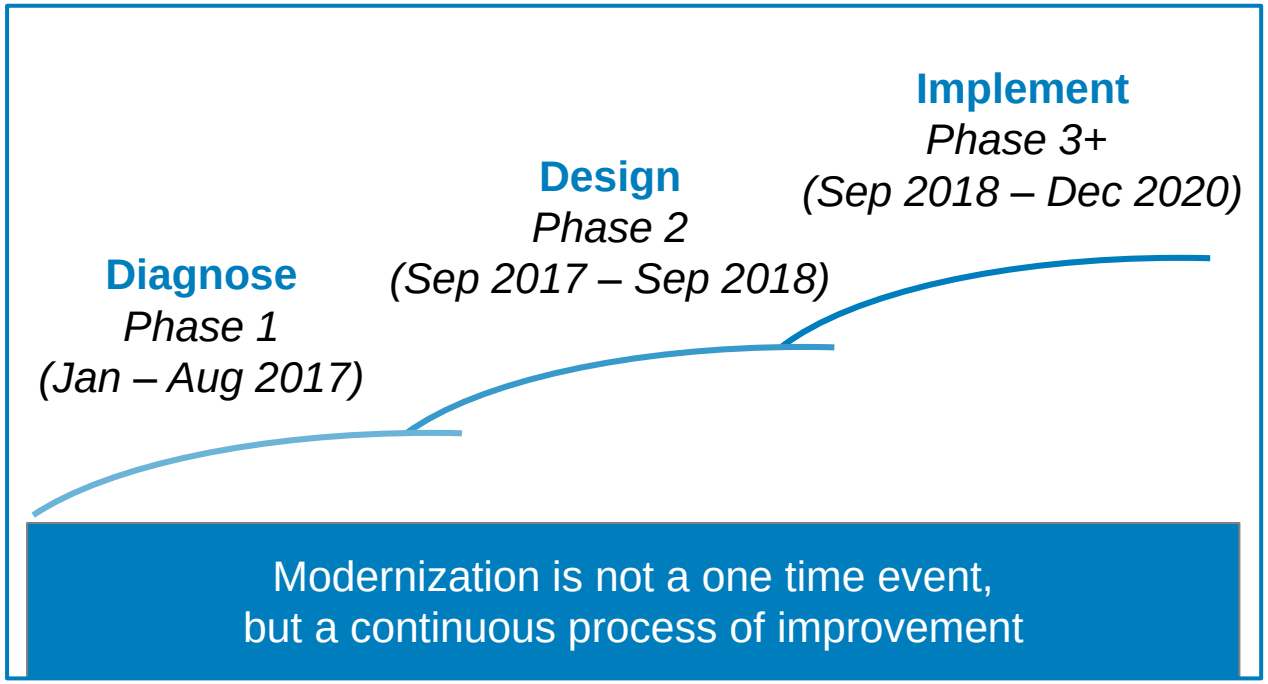
- OND Talent Management
- Assessing Talent

NDRP Modernization Overview and Strategic Objectives

The impetus for the Modernization…

- **Rapid and sustained growth in the volume of drug development activity**
- **Increased complexity of innovative therapies under development**
- **Greater availability of observational and other "real world" data**
- **Increased public engagement in FDA activity**
- **Persistent budget constraints**
- **Talent shortage**

…it intends to maintain the program's status as a standard for regulatory management of drug development and review



Mission and Vision for the Modernization

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.**"**

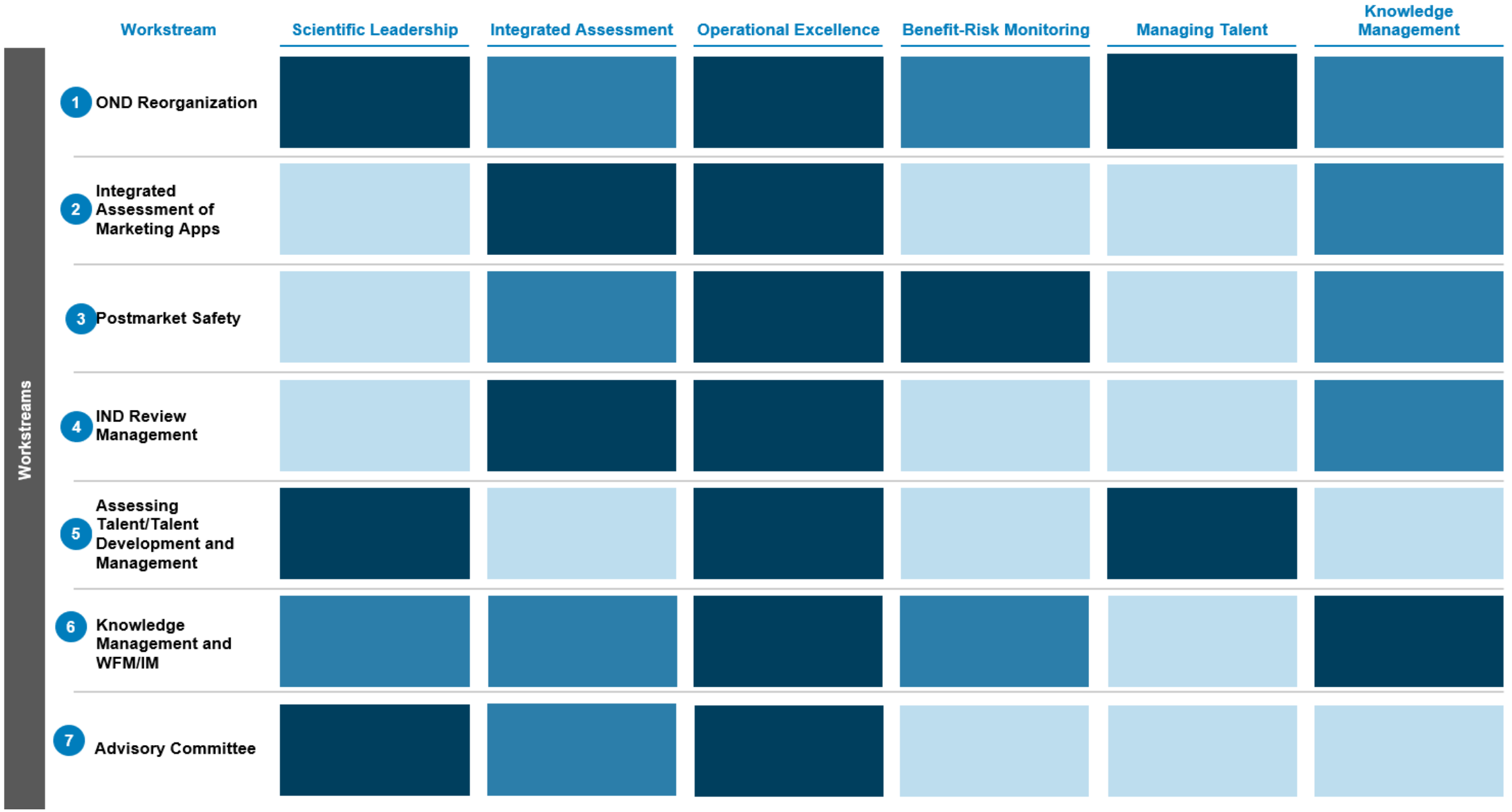
Modernization Vision:

"To Advance our leadership in the science and regulation of New Drugs."

…is translated into six strategic objectives

Scientific Leadership	We will grow our scientific expertise and clarify pathways to regulatory approval.
Integrated Assessment	We will critically, collaboratively and consistently assess whether information in submissions meets statutory and regulatory requirements.
Benefit-Risk Monitoring	We will establish a unified post-market safety surveillance framework.
Managing Talent	We will attract, develop, and retain outstanding people.
Operational Excellence	We will have a dedicated focus on operational excellence.
Knowledge Management	We will facilitate knowledge management.

Workstreams bring the Modernization to life



Integrated Assessment of Marketing Applications

The new Integrated Assessment of Marketing Applications approach focuses on 3 guiding principles: enhanced communication, interdisciplinary collaboration, and issue-based reviews.

- The Integrated Review Template is a **three-part document** consisting of the Executive Summary, Interdisciplinary Assessment, and Appendices.

- **Phased implementation** has allowed an iterative approach through evaluation, feedback, and responsive refinement of the process and template.

- FDA requested public comment on the Integrated Review Template in 2019 and 2020 to gather feedback on how it can continue **supporting our stakeholders' needs.** Respondents include patients, patient groups, scientists, academia, and industry.

  - Most recent public workshop was hosted virtually on October 30th. **Public docket* is open until December 31, 2020**. We will be publishing a meeting summary and summary of the docket comments.

* Visit www.federalregister.gov and search for "FDA–2020–N–1550"

The Interdisciplinary Assessment includes a Patient Experience Data section.

Patient experience data that was **submitted as part of the application**, such as PROs or other COAs, qualitative studies or patient narratives submitted by the Applicant and natural history studies.

Patient experience data **not submitted in the application but may have informed FDA review** nonetheless, such as a PFDD meeting.

4. Patient Experience Data

The Applicant submitted a patient-reported outcome assessment (Table 4). Assessing the impact of FTR + OBT on quality of life was an exploratory endpoint. Three instruments were used to measure the impact of FTR: the EQ-5D-3L, the Functional Assessment of HIV Infection (FAHI), and the Modified Medication Adherence Self-Report Inventory (M-MASRI) Questionnaire on Adherence.

Table 4. Patient Experience Data Submitted or Considered

Data Submitted in the Application		
Check if Submitted	**Type of Data**	**Section Where Discussed, if Applicable**
Clinical outcome assessment data submitted in the application		
☒	Patient-reported outcome	III.16.5: Health Outcomes Endpoints
☐	Observer-reported outcome	
☐	Clinician-reported outcome	
☐	Performance outcome	
Other patient experience data submitted in the application		
☐	Patient-focused drug development meeting summary	
☐	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel)	
☐	Observational survey studies	
☐	Natural history studies	
☐	Patient preference studies	
☐	Other: (please specify)	
☐	**If no patient experience data were submitted by Applicant, indicate here.**	
Data Considered in the Assessment (but Not Submitted by Applicant)		
Check if Considered	**Type of Data**	**Section Where Discussed, if Applicable**
☐	Perspectives shared at patient stakeholder meeting	
☐	Patient-focused drug development meeting summary report	
☐	Other stakeholder meeting summary report	
☐	Observational survey studies	
☐	Other: (please specify)	

Where in the Integrated Review or appendices any discussion related to the patient experience data is included. For example, if clinical trial endpoints included PROs, reference is made to where discussion on those endpoints occurs.

Source: Rukobia Integrated Review Document

Knowledge Management

The New Drugs Regulatory Program Modernization intends to facilitate knowledge management through 4 specific aims

Outcomes of Knowledge Management

1. Greater **capture and integration** of knowledge in NDRP review processes
2. Faster and easier **access and searchability** of targeted information
3. Increased internal and external **transparency and shareability** of data upon request
4. **Improved awareness of relevant precedents and information during decision-making**

What does success look like?

Situation: A reviewer is starting an original NME application review for **myelofibrosis.** She wants to understand the fact base of prior reviews for this **target indication**, including patient inclusion/exclusion criteria, prior trial sizes, rationale for permitting or rejecting study types, etc.

From (Current State):

- **No standard terminology** for target indications
- **Manual search** of all prior myelofibrosis applications
- **Individual reading of each application**, searching for specific sections and key data points
- **Individualized data capture/tracking** without institutional knowledge being collected or shared
- **Estimated 1-2 weeks** to answer key question and no future use of that research

To (Future State):

- **SNOMED CT is fully adopted and implemented** as the standard for coding target indication
- **"Google-like" search** to automatically pull all former applications based on key search variables (e.g., myelofibrosis, trial design protocols)
- **Consolidated results** that pull **consistent information/data** elements per application based on structured data models of the reviews
- **Continuous improvement of searches** and saved inquiries to accelerate future reviewer questions
- **Estimated 3-4 hours** to answer key question, with most of the time spent on reviewing relevant information

Talent: OND Talent Management

OND undertook a multi-year effort to better develop and manage talent throughout OND

- As a knowledge organization, OND's talent is its greatest resource, making OND's approach to talent development and management **critical to successfully fulfilling our public health mission**

- In the latter half of 2018, OND conducted an **assessment of how we develop and manage talent**, reviewing annual performance review ratings (2015-2017) and employee survey data (2017 and 2018) and conducting interviews with OND leaders and focus groups with staff and supervisors within the clinical, pharm/tox, and regulatory operations disciplines

- In April 2019, we established an interdisciplinary group that reviewed the findings of the **current state assessment**, set an **aspiration for the future approach** to talent development and management in OND, and developed a **blueprint for the future talent system** and a high-level competency framework that we believe can serve as the foundation for the development and management of talent across OND

OND's current-state assessment found four key areas for improvement

Does OND's performance management system...	What we've learned...
1 ...establish **clear and consistent performance expectations** for staff?	▪ **Performance expectations are often vague and inconsistent**, but staff generally know what is expected of them day-to-day ▪ **PMAP objectives are not explicitly or consistently linked to career paths** or professional development
2 ...effectively **differentiate high and low performers**, with **calibrated ratings** across supervisors?	▪ OND **ratings are consistently clustered to the top of the range** ▪ There is **no common articulation or understanding of how to apply each PMAP score**
3 ...develop staff through **feedback and coaching**?	▪ **Managers may not have been trained in how to deliver feedback** ▪ PMAPs often **do not convey meaningful feedback** ▪ **Giving and receiving developmental feedback** is not ingrained in the culture of every division
4 ...link **consequences and rewards to performance**?	▪ Staff perceive a **disconnect between actual performance and recognition/rewards** ▪ **Steps are not taken to deal with underperformers** due to the burden of the remediation process

Source: Interviews with OND CPMSs July – September 2018 and Pharm Tox reviewer, team lead, and supervisor focus groups from August – September 2018; RPM focus group April 2019; OND performance ratings data from 2015-2017; 2017 and 2018 Employee Viewpoint Survey

Aspiration and Blueprint for the future approach to talent development and management in OND

OND's talent system should:

- Be fair, transparent, consistent, feasible, and core to OND's strategic priorities
- Provide clear expectations for staff and managers
- Obtain accurate, evidence-based information on staff performance
- Encourage actionable feedback tied to staff development
- Provide opportunities for targeted development

Made possible through a standardized and evidence based approach to talent management

Performance expectations	• Clearly articulated performance expectations by discipline, linked to roles and career paths • Stretch goals in PMAPs that are SMART, tailored to individuals, and linked to OND strategic priorities
Performance appraisal	• Standardized evaluation rubrics that promote objective, evidence based ratings • PMAP input consistently gathered from multiple sources • Calibration of PMAP scores to promote consistency in evaluation process and differentiate high and low performers
Ongoing development	• Regular, actionable, forward looking feedback provided to all staff by team leads and supervisors
Consequence management	• Better recognition of high performers, both formally and informally • Enhanced infrastructure to deal with low performers including leadership and administrative/HR support

Talent Assessment Onboarding Pilot Overview

Our Pilot aimed to develop a systematic approach to reviewer assessment and retain new review staff

CDER's ability to conduct thorough review work, apply sound scientific judgment, and uphold regulatory standards ultimately **depends on the caliber of our reviewers**

In an effort to meet PDUFA VI commitments and replace outgoing staff, the Office of New Drugs (OND) **piloted a systematic pre-hire assessment of high caliber candidates** to better gauge their fit with the organization

In conjunction with the pre-hire assessment, our pilot **developed materials to standardize OND reviewer development and assessment** during the first year, in order to support retention and new employee satisfaction

We developed a pilot approach for reviewer development and assessment based on OND feedback

Focus groups identified needs for **systematic**:

- On-boarding
- Training
- Mentoring

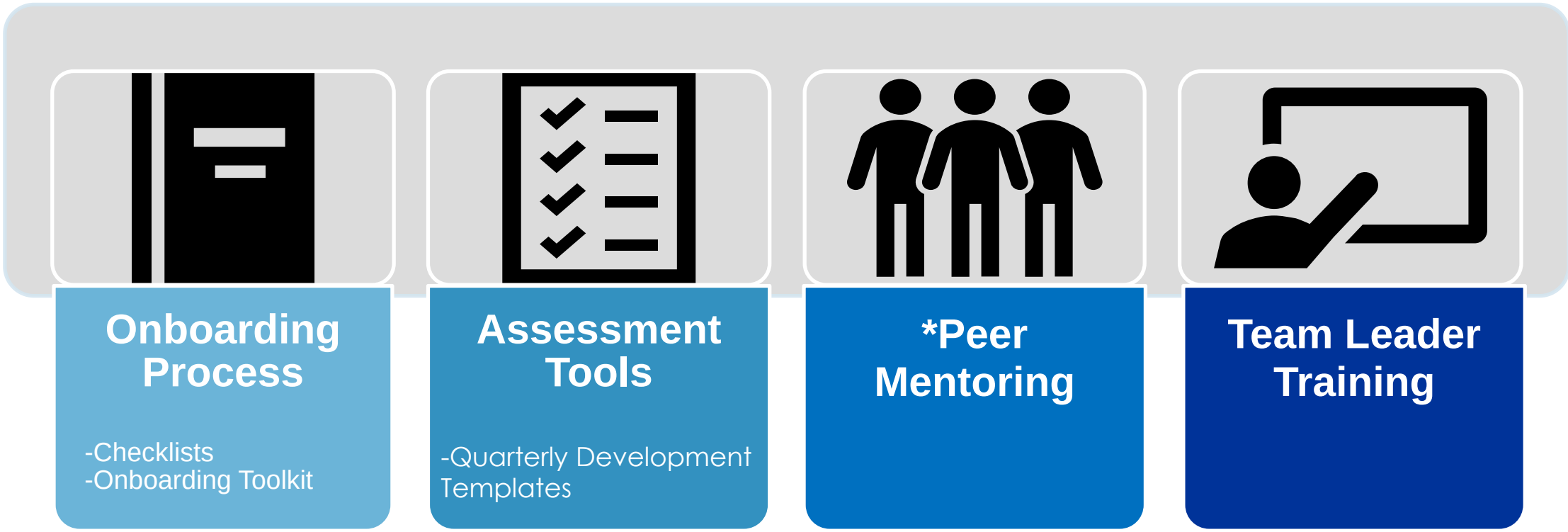
Extensive resources exist but are implemented unevenly.

Key Takeaways:
Reviewers, team leaders, and supervisors identified value in

- **Standardizing approaches** to reviewer on-boarding, development and assessment
- **Clarifying job expectations** for all staff
- **Preparing managers** to better assess and develop new staff

From September 2019-August 2020, our working group conducted an onboarding pilot with five OND divisions to test onboarding materials and processes for clinical reviewers and team leaders

Reviewer competencies will be the foundation of the pilot first year development and assessment activities



**Peer Mentoring framework developed and deployed concurrently in OND*

Checklists

MANAGER CHECKLIST FOR ONBOARDING, DEVELOPING AND ASSESSING NEW REVIEWERS

Team leaders and supervisors should follow this checklist to onboard new review team members. Use the resources in the appendices for more detailed guidance.

Time		Task
2-4 Weeks Prior Confirmed Start Date	☐	Collaborate with admin staff to prepare for new employee arrival: set up the work space, computer, security, and network access for the new team member
	☐	Review learning resources to become familiar with the latest information
	☐	Communicate with the new hire about their start date and expectations for the first week or so
	☐	Email division about new hire with start date, employee's role, and bio
	☐	Match the new hire with an experienced reviewer who will function as a mentor and ask Orientation Mentor to contact new reviewer
	☐	Determine applicable software applications and SharePoint sites to provide to AO to process access
First Day in Division	☐	Plan to meet and welcome the new employee upon arrival
	☐	Meet with employee and review work schedule and plan for the first week. Discuss time and attendance
	☐	Ensure that reviewer can access computer network, email and the phone works; issue an office key; provide a division staff list and helpful points of contact
	☐	Give reviewer a tour of the wing/building and key campus locations (or pair with another team member)
	☐	Introduce new team member to colleagues and leaders
First Week	☐	Continue to introduce new team member to colleagues and leaders
	☐	If possible, have informal lunch with team members
	☐	Plan meaningful work such as division meetings, meeting with training team, assign Clinical Review Handbook as reading, etc.
	☐	**Meeting with Team Leader, Division Director/Deputy and reviewer to go over role, expectations, competencies, required learning, work policies, arrival/departure, work styles, communication, leave, organization/division structure, key leaders/staff, etc.**
	☐	Set up initial schedule of 1:1 meetings
	☐	Ask mentor to check in with employee to see how he/she is doing and help with Intranet, calendar, division information, admin staff, mailboxes, printers, etc.
	☐	Provide 2nd week reading resources: Interactive Clinical Reviewer Learning Plan, Clinical Reviewer Handbook; Reviewer Competencies; New Reviewer Development Template
	☐	Flag division meetings, sponsor meetings, review team meetings, etc. that would be good for new review to attend; be sure to debrief afterward (or ask orientation mentor to do so)
	☐	Ask Admin Staff to share pay schedule, holiday schedule, timekeeping and ITAS information
Week 2	☐	Meet to follow up on questions/clarification on expectations, competencies, required learning, work policies, arrival departure, work styles, communication, etc.
	☐	Send an email outlining the information in the previous bullet
	☐	Introduce New Reviewer Development Template and explain how progress/performance is measured
Weeks 3-12	☐	Schedule weekly meetings with reviewer (first two months)
	☐	Discuss activities – training, projects, needs, expectations; flag division, sponsor, review team meetings & debrief
	☐	Sequence assignments, from simple to complex, as much as possible
	☐	Introduce employee to colleagues in other disciplines
Month 3+	☐	Continue meeting biweekly, or weekly, as appropriate; Help reviewer prepare for participation in internal meetings
	☐	Follow-up on required training to check progress
	☐	Discuss telework (PMAS can help with forms and training)
Months 3, 6, 9, 12	☐	Quarterly Development Check-in with the TL/supervisor to discuss progress toward development goals using the New Reviewer Development Template (Reviewer version).
Mid-Year PMAP	☐	Supervisor collects feedback from multiple sources, including team leader, RPM, admin, other disciplines, etc.
	☐	Supervisor provides performance feedback on achievements, strengths and development areas, with specific guidance on where improvement is needed and how to work toward proficiency.
Annual PMAP	☐	Supervisor collects feedback from multiple sources, including team leader, RPM, admin, other disciplines, etc.
	☐	Supervisor provides performance feedback on achievements, strengths and specific guidance on where improvement is needed and how to work toward proficiency.
	☐	Supervisor provides a formal rating and end-of-year performance feedback.

Adapted from: Getting On Board: A Model for Engaging and Integrating New Employees, May 2008; Partnership for Public Service & Booz Allen Hamilton; December 15, 2018

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Onboarding Toolkit

TEAM LEADER AND SUPERVISOR
ONBOARDING TOOLKIT
FOR NEW EMPLOYEE DEVELOPMENT

ONBOARDING, DEVELOPING AND ASSESSING FIRST-YEAR REVIEWERS

Food and Drug Administration | Office of New Drugs
January 2020

1

Quarterly Development Templates

New Clinical Reviewer Quarterly Developmental Check-in Team Leader Name: _____ Date: _____

Quarter ☐1 ☐2 ☐3 ☐4 Reviewer Name: _____

End of First Year Expectations	Proficiency Level	Rationale/Examples to Support the Rating	Suggestions for development
Scientific and Clinical Knowledge	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Regulatory Knowledge	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Operational Knowledge	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Clinical Review Conduct	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Clinical Trial Methodology, Data Analysis and Interpretation	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Interdisciplinary Collaboration	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Organization/Time Management	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Scientific Engagement	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.
Communication	Choose an item.	Click or tap here to enter text.	Click or tap here to enter text.

We acknowledge that our Q___ development check-in took place on _____.

Reviewer Signature: _____ Printed Name: _____

Team Leader Signature: _____ Printed Name: _____

The new reviewer onboarding toolkit and checklists were helpful

75% of new reviewers said they received the checklist and said it was **helpful for understanding which systems to access and trainings** to take.

Checklists were most helpful when they…

Provided Clarity around resources

Pointed them to what key trainings to take and when to take them

Provided contacts and links to other resources to address new reviewer questions

New reviewers and Team Leads spoke very highly of OND's peer mentor program

94%

of new reviewers surveyed said they had a peer mentor

Having a mentor allowed new reviewers to **ask questions and express concerns** without feeling like they were being evaluated or bothering their supervisor.

Mentors helped by **answering day-to-day questions about assignments and resources**, setting up 1:1 meetings, **providing feedback**, explaining **onboarding expectations.**

Team Leads noted that peer mentors **took some of the burden off** themselves (TLs) and provided new reviewers with **another perspective** on how to coordinate their workload.

Overall recommendations of the pilot include expanding pilot material and process for use across OND

- **Amend onboarding checklists**
  Integrate suggested recommendations to onboarding checklists as feasible.
- **Amend structure of development check-ins**
  Hold check-ins only at the six and twelve month marks.
- **Create a shared knowledge base for each division**
  New reviewers recommended that a shared knowledge base be established for each division, including examples of different types of deliverables, particularly the wording of responses.
- **Consider additional recommendations**
  Recommendations regarding having the TL check in on onboarding logistics, and creating division-specific learning opportunities - such as examples and informal meetings for new reviewers - should be considered.
- **Expand pilot materials to all of OND**
  TLs throughout OND should be trained on how to use pilot materials and they should be housed in a central, easy-to-access repository.

Questions?

Discussion/Any Other Business

Upcoming Topics

Friday, January 15, 2020
12:30-2:30 PM EST

- Efforts to make clinical trials more inclusive and diverse
- Recent guidance on use of decentralized clinical trials (CT), other potential clinical trial flexibilities, and opportunities for greater efficiency
- Strength and reach of patient and rare disease programs (including rare disease cures accelerator) to improve diversity in patient engagement and encourage greater data sharing

PDUFA VII Closing Remarks

December 11, 2020

Dr. Theresa Mullin
Office of the Center Director
Center for Drug Evaluation and Research
Food and Drug Administration