Oncology Center of Excellence
2021 Annual Report

5 Years
of Driving Change
in Oncology Product Development

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Director's Message

In January 2022, the Oncology Center of Excellence marked its fifth anniversary by looking back at what we accomplished and looking ahead to further progress toward achieving our vision to create a collaborative scientific environment to advance the development and regulation of oncology products for patients with cancer.

Since its formation in 2017, the OCE has established more than 30 outward-facing programs and projects to educate, inform, conduct research, and collaborate. The OCE is committed to driving change in cancer drug development that results in more efficient and accessible clinical trials, more effective and safer medical products, and better outcomes for patients with cancer. This begins with rigorous medical product review for efficacy and safety, but also stepping back to look at what's happening across the field of oncology and determining how the OCE can leverage its expertise.

This past year, OCE developed additional projects looking at various aspects of cancer drug development:

- **Project Optimus**–Reforming the dose optimization and dose selection paradigm in oncology
- **Project Significant**–Statistics in Clinical Trials: Promoting collaboration in design and analysis of cancer clinical trials
- **Project Catalyst**–Providing a regulatory platform to connect scientific knowledge, creative insight, and medical professionals to foster early-stage product innovation
- **Rare Cancers Program**–Promoting development of new drug and biological products to treat patients with rare cancers
- **Project Protect**–Providing consistent review of safety signals across drug classes

Two projects launched in 2020 continued to expand the work to influence cancer drug development in positive ways for the benefit of patients with cancer: **Project Equity** and the **Oncology Real-World Evidence Program.**

Regulatory Review Continued Unabated Despite COVID-19

Despite the challenges of the second year of the pandemic, CDER and CBER oncology review teams granted a total of 80 drug approvals in 2021. That includes 15 NMEs, 1 original BLA, 50 supplemental approvals for new indications, 8 supplemental approvals in new populations, and 6 505(b)(2) approvals. Eight approvals included indications for pediatric patients.

CDRH granted marketing approval to 16 in vitro diagnostic devices, including 12 companion diagnostics.

The OCE's **Project Orbis** collaborated with international regulators on 26 of the drug approvals. All of these approvals use the OCE's Assessment Aid, a concise review template that facilitates the FDA assessment of an application. In 2021, Project Orbis added as partners the Israel Ministry of Health Pharmaceutical Administration and the United Kingdom's Medicines and Healthcare Products Regulatory Agency.

Reevaluating Accelerated Approval

Accelerated Approval provides a tradeoff of expediting approvals of drugs with increased uncertainty. Oncology has successfully applied the principles of Accelerated Approval over the last 29 years, making transformative oncology indications available to patients years earlier.

However, in 2021, the OCE identified certain trials, in particular for drugs targeting programmed death 1 or programmed death ligand 1 for which confirmatory trials did not verify benefit. OCE proactively contacted 10 development programs and through multiple discussions and advisory committee meetings, encouraged companies to withdraw 7 of these. One indication was converted to regular approval with additional data and 2 remain under regulatory review. The percentage of drugs that do not ultimately confirm clinical benefit should not be viewed as a failure of the program but rather an expected tradeoff to expedite drug development of promising agents. To increase transparency around oncology Accelerated Approvals, the OCE's **Project Confirm** developed a database of oncology Accelerated Approvals that are ongoing, confirmed, or withdrawn.

Empowering Patients, Survivors, Advocates and Consumers

In 2021, OCE's **Project Community** began the first **National Black Family Cancer Awareness Week** to increase cancer awareness in one of the most vulnerable segments of the US population. This effort coincided with the 50th anniversary of the National Cancer Act and the signing of Presidential Executive Order 13985, "Advancing Racial Equity and Support for Underserved Communities Through the Federal Government, Section 8." In addition, Project Community held eight Conversations on Cancer panel discussions on issues of health equity in racial and ethnic minority popultations, challenges faced by cancer survivors, and progress in drug development for treatment of children with cancer.

Resources and Educational Opportunities for Oncology Professionals

The OCE provides educational opportunities and professional resources to oncology professionals about the role of the FDA in oncology product development. These include learning opportunities for oncologists, oncology fellows, new FDA oncology staff members, and high-school students. In addition to formal programs, the OCE offers webinars and publications. In addition, the OCE runs a unique "call center" to assist oncology care teams in filing Expanded Access requests for investigational therapies for patients with cancer who have no other available therapy.

I welcome your involvement and interest in OCE's work and hope that our Annual Report will inspire you to consider taking part in our programs and projects to improve the lives of patients with cancer.

Richard Pazdur, M.D.
Director,
Oncology Center of Excellence

Oncology of Excellence 2021 Annual Report

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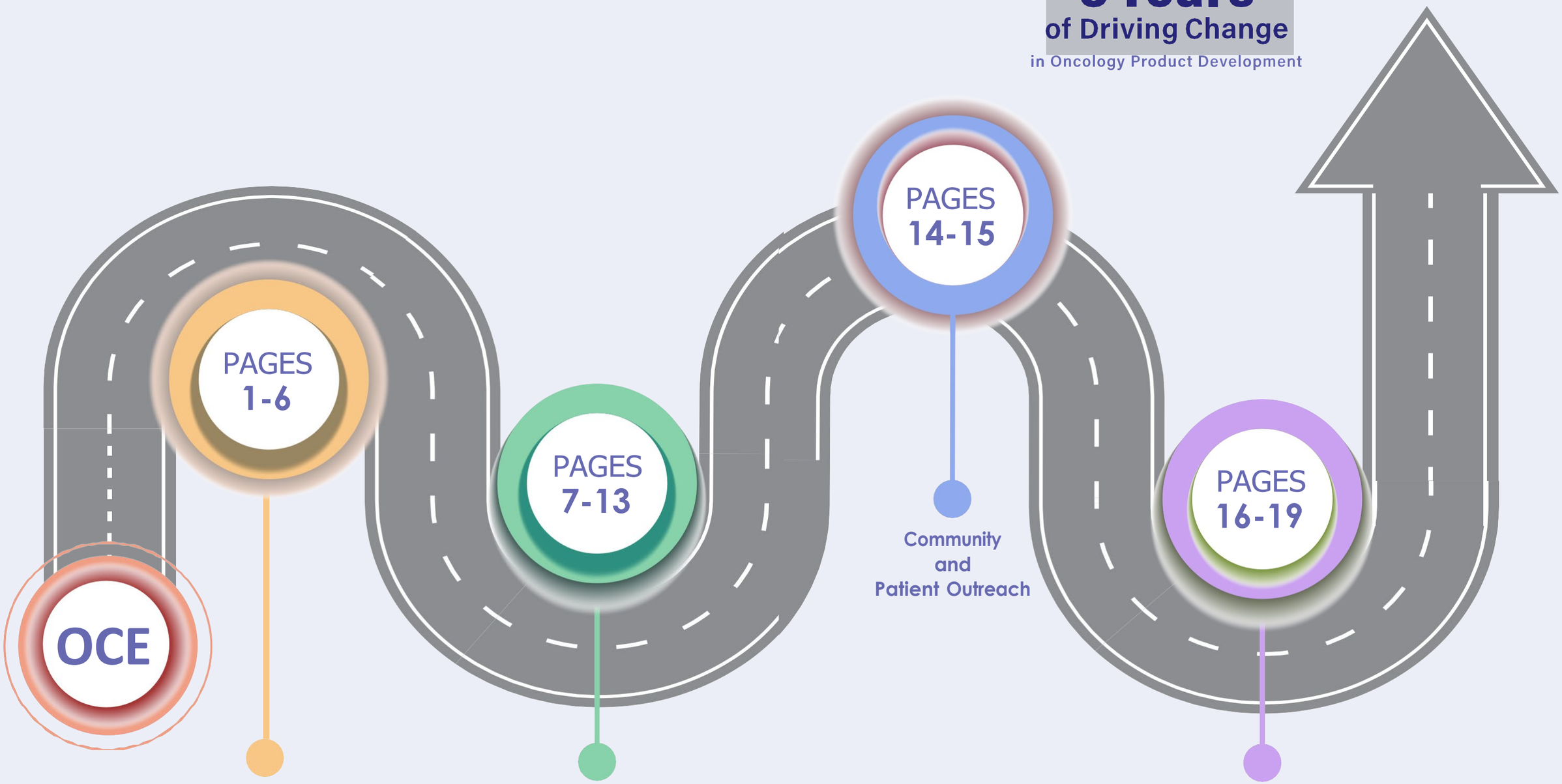


Driving Medical Product Development

The OCE is committed to working with stakeholders to improve oncology product development for the beneft of people with cancer. In addition to rigorous medical product review, our funding supports research and development projects to increase knowledge that will result in better therapies and better outcomes for patients.

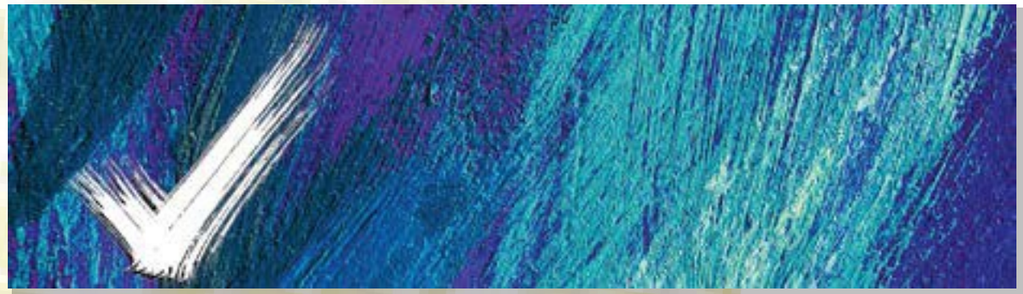
In this section of the OCE Annual Report, we highlight OCE projects that were newly launched or ramped up in 2021. For information about all OCE programs and projects, visit www.fda.gov/OCE.

Project Catalyst

OCE's Project Catalyst provides guidance and educational resources to small pharmaceutical companies and academic life science incubators to support informed anticancer therapy development.

In 2021, the project developed a web page for its educational initiative, Oncology Regulatory Expertise and Early Guidance (OREEG), a self-directed platform providing early-stage oncology companies with product-type advice to inform sound product-specific drug development decisions. This platform will be updated with additional "bench-to-bedside" chats with regulatory science experts and answers to frequently asked questions.

The project welcomes questions regarding oncology drug development plans that are premature for pre-IND submission, if those questions are not covered in the available materials.



Project Confirm

Project Confirm is an OCE initiative to increase the transparency of outcomes related to Accelerated Approval for oncology indications. Project Confirm created a searchable public database listing all Accelerated Approvals granted in oncology since 1992, when the FDA began granting them.

For Accelerated Approvals that are ongoing, information on confirmatory trials required to verify clinical benefit is included. The Project Confirm webpage provides background information on the Accelerated Approval program and addresses several frequently asked questions.

Project Confirm has supported a series of OCE mini-symposia on Accelerated Approvals, presentations on the Accelerated Approval program, and academic publications in press and in preparation. Looking to the year ahead, the project aims to facilitate evaluation of ongoing Accelerated Approvals and to continue efforts to increase public awareness of the program and its outcomes.

2021 Publications

- Beaver JA, Pazdur R. The Wild West of Checkpoint Inhibitor Development. N Engl J Med. 2021;10.1056/NEJMp2116863. doi:10.1056/NEJMp2116863
- Beaver JA, Pazdur R. "Dangling" Accelerated Approvals in Oncology. N Engl J Med. 2021;384(18):e68. doi:10.1056/NEJMp2104846

Project Optimus

Project Optimus, begun by OCE in 2021, is an initiative to reform the dose optimization and dose selection paradigm in oncology drug development. Too often, the current paradigm for dose selection—based on cytotoxic chemotherapeutics—leads to doses and schedules of molecularly targeted therapies that are inadequately characterized before initiating registration trials.

The goal of Project Optimus is to educate, innovate, and collaborate with companies, academia, professional societies, international regulatory authorities, and patients to move

forward with a dose-finding and dose optimization paradigm across oncology that emphasizes selection of a dose or doses that maximizes not only the efficacy of a drug but the safety and tolerability as well.

In April 2021, Project Optimus emphasized the importance of improving dose selection as part of the "Hot Topics in Oncology Regulation" session at the AACR Annual Meeting. For the May 2021 approval of sotorasib for the treatment of metastatic non–small-cell lung cancers harboring the KRAS p.G12C mutation, FDA required a post-marketing study to evaluate lower doses. OCE worked within the FDA on a draft guidance to facilitate alternative dosing regimens for PD-(L)1 drugs based on pharmacokinetic-based criteria.

Throughout 2021, Project Optimus collaborated with OCE's Project Significant on a series of sessions titled, "Designing Dose Optimization Studies in Cancer Drug Development." In November 2021, Project Optimus partnered with Friends of Cancer Research (FOCR) and other key stakeholders to highlight potential strategies for dose optimization in a session titled, "Maximizing Benefit and Improving Tolerability for Patients through Dose Optimization," at the FOCR Annual meeting and to publish an accompanying white paper. Project Optimus's perspective on the urgent need for dose optimization for oncology drugs was featured in the New England Journal of Medicine in September 2021 in an article, "The Drug Dosing Conundrum in Oncology: When Less is More."

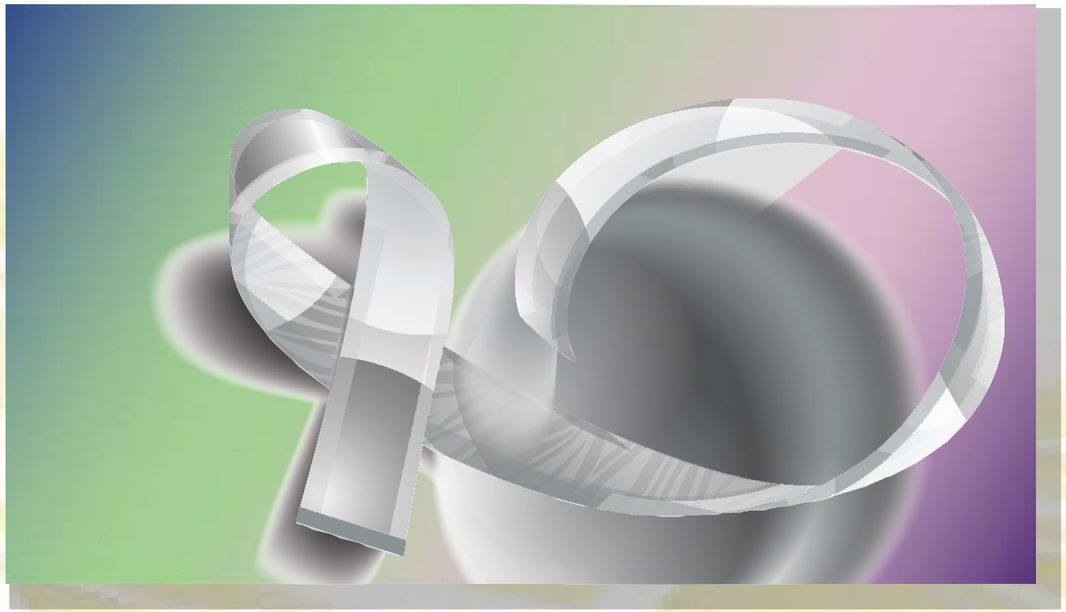
Project Significant

Project Significant (Statistics in Cancer Trials), begun in the fall of 2020, holds discussions with the Biopharmaceutical Section of the American Statistical Association and other oncology stakeholders to further the design and analysis of cancer clinical trials with the goal to advance cancer therapies. Seven publications summarizing these discussions were published in 2021.

Project Protect

Project Protect formed a uniquely structured safety team organized by drug class to provide consistent advice and review of safety signals in the pre- and post-market setting, supporting CDER and CBER reviewers. In 2021, Project Protect provided support for 44 drug applications.

Project Protect engaged external stakeholders to develop safety data standards across CBER and CDER to expedite regulatory review and research. The project also helped develop a Safety Analysis Generator tool customized to oncology-specific applications. Launched in March 2021, this tool aids in the efficient review of applications and provides individual data analysis support for reviewers. Project Protect continues to build a team of data analysts to assist with analytics and regulatory research to further the OCE's mission.



Rare Cancers Program

Launched in late 2021, the Rare Cancers Program leverages the OCE's ongoing initiatives to promote development of safe and effective new drugs and biologics to treat patients with rare cancers.

The Rare Cancers Program works in conjunction with the Offce of Oncologic Diseases to proactively address challenges that are common to rare cancer drug development as a whole and those that are specifc to each rare cancer type. The program also works closely with other FDA offces such as the Offce of Orphan Product Development and the Division of Rare Diseases and Medical Genetics, other international regulatory agencies, and external stake-holders to expedite drug development for rare cancers.

Early in 2022, the program will launch a webpage, which will highlight how the OCE uses various programs and projects to develop a context-specifc approach that is tailored to unique patient needs and aspects of each rare cancer, in addition to other useful resources. The program has an exciting listening session and a Rare Disease Day OCE Panel planned for the frst quarter of 2022, as well other projects.

Project Equity

The OCE established Project Equity in 2020 to ensure that the data submitted to the FDA for approval of oncology medical products adequately reflects the demographic representation of patients for whom the medical products are intended. In 2021, the project worked within and outside of the FDA to promote regulatory policies to ensure satisfactory enrollment of members of historically and underrepresented and vulnerable populations in oncology clinical trials. Several publications, symposia, and invited talks and collaborations grew from these efforts. Visit the Project Equity webpage for a full Progress Report.

2021 Publications

- Gormley N, Fashoyin-Aje L, Locke T, Unger JM, Little RF, Nooka A, Mezzi K, Popa McKiver M, Kobos R, Biru Y, Williams TH, and Anderson KC. Recommendations on Eliminating Racial Disparities in Multiple Myeloma Therapies: A Step toward Achieving Equity in Healthcare. Blood Cancer Discov March 1 2021 (2) (2) 119-124; DOI:10.1158/2643-3230.BCD-20-0123.
- Hoffman Censits J, Kanesvaran R, Bangs R, Fashoyin-Aje L, Weinstock C. Breaking Barriers: Addressing Issues of Inequality in Trial Enrollment and Clinical Outcomes for Patients with Kidney and Bladder Cancer. Am Soc Clin Oncol Educ Book. 2021 Jun;41:e174e181. doi: 10.1200/EDBK_320273.
- Carpten, J.D., Fashoyin-Aje, L., Garraway, L.A. et al. Making cancer research more inclusive. Nat Rev Cancer (2021). 29 June 2021 doi: 10.1038/s41568-021-00369-7.
- Lola Fashoyin-Aje; Julia A. Beaver; Richard Pazdur. Promoting Inclusion of Members of Racial and Ethnic Minority Groups in Cancer Drug Development. JAMA Oncol. Published online July 15, 2021. doi:10.1001/jamaoncol.2021.2137

Oncology Real-World Evidence Program

OCE's Oncology Real World Evidence (RWE) Program, established in 2020, advances the appropriate use of RWE in oncology product development to facilitate patient-centered regulatory decision-making. The program reviews regulatory submissions containing real-world data (RWD) across oncology review divisions within CDER, CBER, and CDRH. The program established initiatives in RWD quality and characterization of real-world response:

- In partnership with the Regan Udall Foundation, the Oncology Quality Characteristics and Assessment of Real-world Data (QCARD) initiative seeks to develop a standardized approach to RWD characterization and evaluation of data quality for regulatory submissions.
- In collaboration with the Friends of Cancer Research, the Real-World Response Project seeks to evaluate the feasibility of improving ascertainment of tumor response within electronic health records and other RWD sources.
- The program established the Translational Evaluation and Assessment of Methods to Facilitate use of Oncology RWD (TEAM FoRWD) to bring together oncology clinical review staff across divisions interested in exploring opportunities to advance RWD regulatory science, policy, research, and education.
- Several research partnerships are underway through Research Collaboration Agreements, Broad Agency Agreements, and Centers of Excellence in Regulatory Science and Innovation.

The Oncology RWE program is active in Project Post-COVIDity to advance our understanding of how COVID-19 affects the health of patients with cancer. Research with several data providers resulted in two publications:

- Hwang C, Izano MA, Thompson MA, Gadgeel SM, Weese JL, Mikkelsen T, Schrag A, Teka M, Walters S, Wolf FM, Hirsch J, Rivera DR, Kluetz PG, Singh H, Brown TD. Rapid real-world data analysis of patients with cancer, with and without COVID-19, across distinct health systems. Cancer Rep (Hoboken). 2021 May 20:e1388. doi:10.1002/cnr2.138
- Ackerman B, Keane C, Beaver JA, Kluetz PG, Rivera D, Paliwal P, Singh H, Mpofu P, Amiri-Kordestani L, Baxi SS. Trends in diagnosis and treatment of early breast cancer (eBC) in the United States (US) during the COVID-19 era. Journal of Clinical Oncology 2021 39:28_suppl, 227-227

Oncology Regulatory Review

The OCE collaborates with the three FDA product centers reviewing drugs, biologic therapies, and devices to develop and execute an integrated regulatory approach to enhance the cross-center coordination of oncology product clinical review.

Highlights of 2021

Drugs:

The Offce of Oncologic Diseases (OOD) in the Center for Drug Evaluation and Research (CDER) approved four new drugs for non-small lung cancer (Tepmetko, Rybrevant, Lumakras, Exkivity), including one non-small cell lung cancer type previously thought to be resistant to treatment.

For skin cancer, OOD approved a therapy (Libtayo) for some types of basal cell carcinoma, the most common form of skin cancer, for certain patient populations.

OOD also approved the frst immunotherapy (Opdivo), or therapy that stimulates or suppresses the immune system, as a frst-line treatment for esophageal (esophagus-related) cancer, gastric (stomach) cancer, and gastroesophageal junction (GEJ) adenocarcinoma, a rare cancer that starts where the esophagus and stomach join together. Also related to stomach and esophageal cancer, OOD approved two other therapies (Enhertu and Keytruda) for certain patients with HER2-positive gastric cancer and GEJ adenocarcinoma, one of which (Keytruda) also was approved for esophageal cancer, advanced kidney cancer, and as an add-on treatment for kidney cancer.

Additionally, OOD approved Keytruda for early-stage, triple negative breast cancer, or cancer that does not respond to hormonal therapies or medications that target HER2 protein receptors.

Other approvals for rare cancers included:

- Two treatments (Truseltiq and Tibsovo) for adults with certain kinds of cholangiocarcinoma, a group of aggressive cancers that start in the bile duct,
- A therapy (Welireg) for use in adults to treat certain tumors that are associated with Von Hippel-Lindau disease an inherited disorder characterized by tumors and cysts,
- A therapy (Darzalex Faspro) to be used together with other treatments for light chain amyloidosis, a cancer occurring when an abnormal protein builds up in the organs, and
- A treatment (Fyarro) for locally advanced unresectable or metastatic perivascular epithelioid cell tumor (PEComa), a group of rare tumors that form in the soft tissues of the stomach, intestines, lungs and other body parts. This is the frst FDA-approved treatment for PEComa.

The Center for Biologics Evaluation and Research (CBER) reviews and regulates cellular cancer therapies in partnership with OCE.

In 2021, CBER and OCE approved a new biologic therapy, Abecma (idecabtagene vicleucel) for adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Also, a new indication was granted for Tecartus (brexucabtagene autoleucel) for treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia. Tecartus was previously approved for treatment of adults with relapsed or refractory mantle cell lymphoma.

In addition, FDA granted accelerated approval to Yescarta (axicabtagene ciloleucel) for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Devices:

The Center for Devices and Radiological Health (CDRH) reviews and regulates oncology devices and diagnostics in partnership with OCE. During 2021, CDRH and OCE authorized 16 oncology-related in vitro diagnostic devices (IVDs) including 12 companion |diagnostic approvals.

Eight companion diagnostic devices were approved in areas of unmet need such as for the treatment of cholangiocarcinoma and to detect KRAS G12C variants in patients with non-small cell lung cancer. The frst tumor agnostic immunohistochemistry companion diagnostic was authorized for the identifcation of patients with solid tumors that are DNA mismatch repair defcient. In addition, a second group labeling claim was approved, for patients with unresectable or metastatic melanoma to detect specifc BRAF variants for the selection of BRAF inhibitors or BRAF/MEK inhibitor combinations.

NMEs/ Original BLA	16 (6 Regular, 12 AA)** (9 RTOR) (6 AAid)
Supplements (new indication)	50 (43 Regular, 7 AA) (16 RTOR) (26 AAid)
Supplements (new population)	8
505b2	6
In vitro diagnostic devices (PMAs)	16 (12 companion diagnostics)
Breakthrough Designation	25 (22 CDER, 3 CBER)
Breakthrough Device Designation	13
Fast Track	58
Priority Review	70 (68 CDER, 2 CBER)
Project Orbis Submissions Granted	26

* Approval numbers reflect approvals from CBER, CDER and CDRH

** There may be a greater amount of regular and accelerated approvals than the total number of NMEs because some NME applications are administratively split due to different actions for different indications within the NME

AA: Accelerated Approval; AAid: Assessment Aid; BLA: Biologics License Application; NME: new molecular entity; PMA: Premarket Approval; RTOR: Real-Time Oncology Review.

Project Orbis Approvals in 2021

OCE's **Project Orbis** provides a framework for concurrent submission and review of oncology products among international partners. FDA approved the following drug-indication combinations through Project Orbis in 2021. Click on the links to read about each approval.

	APPROVAL DATES	PRODUCT NAMES	INDICATION	AAid/ RTOR
1.	1/15/2021	Enhertu[5] (fam-trastuzumabderuxtecan-nxki))	GEJ	Y/N
2.	1/15/2021	Darzalex Faspro[1] (daratumumab and hyaluronidase-fhj)	Amyloidosis	Y/Y
3.	2/3/2021	Tepmetko (tepotinib[1,2])	MET exon 14 skipping NSCLC	Y/Y
4.	3/3/2021	Lobrena (lorlatinib[4])	1L ALK+ NSCLC	Y/Y
5.	3/22/2021	Keytruda (pembrolizumab)	GEJ	Y/Y
6.	4/7/2021	Trodelvy[3] (sacituzumab govitecan) mTNBC		Y/Y
7.	4/16/2021	Opdivo (nivolumab)	GEJ	Y/Y
8.	5/5/2021	Keytruda[5] (pembrolizumab)	GEJ	Y/Y
9.	5/20/2021	Opdivo (nivolumab)	GEJ (adjuvant)	Y/Y
10.	5/21/2021	Rybrevant (amivantimab-vmjw[1,2]) exon 20 insertion mutations	NSCLC,EGFR	Y/N
11.	5/28/2021	Truseltiq (infgratinib[1,2])	cholangiocarcinoma	Y/Y
12.	5/28/2021	Lumakras (sotorasib[1,2])	NSCLC, KRAS G12C	Y/Y
13.	6/30/2021	Rylaze asparaginase erwinia chrysanthemi (recombinant)-rywn[2])	ALL & LBL	Y/Y
14.	7/9/2021	Padcev[3] (enfortumab vedotin)	UC mutated	Y/Y
15.	7/16/2021	Rezurock (belumosudil[2])	cGvHD	Y/Y
16.	7/21/2021	Keytruda[3,4,5](pembrolizumab) + Lenvima[3,4,5] (lenvatinib)	Advanced EC not MSI-H or dMMR	Y/N
17.	7/26/2021	Keytruda[3,4,5] (pembrolizumab)	TNBC	Y/Y
18.	8/13/2021	Welireg[2] (belzutifan)	VHL disease associated RCC	Y/Y
19.	9/15/2021	Exkivity[1,2] (mobocertinib)	NSCLC, EGFR exon 20 insertion mutations	Y/Y
20.	9/22/2021	Jakafi (ruxolitinib)	cGVHD	Y/N
21.	10/12/2021	Verzenio[5] (abemaciclib)	EBCNode+, HR+, HER2-	Y/Y
22.	10/13/2021	Keytruda[3,4] (pembrolizumab)	cervical cancer, tumors express PD-L1 (CPS ≥1)	Y/N
23.	10/15/2021	Tecentriq (atezolizumab)	adjuvant NSCLC, stage II to IIIA	Y/Y
24.	11/17/2021	Keytruda (pembrolizumab)	adjuvant RCC	Y/N
25.	12/3/2021	Keytruda[5] (pembrolizumab)	adjuvant melanoma	Y/Y
26.	12/15/2021	Orencia (abatacept)	aGVHD prophylaxis	Y/N

Pediatric Oncology Program

The OCE Pediatric Oncology Program facilitates early pediatric studies of appropriate new, targeted cancer therapeutics to eliminate long lag times between first-in-human and first-in-children studies of approved cancer drugs. To do this, we attempt to maximize the authority available through the Best Pharmaceuticals for Children Act to increase the number of written requests for pediatric studies of appropriate new drugs developed for adult cancers much earlier in the development timeline.

Pediatric Oncology Approvals in 2021

APPROVAL DATES	PRODUCT NAME(S)	INDICATION
1. 1/14/2021	Xalkori (crizotinib)	For pediatric patients ≥1 year and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma that is ALK-positive
2. 6/30/2021	Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn)	As a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia and lymphoblastic lymphoma in adult and pediatric patients ≥1 month who have developed hypersensitivity to E. coli-derived asparaginase
3. 7/16/2021	Rezurock (belumosudil)	For adult and pediatric patients ≥12 years with chronic graft-versus-host disease after failure of at least two prior lines of systemic therapy
4. 9/17/2021	Cabometyx (cabozantinib)	For adult and pediatric patients ≥12 years and older with locally advanced or metastatic differentiated thyroid cancer that has progressed following prior VEGFR-targeted therapy and who are ineligible or refractory to radioactive iodine
5. 9/22/2021	Jakafi (ruxolitinib)	For chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients ≥12 years
6. 12/2/2021	Rituxan (rituximab)	In combination with chemotherapy for pediatric patients (≥6 months to <18 years) with previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma, Burkitt lymphoma, Burkitt-like lymphoma, or mature B-cell acute leukemia
7. 12/3/2021	Keytruda (pembrolizumab)	For the adjuvant treatment of adult and pediatric (≥12 years) patients with stage IIB or IIC melanoma following complete resection
8. 12/15/2021	Orencia (abatacept)	For the prophylaxis of acute graft versus host disease in combination with a calcineurin inhibitor and methotrexate in adults and pediatric patients (≥2 years) undergoing hematopoietic Stem cell transplantation from a matched or 1 allele-mismatched unrelated donor

Pediatric Oncology Program Reviews in 2021

Initial Pediatric Study Plans (iPSPs)	297
Agreed iPSPs	258
Amended Agreed iPSPs	37
Inadequate Proposed Pediatric Study Requests	37
Written Requests (WRs)	7
Amended WRs	19
Type F Meetings	12

iPSP: initial Pediatric Study Plan; PPSRs: Proposed Pediatric Study Requests; WRs: Written Requests

Guidances

The OCE led or participated in the development of eight oncology-specific guidance documents in 2021. The OCE continued efforts to encourage expansion of eligibility criteria and stress enrollment of a diverse population to ensure that clinical trial results are applicable to the US population. FDA finalized a guidance regarding evaluation of patients with CNS metastases and issued a draft guidance regarding prior therapies that may allow more patients to enroll on trials rather than always having to receive all approved therapies first. See all current oncology guidance documents at OCE Guidances.

- Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1)Blocking Antibodies for Treatment of Patients with Cancer (Draft)
- Evaluating Cancer Drugs in Patients with Central Nervous System Metastases (Final)
- Cancer Clinical Trial Eligibility Criteria: Available Therapy in Non-Curative Settings (Draft)
- Premenopausal Women with Breast Cancer: Developing Drugs for Treatment (Final)
- Core Patient-Reported Outcomes in Cancer Clinical Trials (Draft)
- Chemotherapy-Induced Nausea and Vomiting: Developing Drugs for Prevention (Draft)
- COVID-19: Master Protocols Evaluating Drugs and Biological Products for Treatment or Prevention (Final)
- FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs: Amendments to Sec. 505B of the FD&C Act (Final)

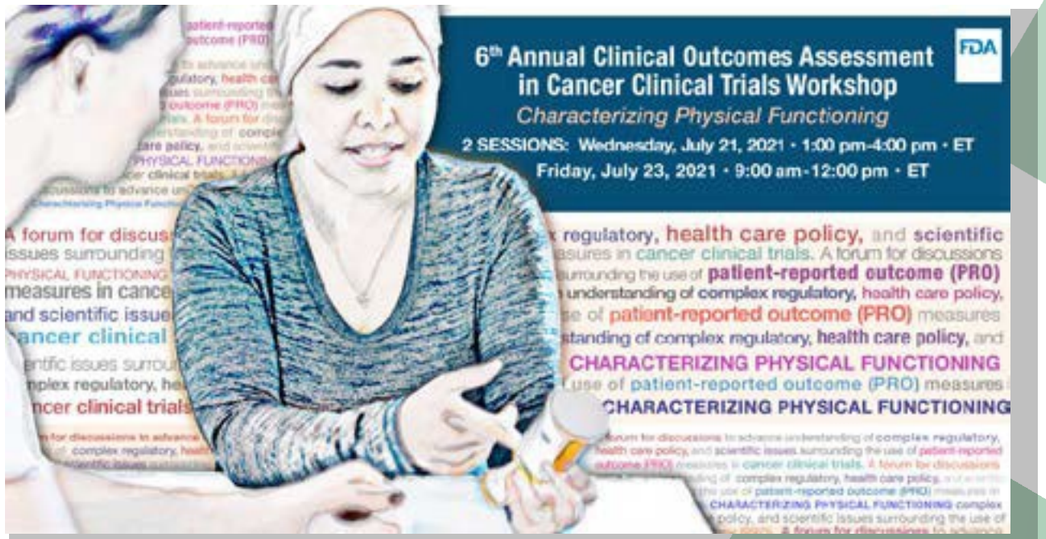
Patient Focused Drug Development (PFDD)

Consistent with OCE's mission to achieve patient-centered regulatory decision making, the OCE PPD program continued to advance efforts to integrate rigorous measurement of symptoms, function and other patient experience data in cancer trials. In 2021, the program expanded its consult service, providing consistent trial design and regulatory review advice on clinical outcome assessments for over 100 oncology products across review divisions in CDER, CBER and CDRH.

Other highlights included fnalizing the frst OCE funded prospective clinical study to quantify physical function in collaboration with Yale and Mayo Clinic, release of an OCE draft guidance for industry on core patient-reported outcomes and completion of the sixth annual Clinical Outcomes Assessment in Cancer Clinical Trials workshop.

Recent Publications by the OCE PFDD Program:

- Clinical Advances in Hematology & Oncology (2021) "The FDA's Patient-Focused Drug Development Initiative
- Blood Cancer Journal (2021) "Review of patient-reported outcomes in multiple myeloma registrational trials: highlighting areas for improvement
- Journal of the National Cancer Institute (2022) Patient-Reported Outcomes in Pediatric Cancer Registration Trials: A US Food and Drug Administration Perspective
- Journal of the National Cancer Institute (2021) Advancing Assessment, Analysis, and Reporting of Safety and Tolerability in Cancer Trials



Community and Patient Outreach

Project Community

Project Community leads the OCE's outreach to patients with cancer, their families and caregivers, and medically underserved communities in the U.S.

In 2021, Project Community began the first National Black Family Cancer Awareness Week to increase cancer awareness in one of the most vulnerable segments of the U.S. population. This initiative created a social media toolkit and included four meetings with external stakeholders plus a June 2021 Conversation on Cancer that garnered 469 attendees and more than 600 YouTube views.

More than 50 organizations engaged with the initiative on social media throughout the year, generating cancer awareness messages to millions of social media viewers. This successful initiative will continue, with the awareness week scheduled for June 16-22, 2022.

Conversations on Cancer

Project Community held eight Conversations on Cancer public panel discussions in 2021, with total attendance at nearly 4,000. Topics included clinical trial barriers for Black Americans, racial injustice in health care for Asian Americans and Pacific Islanders, health challenges and communication strategies for cancer survivors, the future of childhood cancer drug development, cancer disparities in the U.S. Latinx LGBTQ communities, and future cancer equity opportunities.

These discussions are freely available for viewing on the Conversations on Cancer web page or YouTube playlist.

Project Community also conducted four meetings with 25 NCI-designated Cancer Center Outreach Leads and participated in five listening sessions or public-facing meetings with external stakeholders.

Conversations on Cancer Events

Professional Education and Resources

Project Socrates

In 2021, Project Socrates launched into its second year, continuing many of its internal and external educational programs. Most notably, the FDA-AACR Oncology Educational Fellowship welcomed 29 new fellows to its 2021-2022 class in October 2021. Similar to its inaugural year, the Fellowship will span eight sessions over the course of a year and revisit Project ODAC Odyssey and many case discussions of approved oncology products.

OCE's Project Livin' Label now has five episodes available, each discussing the backstory of the development and FDA approval of an oncology product. In 2022, Project Livin' Label welcomes the Oncology Nursing Society (ONS) and Hematology/Oncology Pharmacy Association (HOPA) as it looks to expand its scope by hearing the perspectives of oncology nurses and pharmacists.

Regarding outreach efforts, the FDA-ASCO Hematology/Oncology Fellows Workshop continued in its seventh year, with two half-day virtual sessions and almost 100 attendees at each session.

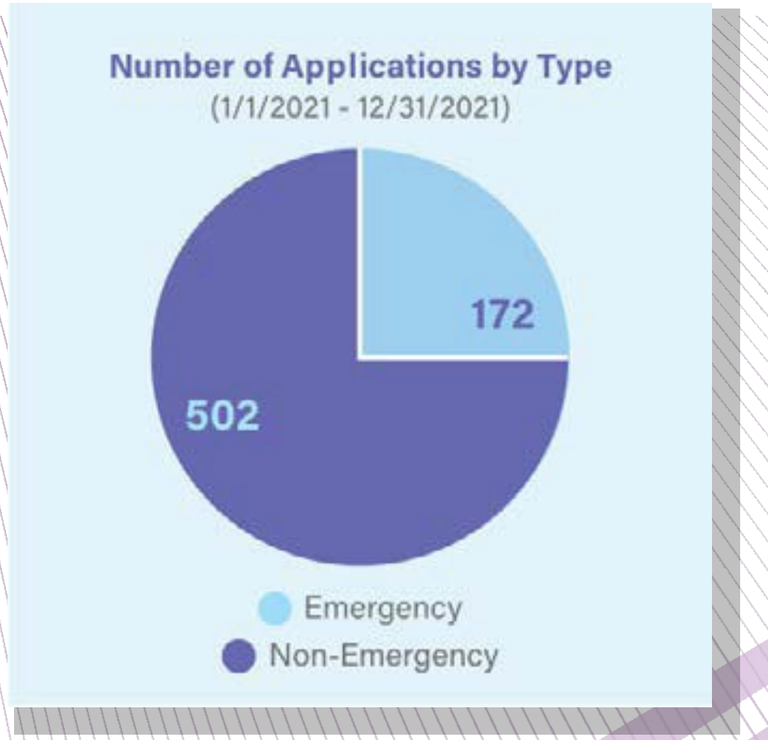
The OCE Icons in Oncology Distinguished Lecture Series welcomed Drs. James Allison, Martine Piccart, Judith Karp, and Lawrence Einhorn, who provided historical perspectives of how research, treatment paradigms, and clinical trials have evolved over time.

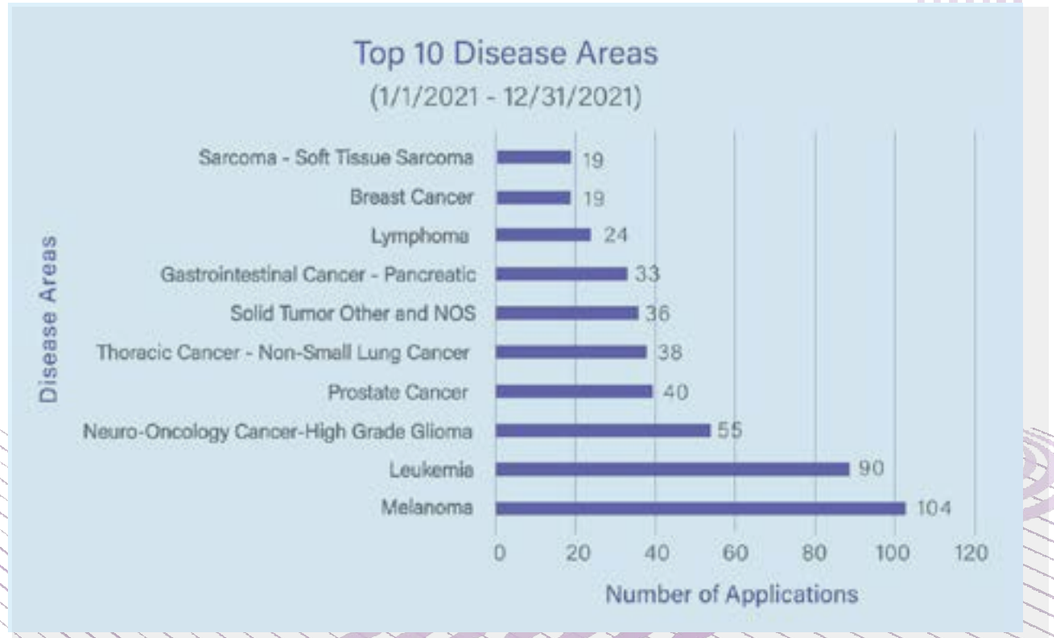
The Office of Oncologic Diseases welcomed 15 new clinical reviewers and analysts to the FDA oncology team, and Project Socrates held approximately 20 classes as part of the OCE Curriculum to educate new reviewers on oncology regulatory policy and science.

During the summer of 2021, the OCE Summer Scholars Program, welcomed 70 students to a three-week virtual learning experience on cancer drug development and career opportunities in government, regulatory medicine, and cancer advocacy. The Scholars Program began in 2017 as an in-person internship for up to 20 high-school students; it has since quadrupled in size and scope. U.S. Students from across the country and abroad are now able to participate in the program.

Project Facilitate

Project Facilitate is a program designed to assist oncology healthcare professionals in submitting Expanded Access requests to the FDA. In addition to providing support via phone or email, Project Facilitate staff also review all CDER oncology single-patient expanded access applications. In 2021, Project Facilitate handled 429 phone calls and 674 Expanded Access applications. Since Project Facilitate was launched, review and processing times have been reduced to less than one day, compared to two to three days on average prior to the program's implementation, consistent with the Project Facilitate mission to improve effciency of review of oncology Expanded Access requests. Project Facilitate staff also increased the number of educational outreach presentations on Expanded Access to clinics and hospital systems





Project Renewal

OCE's Project Renewal is a public health initiative aimed at updating the labeling of long-standing, off-patent oncology drugs. Since its inception in 2018, Project Renewal has continued to refine its process of engaging a multi-disciplinary team of oncologists, clinical fellows in training, and other scientific experts to review older oncology drug labeling. This engagement culminates in an independent FDA review of clinical findings from published studies to ensure revised labeling provides adequate directions for use. In 2021, Project Renewal evaluated over 25 existing indications and potential off-label uses for three oncology drugs and fostered educational experiences for 12 oncologists and 7 hematology/oncology fellows.

To date, Project Renewal has evaluated products which have a reference listed drug (RLD) New Drug Application (NDA) holder. In December 2020, the Making Objective Drug Evidence Revisions for New (MODERN) Labeling Act was passed, providing a regulatory framework for the FDA to update labeling of generic products approved under the abbreviated new drug applications pathway. Project Renewal, in collaboration with the FDA Office of Generic Drugs, looks forward to using the MODERN authority to revise important generic oncology product labeling for cancer therapies that do not have an RLD NDA holder.

FDA Oncology Publications

The OCE's strong support for publications by FDA oncology/hematology staff continued in 2021, resulting in 86 articles in scientific journals. From 2010 through 2021, FDA oncology staff have published a total of 612 articles in scientific journals. OCE's support for publications starts at the level of disease-specific team leaders who encourage and assist oncology reviewers in writing FDA approval summaries on most drug approvals. Staff are also encouraged to develop research articles on pooled analyses of clinical trial data. OCE and divisional leadership in the Office of Oncologic Diseases often write articles providing perspectives on topics in cancer drug development. The OCE Communications Team supports authors with editing and administrative services related to publication.