FY 2018

PERFORMANCE REPORT TO CONGRESS

for the

Office of Combination Products

as required by the

Medical Device User Fee and Modernization Act of 2002

Commissioner's Report

I am pleased to submit the Food and Drug Administration's (FDA or the Agency) Fiscal Year (FY) 2018 Annual Report to Congress for the Office of Combination Products (OCP). This report includes data from the 15th full year since OCP was established, as mandated by the Medical Device User Fee and Modernization Act of 2002, P.L. 107-250 (MDUFMA), enacted on October 26, 2002.

Combination products are therapeutic and diagnostic products that combine a drug, device, and/or biological product. Technological advances continue to merge product types and blur the historical lines of separation between FDA's human medical product Centers, which are made up of the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH). Combination products involve constituent parts that would normally be regulated under different types of regulatory authorities, and frequently by different FDA Centers, which can raise regulatory, policy, and review management challenges. Differences relating to the normal regulatory pathways and considerations for each type of constituent part (drug, device, biological product) can impact the regulatory processes for all aspects of product development and management, including preclinical testing, clinical investigation, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, user fees, and post-approval modifications.

OCP continues to enhance the efficiency, consistency, transparency and predictability of the process for assigning combination products to the appropriate lead Center and for the regulatory process. In this regard, OCP acts to facilitate interactions between industry and FDA to clearly delineate regulatory pathways, monitor and adjust processes to ensure timely and effective premarket review, and ensure the consistent and appropriate postmarket regulation of combination products. In addition to combination products, OCP also has classification and assignment responsibilities for non-combination drug, device, and biologic products.

Combination products are likely to become more complicated as new technologies emerge and existing technologies mature. OCP will continue to focus on the most important issues relating to the regulation of combination products. OCP is committed to actively assisting industry and FDA reviewers in understanding the complexities of this regulatory area.

FDA looks forward to ensuring success in meeting the unique challenges in the review and regulation of combination products.

Stephen M. Hahn, M.D.
Commissioner of Food and Drugs

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Executive Summary

FDA established the Office of Combination Products (OCP) on December 24, 2002, as required by the Medical Device User Fee and Modernization Act of 2002 (Pub. L. 107-250). The statutory mission of OCP is to ensure the prompt assignment of combination products (for drug-device, biologic-device, drug-biologic, or drug-device-biologic products) to Food and Drug Administration (FDA) Centers; the timely, effective, and aligned premarket review of such applications; and the consistent and appropriate postmarket regulation of like products subject to the same statutory requirements to the extent permitted by law.

This document presents OCP's annual performance report to Congress and covers activities and accomplishments during fiscal year (FY) 2018 (i.e., from October 1, 2017, to September 30, 2018). OCP's activities and performance for FY 2018 that are highlighted in this report include the following:

1. **Prompt Assignment of Combination Products.** In FY 2018, OCP continued to clarify the jurisdictional assignment of combination products and to provide prompt Request for Designation (RFD) decisions. OCP issued eight combination product RFD decisions, with every classification and/or assignment decision meeting the 60-day statutory decision time requirement. OCP also provided timely classification and jurisdictional Center assessments for 82 separate Pre-RFD submissions. OCP issued a final guidance in February 2018,[1] on its preliminary product classification assessment (Pre-RFD) process.

2. **Timely and Effective Combination Product Review.** In FY 2018, OCP received 321 requests for product-specific assistance, the responses to which contributed to ensuring the timely and effective review of combination products. This number of requests is a 39 percent decrease from the 525 requests received in FY 2017. OCP also fully implemented a revised inter-Center consult process that was piloted in FY 2017. This new process enhanced the efficiency, coordination, and consistency of the review of combination products. The corresponding revised staff manual guide (i.e., SMG 4101) was published in June 2018. Other OCP activities relating to premarket review included chairing and/or participating in several inter-Center working groups to examine complex regulatory issues, clarify regulatory standards, address challenging categories of products, identify and resolve specific product issues, update the premarket review process, and address developmental considerations for combination products.

   FDA received 498 original premarket applications for combination products in FY 2018. This number of applications reflects a 14 percent decrease from the 566 applications of the types reported in FY 2017.[2] Inter-Center consulting reviews for combination products increased to 1,445 for FY 2018 from 1,419 in FY 2017.

[1] This final guidance is available at https://www.fda.gov/media/102706/download.

[2] The FY 2017 numbers were changed to reflect updates to data presented in the FY 2017 OCP performance report. The updated data for FY 2017 is located in Appendix A of the FY 2018 performance report.

a. Examples of combination product types can be found at the OCP website at www.fda.gov/CombinationProducts/default.htm.

3. **Consistent and Appropriate Postmarket Regulation**. In FY 2018, OCP provided clarification and support for 86 separate postmarket matters. OCP continued to chair FDA working groups to address current good manufacturing practices (CGMPs) and postmarketing safety reporting (PMSR) requirements for combination products. Notably, FDA (1) published a draft guidance in March 2018[3] on the implementation of its December 2016 final rule on PMSR for combination products and (2) issued a proposed list of alternative or streamlined mechanisms for complying with CGMPs in June 2018[4] as required by the 21st Century Cures Act (Cures Act) (Pub. L. 114-255). OCP also continued to work with the medical product Centers on registration and listing issues, postmarket manufacturing compliance, and other postmarket regulatory issues pertaining to specific combination products.

4. **Procedural and Policy Activities and Accomplishments**. The cross-cutting decisional Combination Products Policy Council, consisting of senior leaders from all three human medical product Centers, the Office of Medical Products and Tobacco, the Office of Special Medical Programs, and OCP, continued to provide direction regarding complex policy and procedural questions for combination products. Topics addressed included the implementation of section 3038 of the Cures Act, as well as human factors, the inter-Center consult process, the availability of premarket pathways for combination products, the inter-component coordination on combination product policy activities, and regulatory considerations for cross-labeled and other separately distributed medical products intended for combined use. OCP also continued to conduct external outreach activities through a variety of educational and informational presentations to national and international audiences. These activities were intended to foster greater efficiency of the combination product development and premarket review process by enhancing understanding of the complex regulatory and scientific issues that often arise regarding combination products.

[3] This draft guidance is available at https://www.regulations.gov/document?D=FDA-2008-N-0424-0023.

[4] 83 FR 27609 (June 13, 2018), available at https://www.federalregister.gov/documents/2018/06/13/2018-12634/alternative-or-streamlined-mechanisms-for-complying-with-the-current-good-manufacturing-practice.

Table of Contents

Abbreviations

510(k) – Premarket Notification

ANDA – Abbreviated New Drug Application

BLA – Biologics License Application

BsUFA – Biosimilar User Fee Act

CBER – Center for Biologics Evaluation and Research

CDER – Center for Drug Evaluation and Research

CDRH – Center for Devices and Radiological Health

CFR – Code of Federal Regulations

CGMP – Current Good Manufacturing Practice

FDA – Food and Drug Administration

FY – Fiscal Year (October 1 to September 30)

GDUFA – Generic Drug User Fee Act

HDE – Humanitarian Device Exemption

IDE – Investigational Device Exemption

IND – Investigational New Drug

ISO – International Organization for Standardization

MDUFA – Medical Device User Fee Amendments

MDUFMA – Medical Device User Fee and Modernization Act

NDA – New Drug Application

NSE – Not Substantially Equivalent

OCC – Office of the Chief Counsel

OCP – Office of Combination Products

PDUFA – Prescription Drug User Fee Act

PMA – Premarket Approval Application

PMC – Postmarketing Commitment

PMR – Postmarketing Requirement

Pre-RFD – Pre-Request for Designation

RFD – Request for Designation

SE – Substantially Equivalent

Introduction

On October 26, 2002, the Medical Device User Fee and Modernization Act (MDUFMA) (Pub. L. 107-250) was signed into law. Among other things, MDUFMA required the Food and Drug Administration (FDA or Agency) to establish an office "to ensure the prompt assignment of combination products to agency centers, the timely and effective premarket review of such products, and consistent and appropriate postmarket regulation of like products to the extent permitted by law." In response, FDA established the Office of Combination Products (OCP) within the Office of the Commissioner. On December 13, 2016, the 21st Century Cures Act (Cures Act) (Pub. L. 114-255) was signed into law. Among other things, the Cures Act clarified and expanded the duties of OCP to include ensuring the alignment of premarket review of combination products. Information about OCP, including the authorizing text of MDUFMA as amended by the Cures Act, can be found on the OCP website at www.fda.gov/CombinationProducts/default.htm.

Description of Combination Products

21 CFR 3.2(e) states that combination products include:

(1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;

(2) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;

(3) A drug, device, or biological product packaged separately that, according to its investigational plan or proposed labeling, is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or,

(4) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Some combination products have the potential to provide enhanced therapeutic advantages compared to non-combination medical products (devices, drugs, and biological products) and incorporate cutting-edge, novel technologies that hold great promise for advancing patient care. Combination products may include drug delivery systems, gene therapy systems, personalized

medicine drug-device combinations, biological-device combinations, applications of nanotechnology, and other innovative products.

Statutorily Mandated Functions of OCP

MDUFMA and the Cures Act have established broad responsibilities for OCP that cover the regulatory life cycle from product jurisdiction decisions to duties relating to premarket review and postmarket oversight of combination products. However, the primary responsibilities for scientific premarket review and postmarket regulation of combination products remain in the three human medical product Centers – the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH) – to which they are assigned by OCP.

Specifically, section 503(g)(8) of the Federal Food, Drug, and Cosmetic Act requires OCP to, among other things, complete the following functions:

(1) Promptly assign a Center with primary jurisdiction for a combination product;

(2) Ensure the timely and effective premarket review of combination products by overseeing the timeliness of reviews and the alignment of Agency feedback to the product sponsor and by coordinating reviews involving more than one Center;

(3) Ensure the consistency and appropriateness of postmarket regulation of like products subject to the same statutory requirements to the extent permitted by law;

(4) Resolve disputes regarding the timeliness of premarket review of combination products; and

(5) Review and modify/revise/eliminate, as needed, agreements, guidance documents, or practices specific to the assignment of combination products.

Among other activities, OCP serves as a focal point for addressing combination product issues raised by FDA reviewers and stakeholders and works with the relevant Centers to develop guidance documents, regulations, processes, and procedures to clarify and enhance the efficiency, consistency, and transparency of combination products regulation.

In addition, OCP has responsibility for FDA action on every Request for Designation (RFD) submitted by industry in accordance with 21 CFR part 3, “Product Jurisdiction.” RFDs may request classification of a particular product as a biological product, device, drug, or combination product, or a determination of its Center assignment or both.

Performance Presented in This Report

This report presents fiscal year (FY) 2018 OCP activities and accomplishments, including key measures that should be made public. These reportable measures support the mandated functions of OCP. Specifically, this report presents information and data on OCP activities related to the following:[5]

- Prompt assignment of combination products
    - Timeliness of the assignment of combination products
- Timely and effective premarket review
    - Number and types of combination products under review
    - Timeliness of the reviews of combination products
    - Number of premarket reviews of combination products that involved a consulting Center
- Consistent and appropriate postmarket regulation
- Effective resolution of review disputes
    - Timeliness of dispute resolutions regarding combination products

Unless otherwise noted, all performance data are as of September 30, 2018.

[5] FDA has initiated various activities related to its implementation of the Cures Act requirements for combination products, and this report has been modified to provide new information to reflect the Cures Act requirements and expectations. As the Cures Act implementation proceeds, the Agency will consider what additional information or adjustments may be appropriate for subsequent reports.

Prompt Assignment of Combination Products

OCP is required to respond to RFDs to classify a particular product as a biological product, device, drug, or combination product and to assign a particular product to the appropriate Center (i.e., CBER, CDER, or CDRH). OCP assigns primary jurisdiction for combination products (i.e., Center assignment) based on the product's primary mode of action (PMOA) (see 21 U.S.C. 353(g)(1) and 21 CFR 3.4(a)) in response to RFDs. RFD submissions are subject to a statutory 60-day deadline.[6] OCP also provides responses to Pre-RFD requests for assistance regarding product classification and assignment.[7]

Requirement Workload Trends: FY 2013 to FY 2018

In the table below, the total number of OCP's RFD determinations (i.e., classifications and assignments) in FY 2018 is compared to the previous 5-year average. The total number of RFD determinations in FY 2018 remained the same compared to FY 2017. However, the individual numbers of combination product and non-combination product determinations varied compared to their respective 5-year average. Specifically, the RFD determinations for combination products increased by 14 percent over the previous 5-year average; this is in contrast to the RFD determinations for non-combination products for which none were issued in FY 2018.

RFD Determinations [8]

RFD Submissions	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18	FY 13 to FY 17 5-Year Average	FY 18 Compared to 5-Year Average
Total RFD Combination Product Classifications/ Assignments	17	8	2	2	5	8	7	+14%
Total RFD Non-Combination Product Classifications/ Assignments	14	9	7	2	3	0	7	-100%

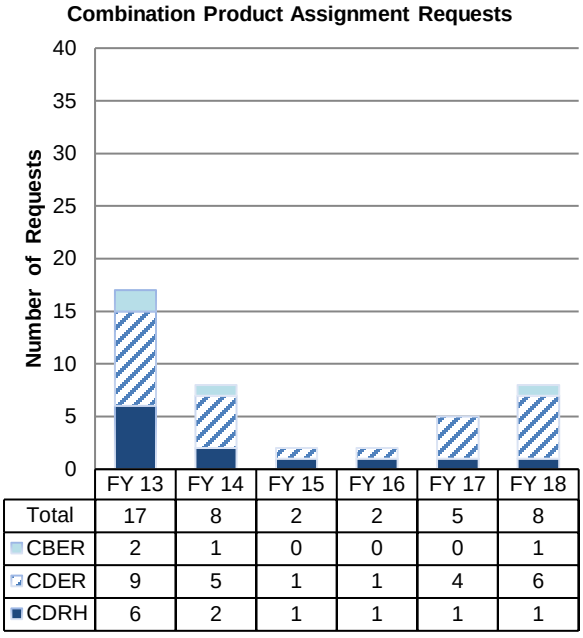
[6] OCP also provides assistance to product sponsors regarding preparation of RFDs and works with sponsors who disagree with FDA's PMOA determination on potential studies addressing PMOA matters (see 21 U.S.C. 353(g)(1)(F)).

[7] Responses to Pre-RFD submissions for product classification and jurisdictional assignments do not have a required time frame. However, OCP attempts to respond to Pre-RFD submissions in the same time frame as RFDs (i.e., within 60 days). Information about FY 2018 Pre-RFD submissions (including the timeliness of OCP responses) is provided in the section below titled Pre-RFD Workload Performance.

[8] Over the reported 5-year time frame, the decrease in RFD decisions has been accompanied by an increase in the number of Pre-RFD assessments provided by OCP. See the section below titled OCP Pre-RFD Workload Performance for more information.

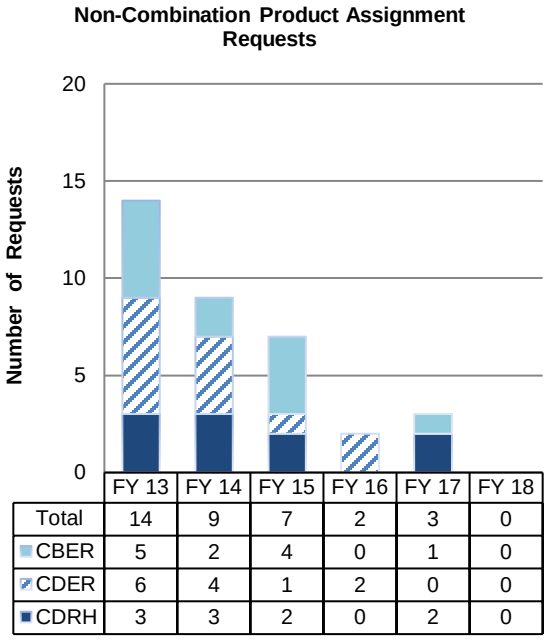
OCP received 56 RFD submissions in FY 2018.[9] Of these submissions, decisions were issued for 8 of them (14 percent), 44 of them were found to have insufficient information for filing (79 percent), 3 of them were pending at the end of FY 2018 (5 percent),[10] and 1 of them was withdrawn by the product sponsor prior to filing (2 percent). OCP also issued one response to a Request for Reconsideration of one of those RFD decisions by the 15-day review period as specified by regulations.

The total number of RFD combination product classifications and assignments issued in FY 2018 increased by 3 compared to FY 2017.



	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18
Total	17	8	2	2	5	8
CBER	2	1	0	0	0	1
CDER	9	5	1	1	4	6
CDRH	6	2	1	1	1	1

The total number of RFD non-combination product classifications and assignments issued in FY 2018 decreased by 3 compared to FY 2017.



	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18
Total	14	9	7	2	3	0
CBER	5	2	4	0	1	0
CDER	6	4	1	2	0	0
CDRH	3	3	2	0	2	0

[9] Of these 56 submissions, all were received in 2018, and none were carried over from the prior fiscal year.

[10] These three submissions were undergoing review at the end of FY 2018 and were carried over to FY 2019.

In FY 2018, the 8 RFD determinations were all issued by the statutorily mandated 60-day deadline. The average RFD review time was 58 days, with a median review time of 59 days. The following tables provide timeliness data by product type of the issued RFD decision.

Timeliness of Combination Product Determinations

Determination	Product Assignments Issued*	Percent On Time*
Drug-Device	7	100%
Drug-Biologic	0	NA
Device-Biologic	1	100%
Drug-Device-Biologic	0	NA
Total	**8**	**100%**

* Does not include request for reconsideration responses, which are issued within the 15-day time frame provided by 21 CFR 3.8. One request for reconsideration was submitted for a combination product in FY 2018.

Timeliness of Non-Combination Product Determinations

Determination	Product Assignments Issued*	Percent On Time*
Drug	0	NA
Biologic	0	NA
Device	0	NA
Total	**0**	**NA**

* Does not include request for reconsideration responses, which are issued within the 15-day time frame provided by 21 CFR 3.8. No requests for reconsideration were submitted for a non-combination product in FY 2018.

Pre-RFD Workload Performance

In addition to responding to RFDs, OCP provided preliminary feedback/assessments in response to Pre-RFD submissions for product classification and jurisdictional assignment. The Pre-RFD process may be preferable in some circumstances to the more formal RFD process. For example, Pre-RFD submissions allow for more discussions (e.g., teleconferences) between FDA and a sponsor if questions arise during review. In the tables below, OCP Pre-RFD submission review workloads in FY 2018 are provided. FY 2018 is the second full year of the "formalized" Pre-RFD program.[11] As such, available data allowing for a multi-year comparison (e.g., a comparison to 5-year averages) are not yet available. However, this year-to-year comparison data will be provided in future reports as they become available.

OCP Pre-RFD Submission Assessments

	FY 17	FY 18
Combination Product Assessments	44	48
Non-Combination Product Assessments	34	28
Unclassified Assessments*	-	6
Total Pre-RFD Assessments	**78**	**82**

* Six Pre-RFD assessments did not result in a classification as a drug, device, biological product, or combination product, and/or a Center assignment. For instance, products that fell under this category may (1) not have met the criteria for regulation solely under section 361 of the Public Health Service Act and 21 CFR part 1271 or (2) have been for submissions in which a sponsor may have pursued only a product assignment and not a classification.

[11] Formalization of the Pre-RFD program as a distinct OCP activity occurred during FY 2016. Consistent with past practice, Pre-RFD data presented in the FY 2016 report continued to be grouped with Center-requested consultations (i.e., product classification and jurisdictional requests that originate with the FDA Centers and not with product sponsors). However, Pre-RFD and Center-requested consultations are two different OCP activities. Therefore, these two different data groups have been independently reported since FY 2017. Center-requested consultations are discussed in the following section.

Of the 82 total FY 2018 Pre-RFD assessments, 98 percent were issued by OCP's internally established 60-day goal, which started on the date of receiving sufficient information to provide requested feedback[12] (see the following tables). In FY 2018, the 60-day review goal was missed for 2 submissions out of 82. The average review time for Pre-RFD assessments was 37 days, with a median review time of 54 days. The following tables show Pre-RFD assessments for combination products and non-combination products based on the product's classification and the Center assignment.

Number of Combination Product Pre-RFD Assessments

Classification	Assignments Issued	Percent Issued in 60 Days
Drug-Device	40	100%
Drug-Biologic	0	NA
Device-Biologic	5	100%
Drug-Device-Biologic	3	100%
Total	**48**	**100%**

Number of Combination Product Pre-RFD Assessments by Center Assignment

Center Assignment	Consultations Issued
CDER	35
CBER	4
CDRH	9
Total	**48**

Number of Non-Combination Product Pre-RFD Assessments

Classification	Assignments Issued	Percent Issued in 60 Days
Drug	9	89%
Biologic	5	100%
Device	14	93%
Total	**28**	**93%**

[12] OCP does not have a mandated review time frame for Pre-RFD assessments. However, OCP attempts to review Pre-RFD assessments within the same time frame as RFD submissions (i.e., 60 days).

Number of Non-Combination Product Pre-RFD Assessments by Center Assignment

Center Assignment	Consultations Issued
CDER	9
CBER	6
CDRH	13
Total	**28**

Internal Center-Requested Classification and Assignment Consultations

In addition to responding to RFDs and Pre-RFDs submitted by industry/sponsors, OCP provided classification and assignment feedback for combination and non-combination products in response to requests from Centers in relation to premarket submissions. Centers may consult OCP for assistance in determining if the product submitted to a Center for review is appropriately assigned to that Center, whether the sponsor would need to be referred to OCP for a classification or assignment determination, or both. The number of the consultations provided by OCP is presented in the table below. As with the Pre-RFD data presented above, FDA intends to provide, in future reports, metrics for multiple fiscal years, as such data become available.

Center-Requested Classification and Assignment Consultations

Center Assignment	FY 17	FY 18
CDER	29	31
CBER	3	3
CDRH	16	14
Unassigned[13]	0	2
Total	**48**	**50**

Additional Classification and Assignment Activities

This category reports on all other activities not falling within the classification and assignment activities reported above. Examples of this category of activity include responding to questions about process (e.g., how to prepare an RFD or Pre-RFD) and providing feedback to sponsors regarding the design of studies (e.g., to evaluate PMOAs). This category also includes responses to individual email queries and meetings and teleconferences that OCP holds with sponsors.

[13] The term *unassigned* indicates that a determination/assessment of Center assignment was not made. This may be the case, for example, if the question before OCP concerns solely product classification.

Additional Number of Product Classification and Assignment Activities

	FY 17	FY 18
Jurisdiction/Classification Issues	528	529

Accomplishments

Type of Activity	FY 2018 Accomplishments
Issuing required RFD assignments within 60 days	OCP issued all RFD assignments by the statutory 60-day determination deadline.
Clarifying standards for product classification and preparing guidance on this issue	In late FY 2017, OCP published a final guidance on the classification of drugs and devices and additional issues related to product classification.[14] OCP continued to chair a working group, including staff from CDER, CDRH, CBER, and the Office of Chief Counsel (OCC), to clarify interpretive standards; to address the classification and assignment of challenging categories of products; to continue pursuing and supporting related policy initiatives, including the issuance of a final guidance on regulatory considerations for human cells, tissues, and tissue-based products (including classification);[15] and to clarify standards for cross-labeled combination product status.
Enhancing the timeliness, consistency, and clarity of jurisdictional decisions across FDA	OCP continued to facilitate product classification and jurisdictional meetings with CBER, CDER, CDRH, and OCC staff to exchange information and discuss challenging product classification and assignment issues before FDA. OCP continued to provide training to review staff, including personnel from CBER, CDER, and CDRH, as well as Office of Regulatory Affairs inspectors, on product classification and assignment. See also the discussion of the issuance of a guidance on the Pre-RFD program and classification of products and other policy activities relating to product classification and assignment under Policy Activities and Accomplishments.

[14] This guidance is available at https://www.fda.gov/media/80384/download.

[15] This guidance is available at https://www.fda.gov/media/124138/download.

Combination Product Premarket Review

OCP is responsible for ensuring the timely, effective, and aligned premarket review of combination products, which includes overseeing the timeliness of reviews and aligning feedback by coordinating reviews involving more than one Center.

In 2002, FDA established policies and procedures for FDA staff to follow when requesting, receiving, handling, processing, and tracking formal reviews of combination products, devices, drugs, and biological products. This policy was formally incorporated into the FDA Staff Manual Guide, Agency Program Procedures, Volume IV, effective June 18, 2004.

In FY 2017, in light of feedback from stakeholders and internal FDA staff regarding the consistency, efficiency, and coordination within FDA of premarket reviews for combination products, FDA piloted a revised inter-Center consultative process to ensure that consultations occur as appropriate, improve the early identification of the appropriate inter-Center review team, enhance the efficiency of consult request issuance and the clarity of questions asked, and better ensure FDA's responsiveness and documentation of completed consults. Based on the results of this pilot, an updated process has been implemented and incorporated into the appropriate FDA Staff Manual Guide in FY 2018.

Number and Types of Combination Products Submitted for Review

FDA is required to report the number and types of combination products submitted for review. The following information refers to FDA performance data presented in this subsection.

- Data on the number and types of combination products submitted for review for FY 2018 by CBER, CDER, and CDRH (includes submissions filed or received in FY 2018).

- When reporting timeliness in days for the review for CBER-led or CDER-led combination products, the Prescription Drug User Fee Act (PDUFA VI) goals were referenced for priority and standard new drug applications (NDAs) and applicable biologics license applications (BLAs), the Generic Drug User Fee Act (GDUFA II) goals were referenced for 2018 goals for abbreviated new drug applications (ANDAs), and the Biosimilar User Fee Act (BsUFA II) goals were referenced for 2018 goals for biosimilar BLAs. For CBER-led or CDRH-led combination products, the Medical Device User Fee Amendments (MDUFA IV) goals were referenced for expedited and original premarket approval applications (PMAs), premarket notifications (510(k)s), De Novo classification requests (De Novos), and device BLAs.
- Some product review goals, such as for NDAs, were defined by the number of months to review the product. Because of the differences in the numbers of days in each month (28 to 31), 10 months represented a range from 304 days (such as February 1 to December 1) to 306 days (such as March 15 to January 15), and 6 months represented a range from 182 days (such as February 15 to August 15) to 184 days (such as July 15 to January 15).

- Median review time was based on FDA first cycle review performance for PDUFA VI goals. For MDUFA IV goals, median review times were based on total MDUFA IV decision review time. Actual review time was used when only one action was measured.

Requirement Workload Trends: FY 2013 to FY 2018

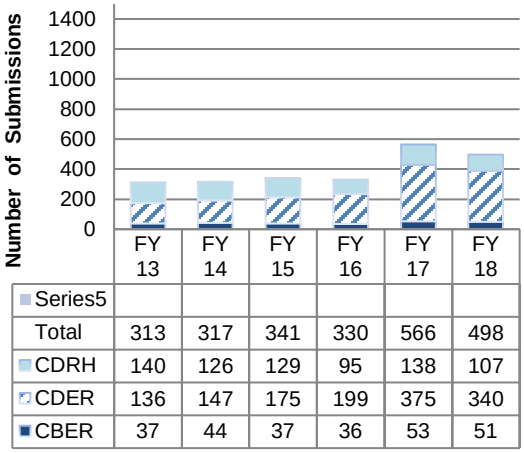
FY 2018 Submission Review Workloads

Submission/Request	FY 13	FY 14	FY 15	FY 16*	FY 17[16]	FY 18
Total Combination Products (by Center) Submitted for Review	313	317	341	330	566	498

* FY 2016 numbers were changed to reflect updates to data presented in the FY 2016 OCP Performance Report.

The total number of combination products submitted for review decreased slightly in FY 2018. Of all combination product submissions, 68 percent were received by CDER, 22 percent were received by CDRH, and 10 percent were received by CBER.

Combination Product Application Submissions



	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18
Series5						
Total	313	317	341	330	566	498
CDRH	140	126	129	95	138	107
CDER	136	147	175	199	375	340
CBER	37	44	37	36	53	51

[16] Reported FY 2017 and FY 2018 data include additional submission types, i.e., abbreviated new drug applications (ANDAs) and De Novo classification (De Novos) requests, that were not previously reported in past years, and also track user fee performance for biosimilar products separately from other biological products. FDA has made these changes in light of submission trends and clarification provided by the Cures Act regarding availability of premarket pathways for combination products. See Appendix A for updated FY 2017 data. As such the data shown for FY 2018 are not directly comparable to the past years shown in this table.

The table below presents the 498 original applications for combination products received in FY 2018, broken down by the identified ten application types and by the product's initial classification into one of nine categories of combination product.[17] The same table reflecting applications received in FY 2017 is updated in Appendix A to reflect corrections and actions as of September 30, 2018. The majority of the applications (47 percent) received in FY 2018 were original investigational new drug (IND) applications, followed by ANDAs (22 percent). Also, the most common combination product category was the pre-filled drug delivery device/system (23 percent).

Workload by Combination Product Category Number

Application Type	1	2	3	4	5	6	7	8	9	Totals
Original NDAs	2	18	0	0	0	0	2	0	0	**22**
Original BLAs	1	0	5	0	0	1	0	0	0	**7**
Original PMAs	0	2	1	0	0	0	0	0	0	**3**
Original 510(k)s	7	1	0	53	1	1	2	0	8	**73**
Original INDs	19	29	34	4	6	48	6	81	6	**233**
Original IDEs	6	0	0	15	3	0	4	3	15	**46**
Original HDEs	0	0	0	0	0	0	0	0	0	**0**
ANDAs	46	65	0	0	0	0	0	0	0	**111**
Biosimilar BLAs	0	0	1	0	0	0	0	0	0	**1**
De Novos	0	0	0	2	0	0	0	0	0	**2**
Total	**81**	**115**	**41**	**74**	**10**	**50**	**14**	**84**	**29**	**498**

Combination Product Category Key:

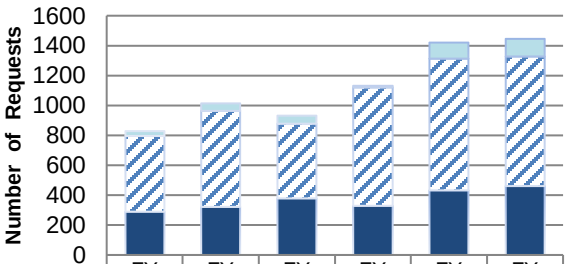
1 = convenience kit or co-package
2 = pre-filled drug delivery device/system
3 = pre-filled biologic delivery device/system
4 = device coated/impregnated/otherwise combined with drug
5 = device coated or otherwise combined with biologic
6 = drug/biologic combination
7 = separate products requiring mutually conforming labeling
8 = possible combination based on mutually conforming labeling of separate products
9 = other type of combination product

[17] The classifications are presented as initial because adjustments were made to these numbers for each fiscal year to reflect corrections and subsequent actions that may have informed the classification status, such as the ultimate status of products initially placed in category 8 (for certain possible combination products).

Inter-Center Consultation Requests

The total number of inter-Center consultation requests related to combination products increased for FY 2018 to the highest number in the past 6 years. The number of inter-Center consultation requests in FY 2018 (1,445) increased by 36 percent as compared to the previous 5-year average of 1,064.

Inter-Center Consultation Requests by Lead/Reviewing Center



	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18
Total	828	1,013	932	1,130	1,419	1,445
CBER	31	48	53	9	105	118
CDER	506	643	499	793	881	867
CDRH	291	322	380	328	433	460

In the table below, the total review workload for inter-Center consultation requests in FY 2018 is compared to the previous 5-year averages.

FY 2018 Inter-Center Consult Workloads

Submission/Request	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18	FY 13 to FY 17 5-Year Average	FY 18 Compared to 5-Year Average
Total Inter-Center Consult Requests	828	1,013	932	1,130	1,419	1,445	1,064	+ 36%

In the table below, the number of Inter-Center consult requests during FY 2018 is broken down by lead Center (i.e., Center requesting the consult) and consulted Center (i.e., reviewing Center).

Number of Premarket Review Inter-Center Consults for Combination Products by Lead and Consulted Centers

Lead Center	Consulted Center			
	CBER	CDER	CDRH	Number of Consults
CBER	--	27	91	118
CDER	24	--	843	867
CDRH	5	455	--	460
Total	**29**	**482**	**934**	**1,445**

Timeliness in Days for the Review of Combination Products

FDA is required to report the timeliness in review time for combination products. The table below summarizes the review type and review performance target for original NDAs, ANDAs, PDUFA BLAs, BsUFA BLAs, PMAs, De Novos, and 510(k)s. PDUFA VI, GDUFA II, BsUFA II, and MDUFA IV established review performance goals for many types of drug, device, and biological product premarket applications. These goals reflect current expectations about the portion of premarket applications that will be reviewed within a specified time frame. Performance goals apply to only a portion of all applications of a certain type, and they do not require that every application be reviewed in accordance with the applicable timeframe. Typical goals range from 50 percent to 90 percent and vary by year.

- For MDUFA IV performance goals, refer to https://www.fda.gov/media/102699/download.
- For PDUFA VI performance goals, refer to https://www.fda.gov/media/99140/download.
- For GDUFA II performance goals, refer to https://www.fda.gov/media/101052/download.
- For BsUFA II performance goals, refer to https://www.fda.gov/media/100573/download.

Performance Goals for Original Applications[†]

User Fee Act	Original Application Type	Review Type	Review Within
PDUFA VI	NDAs	Priority	6 months
PDUFA VI	NDAs	Standard	10 months
PDUFA VI	BLAs	Priority	6 months
PDUFA VI	BLAs	Standard	10 months
MDUFA IV	Expedited and Original PMAs	Standard with No Advisory Committee Input	180 days
MDUFA IV	Expedited and Original PMAs	Standard with Advisory Committee Input	320 days
MDUFA IV	510(k)s	Standard	90 days
MDUFA IV	BLAs	Priority	6 months
MDUFA IV	BLAs	Standard	10 months
BsUFA II	Biosimilar BLAs	Standard	10 months
GDUFA II	ANDAs	Standard	10 months
MDUFA IV	De Novos	Standard	150 days

[†] The timelines for new medical entities and BLAs that fall under PDUFA VI's Program Review Model are 10 months for standard applications and 6 months for priority reviews from the 60-day filing date (or 12 months and 8 months, respectively, from the date of submission of the application).

FDA premarket review performance information for CBER, CDER, and CDRH is based on a fiscal year receipt cohort. This methodology calculates performance information for submissions for the fiscal year in which FDA received them, regardless of when FDA acted on or approved the submissions. This section updates FDA's review performance on the FY 2017 combination product submissions and presents FDA's review performance on the FY 2018 combination product submissions through September 30, 2018.

FY 2017 and FY 2018 Review Performance

The table below shows final FY 2017 review goal performance.

Original Application Type	Review Type	Review Within	Number of Combination Products	Median or Actual Review Time (Days)	Range of Review Time (Days)
NDAs	Priority	6 months	4	184	182 to 184
NDAs	Standard	10 months	30*	304	276 to 365
BLAs	Priority	6 months	4*	240	239 to 240
BLAs	Standard	10 months	5*	363	363
Expedited and Original PMAs	Standard	180 or 320 days†	9*	179	170 to 180
510(k)s	Standard	90 days	78*	81	15 to 220
Biosimilar BLAs	Standard	10 months	7*	302	302
ANDAs	Standard	10 months	67*	301	267 to 316
De Novos	Standard	N/A‡	1	126	126

* Included in this count are NDAs, ANDAs, BLAs, PMAs, and 510(k)s that are pending filing because the assumption is that they will go on to be filed. These are preliminary numbers that may change if the reported filed figures differ from the receipt figures.

† These figures represent a review occurring within 180 days for decisions without advisory committee input and a review occurring within 320 days for decisions with advisory committee input.

‡ De Novo requests did not have an associated performance goal in FY 17.

The table below shows preliminary FY 2018 review goal performance through September 30, 2018.

Original Application Type	Review Type	Review Within	Number of Combination Products	Median or Actual Review Time (Days)	Range of Review Time (Days)
NDAs	Priority	6 months	5	182	12 to 333
NDAs	Standard	10 months	17	183.5	60 to 306
BLAs	Priority	6 months	3	244	214 to 333
BLAs	Standard	10 months	4	277	277
Expedited and Original PMAs	Standard	180 or 320 days	3	179	170 to 180
510(k)s	Standard	90 days	73	84.5	45 to 90
Biosimilar BLAs	Standard	10 months	1	361	361
ANDAs	Standard	10 months	111	300	227 to 348
De Novos	Standard	150 days	2	118	84 to 151

Premarket Review Facilitation/Assistance

OCP continues to facilitate the premarket review of combination products that raise complex regulatory issues. OCP fosters early interactions between industry and FDA to help clearly delineate regulatory pathways for the development of combination products and expeditiously review premarket submissions for these products. Responding to requests from both industry and FDA review staff, OCP provides guidance on regulatory challenges unique to combination products. OCP also serves as a resource for FDA staff (1) on the appropriate use and interpretation of combination product categorization for premarket submissions and (2) in determining the correct combination product categories for data reporting purposes. Finally, OCP leads or participates in meetings and discussions to ensure efficient, effective communication between sponsors and FDA review staff. The number of OCP FY 2018 documented premarket review facilitation and assistance figures are presented below.

Number of OCP Documented Premarket Activities

	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18	FY 13 to FY 17 5-Year Average	FY 18 Compared to 5-Year Average
Premarket Review Issues	157	402	225	266	525	321	315	+ 2%

Number of OCP Documented Premarket Activities

	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18	FY 13 to FY 17 5-Year Average	FY 18 Compared to 5-Year Average
Premarket Review Issues	157	402	225	266	525	321	315	+ 2%

OCP received 321 requests for product-specific assistance from sponsors, the responses to which contributed to ensuring the timely, effective, and aligned review of combination products. Notably, OCP addressed issues such as the following:

- Novel drug and biological products combined with new technology delivery systems (e.g., emergency use products and complex generic combination products that include devices)
- Alignment of preclinical and biocompatibility data requests
- Review of combination products for rare disease populations
- Alignment of potential clinical hold review assessments
- Accuracy, consistency, and clarity of labeling of separately distributed constituent parts

- Alignment of warning letter considerations with ongoing developmental considerations for combination products

- Ongoing development considerations of combination products that incorporate mobile communication technologies

- In addition, OCP oversees inter-Center consults by facilitating coordination among review Centers (i.e., to ensure that reviews of premarket applications are completed in a timely manner and meet applicable user fee timelines). Specifically, OCP tracks and monitors all ongoing inter-Center consult requests; clarifies internal operating procedures, roles, and responsibilities; identifies consulting divisions and contacts; clarifies due dates and completion status; facilitates access to review documents; and resolves other barriers to timely completion of consults. OCP periodically reviews inter-Center consult data requests. OCP also conducts additional assessments, as needed, to ensure that the inter-Center consult request process supports the timely, consistent, and effective review of combination products.

- OCP provides assistance to the FDA Centers and industry regarding regulatory and scientific issues relating to specific combination products or to specific categories of combination products. For example, OCP responded to external industry requests to host cross-Center early product-specific development discussions on the implications of the Agency's 21 CFR part 15 hearing for devices referencing drugs.[18] Detailed accomplishments during FY 2018 are presented in the table below.

Type of Activity	FY 2018 Accomplishments
Providing Significant Premarket Review Facilitation or Assistance	Provided significant assistance with respect to the following categories of products and other premarket regulatory issues: • Novel drug-device cancer therapies • Injector delivery systems (e.g., intrathecal and on-body-wearable pump infusion systems) • Medical imaging drugs with photodynamic device activating and imaging systems • Facilitation of premarket CGMP assessments • Application of 21 CFR Part 4 to premarket submissions under review • Inter-Center review of manufacturing process compliance • Inter-Center safety evaluator processes • Ongoing regulatory considerations for a monograph drug for use with a device constituent part or for a Class I device for use with a drug • Unique device identifiers and standardized numerical identification • Alignment of IND and IDE review requirements for combination products

[18] See 82 FR 44803 (September 26, 2017).

Combination Product Postmarket Activities

OCP is tasked with ensuring the consistency and appropriateness of postmarket regulation of combination products, and FDA is required to describe any improvements in the consistency of postmarket regulation of combination products.

OCP meets the requirement to ensure consistency and appropriateness by undertaking a variety of compliance-related and postmarket activities to help ensure the safety and quality of combination products. The compliance-related and postmarket activities include (1) leading Agency efforts to develop and publish regulations and to issue guidance for postmarket safety and CGMPs for combination products (as discussed more fully in the Policy Activities and Accomplishments section below), (2) coordinating and overseeing FDA actions relating to novel and complex postmarket safety issues and CGMP compliance questions, and (3) facilitating and leading meetings between industry and FDA regarding these matters. For example, OCP provides support to FDA field inspectors on CGMP facility inspection issues and on the seizure of products at ports of entry to stop adulterated/misbranded products from entering the United States, assists Agency responses to product defect issues, and provides assistance on enforcement issues, including the development of compliance and enforcement action communications such as warning letters.

OCP's FY 2018 accomplishments related to the consistency and appropriateness of postmarket regulation are included below (see also the Policy Activities and Accomplishments section below).

Documented Product-Specific Postmarket Regulatory Activities

	FY 13	FY 14	FY 15	FY 16	FY 17	FY 18	FY 13to FY 17 5-Year Average	FY 18 Compared to 5-Year Average
Postmarket Regulatory Activities	57	110	71	50	74	86	72	+19%

OCP addressed 86 product-specific, postmarket-related matters involving such issues as the application of CGMPs and quality system regulations for inspections of combination products, the appropriate mechanisms and responsibilities for reporting adverse events, and the requirements for registration and listing. This represents a 19 percent increase in the number of such engagements as compared to the prior 5-year average. In addition, at the request of the Centers, OCP facilitated or led working groups to assess safety signal evaluations to determine the Agency's response approach.

These efforts have helped improve the consistency of postmarket regulation in a number of ways, including the following:

- Enhancing coordination among Agency components in support of CGMP inspectional and compliance policies and practices

- Clarifying stakeholder and FDA understanding of CGMP obligations (see also the final guidance mentioned in the Policy Activities and Accomplishments section below)

- Clarifying stakeholder and FDA understanding of PMSR requirements (see also the final rule mentioned in the Policy Activities and Accomplishments section below)

- Aligning the assessment of postmarket safety signals and risk assessments

Effective Resolution of Review Disputes

When requests are received, OCP is required to resolve disputes regarding the timeliness of the premarket review of a combination product. OCP facilitates communications between sponsors and FDA review staff to identify, clarify, and resolve specific concerns associated with review timeliness. The facilitation of issues helps prevent the need for a more formal dispute resolution.

In addition to disputes related to timeliness, OCP may also receive requests for dispute resolution and/or mediation for other review issues (e.g., inter-Center review dispute resolution or requests by product sponsors for assistance in understanding a review division's intent regarding issued decisions).

Percentage of Combination Products Reviewed for which a Dispute Resolution was Requested

FDA is required to identify the percentage of combination products for which a dispute resolution, with respect to premarket review, was requested by the combination product's sponsor.[19] FDA received no requests for dispute resolution in FY 2018. Therefore, the percentage is zero of total combination product submissions (i.e., based on the total number of combination product submissions reported in the Product Premarket Review section of this report). The Timely and Effective Premarket Review section of this report provides examples of FDA's informal facilitation and resolution of issues related to premarket review.

[19] This reporting requirement was established by the Cures Act and replaces the prior requirement to report on the timeliness in days of dispute resolutions regarding combination products.

Policy Activities and Accomplishments

Regulatory Initiatives

OCP activities include leading and assisting with policy initiatives important to the regulation of combination products. Examples of such activities pursued in FY 2018 are discussed in this section (and included in the following tables).

Supporting Legislative Initiatives

OCP participated in development of FDA positions in response to Congressional inquiries. Furthermore, OCP continued its efforts, in coordination with the medical product Centers, to implement section 3038 of the Cures Act regarding combination products. Activities in this regard included: the issuance of new rules and guidance documents; and the enhancement of standard operating procedures, information technology, staff training, and outreach. OCP also participated in the implementation of section 706 of the FDA Reauthorization Act of 2017 (Pub. L 115-52).

Streamlining Regulations

OCP published a proposed rule to amend FDA's jurisdictional regulations in 21 CFR part 3, as well as to update and clarify these regulations in light of legislative and other policy developments.[20]

Providing Clarifying Guidances

OCP collaborated with the medical product Centers to develop and publish the following guidance documents:

- Draft guidance on PMSR for combination products[21]
- Final guidance on the Pre-RFD program[22]

Completing Other Policy Activities

OCP completed additional policy activities, including the following:

[20] 83 FR 22428 (May 15, 2018), available at https://www.govinfo.gov/content/pkg/FR-2018-05-15/pdf/2018-10321.pdf.

[21] The final guidance which published in 2019 is available at https://www.fda.gov/media/111788/download.

[22] This final guidance is available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm534661.htm.

- Issuance of a staff manual guide (i.e., SMG 4103) on FDA's inter-component coordination for combination product review[23]

- Issuance of a Cures Act-mandated notice of proposed alternative and streamlined approaches to CGMP compliance[24]

- Initiation of an evaluation of assessment procedures to monitor and enhance combination product regulatory activities in accordance with the Cures Act mandates for OCP

- Initiation of an evaluation of procedural and information technology measures to enable implementation of a final PMSR rule for combination products

Additional Classification and Assignment Regulatory Initiatives

Type of Activity	FY 2018 Accomplishments
Developing regulations and guidance	Additional OCP classification and assignment-related activities included participating in the following Agency rulemaking and guidance initiatives: • Rule on the regulatory status of wound care products • Rulemaking on the meaning of *protein* in the definition of *biological product* in the Public Health Service Act (Pub. L. 78-410)[25] • Final guidance on minimal manipulation and homologous use for human cells, tissues, and cellular and tissue-based products [26]
Participating in other inter-Center and Agency-wide working groups to clarify issues related to product jurisdiction	OCP jurisdiction-related activities included participating in the following: • Enhancing the efficiency and transparency of the Pre-RFD Program • Classification-related issues for e-cigarettes and other products that include tobacco

[23] SMG 4103 is available at https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffManualGuides/UCM602810.pdf.

[24] 83 FR 27609 (June 13, 2018), available at https://www.federalregister.gov/documents/2018/06/13/2018-12634/alternative-or-streamlined-mechanisms-for-complying-with-the-current-good-manufacturing-practice.

[25] Available at https://www.govinfo.gov/content/pkg/FR-2018-12-12/pdf/2018-26840.pdf

[26] Available at https://www.fda.gov/media/124138/download

Additional Premarket Review Regulatory Initiatives

Type of Activity	FY 2018 Accomplishments
Developing guidance and regulations	OCP chaired or led the following guidance-related activities: • Continued to chair a cross-Center working group to finalize a guidance on human factors studies for combination products • Continued to chair a cross-Center working group to begin development of a draft guidance for technical aspects of intravaginal ring drug-delivery combination products • Chaired a cross-Center working group to develop a guidance for the technical considerations for demonstrating reliability of combination product emergency-use injectors • Led the development of a Cures Act-mandated guidance on presubmissions for combination product and combination product agreement meetings OCP participated in the development of: • Rule on De Novo classification • Draft guidance on the premarket principles and pathway availability for combination products • Draft guidance on pre-submission facility inspection for generic drugs[27] • Draft guidance on metered dose inhalers and dry powder inhalers[28] • Provision of combination product comments for citizen petition responses for specific types of generic combination products • Draft guidance on comparative assessments, including human factors for generic drug-led and interchangeable biologic-led combination products[29] • Final guidance on the selection of appropriate package type terms and recommendations for labeling injectable medical products packaged in multiple-dose, single-dose, and single-patient use containers for human use • Technical considerations for visual inspection for particulates in injectable solutions • Final guidance on regulatory considerations for human cells, tissues, and tissue-based products (including classification)[30] • Comments on ISO standards development for certain syringes.
Assessing regulatory pathways for new products intended to be used with another sponsor's already-approved product	OCP continued to work with the Centers and OCC to assess approaches for resolving complex legal and public health issues associated with the marketing of products intended for use with other legally marketed products. This work also included preparations for a 21 CFR part 15 hearing.

[27] Available at https://www.fda.gov/media/105794/download
[28] Available at https://www.fda.gov/media/70851/download
[29] Available at https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621902.pdf
[30] Available at https://www.fda.gov/media/124138/download

Type of Activity	FY 2018 Accomplishments
Participating in other inter-Center and Agency-wide working groups to clarify issues related to combined use of medical products	OCP led or participated in working groups with Centers and other Agency components regarding the following: • The appropriate regulatory pathway for novel technology diagnostics and biomarkers for use with drug or biological products • Companion diagnostics • The expansion of non-prescription drug availability • The development of Agency thinking on the regulation of software as drug labeling • Agency-wide working groups such as FDA's Task Force on Antimicrobial Resistance
Developing the consultative/collaborative review process and procedures	OCP, with the medical product Centers and other components of the Office of the Commissioner, completed an Inter-Center consult process pilot intended to enable timely and consistent coordination and the efficient, consistent review of submissions, and launched the revised process. This activity included developing and presenting training materials, facilitating, monitoring, and assessing consult activities.

Additional Postmarket Review Regulatory Initiatives

Type of Activity	FY 2018 Accomplishments
Participation in other Inter-Center and Agency-wide working groups to clarify postmarket review issues related to combination products and guidance development	OCP participated in the following postmarket review activities: • Continued to chair working groups relating to PMSR for combination products, focusing on the development of a draft guidance regarding the final rule and efforts to implement that rule, including the development of internal standard operating procedures • Continued to chair a working group and leadership body to support implementation of the final rule on CGMPs for combination products, including inspectional activities and expectations relating to premarket submissions • Continued to work with Centers on track-and-trace regimes with respect to combination products, including Unique Device Identifier, numeric drug coding, and serialized numeric identifiers • Continued to co-chair a committee on combination products of the Association for the Advancement of Medical Instrumentation that continued work on a technical information report on risk management for combination products

Additional Activities and Accomplishments

Information Technology

OCP continued to coordinate and participate in cross-cutting information technology (IT) initiatives to enhance infrastructure and update guidances as appropriate to improve the efficiency, consistency, and reliability of information systems and communications within and among medical product Centers and between FDA and combination product sponsors and other interested stakeholders. OCP led efforts to improve staff access to IT systems needed for the review of combination products, to update PMSR Agency IT systems, and to develop new guidances on how stakeholders should engage with FDA in light of the final rule on PMSR for combination products.

External Outreach

OCP conducted outreach on FDA's assignment and regulation of combination products by meeting and otherwise engaging with trade associations and coalitions (e.g., Combination Products Coalition, Advanced Medical Technology Association, Association for Advancement of Medical Instrumentation, Pharmaceutical Research and Manufacturers of America, and BIO) representing the drug, device, biological product, and combination product industries, as well as by participating in industry conferences. Discussions and presentations focused on a wide range of topics, including emerging issues in combination product regulation, the role of OCP, policies and guidance documents under consideration, rulemakings, specific categories of combination products, particular regulatory issues, and stakeholder priorities for further action. Examples of FY 2018 outreach activities are included in the table below.

Type of Activity	FY 2018 Accomplishments
Conducting presentations and outreach activities	OCP participated in a number of outreach activities. The following are examples of venues/events for which OCP provided presentations and/or educational outreach: • Association for the Advancement of Medical Instrumentation/FDA International Conference on Medical Device Standards and Regulation, 2018 • 2018 Drug Information Association Annual Conference on Combination Products • Parenteral Drug Association/FDA Joint Regulatory Conference 2018 • Drug Information Association Annual Meeting 2018 • Xavier University Health Combination Products Summit (September 2018) • 2018 Drug Information Association Complex Drug-Device Generic Combination Products Conference • Medical Device Manufacturers Association 2018 FDA Forum

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Appendix

Appendix A: FY 2017 Updated Performance Detail

The table below reflects the 566 original applications received in FY 2017 initially classified into one of nine categories of combination products.

Workload by Combination Product Category Number

Application Type	1	2	3	4	5	6	7	8	9	Totals
Original NDAs	7	23	0	2	0	0	0	0	2	**34**
Original BLAs	0	0	8	0	0	1	0	0	0	**9**
Original PMAs	0	0	0	5	1	0	2	0	2	**10**
Original 510(k)s	6	0	2	58	3	0	7	3	14	**93**
Original INDs	33	46	23	12	14	66	0	92	11	**297**
Original IDEs	6	0	0	27	0	0	4	3	7	**47**
Original HDEs	0	0	0	0	0	0	0	0	0	**0**
ANDAs	27	40	0	0	0	0	0	0	1	**68**
Biosimilar BLAs	6	0	1	0	0	0	0	0	0	**7**
De Novos	1	0	0	0	0	0	0	0	0	**1**
Total	**86**	**109**	**34**	**104**	**18**	**67**	**13**	**98**	**37**	**566**

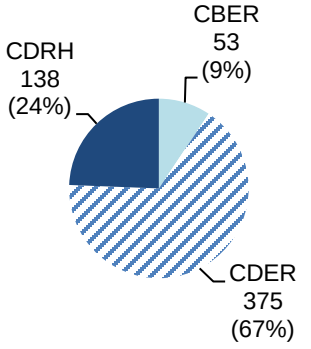
Combination Product Category Key:

- **1 = convenience kit or co-package**
- **2 = pre-filled drug delivery device/system**
- **3 = pre-filled biologic delivery device/system**
- **4 = device coated/impregnated/otherwise combined with drug**
- **5 = device coated or otherwise combined with biologic**
- **6 = drug/biologic combination**
- **7 = separate products requiring mutually conforming labeling**
- **8 = possible combination based on mutually conforming labeling of separate products**
- **9 = other type of combination product**

Workload by Center Lead

The pie chart to the right shows the number and percentage of combination product applications received in FY 2017 by Center lead, as of September 30, 2018.

Combination Product Applications (n = 566)



Department of Health and Human Services
Food and Drug Administration

This report was prepared by FDA's Office of Combination Products in collaboration with the Office of Planning and Evaluation, the Center for Biologics Evaluation and Research, the Center for Drug Evaluation and Research, and the Center for Devices and Radiological Health. For information on obtaining additional copies, contact:

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