Report to Congress

Premarket Approval of Pediatric Uses of Devices

FY 2021

Submitted Pursuant to
Section 515A of the Federal Food, Drug, and Cosmetic Act

Executive Summary

Section 515A(a)(3) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) requires the Food and Drug Administration (FDA or Agency) to submit an annual report to Congress on the premarket approvals for devices labeled[1] for pediatric use, among other requirements. This report also includes information on the premarket approval of devices where there is a pediatric subpopulation[2] that suffers from the disease or condition that the device is intended to treat, diagnose, or cure. To meet this requirement, this report includes statistical data on these approvals, which were approved by FDA's Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER) during fiscal year (FY) 2021 (i.e., October 1, 2020, through September 30, 2021). This is the eleventh such report submitted by FDA to Congress.

As noted in this report, during FY 2021, FDA approved 59 premarket device applications. In particular, in FY 2021,

- FDA approved 56 original premarket approval (PMA) applications and panel-track supplements for devices and three humanitarian device exemption (HDE) applications for devices, totalling 59 device approvals.

- Of those 59 device approvals, FDA approved 14 PMA applications and one HDE application (or 15/59, 25 percent) for devices that were indicated for use in a pediatric population or subpopulation.[3,4]

- Of the remaining 44 device approvals, 42 PMA applications and two HDE applications were for devices that were indicated for use in adults. Of these 44 device approvals, the 42 PMA applications and two HDE applications (or 100 percent) were for devices that were determined to treat, diagnose, or cure a disease or condition for which there is a pediatric subpopulation that also suffers from such a disease or condition.[5]

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[1] See section 201(k) of the FD&C Act for the definition of *label*; see 21 CFR 1.3 for the definition of *labeling*.

[2] Section 520(m)(6)(E)(i) of the FD&C Act (and 21 CFR 814.3(s)) defines *pediatric patients* as patients 21 years of age or younger at the time of their diagnosis or treatment. Section 515A(c) of the FD&C Act defines, by reference to section 520(m)(6)(E)(ii) of the FD&C Act, a *pediatric subpopulation* as one of the following subpopulations: neonates, infants, children, and adolescents.

[3] More information about these FY 2021 pediatric device approvals, including these devices' review times and the pediatric population for which they were indicated at the time of their initial approval, appears in Appendix A of this report.

[4] See section 515A(a)(3)(C) and 515A(a)(3)(D) of the FD&C Act.

[5] See section 515A(a)(3)(A) of the FD&C Act.

- For one of the above-mentioned 14 PMA applications approved for a device indicated for use in a pediatric population or subpopulation, FDA relied on data from adults to support its determination that the devices were reasonably assured to be safe and effective in pediatric patients.[6]

- For no device approvals, FDA relied on data from one pediatric subpopulation to support a determination of a reasonable assurance of safety and effectiveness in another pediatric subpopulation.[7]

- From the 56 PMA application approvals, no PMA application for a device that was indicated solely for a pediatric population was exempted from user fees.[8]

- The median time to review the 14 PMA applications for devices that were indicated for use in a pediatric population or subpopulation was 180 FDA Days[9] and 323 Total Elapsed Days.

- The median time to review the one HDE application for a device that was indicated for use in a pediatric population or subpopulation was 148 FDA Days and 597 Total Elapsed Days.[10]

- Based on a review of the data available to FDA, such as the PMA and HDE periodic reports[11] received in FY 2021, approved pediatric labeling could confer a benefit to pediatric patients for 33 of the 44 approved devices that were not labeled for such use.[12]

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[6] See section 515A(a)(3)(G) of the FD&C Act.

[7] See section 515A(a)(3)(H) of the FD&C Act.

[8] See section 515A(a)(3)(E) of the FD&C Act. Please note that under section 738(a)(2)(B)(i) of the FD&C Act, HDE applications are exempt from user fees.

[9] FDA's Medical Device User Fee Amendments of 2017 (MDUFA IV) commitment letter defined *FDA Days* as calendar days when a submission is considered to be under review at the Agency for submissions that have been filed. Tracking of FDA Days begins on the date of the receipt of the submission or the amendment to the submission that enables the submission to be filed. See FDA's final guidance document entitled *FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals* (October 2017), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-actions-premarket-approval-applications-pmas-effect-fda-review-clock-and-goals.

[10] See section 515A(a)(3)(F) of the FD&C Act.

[11] PMA applications are subject to any periodic postmarket reporting requirements imposed in the PMA approval order (see 21 CFR 814.82(a) and 21 CFR 814.84(b)). Similarly, under 21 CFR 814.126(b), "the holder of an approved HDE" application must submit a periodic report in accordance with the HDE approval order.

[12] Section 515A(a)(3)(B) of the FD&C Act.

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I. Introduction

The Food and Drug Administration Amendments Act of 2007 (FDAAA) amended section 515A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360e-1).[1] Section 515A(a)(2) of the FD&C Act, as added by FDAAA, requires persons who are submitting a certain device application and seeking approval for that application to include in their application, if readily available, (1) a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure and (2) the number of affected pediatric patients.[2] Section 515A(a)(3) of the FD&C Act, as added by FDAAA, requires the Food and Drug Administration (FDA or Agency) to submit an annual report to Congress on the premarket approvals for devices labeled for pediatric use or for which there is a pediatric subpopulation that suffers from the disease or condition that the device is intended to treat, diagnose, or cure.[3] On August 18, 2017, section 515A(a)(3) of the FD&C Act was amended by the FDA Reauthorization Act of 2017 (FDARA) to now also require, among other things, FDA to provide, in that annual report, information related to the number of devices approved with a pediatric indication.[4] Specifically, section 515A(a)(3) of the FD&C Act, as amended, states that,

> *Not later than 18 months after the date of the enactment of this section and annually thereafter, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report that includes—*
>
> *(A) the number of devices approved in the year preceding the year in which the report is submitted, for which there is a pediatric subpopulation that suffers from the disease or condition the device is intended to treat, diagnose, or cure;*
>
> *(B) any information, based on a review of data available to the Secretary, regarding devices used in pediatric patients but not labeled for such use for which the Secretary determines that approved pediatric labeling could confer a benefit to pediatric patients;*

[1] Public Law 110-85, 121 Stat. 859.

[2] Section 520(m)(6)(E)(i) of the FD&C Act (and 21 CFR 814.3(s)) defines *pediatric patients* as patients 21 years of age or younger at the time of their diagnosis or treatment. Section 515A(c) of the FD&C Act defines, by reference to section 520(m)(6)(E)(ii) of the FD&C Act, a *pediatric subpopulation* as one of the following subpopulations: neonates, infants, children, and adolescents.

[3] See section 201(k) of the FD&C Act for the definition of *label*; see 21 CFR 1.3 for the definition of *labeling*.

[4] Public Law 115-52, 131 Stat. 1037.

(C) the number of pediatric devices that receive a humanitarian use exemption under section 520(m) [of the FD&C Act];

(D) the number of devices approved in the year preceding the year in which the report is submitted, labeled for use in pediatric patients;

(E) the number of pediatric devices approved in the year preceding the year in which the report is submitted, exempted from a fee pursuant to section 738(a)(2)(B)(v) [of the FD&C Act];

(F) the review time for each device described in subparagraphs (A), (C), (D), and (E);

(G) the number of devices for which the Secretary relied on data with respect to adults to support a determination of a reasonable assurance of safety and effectiveness in pediatric patients; and

(H) the number of devices for which the Secretary relied on data from one pediatric subpopulation to support a determination of a reasonable assurance of safety and effectiveness in another pediatric subpopulation.

For the items described in this paragraph, such report shall disaggregate the number of devices by pediatric subpopulation.

This is the eleventh report of FDA submitted to Congress pursuant to section 515A(a)(3) of the FD&C Act since FDAAA's enactment. This fiscal year (FY) 2021 report, as required under section 515A of the FD&C Act, includes information and accounting on FDA's FY 2021 premarket approvals for devices that were, among other requirements, indicated for use in pediatric patients or that are intended to treat, diagnose, or cure diseases from which pediatric patients suffer.[5] This report also includes background information regarding section 515A of the FD&C Act and FDA's implementation of that provision. Information submitted under section 515A(a) of the FD&C Act assisted in the development of this report.

[5] The phrase *indications for use*, as defined in 21 CFR 814.20(b)(3)(i), describes the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended.

II. Background

Section 515A of the FD&C Act, and other provisions in FDAAA and FDARA, are intended to encourage the development of devices for use in pediatric patients. For example, the Congressional House Report for FDAAA described the need for the legislation as follows:[6]

> *Pediatric medical devices are used to treat or diagnose diseases and conditions in patients from birth through age 21 years. Some products are designed specifically for children, while others are borrowed from adult applications or produced for more general use.*
>
> *Children have specific medical needs that must be considered when medical and surgical devices are prescribed. Devices that have not been studied for use in children may not accommodate the unique needs of children, such as allowing for expandable growth and accommodating their active lifestyles and differing metabolism.*

Section 520(m)(6)(E)(i) of the FD&C Act and 21 CFR 814.3(s) define *pediatric patients*, for device approval purposes, as patients who are 21 years of age or younger (i.e., from birth through the day prior to their 22nd birthday) at the time of diagnosis or treatment. Additionally, a *pediatric subpopulation* is defined by section 520(m)(6)(E)(ii) of the FD&C Act (and adopted by reference in section 515A(c) of the FD&C Act) as one of the following subpopulations: neonates, infants, children, and adolescents. Generally, FDA views the approximate age ranges for these pediatric subpopulations as follows:[7]

- Neonates (birth until 1 month of age);
- Infants (greater than 1 month of age until 2 years of age);
- Children (greater than 2 years of age until 12 years of age); and
- Adolescents (greater than 12 years of age through 21 years of age (i.e., up to but not including the 22nd birthday)).

On January 10, 2014, FDA issued a final rule in the *Federal Register*[8] that amended 21 CFR part 814's regulations on the premarket approval of devices to now require persons who are submitting a certain device application and seeking approval for that application to include in their application, if readily available, (1) a description of any

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[6] House Committee on Energy and Commerce, "Food and Drug Administration Amendments Act of 2007," H.R.100-225, 110th Congress, 1st Session, on page 8.

[7] See FDA's final guidance document entitled *Premarket Assessment of Pediatric Medical Devices*, available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-assessment-pediatric-medical-devices.

[8] *Pediatric Uses of Devices; Requirement for Submission of Information on Pediatric Subpopulations That Suffer from a Disease or Condition That a Device Is Intended To Treat, Diagnose, or Cure* (79 FR 1735 at 1735-1741) (January 10, 2014).

pediatric subpopulations that suffer from the disease or condition that a device is intended to treat, diagnose, or cure and (2) the number of affected pediatric patients. These regulations reflect requirements under section 515A of the FD&C Act, as amended by FDAAA and FDARA.

On March 24, 2014, FDA issued a final guidance document entitled *Premarket Assessment of Pediatric Medical Devices*, which provides information for applicants regarding the pediatric information requirement mandated under section 515A of the FD&C Act and its implementing regulations.[9] On May 1, 2014, FDA issued a final guidance document entitled *Providing Information about Pediatric Uses of Medical Devices*.[10]

Later, on June 21, 2016, FDA issued a final guidance document entitled *Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices*.[11] This guidance document seeks to provide clarity and predictability for device sponsors and to ensure consistency within FDA regarding the specific criteria that should be considered when deciding whether leveraging existing clinical data to support pediatric device indications in premarket approval (PMA) applications, humanitarian device exemption (HDE) applications, and De Novo requests is appropriate and, if so, to what extent.

III. Summary of the Information Required by Section 515A(a)(3) of the FD&C Act

Consistent with section 515A of the FD&C Act, this report provides data on premarket device approvals that were approved by FDA's Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER) during FY 2021. In particular, in FY 2021,

- FDA approved 56 original premarket approval (PMA) applications and panel-track supplements for devices and three humanitarian device exemption (HDE) applications for devices, totalling 59 device approvals.

[9] This final guidance document, published in March 2014, is available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-assessment-pediatric-medical-devices.

[10] This final guidance document, published in May 2014, is available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-information-about-pediatric-uses-medical-devices.

[11] This final guidance document, published in June 2016, is available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/leveraging-existing-clinical-data-extrapolation-pediatric-uses-medical-devices.

- Of those 59 device approvals, FDA approved 14 PMA applications and one HDE application (or 15/59, 25 percent) for devices that were indicated for use in a pediatric population or subpopulation.[12,13]

- Of the remaining 44 device approvals, 42 PMA applications and two HDE applications were for devices that were indicated for use in adults. Of these 44 device approvals, the 42 PMA applications and two HDE applications (or 100 percent) were for devices that were determined to treat, diagnose, or cure a disease or condition for which there is a pediatric subpopulation that also suffers from such a disease or condition.[14]

- For one of the above-mentioned 14 PMA applications approved for a device indicated for use in a pediatric population or subpopulation, FDA relied on data from adults to support its determination that the devices were reasonably assured to be safe and effective in pediatric patients.[15]

- For no device approvals, FDA relied on data from one pediatric subpopulation to support a determination of a reasonable assurance of safety and effectiveness in another pediatric subpopulation.[16]

- From the 56 PMA application approvals, no PMA application for a device that was indicated solely for a pediatric population was exempted from user fees.[17]

- The median time to review the 14 PMA applications for devices that were indicated for use in a pediatric population or subpopulation was 180 FDA Days[18] and 323 Total Elapsed Days.

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[12] More information about these FY 2021 pediatric device approvals, including these devices' review times and the pediatric population for which they were indicated at the time of their initial approval, appears in Appendix A of this report.

[13] See section 515A(a)(3)(C) and 515A(a)(3)(D) of the FD&C Act.

[14] See section 515A(a)(3)(A) of the FD&C Act.

[15] See section 515A(a)(3)(G) of the FD&C Act.

[16] See section 515A(a)(3)(H) of the FD&C Act.

[17] See section 515A(a)(3)(E) of the FD&C Act. Please note that under section 738(a)(2)(B)(i) of the FD&C Act, HDE applications are exempt from user fees.

[18] FDA's Medical Device User Fee Amendments of 2017 (MDUFA IV) commitment letter defined *FDA Days* as calendar days when a submission is considered to be under review at the Agency for submissions that have been filed. Tracking of FDA Days begins on the date of the receipt of the submission or the amendment to the submission that enables the submission to be filed. See FDA's final guidance document entitled *FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals* (October 2017), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-actions-premarket-approval-applications-pmas-effect-fda-review-clock-and-goals.

- The median time to review the one HDE application for a device that was indicated for use in a pediatric population or subpopulation was 148 FDA Days and 597 Total Elapsed Days.[19]

- Based on a review of the data available to FDA, such as the PMA and HDE periodic reports[20] received in FY 2021, approved pediatric labeling could confer a benefit to pediatric patients for 33 of the 44 approved devices that were not labeled for such use.[21]

From FY 2008 to FY 2021, 703 PMA and HDE applications have been approved by CDRH and CBER combined, with an average of 50.21 device approvals per year.[22] Of these device approvals, 185[23] were approved with an indication for use in a pediatric population or subpopulation at the initial time of the marketing authorization. Since FY 2008, as shown in Figure 1A, there has generally been an increase in PMA and HDE application approvals for devices with non-pediatric indications reviewed by CDRH and CBER.[24] From FY 2008 to FY 2021, the greatest number (i.e., 73) of PMA or HDE application approvals was in FY 2016, and the lowest number of PMA or HDE application approvals (i.e., 21) was in FY 2010.[25]

Figure 1A demonstrates the PMA and HDE application approvals, from FY 2008 to FY 2021, with pediatric indications (blue) and non-pediatric (red) indications of devices reviewed by CDRH and CBER.

[19] See section 515A(a)(3)(F) of the FD&C Act.

[20] PMA applications are subject to any periodic postmarket reporting requirements imposed in the PMA approval order (see 21 CFR 814.82(a) and 21 CFR 814.84(b)). Similarly, under 21 CFR 814.126(b), "the holder of an approved HDE" application must submit a periodic report in accordance with the HDE approval order.

[21] Section 515A(a)(3)(B) of the FD&C Act.

[22] See Table 1 in Appendix B.

[23] This number was obtained by totaling the PMA and HDE application approvals for devices indicated for pediatric patients from FY 2008 to FY 2021; see Table 1 in Appendix B.

[24] See also Table 1 in Appendix B.

[25] These numbers represent the combined PMA or HDE application approvals by CDRH and CBER in FY 2017 and in FY 2010.

Figure 1A. PMA and HDE Application Approvals from FY 2008 to FY 2021 for Devices with Pediatric Indications and Non-Pediatric Indications.

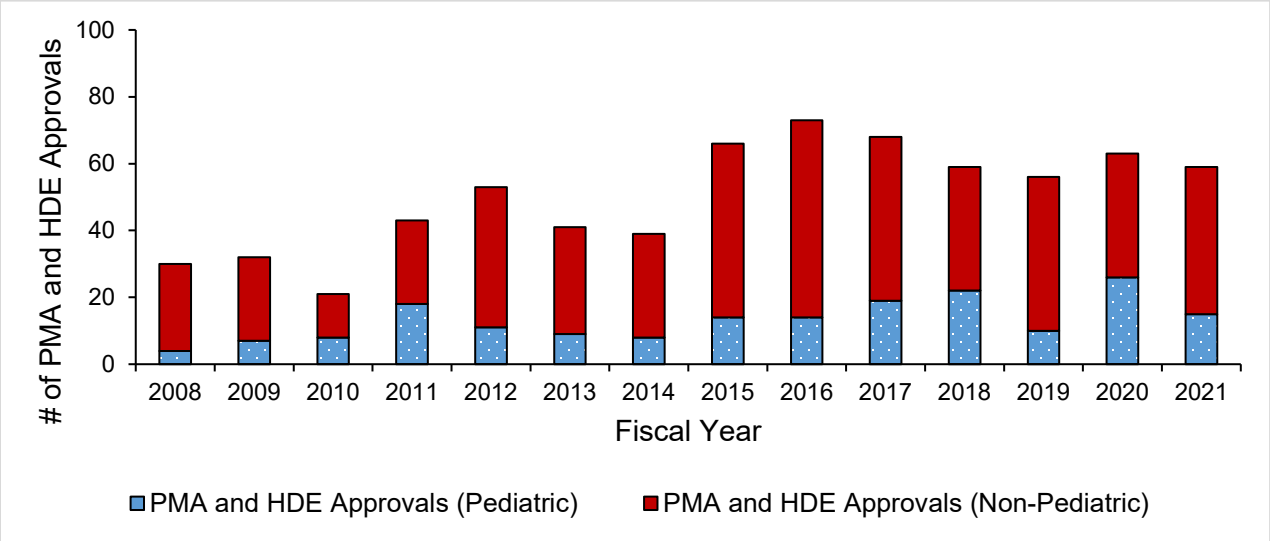
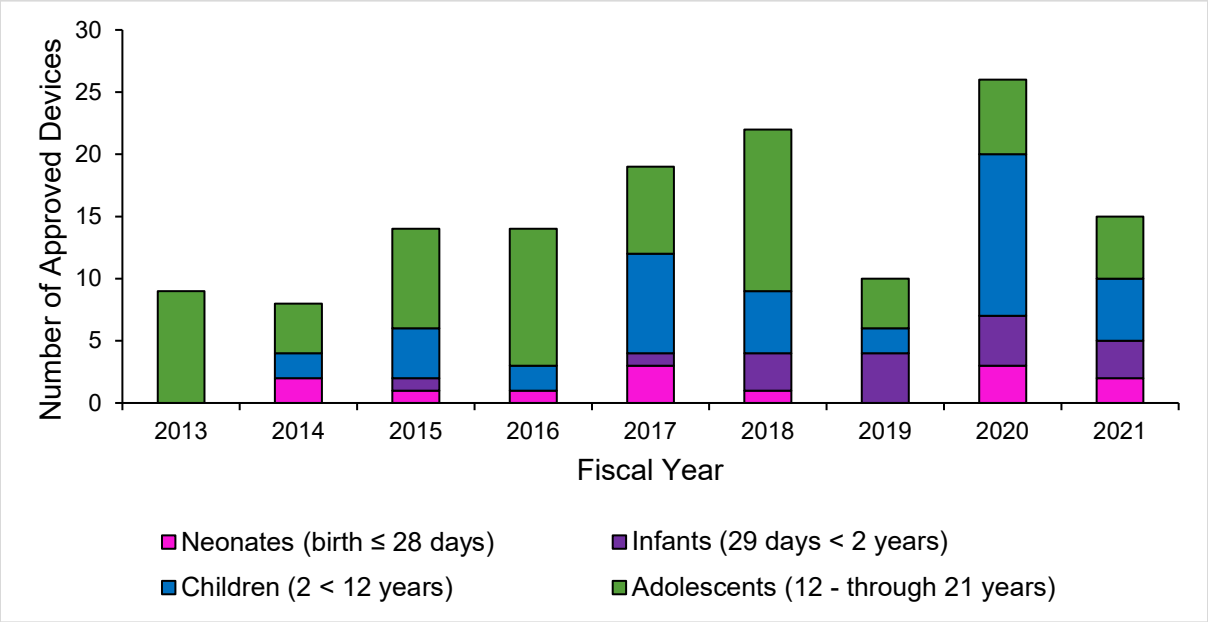


Figure 1B shows, by the age of each pediatric subpopulation, the PMA and HDE application approvals for devices indicated for these subpopulations; these devices were reviewed by CDRH and CBER from FY 2008 to FY 2021. The PMA and HDE application approvals are categorized by the youngest age for which there was an indication for use. In rare cases, a device may have only been used in a specific subpopulation.[26]

[26] See also Table 2 of Appendix B for a more detailed breakdown, by the age of each pediatric subpopulation, of PMA and HDE application approvals for devices indicated for these subpopulations; these devices were reviewed by CDRH and CBER from FY 2013 to FY 2021.

Figure 1B. PMA and HDE Application Approvals by the Youngest Suggested Pediatric Subpopulation from FY 2013 to FY 2021.



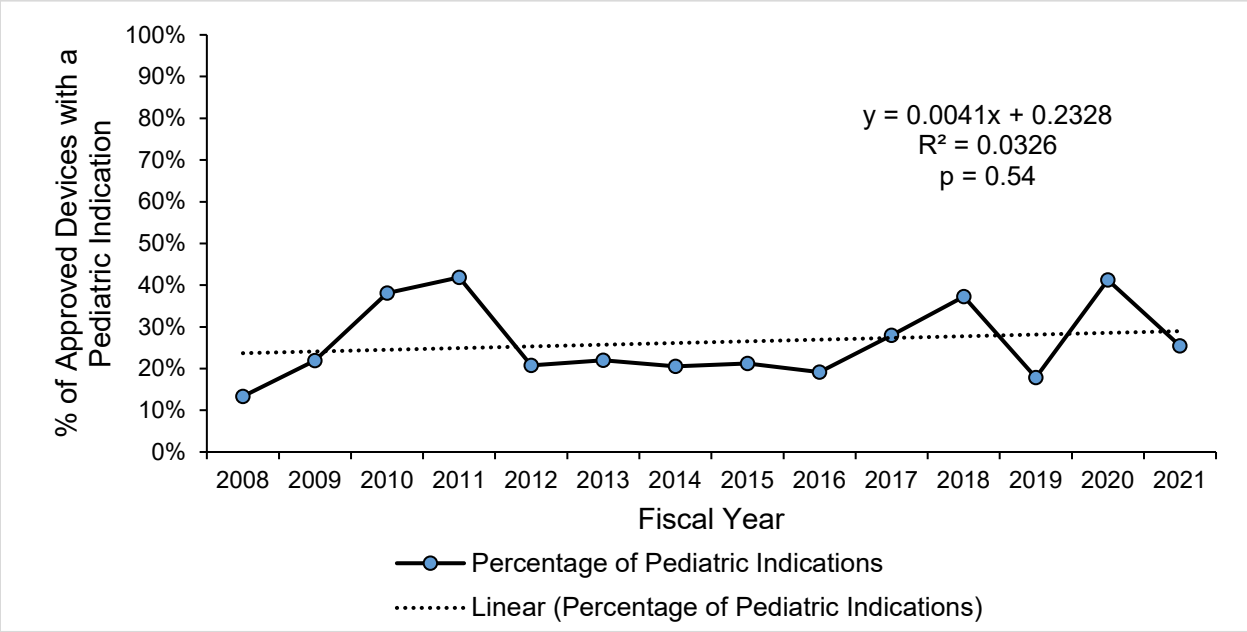
Appendix A includes a detailed summary of each of the FY 2021 PMA and HDE application approvals for devices that were indicated for use in a pediatric population or pediatric subpopulation.

Since FY 2008, the largest number (i.e., 26) of PMA and HDE application approvals by CDRH and CBER for devices with an indication that included a pediatric population or subpopulation was in FY 2020.[27] As shown in Figure 2, the largest percentage of PMA and HDE application approvals (i.e., 42%) for devices with an indication that included a pediatric population or subpopulation was in FY 2011.[28]

[27] See Table 1 in Appendix B.

[28] See also Table 1 in Appendix B.

Figure 2. Percentage of PMA and HDE Applications Indicated for Use Within the Pediatric Population (Mean = 26% (185/703)).



On average for the last 14 fiscal years, only 26 percent of the total PMA and HDE application approvals in each fiscal year have been for a device with an indication that includes a pediatric population or subpopulation. The percentage of pediatric indications increased between FY 2008 and FY 2011, but starting in FY 2012, the percentage of PMA and HDE application approvals for devices with pediatric indications declined to 21 percent, only rising again to 28 percent in FY 2017 and 37 percent in FY 2018. The percentage of pediatric indications decreased to 18 percent in FY 2019, increased to 41 percent in FY 2020, and decreased to 25 percent in FY 2021.

IV. Conclusion

Since FY 2008, FDA has submitted reports to Congress providing information concerning FDA's annual premarket approvals of devices that were indicated for pediatric use. This eleventh such report, submitted under section 515A(a)(3) of the FD&C Act, includes data on the devices approved by CDRH and CBER, in FY 2021, that had an indication for use in the pediatric population or its subpopulations. Based on the information summarized in this report, there have been limited changes since FY 2008 in FDA's PMA or HDE application approvals for devices indicated for use in a pediatric population or subpopulation. Since the passage of FDAAA, the number of devices approved for the pediatric population has generally increased; however, the

percentage of devices indicated for use in the pediatric population, out of the total number of devices approved each fiscal year, has remained relatively constant.[29]

FDA is committed to continue working with the pediatrics community to support the advancement, development, and availability of devices for use in the pediatric population. FDA takes seriously its responsibility to ensure that the devices on the market, including those for the pediatric population, demonstrate a reasonable assurance of safety and effectiveness. For the latest information on FDA's efforts related to pediatric devices, refer to FDA's Pediatric Medical Devices web page.[30]

[29] See Table 1 in Appendix B.

[30] https://www.fda.gov/medical-devices/products-and-medical-procedures/pediatric-medical-devices.

Appendix A: Approvals of, and Review Times for, PMA and HDE Applications for Devices Indicated for Use in Pediatric Populations in FY 2021

All devices included in this appendix are approved and labeled for use in a pediatric population.[31] Below, CDRH and CBER include information on the youngest suggested pediatric subpopulations for the listed devices, as designated under section 515A(c) of the FD&C Act, based on these Centers' analyses of publicly available information, such as the device's Summary of Safety and Effectiveness Data, Summary of Safety and Probable Benefit, and labeling, as well as additional factors, including but not limited to average pediatric anthropometric measurements and device dimensions.

VioOne™ HIV Profile™ Supplemental Assay

The VioOne™ HIV Profile™ Supplemental Assay is an enzyme-linked immunosorbent assay (ELISA) for confirmation and differentiation of individual antibodies directed to Human Immunodeficiency Virus Type 1 (HIV-1 Group M & Group O) and Type 2 (HIV-2) in human serum or plasma. The VioOne™ HIV Profile™ Supplemental Assay is intended as an aid in the diagnosis of infection with HIV-1 and/or HIV-2. It is intended as an additional, more specific test to confirm the presence of antibodies to HIV-1 and HIV-2 for specimens repeatedly reactive in diagnostic procedures, including pediatric patients (ages 2-20).

This device is not intended for use as a first line diagnostic test or for screening donors of blood, blood products, or human cells or tissues or cellular and tissue-based products (HCT/Ps).

Manufacturer	Avioq, Inc.
Number	BP180279
Filing Date	11/16/2018
Approval Date	10/19/2020
Youngest Suggested Pediatric Subpopulation:	Child
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	350
Total Elapsed Days	703

[31] Additional information pertaining to these devices can be found in the Summary of Safety and Effectiveness Data or the Summary of Safety and Probable Benefit by searching the PMA or HDE number, respectively. The PMA and HDE application approvals are listed in chronological order from the earliest approval date. In addition, please consult FDA's Medical Device Databases web (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases) for more information.

FoundationOne®CDx (F1CDx)

FoundationOne®CDx (F1CDx) is a qualitative next generation sequencing based *in vitro* diagnostic test that uses targeted high throughput hybridization-based capture technology for detection of substitutions, insertion and deletion alterations (indels) and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling. Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms. Genomic findings other than those listed in Table 1 are not prescriptive or conclusive for labeled use of any specific therapeutic product.

Table 1. Companion diagnostic indications

Indication	Biomarker	Therapy
Non-small cell lung cancer (NSCLC)	EGFR exon 19 deletions and EGFR exon 21 L858R alterations	Gilotrif® (afatinib), Iressa® (gefitinib), Tagrisso® (osimertinib), or Tarceva® (erlotinib)
	EGFR exon 20 T790M alterations	Tagrisso® (osimertinib)
	ALK rearrangements	Alecensa® (alectinib), Xalkori® (crizotinib), or Zykadia® (ceritinib)
	BRAF V600E	Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib)
	MET single nucleotide variants (SNVs) and indels that lead to MET exon 14 skipping	Tabrecta™ (capmatinib)
Melanoma	BRAF V600E	Tafinlar® (dabrafenib) or Zelboraf® (vemurafenib)
	BRAF V600E and V600K	Mekinist® (trametinib) or Cotellic® (cobimetinib) in combination with Zelboraf® (vemurafenib)
Breast cancer	ERBB2 (HER2) amplification	Herceptin® (trastuzumab), Kadcyla® (ado-trastuzumabemtansine), or Perjeta® (pertuzumab)
	PIK3CA C420R, E542K, E545A, E545D [1635G>T only], E545G,	Piqray® (alpelisib)

	E545K, Q546E, Q546R, H1047L, H1047R, and H1047Y alterations	
Colorectal cancer	KRAS wild-type (absence of mutations in codons 12 and 13)	Erbitux® (cetuximab)
	KRAS wild-type (absence of mutations in exons 2, 3, and 4) and NRAS wild-type (absence of mutations in exons 2, 3, and 4)	Vectibix® (panitumumab)
Ovarian cancer	BRCA1/2 alterations	Lynparza® (olaparib) or Rubraca® (rucaparib)
Cholangiocarcinoma	FGFR2 fusions and select rearrangements	Pemazyre™ (pemigatinib)
Prostate cancer	Homologous Recombination Repair (HRR) gene (BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D and RAD54L) alterations	Lynparza® (olaparib)
Solid tumors	TMB > 10 mutations per megabase	Keytruda® (pembrolizumab)
	NTRK1/2/3 fusions	Vitrakvi® (larotrectinib)

The test is also used for detection of genomic loss of heterozygosity (LOH) from formalin-fixed, paraffin-embedded (FFPE) ovarian tumor tissue. Positive homologous recombination deficiency (HRD) status (F1CDx HRD defined as tBRCA-positive and/or LOH high) in ovarian cancer patients is associated with improved progression-free survival (PFS) from Rubraca (rucaparib) maintenance therapy in accordance with the Rubraca product label.

The F1CDx assay will be performed at Foundation Medicine, Inc. sites located in Cambridge, MA and Morrisville, NC.

Manufacturer	Foundation Medicine, Inc.
Number	P170019/S017
Filing Date	1/31/2020
Approval Date	10/23/2020
Youngest Suggested Pediatric Subpopulation:	Infant
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	180
Total Elapsed Days	266

LIAISON® XL MUREX HIV Ab/Ag HT and LIAISON® XL MUREX Control HIV Ab/Ag HT

The LIAISON® XL MUREX HIV Ab/Ag HT is an *in vitro* chemiluminescent immunoassay for the simultaneous qualitative detection of HIV p24 antigen and antibodies to HIV-1 (Groups M and O) and HIV-2 in human serum (without or with gel-

SST) or plasma (lithium and sodium heparin, sodium citrate, and potassium EDTA), on the LIAISON® XL Analyzer. It is intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection in pediatric subjects (2-21 years) and in pregnant women.

The assay cannot distinguish between the detection of HIV p24 antigen and HIV-1/HIV-2 antibodies.

The LIAISON® XL MUREX HIV Ab/Ag HT assay is not intended for screening donors of blood or blood products, or human cells or tissues or cellular and tissue-based products (HCT/Ps), or organ donors for HIV.

The LIAISON® XL MUREX Control HIV Ab/Ag HT is intended for use as assayed quality control samples to monitor the performance of the LIAISON® XL HIV Ab/Ag HT assay. The performance characteristics of LIAISON® controls have not been established for any other assays or instrument platforms different from LIAISON® XL.

Manufacturer	DiaSorin, Inc.
Number	BP190437
Filing Date	12/20/2019
Approval Date	11/25/2020
Youngest Suggested Pediatric Subpopulation:	Child
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	175
Total Elapsed Days	341

Sonalleve MR-HIFU

Sonalleve MR-HIFU is intended to be used for the treatment of osteoid osteomas in the extremities.

Manufacturer	Profound Medical Inc.
Number	H190003
Filing Date	4/10/2019
Approval Date	11/27/2020
Youngest Suggested Pediatric Subpopulation:	Infant
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	148
Total Elapsed Days	597

GORE® EXCLUDER® Conformable AAA Endoprosthesis

The GORE® EXCLUDER® Conformable AAA Endoprosthesis is intended to exclude the aneurysm from the blood circulation in patients diagnosed with infrarenal abdominal aortic aneurysm (AAA) disease and who have appropriate anatomy as described below:

- Adequate iliac / femoral access

- Infrarenal aortic neck treatment diameter range of 16–32 mm and a minimum aortic neck length of 15 mm
- Proximal aortic neck angulation is ≤60˚
- Iliac artery treatment diameter range of 8–25 mm and iliac distal vessel seal zone length of at least 10 mm

Manufacturer	W.L. Gore and Associates, Inc
Number	P200030
Filing Date	6/29/2020
Approval Date	12/22/2020
Youngest Suggested Pediatric Subpopulation:	Adolescent
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	176
Total Elapsed Days	176

AED Battery Exchange (Models 9146-ABE, G5-ABE, 5070-ABE, FR3-ABE)

The automated external defibrillator (AED) battery supplies power to an AED as required during self maintenance, automated diagnoses, and defibrillation. The 9146-ABE is indicated for use with the Cardiac Science Powerheart G3, models 9390A, 9390E, 9300A, and 9300E. The G5-ABE is indicated for use with the Cardiac Science Powerheart G5, models G5A-80A, G5A-80C, G5S-80A, and G5S-80C. The 5070-ABE is indicated for use with the Philips HeartStart OnSite/Home, models M5066A, M5068A, and the FRx, model 861304. The FR3-ABE is indicated for use with the Philips HeartStart FR3, models 861388 and 861389.

Manufacturer	AED Battery Exchange, LLC
Number	P190013
Filing Date	4/03/2020
Approval Date	2/2/2021
Youngest Suggested Pediatric Subpopulation:	Neonate
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	180
Total Elapsed Days	305

Elecsys HIV Combi PT

Elecsys HIV combi PT is an immunoassay for the *in vitro* qualitative determination of HIV-1 p24 antigen and antibodies to HIV-1 (HIV-1 groups M and O) and HIV-2 in human serum and plasma. Elecsys HIV combi PT is intended to be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1/HIV-2 infection in subjects greater than 2 years of age and in pregnant women.

The Elecsys HIV combi PT assay is not intended for the screening of blood or plasma donors.

Manufacturer	Roche Diagnostics Operations, Inc.

Number	BP160050/S013
Filing Date	9/25/2020
Approval Date	2/19/2021
Youngest Suggested Pediatric Subpopulation:	Child
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	147
Total Elapsed Days	147

Elecsys Anti-HBs II, PreciControl Anti-HBs, and Anti-HBs CalCheck

Elecsys Anti-HBs II:
Immunoassay for the *in vitro* quantitative determination of total antibodies to the hepatitis B surface antigen (HBsAg) in human adult, pregnant women, and pediatric (ages 2 to 21 years) serum and plasma (K2-EDTA and K3-EDTA). Assay results may be used as an aid in the determination of susceptibilty to hepatitis B virus (HBV) infection for individuals prior to or following HBV vaccination; or where vaccination status is unknown. Assay results may be used with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. A reactive assay result will allow a differential diagnosis in individuals displaying signs and symptons of hepatitis in whom etiology is unknown. The detection of anti-HBs is indicative of laboratory diagnosis of seroconversion from hepatitis B virus (HBV) infection or from vaccination. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 601 immunoassay analyzer.

PreciControl Anti-HBs:
PreciControl Anti-HBs is used for quality control of the Elecsys Anti-HBs immunoassay on the Elecsys and cobas e immunoassay analyzers and of the Elecsys Anti-HBs II immunoassay on the cobas e 601 immunoassay analyzer. The performance of PreciControl Anti-HBs has not been established with any other anti-HBs assay.

Anti-HBs CalCheck:
Anti-HBs CalCheck is an assayed control material for use in the verification of the calibration established by the Elecsys Anti-Hbs immunoassay on the cobas e immunoassay analyzers and by the Elecsys Anti-Hbs II immunoassay on the cobas e 601 immunoassay analyzer.

Manufacturer	Roche Diagnostics
Number	P190034
Filing Date	12/30/2019
Approval Date	2/23/2021
Youngest Suggested Pediatric Subpopulation:	Child
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	164
Total Elapsed Days	421

Harmony Transcatheter Pulmonary Valve (TPV) System

The Harmony Transcatheter Pulmonary Valve (TPV) System is indicated for use in the management of pediatric and adult patients with severe pulmonary regurgitation (i.e., severe pulmonary regurgitation as determined by echocardiography and/or pulmonary regurgitant fraction ≥30% as determined by cardiac magnetic resonance imaging) who have a native or surgically-repaired right ventricular outflow tract and are clinically indicated for surgical pulmonary valve replacement.

Manufacturer	Medtronic, Inc.
Number	P200046
Filing Date	11/18/2020
Approval Date	3/26/2021
Youngest Suggested Pediatric Subpopulation:	Adolescent
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	128
Total Elapsed Days	128

RECELL® Autologous Cell Harvesting Device

The RECELL® Autologous Cell Harvesting Device is indicated for the treatment of acute thermal burn wounds. The RECELL® Device is used by an appropriately-licensed healthcare professional at the patient's point-of-care to prepare autologous RES® Regenerative Epidermal Suspension for direct application to acute partial-thickness thermal burn wounds in patients 18 years of age and older or application in combination with meshed autografting for acute full- thickness thermal burn wounds in pediatric and adult patients.

Manufacturer	Avita Medical
Number	BP170122/S287
Filing Date	12/14/2020
Approval Date	6/9/2021
Youngest Suggested Pediatric Subpopulation:	Infant
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	177
Total Elapsed Days	177

Neuro Cochlear Implant System

The Neuro Cochlear Implant System (NCIS) is indicated for individuals eighteen (18) years of age or older, with bilateral severe-to-profound sensorineural hearing loss, who obtain limited benefit from appropriately fitted hearing aid(s).

Severe-to-profound hearing loss is determined by a pure-tone average (PTA) superior or equal (≥) to 70 dB HL at 500, 1000 and 2000 Hz. *Limited benefit from amplification* is defined by scores of 50% or less on Hearing in Noise Test (HINT) sentences in quiet or noise, in the best-aided listening condition. Unless already appropriately fitted with hearing aids, it is recommended that candidates undergo a hearing aid trial period of three (3) months.

Manufacturer	Oticon Medical
Number	P200021
Filing Date	3/23/2020
Approval Date	6/23/2021
Youngest Suggested Pediatric Subpopulation:	Adolescent
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	180
Total Elapsed Days	457

ADVIA Centaur® Anti-Hbe2 (AHBe2) Assay

The ADVIA Centaur® Anti-HBe2 (aHBe2) assay is an *in vitro* diagnostic immunoassay for the qualitative detection of antibodies to the e antigen of the hepatitis B virus (HBV) in human pediatric (2–21 years old) and adult serum, EDTA plasma, or lithium heparin plasma using the ADVIA Centaur systems (XP/XPT/CP). Assay results, in conjunction with other laboratory results and clinical information may be used as an aid in the diagnosis of hepatitis B virus (HBV) infection in patients with signs or symptoms of hepatitis B infection, or with risk factors for HBV infection, or with known HBV infection. Results of the assay, in conjunction with other diagnostic information, may be used to aid in determining HBV seroconversion.

This assay is not intended for screening donors of blood or blood products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).

Manufacturer	Siemens Healthcare Diagnostics, Inc.
Number	P200017
Filing Date	3/9/2020
Approval Date	7/14/2021
Youngest Suggested Pediatric Subpopulation:	Child
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	197
Total Elapsed Days	492

Relay®Pro Thoracic Stent-Graft System

The Relay®Pro Thoracic Stent-Graft System is indicated for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating atherosclerotic ulcers in the descending thoracic aorta in patients having appropriate anatomy, including:

- Iliac or femoral access vessel morphology that is compatible with vascular access techniques, devices, and/or accessories;
- Non-aneurysmal aortic neck diameter in the range of 20 – 42 mm;
- Non-aneurysmal proximal aortic neck lengths of:
    - 15 mm for the 24 – 28 mm device diameters (Bare Stent Configuration)
    - 20 mm for the 30 – 38 mm device diameters (Bare Stent Configuration)
    - 25 mm for the 40 – 46 mm device diameters (Bare Stent Configuration)

- 25 mm for the 24 – 38 mm device diameters (Non-Bare Stent Configuration)
- 30 mm for the 40 – 46 mm device diameters (Non-Bare Stent Configuration)

- Non-aneurysmal distal aortic neck lengths of:
  - 25 mm for the 24 – 38 mm device diameters
  - 30 mm for the 40 – 46 mm device diameters

Manufacturer	Bolton Medical, Inc.
Number	P200045
Filing Date	11/20/2020
Approval Date	8/5/2021
Youngest Suggested Pediatric Subpopulation:	Adolescent
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	180
Total Elapsed Days	258

Organ Care System (OCS) Heart System

The TransMedics Organ Care System (OCS) Heart System is indicated for the preservation of donor-after-brain-death (DBD) hearts deemed unsuitable for procurement and transplantation at initial evaluation due to limitations of prolonged cold static cardioplegic preservation (e.g., > 4 hours of cross-clamp time).

Manufacturer	TransMedics, Inc.
Number	P180051
Filing Date	12/26/2018
Approval Date	9/3/2021
Youngest Suggested Pediatric Subpopulation:	Adolescent
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	795
Total Elapsed Days	982

ConMed PadPro Multifunction Electrodes, ConMed PadPro Multifunction Electrode Adapters

<u>Adult / Child Models, 2001 (Radiotransparent) and 2516 (Radiotranslucent)</u>:
The ConMed PadPro radiotransparent and radiotranslucent external multifunction electrodes (MFEs) are indicated for use by trained medical professionals in medical facilities or medical transport environments to deliver energy for defibrillation, cardioversion, external pacing, and ECG monitoring applications. The MFE is a non-sterile, disposable device for single patient use only. The electrodes provide the conductive interface between the defibrillator and/or the external transcutaneous (noninvasive) cardiac pacemaker and the patient's skin. This device is intended for use on defibrillators whose output is classified as low power (up to 360 joule maximum).
AED Use:
When used in AED mode i.e., for victims of cardiac arrest where there is apparent lack of circulation as indicated by unconsciousness, absence of breathing, and

absence of pulse, the electrode is intended for use on patients weighing 25kg (55 lbs.) or more. PadPro MFEs are not intended to be used for public access pediatric AED defibrillation purposes.

Manual Use:

- When used in manual mode, i.e., under direction of a qualified health care professional, the electrode is intended for use on adult / child patients weighing 10kg (22 lbs.) or more.

Adult / Child Model 2502 (Sterile):

The ConMed PadPro radiotransparent external multifunction electrodes (MFEs) are indicated for use by trained medical professionals in medical facilities or medical transport environments to deliver energy for defibrillation, cardioversion, external pacing, and ECG monitoring applications. The MFE is a sterile, disposable device for single patient use only. The electrodes provide the conductive interface between the defibrillator and/or the external transcutaneous (noninvasive) cardiac pacemaker and the patient's skin. This device is intended for use on defibrillators whose output is classified as low power (up to 360 joule maximum).

AED Use:

When used in AED mode i.e., for victims of cardiac arrest where there is apparent lack of circulation as indicated by unconsciousness, absence of breathing, and absence of pulse, the electrode is intended for use on patients weighing 25kg (55 lbs.) or more. PadPro MFEs are not intended to be used for public access pediatric AED defibrillation purposes.

Manual Use:

- When used in manual mode, i.e., under direction of a qualified health care professional, the electrode is intended for use on adult / child patients weighing 10kg (22 lbs.) or more.

Infant Model 2603 and Mini-Infant Model 2602:

The ConMed PadPro radiotranslucent external multifunction electrodes (MFEs) are indicated for use by trained medical professionals in medical facilities to deliver energy for defibrillation, cardioversion, external pacing, and ECG monitoring applications. The MFE is a non-sterile, disposable device for single patient use only. The electrodes provide the conductive interface between the defibrillator and/or the external transcutaneous (noninvasive) cardiac pacemaker and the patient's skin.

Not for use in AED mode.

Manual Use:

- When used in manual mode, i.e., under direction of a qualified health care professional, the electrode is intended for use on infant patients (3-10kg) and mini-infant patients (<3kg). Follow American Heart Association (AHA) guidelines for administration of energy levels, which recommends a first dose of 2J/kg, and subsequent doses of 4J/kg. During Refractory ventricular fibrillation, do not exceed a maximum energy level of 10J/kg.

PadPro MFE Adapters The ConMed PadPro adapters are indicated for use by trained medical professionals in medical facilities or medical transport environments to adapt

connection systems associated with a specific defibrillator/therapy cable to a different style connection system. The PadPro MFE adapters are intended for delivery of energy for defibrillation, cardioversion, external pacing, and ECG monitoring applications. The PadPro MFE adapter is a non-sterile, reusable device, providing conductive interface between the defibrillator and/or therapy cable and MFE electrode. This device is intended for use on defibrillators whose output is classified as low power (up to 360 joule maximum).

Manufacturer	ConMed Corporation
Number	P200004
Filing Date	1/31/2020
Approval Date	9/26/2021
Youngest Suggested Pediatric Subpopulation:	Neonate
Exempt from User Fees Because Intended Solely for Pediatric Use?	No
FDA Days	180
Total Elapsed Days	604

Appendix B: PMA and HDE Application Approvals for Devices with a Pediatric Indication from FY 2008 to FY 2021 by CDRH and CBER

Table 1. Total PMA and HDE Application Approvals and PMA and HDE Application Approvals for Devices with a Pediatric Indication from FY 2008 to FY 2021 (per Center).

Fiscal Year	Approved PMA and HDE Devices by Center		Total Approved PMA and HDE Devices	Approved Pediatric PMA and HDE Devices by Center		Total Approved Pediatric PMA and HDE Devices
	CDRH	CBER		CDRH	CBER	
2008	29	1	30	4	0	4 (13%)
2009	31	1	32	7	0	7 (22%)
2010	20	1	21	7	1	8 (38%)
2011	41	2	43	17	1	18 (42%)
2012	52	1	53	11	0	11 (21%)
2013	39	2	41	8	1	9 (22%)
2014	37	2	39	8	0	8 (21%)
2015	61	5	66	11	3	14 (21%)
2016	71	2	73	13	1	14 (19%)
2017	66	2	68	18	1	19 (28%)
2018	57	2	59	20	2	22 (37%)
2019	55	1	56	10	0	10 (18%)
2020	60	3	63	24	2	26 (41%)
2021	53	6	59	11	4	15 (25%)

In Table 2, the devices were categorized by the youngest age for which there was an indication for use.

Table 2. PMA and HDE Application Approvals Indicated for Pediatric Subpopulations by Age from FY 2013 to FY 2021.

Pediatric Subpopulation	PMA	HDE	Total
FY 2013			
Neonates (birth - 28 days)	**0**	**0**	**0**
Infants (29 days to <2 years)	**0**	**0**	**0**
Children (2 - 12 years)	**0**	**0**	**0**
Adolescents (12 - 21 years)	**9**	**0**	**9**
FY 2014			
Neonates (birth - 28 days)	**1**	**1**	**2**
Infants (29 days to <2 years)	**0**	**0**	**0**
Children (2 - 12 years)	**1**	**1**	**2**
Adolescents (12 - 21 years)	**4**	**0**	**4**
FY 2015			
Neonates (birth - 28 days)	**1**	**0**	**1**
Infants (29 days to <2 years)	**1**	**0**	**1**
Children (2 - 12 years)	**4**	**0**	**4**
Adolescents (12 - 21 years)	**7**	**1**	**8**
FY 2016			
Neonates (birth - 28 days)	**0**	**1**	**1**
Infants (29 days to <2 years)	**0**	**0**	**0**
Children (2 - 12 years)	**2**	**0**	**2**
Adolescents (12 - 21 years)	**11**	**0**	**11**
FY 2017			
Neonates (birth - 28 days)	**2**	**1**	**3**
Infants (29 days to <2 years)	**1**	**0**	**1**
Children (2 - 12 years)	**8**	**0**	**8**
Adolescents (12 - 21 years)	**6**	**1**	**7**
FY 2018			
Neonates (birth - 28 days)	**1**	**0**	**1**
Infants (29 days to <2 years)	**3**	**0**	**3**
Children (2 - 12 years)	**4**	**1**	**5**
Adolescents (12 - 21 years)	**13**	**0**	**13**
FY 2019			
Neonates (birth - 28 days)	**0**	**0**	**0**
Infants (29 days to <2 years)	**4**	**0**	**4**
Children (2 - 12 years)	**1**	**1**	**2**
Adolescents (12 - 21 years)	**3**	**1**	**4**
FY 2020			
Neonates (birth - 28 days)	**3**	**0**	**3**
Infants (29 days to <2 years)	**4**	**0**	**4**
Children (2 - 12 years)	**13**	**0**	**13**
Adolescents (12 - 21 years)	**6**	**0**	**6**

FY 2021			
Neonates (birth - 28 days)	**2**	**0**	**2**
Infants (29 days to <2 years)	**2**	**1**	**3**
Children (2 - 12 years)	**5**	**0**	**5**
Adolescents (12 - 21 years)	**5**	**0**	**5**

This report was prepared by FDA's Center for Devices and Radiological Health, in coordination with FDA's Center for Biologics Evaluation and Research. For more information, please contact:

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