Report to Congress

Best Pharmaceuticals for Children Act and Pediatric Research Equity Act

July 1, 2020 – June 30, 2025





Executive Summary

Section 508 of the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted in 2012, requires the Secretary of Health and Human Services (HHS) to report on the Food and Drug Administration's (FDA's) implementation of sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (FD&C Act), which are commonly known as the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), respectively. This report was first required to be submitted to Congress by July 9, 2016, and then every 5 years thereafter. In addition to the FDASIA requirements, the FDA Reauthorization Act of 2017 (FDARA) and the Consolidated Appropriations Act, 2026 (2026 Appropriations Act) added more reporting requirements for HHS. This report submitted pursuant to these laws, and covering July 1, 2020, through June 30, 2025, provides a comprehensive assessment of these landmark pediatric statutes that have fundamentally transformed pediatric drug[1] development.

BPCA incentivizes sponsors to conduct pediatric studies through FDA's issuance of Written Requests, offering the potential for six months of marketing exclusivity upon completion of the studies requested therein. PREA requires sponsors of certain new drug applications and biologics license applications to submit (1) pediatric assessments regarding a drug's safety, effectiveness, dosing, and administration in pediatric populations or (2) reports on molecularly targeted pediatric cancer investigations designed to yield clinically meaningful study data regarding dosing, safety, and preliminary efficacy in pediatric populations. Together, these statutes encourage more informative labeling of drug and biological products for use in children.

Pediatric Studies and Labeling

Enactment of BPCA and PREA has led to substantial progress in the number, timeliness, and successful completion of studies of drugs in pediatric populations. In 2022, FDA announced an historic milestone as more than 1,000 labeling changes had been completed pursuant to BPCA and PREA to incorporate pediatric use information. As of June 30, 2025, 1,364 pediatric labeling changes have been completed as a result of the successful implementation of both BPCA and PREA, with 429 occurring during this reporting period (292 for drugs, 137 for biologics). These labeling changes have provided essential prescribing information for diverse conditions including allergic conditions, asthma, cancer, diabetes, heart failure, hypertension, and infectious diseases. Notable approvals are provided in Section II.A.1 of the report, and all pediatric labeling changes occurring from July 1, 2020, through June 30, 2025, are provided in Appendix A.

[1] In this report, references to *drugs* and *products* include drugs approved under section 505 of the FD&C Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262). As such, this report addresses the requirement under section 508(b)(6) of FDASIA to provide an assessment of the effectiveness of studying biological products in pediatric populations.

Timeliness of Pediatric Drug Development

The average time between adult approval and pediatric labeling decreased from approximately six to five years for the current reporting period, suggesting some progress toward more timely pediatric drug development. However, this improvement must be viewed in the context of broader completion data showing that while 90% of drugs are expected to complete pediatric studies by 10 years post-approval, only 53% had any labeling changes reflecting PREA-mandated study data at that time point. The number of deferral extension requests has increased substantially, particularly from 2022 through 2024, with approximately 20 percent higher annual requests compared to the previous reporting period. While the COVID-19 pandemic contributed to some of the increases, data show that deferral extension requests have been steadily rising since 2015, suggesting underlying structural challenges in pediatric study conduct. FDA has issued 97 noncompliance letters to 67 sponsors since the last report, with 30% of these sponsors receiving multiple letters, indicating that current enforcement mechanisms may lack sufficient deterrent effect for some companies.

Development of Pediatric Cancer Drugs

The Research to Accelerate Cures and Equity (RACE) Act, which was a part of FDARA, has achieved remarkable success, fundamentally changing the landscape of pediatric oncology drug development. The RACE Act amended PREA to grant FDA the authority to require sponsors to submit reports to FDA on pediatric investigations for certain new drugs directed at a molecular target determined to be substantially relevant to the growth or progression of one or more pediatric cancers, including drugs with orphan designation. During this reporting period, FDA reached agreement on 141 initial Pediatric Study Plans for new molecularly targeted oncology products subject to FDARA requirements, with 81 (57%) containing plans to conduct pediatric investigations. Notably, 65 (80%) of these products would have qualified for a PREA exemption or waiver prior to the RACE Act implementation. During the reporting period, 29 oncology drugs were approved for pediatric use, of which 15 were supported by data generated in accordance with BPCA or PREA. From July 1, 2020, through November 24, 2025, four products received approval for pediatric cancer indications based on data generated by PREA post-marketing requirement studies.

Development of Drugs for Rare Pediatric Diseases

The exemption from PREA's pediatric assessment requirements for orphan-designated drugs (i.e., those designated for use in rare diseases) continues to limit the FDA's authority to require pediatric drug development for non-oncologic rare diseases. Over one-third of approved orphan indications relevant to pediatric populations lack complete pediatric labeling information, but approximately 50-75% of rare diseases occur in pediatric populations. This exemption from pediatric assessment requirements has become increasingly common as drugs that treat rare diseases represent an increasing proportion of novel drug approvals.

Other laws have been implemented to incentivize the study of drugs intended to treat rare pediatric diseases. The rare pediatric disease (RPD) priority review voucher (PRV) in particular (see section 529 of the FD&C Act) has garnered significant interest, with FDA having granted 917 rare pediatric disease designations and awarded 61 priority review vouchers since the voucher's inception in 2012 through June 30, 2025 (see Appendix B). Importantly, the requirements to qualify for an RPD PRV generally exclude drugs containing a previously-approved active moiety or active ingredient, and approximately 70% of approved products that qualified for an RPD PRV were the first approved therapy for the disease, representing significant progress in developing disease-modifying therapies. The statutory authority for the RPD PRV was reauthorized on February 3, 2026, as part of the "Consolidated Appropriations Act, 2026," (PL 119-75) (2026 Appropriations Act). The reauthorization extends the program to permit FDA's award of RPD PRVs until September 30, 2029. As it currently exists, the RPD PRV program must be reauthorized periodically by legislative action, which creates unpredictability in long-term planning and resource allocation for companies developing these drugs and biologics. FDA supports making the RPD PRV program permanent, as reflected in legislative proposals included in the FY2027 FDA budget.

Development of Drugs for Neonates

Despite overall progress in pediatric labeling, significant gaps remain in neonatal therapeutics development. Only 12% of the 1,364 pediatric labeling changes pursuant to BPCA and PREA included neonatal information, and approximately 40% of drugs with new neonatal indications relied on extrapolated data rather than clinical studies conducted in neonates. Only two drugs were approved for neonatal-specific conditions during the reporting period, leaving major diseases like bronchopulmonary dysplasia, necrotizing enterocolitis, and hypoxic ischemic encephalopathy without approved therapies. The limited impact reflects that drugs under development for adult conditions may not be relevant to neonates, and current laws may not provide sufficient incentive for pharmaceutical companies to develop drugs specifically addressing conditions characterized by unique neonatal pathophysiology. FDA has enhanced neonatal support through expansion of its neonatology consultation service to three dedicated neonatologists and development of specialized guidance documents, including finalized guidance on clinical pharmacology considerations and neurodevelopmental safety studies in neonatal product development. In addition, FDA has collaborated with the International Neonatal Consortium to develop critical tools for neonatal drug development, including the neonatal adverse event severity scale for standardized safety evaluations.

The NIH Pediatric Drug Testing Research Program

Section 409I of the Public Health Service Act authorizes the National Institutes of Health (NIH) to prioritize therapeutic areas and sponsor pediatric clinical trials under BPCA. This program, commonly referred to as the BPCA/409I program, has demonstrated remarkable productivity, generating 26 labeling changes for off-patent medications since its inception, 11 of which were approved during the current reporting period. These

achievements include critical dosing improvements for antibiotics used in neonates and pre-term infants, safety and efficacy data for psychotherapeutic agents, and innovative pharmacokinetic modeling approaches leveraging real-world evidence. The program has expanded to include lactation studies, with recent labeling updates to the lactation section of labeling of oxycodone and ondansetron to incorporate information on the transfer of these drugs into breastmilk. The Pediatric Trials Network has developed and implemented over 50 pediatric clinical trials across more than 300 clinical sites, submitting 39 clinical study reports to FDA for labeling consideration.

Pediatric Advisory Committee (PAC) and Post-Marketing Pediatric Safety Surveillance

FDA continues to implement the congressionally mandated pediatric-focused post-marketing safety review of drugs and biologics covering the 18-month period after pediatric labeling changes pursuant to BPCA and PREA. An FDA retrospective analysis examined all post-marketing pediatric-focused safety reviews conducted over a 6-year period from October 1, 2013, through September 30, 2019. Among 163 products reviewed following pediatric labeling changes, new safety signals were identified for only 5 products, contributing to less than 1% of the 585 safety-related labeling changes for these products during the study period. None were specific to the pediatric population.

Since the 2021 BPCA and PREA report to Congress, FDA reviewed 184 products for post-marketing pediatric safety, with evaluations consistently confirming safety profiles without identifying new pediatric-specific safety signals requiring labeling changes. Meanwhile, FDA's routine pharmacovigilance consistently identifies a greater number of safety signals relevant to the adult and pediatric populations. The 18-month pediatric-focused safety reviews are redundant with the Agency's established post-marketing safety surveillance. FDA recommended removing this requirement in the legislative proposals included in the FY2027 budget. FDA currently employs a risk-based framework that considers each product's characteristics, use patterns, and risk profile to inform safety surveillance. Additionally, FDA continues to develop and implement processes needed to support efficient and effective post-marketing safety surveillance, including for pediatric populations.

Advances in Regulatory Science for Pediatric Drug Development

FDA has made significant advances in regulatory science to enhance pediatric drug development efficiency and effectiveness. Overall, the Agency has developed more than 80 guidance documents with pediatric-specific information, including new guidance on the use of pediatric extrapolation, a strategy that, when appropriately applied, can be used to leverage existing data and potentially increase the speed and efficiency of pediatric drug development. FDA has actively worked with sponsors to identify opportunities for pediatric extrapolation and innovative study designs, notably for pediatric hypertension and pediatric heart failure. The Agency has hosted numerous stakeholder workshops, including the Advancing the Development of Pediatric Therapeutics (ADEPT) series and other collaborative meetings to bring together

industry, academia, patient advocates, and regulatory experts to identify practical solutions to pediatric development challenges.

Global Alignment of Pediatric Research and Drug Development

FDA continues engaging with international stakeholders to ensure children worldwide participate in well-designed clinical trials that meet international regulatory standards. The Agency coordinates monthly Pediatric Cluster conference calls with regulatory agencies from the European Union, Japan, Canada, Australia, and Switzerland. During the reporting period, the Pediatric Cluster discussed 176 products proposed for pediatric study and 37 general topics, issuing 76 Common Commentary documents to provide coordinated advice to sponsors. This collaboration has been particularly important for pediatric cancer drug development, with 64 oncology products discussed during 36 calls and 22 Common Commentaries issued for cancer drugs. FDA participates in numerous international initiatives, including the ACCELERATE Platform for pediatric cancer therapy development and the International Council for Harmonisation's E11A Expert Working Group on pediatric extrapolation.

Program Improvements for Continued Advancement of Product Development for Children

FDA is evaluating several potential programmatic and/or statutory improvements to enhance pediatric drug development: (1) **Impact of the Orphan Exemption under PREA**. The Agency wants robust orphan product development and evidence for all relevant pediatric age groups with rare diseases, and is evaluating potential strategies that further those goals; (2) **Modernization of Pediatric Pharmacovigilance**. The Agency is proposing to modernize post-market safety monitoring of medical products used in children by removing the time-based requirement for post-market safety reviews under BPCA and PREA, allowing FDA to dedicate resources to real-time, risk-based surveillance activities conducted as safety signals emerge; (3) **Enhancement of Product Development for Neonatal Conditions**. The Agency continues leveraging its authorities to encourage studies in neonates, when appropriate, and is advancing regulatory science research and guidance development to provide critical foundation for neonatal therapeutics development. FDA recognizes that enhancing product development for neonatal conditions may require specialized approaches beyond BPCA and PREA, given that many neonatal diseases have no adult counterparts and existing incentive structures may not adequately reach this population; (4) **More Timely Pediatric Product Development**. The Agency is considering strategies to increase compliance with studies required under PREA. Historically, enforcement mechanisms have relied primarily on public posting of PREA noncompliance letters issued by FDA, with limited to no financial consequences for sponsors who fail to complete required studies. Until the passage of the 2026 Appropriations Act, the law prohibited PREA noncompliance from serving as the basis for penalties or withdrawal of approval, so the “penalty” for noncompliance with PREA was, in effect, no penalty at all. However, the 2026 Appropriations Act authorized the Agency to take enforcement action, under certain limited circumstances, for PREA noncompliance occurring on or after August 2,

2026. The Agency is currently examining this new authority and working to develop policy regarding its implementation. FDA also continues to consider other strategies to improve compliance while working with sponsors who experience legitimate delays in product development. The Agency will focus international efforts on aligning development plans across global regulatory authorities to increase efficiency and success of pediatric drug development, with potential approaches including expanded product-specific discussions involving multiple regulatory bodies early in development programs. FDA also continues to evaluate the balance of incentives and requirements already in place to increase the availability of approved treatments for children, recognizing the complementary nature of both frameworks in achieving this goal.

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Acronym List

BLA	Biologics License Application
BPCA	Best Pharmaceuticals for Children Act
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
COVID-19	Coronavirus Disease 2019
DE	Deferral Extension
EMA	European Medicines Agency
FAERS	FDA Adverse Event Reporting System
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA	Food and Drug Administration
FDARA	FDA Reauthorization Act of 2017
FDASIA	Food and Drug Administration Safety and Innovation Act
IND	Investigational New Drug
iPSP	Initial Pediatric Study Plan
NDA	New Drug Application
NIH	National Institutes of Health
OCE	Oncology Center of Excellence
PAC	Pediatric Advisory Committee
PeRC	Pediatric Review Committee
PMR	Post Marketing Requirement
PPSR	Proposed Pediatric Study Request
PREA	Pediatric Research Equity Act
PRV	Priority Review Voucher
RACE	Research to Accelerate Cures and Equity
VAERS	Vaccine Adverse Event Reporting System
WR	Written Request

I. Introduction

Pediatric drug studies and labeling are governed, in large part, by two sections of the Federal Food, Drug, and Cosmetic Act (FD&C Act): section 505A and section 505B. First, to incentivize sponsors to conduct pediatric studies of drugs when the U.S. Food and Drug Administration (FDA or Agency) determines the studies may produce benefits in pediatric populations, section 505A of the FD&C Act (commonly referred to as the Best Pharmaceuticals for Children Act (BPCA)), gives FDA the authority to issue Written Requests (WRs) to sponsors to conduct those studies. Upon completion of those studies, a sponsor can potentially qualify for six months of additional marketing exclusivity attached to other exclusivity it may have had. BPCA allows FDA to request pediatric studies of drugs that cannot be required under section 505B of the FD&C Act (commonly referred to as the Pediatric Research Equity Act (PREA)). Second, PREA requires that sponsors of certain new drug applications (NDAs), biologics license applications (BLAs), or supplements thereto to submit, as applicable: (1) assessments regarding the drug's safety, effectiveness, dosing, and administration in pediatric populations or (2) reports on the molecularly targeted pediatric cancer investigation that is designed to yield clinically meaningful pediatric study data regarding dosing, safety, and preliminary efficacy to inform potential pediatric labeling.[2] Together, BPCA and PREA serve to increase the availability of pediatric-specific labeling of drug and biological products for use in neonates, infants, children, and adolescents.[3]

In the first BPCA and PREA report to Congress in 2016,[4] FDA provided a detailed overview of the history of pediatric laws, rules, and regulations. That report highlighted FDA's efforts as early as 1994 to add pediatric use information in labeling and described the first pediatric drug development incentive legislation that was enacted as part of the Food and Drug Administration Modernization Act (FDAMA) in 1997. These early efforts paved the way for the subsequent enactment of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act in 2002 and 2003, respectively, both of which became permanent in 2012, with modifications, under the Food and Drug Administration Safety and Innovation Act (FDASIA).[5] The provisions established by BPCA and PREA,

[2] Sponsors must submit pediatric assessments or reports on the molecularly targeted pediatric cancer investigation with any application (or supplement to an application) for which such assessments or reports are required by PREA, unless FDA defers or waives the requirement. See sections 505B(a)(1), 505B(a)(4), and 505B(a)(5) of the FD&C Act.

[3] There are other laws that impact pediatric studies of drugs and biologics, such as section 529 of the FD&C Act (i.e., the rare pediatric disease priority review voucher program) and sections 526 and 527 of the FD&C Act (which authorize orphan drug designation and orphan exclusivity). A further discussion of these laws is included, when relevant, in this report.

[4] See "BPCA and PREA Status Report to Congress July 9, 2012 – June 30, 2015" at https://www.fda.gov/science-research/pediatrics/best-pharmaceuticals-children-act-and-pediatric-research-equity-act.

[5] FDASIA (Pub. L. 112-144). 126 Stat. 993 (July 9, 2012).

sections 505A and 505B of the FD&C Act, have subsequently been amended several times.[6]

Section 508 of FDASIA requires the Secretary of Health and Human Services to report by July 9, 2016, and every 5 years thereafter, on various activities resulting from the implementation of sections 505A (BPCA) and 505B (PREA) of the FD&C Act. The 2016 BPCA and PREA status report to Congress highlighted the progress made in the study of drugs in the pediatric population with a focus on the impact of the pediatric-specific provisions under FDASIA.[7] The 2021 BPCA and PREA status report to Congress provided an assessment of the implementation and impact of the pediatric statutes on specific measures in accordance with requirements established under FDASIA, as well as the additional reporting requirements created under FDARA.[8] The report also highlighted additional successes stemming from BPCA and PREA and offered suggestions for advancing pediatric drug development by ensuring that the objectives underlying the statutes are effectively and efficiently implemented.

The current report provides data covering the five-year period from July 1, 2020, through June 30, 2025,[9] and assesses the implementation and impact of BPCA and PREA on specific measures in accordance with requirements established under FDASIA, as well as the additional reporting requirements created under FDARA. This report highlights the progress made in pediatric drug development, including detailed analyses of pediatric labeling changes, timeliness of study completion, and advances in special populations such as children with cancer, rare diseases, and neonates. The report also describes the achievements of the NIH BPCA/409I pediatric drug testing research program, FDA's post-marketing pediatric safety review activities conducted in collaboration with the Pediatric Advisory Committee, and advances in regulatory science that have enhanced pediatric drug development efficiency. Additionally, this report examines FDA's continued efforts to foster global alignment of pediatric research and drug development through international collaboration, presents input received from interested parties during the September 2025 public meeting, and offers recommendations for program improvements to ensure that the objectives underlying BPCA and PREA are effectively and efficiently implemented to advance development of safe and effective medicines and vaccines for all children who need them.

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[6] Food and Drug Administration Amendments Act of 2007 (FDAAA) (Pub. L. 110-85). 121 Stat. 823 (September 27, 2007); Patient Protection and Affordable Care Act (Pub. L. 111-148). 124 Stat. 119 (March 23, 2010); FDASIA (July 9, 2012); FDARA (Pub. L. 115-52). 131 Stat. 1005 (August 18, 2017).

[7] See “BPCA and PREA Status Report to Congress July 9, 2012 – June 30, 2015” at https://www.fda.gov/science-research/pediatrics/best-pharmaceuticals-children-act-and-pediatric-research-equity-act.

[8] See “BPCA and PREA Status Report to Congress July 1, 2015 – June 30, 2020” at https://www.fda.gov/science-research/pediatrics/best-pharmaceuticals-children-act-and-pediatric-research-equity-act.

[9] Unless otherwise noted, the data provided in this report extend 5 years from the end of the reporting period for the 2021 report to Congress (i.e., from July 1, 2020, through June 30, 2025). To facilitate an assessment of the early impact of FDARA on pediatric cancer research, the report includes information for pediatric oncology approvals beyond the reporting period.

II. Implementation and Impact of Pediatric Statutes: Mandated Reporting Elements and Other Requirements Under the Law

In accordance with the reporting requirements specified under FDASIA and FDARA, this section (1) provides an assessment of the implementation and impact of BPCA and PREA in improving pediatric use information in labeling; (2) describes FDA's implementation of the requirements under FDARA not only to achieve earlier submissions by sponsors of pediatric studies under BPCA but also to improve pediatric research and the labeling of drugs for pediatric cancer; (3) describes successes and limitations to studying drugs for rare pediatric diseases; (4) provides an overview of the progress and challenges in developing drugs for neonates; and (5) describes achievements of the program under section 409I of the Public Health Service Act (BPCA/409I program) at the National Institutes of Health (NIH). This section also describes FDA's continued progress in the congressionally mandated[10] post-marketing pediatric safety review process with reporting to the Pediatric Advisory Committee (PAC).

A. Pediatric Labeling and Timeliness of Pediatric Drug Development

1. Progress in Improving Pediatric Use Information in Labeling

Enactment of BPCA and PREA has led to substantial progress in the number, timeliness, and successful completion of studies of drugs in pediatric populations. In 2022, FDA announced an historic milestone of more than 1,000 pediatric labeling changes completed pursuant to BPCA and PREA. As of June 30, 2025, 1,364 pediatric labeling changes have been approved as a result of the successful implementation of both BPCA and PREA.[11]

A pediatric labeling change, as used here, refers to any update to a drug's labeling to add information about safety, effectiveness, or dosing for pediatric patients. Many labeling changes represent an approval of a new indication for a specific pediatric population. Other labeling changes may not include a new indication. For example, some labeling changes may provide information on failed pediatric studies and/or new safety information advising against use in certain pediatric populations.

[10] See section 505A(l) and 505B(i) of the FD&C Act.

[11] FDA routinely posts updated pediatric labeling change information on its website at https://www.fda.gov/science-research/pediatrics/pediatric-labeling-changes. FDA periodically reviews the completeness and accuracy of its pediatric clinical trial database which can lead to minor shifts in the reported data, including the overall number of pediatric labeling changes over time.

Since the 2021 BPCA and PREA report to Congress, 429 pediatric labeling changes (292 involving drugs and 137 involving biologics)[12] have been approved. The labeling changes have provided important information to support pediatric use for a variety of diseases or conditions, including but not limited to allergic conditions (e.g., allergic rhinitis, anaphylaxis, food allergies), asthma, cancer (e.g., acute lymphoblastic leukemia, brain cancer, melanoma), chronic kidney disease, diabetes (type 1 and type 2), heart failure, hypertension, obesity, rare diseases (e.g., Rett syndrome), rheumatologic conditions (e.g., polyarticular juvenile idiopathic arthritis, psoriatic arthritis, systemic lupus erythematosus), seizures, and infectious diseases (e.g., influenza, HIV, COVID-19). These labeling changes support the health of children by ensuring that pediatric healthcare providers have the information they need to support dosing, safety, and efficacy of medications when treating children. The following list provides selected examples of pediatric approvals since the 2021 BPCA and PREA report to Congress:

- **Benlysta** (belimumab) injection was the first approved treatment for patients aged five to 17 years with active lupus nephritis, a serious kidney disease associated with lupus, who are receiving standard therapy. The drug was previously approved for adults with this disease.
- **Beyfortus** (nirsevimab-alip) injection was the first approved drug to prevent respiratory syncytial virus (RSV) lower respiratory tract disease in all (i.e., not only high-risk) babies born during or entering their first RSV season and certain high-risk children up to age 24 months. While most patients with RSV infection experience mild cold-like symptoms, some infants, especially with their first RSV infection, develop lower respiratory tract disease such as pneumonia and bronchiolitis (swelling of the lungs' small airway passages).
- **Blincyto** (blinatumomab) injection was approved as part of the consolidation phase of treatment for CD19+ Philadelphia chromosome-negative B-cell acute lymphoblastic leukemia (B-ALL) in adult and pediatric patients aged one month and older, creating a new standard frontline treatment option, offering an improvement in overall survival compared to chemotherapy alone.
- **Epclusa** (sofosbuvir and velpatasvir) tablets and oral pellets and **Mavyret** (glecaprevir and pibrentasvir) tablets and oral pellets were the first all-oral, pan-genotypic (genotypes 1-6) hepatitis C virus treatment regimens for pediatric patients aged three years and older. Hepatitis C virus causes liver inflammation that can lead to diminished liver function or liver failure.
- **Linzess** (linaclotide) capsules were approved as the first treatment for pediatric functional constipation in patients aged six to 17 years. Pediatric functional

[12] A single drug may undergo several pediatric labeling changes. For example, a drug's labeling may be updated once when studies in older children have been reviewed by FDA and again years later after studies in younger children are completed.

constipation occurs when patients have infrequent bowel movements with hard stools that can be difficult or painful to pass.

- **Mekinist** (trametinib) tablets and **Tafinlar** (dabrafenib) tablets received the first tissue-agnostic indication (i.e., based on presence of a molecular alteration in the tumor rather than the cancer location) for adult and pediatric patients with refractory advanced cancers harboring the BRAF V600E molecular alteration. Both drugs also were approved in combination for the treatment of pediatric patients aged one year and older with BRAF V600E-mutant low grade glioma (a non-cancerous brain tumor that can result in significant morbidity) who require systemic therapy.
- **Neffy** (epinephrine) nasal spray was approved for emergency treatment of type 1 allergic reactions, including anaphylaxis, in patients aged four years and older weighing at least 15 kilograms (kg). Neffy is the first non-injection epinephrine to treat anaphylaxis, a severe, life-threatening allergic reaction that can occur suddenly and rapidly.
- **Palforzia** (Peanut [Arachis hypogaea] allergen powder-dnfp) was the first oral immunotherapy approved to mitigate allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanuts in patients one year and older with a confirmed diagnosis of peanut allergy.
- **Pradaxa** (dabigatran etexilate) capsules were approved to prevent and treat blood clots in certain specified patients as young as age eight years. Pradaxa is the first oral blood thinning medication approved for children.
- **Wegovy** (semaglutide) injection was approved, in combination with a reduced calorie diet and increased physical activity, in patients aged 12 years and older with obesity to reduce excess body weight and maintain weight reduction long term.
- **Xolair** (omalizumab) injection was approved for IgE-mediated food allergy in patients aged one year and older for the reduction of allergic reactions (type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. Xolair is the first approved medication to reduce allergic reactions to more than one type of food in case of accidental exposure.

Importantly, some pediatric labeling changes provided information about studies that failed to demonstrate efficacy in the pediatric population or raised safety concerns. For example, long-acting stimulants have been approved for treatment of attention deficit hyperactivity disorder (ADHD) in pediatric patients aged six years and older, and had PREA requirements to study pediatric patients four and five years of age with ADHD. However, these studies showed higher rates of adverse reactions such as weight loss in four- and five-year-olds. Based on these findings, FDA issued a drug safety communication and updated the labeling of extended-release stimulants for treatment of

ADHD to add a limitation of use recommending against their use in patients younger than 6 years of age.[13]

Another example is inclusion of pediatric labeling information for cancer drugs that have received multiple indications for adult cancers (e.g., cemiplimab, a checkpoint inhibitor) but failed to demonstrate efficacy in pediatric cancers. Including this information in product labeling helps to reduce duplicative clinical trials and off-label use of drugs with serious known risks that are not likely to benefit pediatric patients.

See Appendix A for a complete list of labeling changes that occurred pursuant to BPCA and PREA during the current reporting period.

2. Pediatric Study Planning and Conduct Under BPCA and PREA

a. FDA's Responses to Proposed Pediatric Study Requests (PPSRs)

Sponsors seeking a Written Request (WR) under BPCA may submit to FDA a proposed pediatric study request (PPSR) describing the studies the sponsor proposes to conduct to qualify for pediatric exclusivity. Under the BPCA, as amended by FDARA, FDA is required to respond to all PPSRs within 120 days of receipt and to provide to the Pediatric Review Committee (PeRC) any response issued to a PPSR, including all letters informing sponsors that a PPSR was inadequate to receive a WR.[14]

From July 1, 2020, to June 30, 2025, FDA received 251 PPSRs. The mean time from receipt of a PPSR to an initial response (either a WR or an inadequate PPSR letter) was 119.7 days (range 22-542 days). FDA responded to 83% (208/251) of the PPSRs within 120 days as required under FDARA (see Figure 1). FDA's response was delayed by more than 30 days for 9.6% (24/251) of the PPSRs. During the same time frame (i.e., from July 1, 2020, to June 30, 2025), FDA issued 50 WRs. Of the WRs issued, 27% (12/45) were issued in response to the first PPSR (see Figure 2). FDA issued five WRs without a PPSR from a sponsor. In these cases, FDA recognized that the WR would otherwise expire and negotiated a new WR with the sponsor without the need for a PPSR.

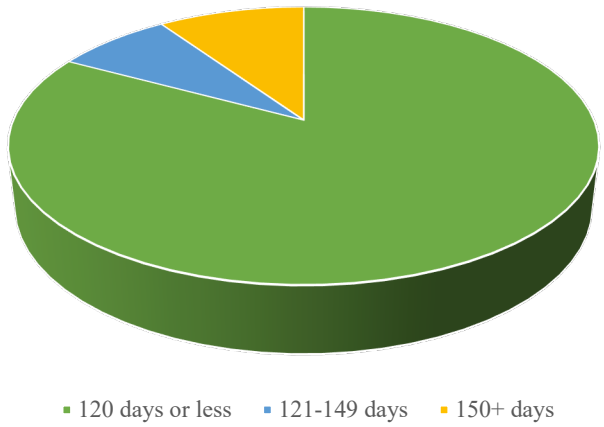
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[13] See https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-expanded-labeling-about-weight-loss-risk-patients-younger-6-years-taking-extended.

[14] See section 505A(d)(3) and section 505A(f)(7). Section 505(c) of FDARA also required FDA, acting through the PeRC, to develop and implement a plan to achieve, when appropriate, a sponsor's earlier submission of pediatric studies under BPCA. Specifically, this plan was intended to identify ways to achieve (1) earlier discussion of PPSRs and WRs between FDA and sponsors and, if appropriate, a discussion of such requests at the meetings required under section 505B(e)(2)(C) of the FD&C Act; (2) earlier issuance of WRs for pediatric studies under BPCA, including for investigational new drugs prior to the submission of an application; and (3) shorter timelines, when appropriate, for completion of studies pursuant to a WR.

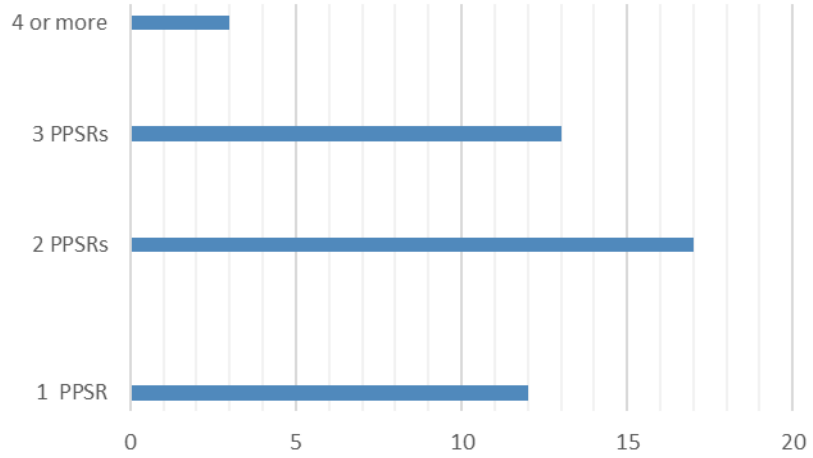
Compared to the 2021 BPCA and PREA report to Congress, the total number of PPSR submissions (251) was greater, though this is partly due to the shorter period of time for the last report (170 PPSR submissions from FDARA implementation on July 1, 2017, through June 30, 2020); the annual rate of PPSR submissions was similar (50 vs. 57 per year). FDA responded to a similar proportion of submitted PPSRs within 120 days (83% vs. 86%). These data demonstrate that FDA continues to respond to PPSR submissions in a timely fashion.

Figure 1: Time (Days) From Receipt of a PPSR to FDA's Response (n=251)



Importantly, sponsors often need to negotiate with FDA the details of a WR (including the appropriate conditions/indications and types of studies needed) prior to FDA's issuance of a WR. When this need arises, sponsors may receive an inadequate PPSR letter. If a sponsor intends to pursue a WR after receipt of an inadequate PPSR letter, then the sponsor may respond by submitting another PPSR. During this reporting period, FDA issued a lower percentage of WRs following the first PPSR submission compared to the last reporting period (27% vs. 44%). Seventeen sponsors submitted two PPSRs before receiving a WR; 13 sponsors submitted three PPSRs before receiving a WR; and three sponsors submitted four or more PPSRs before receiving a WR (see Figure 2). The mean time from submission of the first PPSR to issuance of a WR was 143 days (median 119.5 days; range 116-310 days). While the percentage of WRs issued following the first PPSR submission decreased, a similar pattern of issuance of WRs after 2, 3, or 4 PPSRs were seen in both reporting periods.

Figure 2: Number of PPSRs Submitted Before Issuance of a WR (n=45)



Overall, these data confirm that FDA continues to meet timelines established for the review of PPSRs as required under FDARA. In addition, these data suggest that many PPSRs do not lead to the issuance of a WR. There was an increase in PPSR submissions (n=251) in this reporting period and this higher number of PPSR submissions did not ultimately result in an increase in the number of WRs issued. While it is not clear why the increase in PPSR submissions did not lead to an increase in the number of WRs issued, sponsors may choose not to pursue a WR after receiving FDA's feedback for a variety of reasons and sponsors do not share these decisions or the factors leading to these decisions with FDA. A WR may include requests for studies for one or more indications that may benefit children and may include indications that are not being pursued in adult populations. FDA responses to PPSRs often cite the need to address other pediatric indications for which a drug may provide benefit, and this may be a factor in sponsor decisions not to pursue a WR.

b. WRs Issued Under BPCA and Sponsor Responses

Section 508(b)(4) of FDASIA requires that FDA report on the number of WRs issued, accepted, and declined and provide a listing of any important gaps in pediatric information as a result of such declined requests.[15] From July 1, 2020, through June 30, 2025, FDA issued 50 WRs under BPCA. Compared to the prior reporting period, there was a substantial decline in the number of WRs issued (50 vs. 96). While draft

[15] For the current reporting period (i.e., from July 1, 2020, to June 30, 2025), FDA has not referred any pediatric studies pursuant to section 505A(n) of the FD&C Act.

guidance[16] has discussed FDA's intention to not issue a WR solely for planned studies that are required under PREA upon finalization of the guidance, this approach has not been implemented and does not account for the decline in WRs issued during the current reporting period. In light of the slightly higher number of PPSRs submitted in this reporting period and data in Figure 2 showing WRs issued after multiple PPSRs, this suggests that FDA is identifying concerns with proposed pediatric study requests leading to a greater number of inadequate PPSR responses from FDA. There are multiple factors that contribute to issuing an inadequate PPSR response, including concerns related to proposed study designs and additional conditions for which a product may provide benefit. Other factors also may contribute, such as disagreement with study design elements (e.g., study endpoints, the length of the study, and/or adequacy of safety monitoring). As noted above, the PeRC continues to review all PPSR submissions, as required under FDARA. This PeRC review is intended to provide a consistent approach to issuance of WRs or inadequate letters.

Of the 50 WRs issued during the reporting period, 36 WRs were accepted by the sponsor, 13 WRs were amended based on sponsor feedback and were ultimately accepted by the sponsor, and one was declined. Similar to the prior reporting period, these data demonstrate that sponsors overwhelmingly accepted WRs issued by FDA suggesting that FDA issues WRs that are feasible. An analysis of information gaps related to declined WRs is not provided, since only one was declined. Furthermore, of the 50 WRs issued during this reporting period, six (12%) were issued prior to FDA's approval of an original NDA or BLA for an adult indication, demonstrating FDA's readiness to issue WRs earlier in a drug development program.

Data on amendments to issued WRs were also evaluated. Of the 50 WRs issued during the reporting period, 25 (50%) have been amended at least one time (range 1-3). The average time from the sponsor's request for an amendment to issuance of an amended WR was 124.6 days (range 5-392 days). These data suggest that amendments to WRs can be successfully negotiated and that changes to overall drug development plans can be incorporated into WRs that are issued by FDA. For example, drug development programs were changed for certain antipsychotic drugs for treatment of schizophrenia because of FDA's determination that pediatric extrapolation was acceptable. In such cases (see section II.A.3.b), collection of dosing and safety data in pediatric trials was sufficient to support approval, rather than conducting randomized, controlled trials to demonstrate safety and effectiveness. FDA amended WRs for such drugs to reflect this updated approach.

[16] See Draft Guidance Document "Pediatric Drug Development: Regulatory Considerations - Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act (May 2023) at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-regulatory-considerations-complying-pediatric-research-equity-act-and. When final, this guidance will reflect the Agency's current thinking on this topic.

c. Pediatric Study Planning Under PREA

Section 508(b)(3) of FDASIA requires that FDA provide an assessment of the timeliness and effectiveness of pediatric study planning under PREA. This provision requires that FDA report on the number of required studies that have not met the initial deadline, including the number of deferrals and deferral extensions[17] granted and the reasons such extensions were granted; the number of waivers granted;[18] and the number of noncompliance letters issued.[19]

Initial Pediatric Study Plan (iPSPs)

The total number of iPSPs reviewed by FDA and agreed[20] from January 1, 2020, to June 30, 2025, is presented in Table 1 by calendar year.

Table 1: iPSPs Submitted to FDA*

Calendar Year	iPSPs	Agreed iPSPs	Amended Agreed iPSPs	Non-Agreed iPSPs
2020	356	283	36	21
2021	411	333	33	34
2022	348	289	27	37
2023	300	242	36	28
2024	340	290	28	31
2025	189	134	12	8
Totals	**1944**	**1571**	**172**	**159**

[17] Section 505 of FDASIA amended PREA to ensure the completion of pediatric studies and authorized FDA to grant an extension of assessments deferred under PREA.

[18] See https://www.fda.gov/science-research/pediatrics/pediatric-tracking-requirements-under-fdaaa.

[19] Section 505B(d)(1) of the FD&C Act requires FDA to issue, and publicly post, noncompliance letters for failure to comply with certain PREA requirements, including the failure to submit required pediatric assessments under PREA.

[20] After a sponsor submits an iPSP, the FDA has 90 days to review the iPSP and provide a written response to the iPSP, or meet with the sponsor to discuss the iPSP, as appropriate. This review process includes consultation with the PeRC. The sponsor then has a second 90-day period during which it may review FDA's comments and initiate any needed negotiations to discuss the iPSP. By the end of this second 90-day review period, the sponsor must submit an agreed iPSP. FDA then has 30 days after receipt of the agreed iPSP to review and issue correspondence confirming agreement or issue correspondence stating disagreement. If the FDA does not agree, the iPSP is considered a non-agreed iPSP. See section 505B(e) of the FD&C Act.

* Data shown in Table 1 are collected by calendar year. The numbers provided for 2020 include the entire calendar year; in the 2021 BPCA and PREA report to Congress, only the first 6 months of 2020 were reported. Similarly, only the first 6 months of 2025 are reported here. Due to the timeline described in section 505B(e) of the FD&C Act, the number of agreed and non-agreed iPSPs may not equal the number of iPSPs each year because iPSPs submitted later in the calendar year may be acted upon in the following year.

The data on the number of iPSPs submitted to FDA show a fairly consistent number of iPSP submissions over the reporting period (averaging approximately 350 iPSP submissions per calendar year for 2020 to 2024). The data for 2025 to date also appear consistent with previous years. The last report noted an increase in the number of iPSP submissions in 2019 relative to the prior years, which was largely attributed to the implementation of the pediatric oncology-related provisions of FDARA. This increase in iPSP submissions noted in 2019 has continued throughout this reporting period. These data show agreement is reached on the vast majority of submitted iPSPs and that this has been stable over time. Over the reporting period, less than 10% of the submitted iPSPs were issued a nonagreement letter. These data also show a low number of agreed iPSPs are amended in any given calendar year, suggesting that agreed iPSPs do not often need to be changed.

Waivers and Deferrals Granted

PREA authorizes FDA to waive or defer the requirement to submit pediatric assessments or reports on the molecularly targeted pediatric cancer investigation, based on established criteria, for some or all pediatric age groups.[21] FDA tracks the number of waivers and deferrals granted under PREA. For the current reporting period, the data are provided in Table 2. These data were not included in the last report and therefore, there are no comparisons made with the previous reporting period. However, these data suggest that there has been consistent and steady decisions about granting of waivers and deferrals over the last 5 years.

Table 2: PREA Waivers and Deferrals Granted by FDA*

Year	2020	2021	2022	2023	2024	2025 (Jan 1-June 30)
Waivers Granted	120	127	124	137	139	58

Year	2020	2021	2022	2023	2024	2025 (Jan 1-June 30)
Deferrals Granted	51	44	53	51	55	36

[21] See sections 505B(a)(5) and 505B(a)(4) of the FD&C Act.

* Table 2 includes the total number of waivers and deferrals by indication. For example, a product may have three indications that are subject to PREA; one indication may be granted a full waiver, the second indication may include a partial waiver and a deferral, and the third indication may include no waivers and only a deferral.

Deferral Extensions

The total number of deferral extension (DE) requests that were received, granted, and denied by FDA from January 1, 2020, to June 30, 2025, by calendar year and by FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) is presented in Table 3.

Table 3: DE Requests Received, Granted, and Denied by CDER (CBER) by Calendar Year*

Calendar Year	DE Requests Granted	DE Requests Denied	DE Requests Received
2020	69 (2)	30 (1)	111 (3)
2021	65 (3)	28 (0)	80 (3)
2022	88 (6)	20 (1)	123 (7)
2023	92 (4)	18 (0)	126 (5)
2024	82 (5)	41 (0)	127 (6)
2025	38 (1)	11 (1)	49 (3)
Totals	**434 (21)**	**148 (3)**	**616 (27)**

* Data shown in Table 3 are collected by calendar year. The numbers provided for 2020 include the entire calendar year; in the 2021 BPCA and PREA report to Congress, only the first 6 months of 2020 were reported. Similarly, because the numbers reflect DE requests through June 2025, the 2025 numbers reflect only the first 6 months of the year. The Agency has 45 days to respond to a DE request. Therefore, the number of DE requests granted and denied may not equal the number of DE requests in a given year because a DE request that is submitted in the last 45 calendar days of a year may be acted upon in the following year.

The number of DE requests received between 2020 and the first half of 2025 has increased, particularly in years 2022 through 2024, in comparison to the prior reporting period. Though there is variability from year to year in the number of DE requests received, the number of requests each year from 2022 through 2024 was approximately 20% higher than the highest number of DE requests received in a single calendar year (2019) in the last reporting period. Based on justifications provided by sponsors in their DE requests, the COVID-19 pandemic contributed substantially to the increase in DE requests during this reporting period. The justifications by sponsors for these DE requests noted issues with study participants, sites, and/or management as the basis for study delays. For example, a study site may have had to interrupt research

operations during the COVID-19 pandemic.[22,23] Many DE justifications specifically described how the COVID-19 pandemic delayed completion of the pediatric trial.

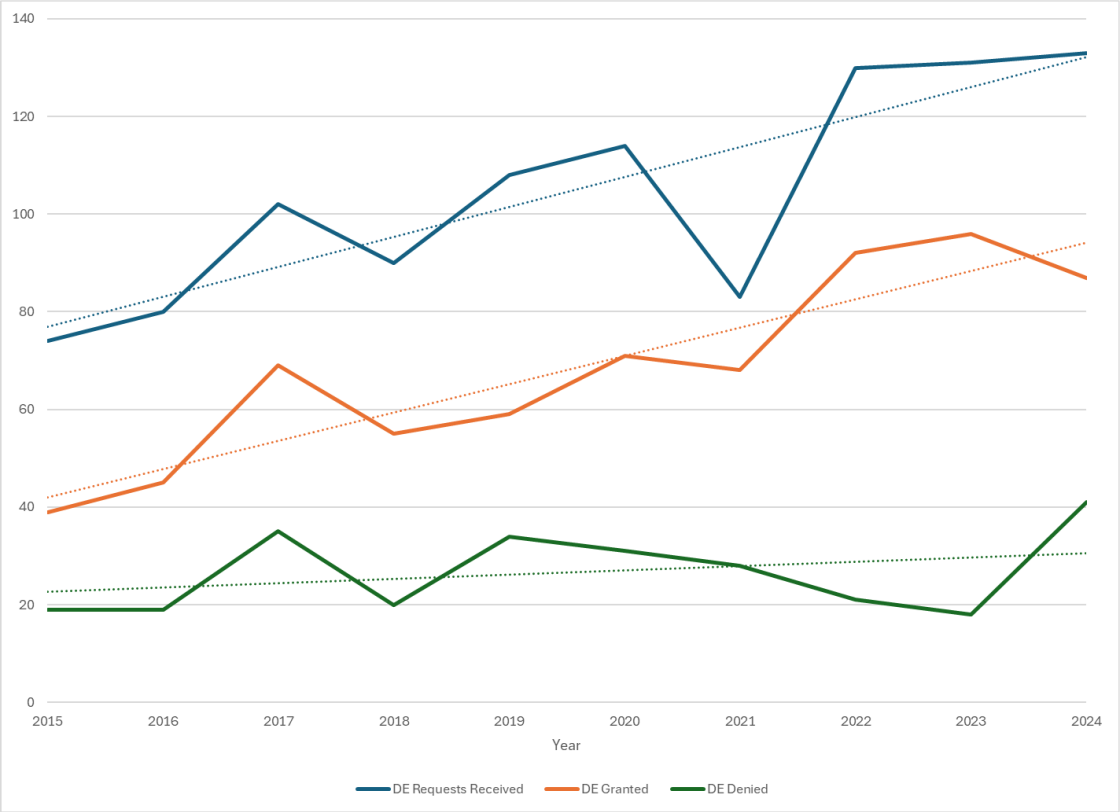
Consistent with the increase in DE requests, there was also an increase in the number of DE requests granted during the reporting period, particularly in years 2022 through 2024. Overall, approximately 75% of the DE request decisions resulted in FDA granting a deferral extension. Compared to the prior reporting period, FDA granted a higher percentage (75% vs. 70%) of DE requests, which is attributed to FDA's agreement that study delay justifications due to disruptions caused by the COVID-19 pandemic were reasonable. Correspondingly, the percentage of DE requests denied was approximately 25%. The number of DE requests denied vary from year to year, ranging from 18 in 2023 to 41 in 2024. The annual number of DE requests denied are in a similar range to the annual number of DE requests denied in the last reporting period (19 to 34). The number of DE denials annually over this reporting period and the last reporting appear similar.

Importantly, although the COVID-19 pandemic may partly explain the increase in the number of DE requests observed in recent years, upon reviewing DE request data provided in prior reports, the number of DE requests has been steadily increasing since 2015 (See Figure 3). FDA continues to work with sponsors who experience delays in product development.

[22] Audisio K, Lia H, Robinson NB, et al. (2022) Impact of the COVID-19 pandemic on non-COVID-19 clinical trials. J. Cardiovasc. Dev. Dis. 9(1):19. DOI: 10.3390/jcdd9010019.

[23] Riccaboni M and Verginer L. (2022) The impact of the COVID-19 pandemic on scientific research in the life sciences. PLoS ONE 17(2): e0263001. DOI:10.1371/journal.pone.0263001.

Figure 3: DE Requests Received, Granted, and Denied (2015-2024)

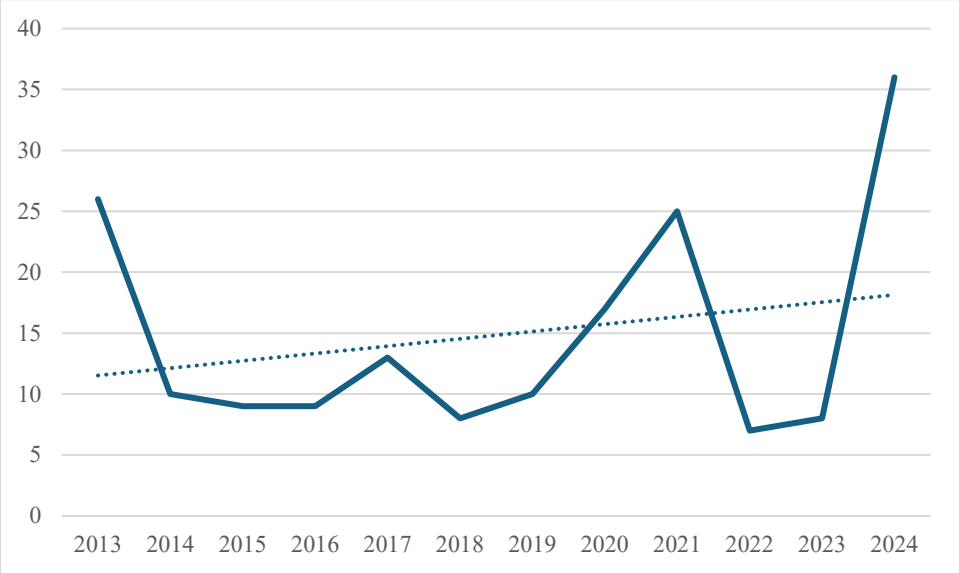


Noncompliance Letters

If an applicant fails to fulfill required deferred pediatric studies under PREA, FDA issues a noncompliance letter that informs the applicant of such failure and posts the noncompliance letter and the applicant's response on FDA's website. The first noncompliance letters were publicly posted on FDA's website on August 26, 2013.[24] Between April 5, 2013, and June 30, 2025, FDA issued a total of 187 noncompliance letters. As shown in Figure 4, the number of noncompliance letters has been somewhat variable over time. However, FDA issued 97 noncompliance letters (52% of the total since April 2013) to 67 sponsors since the 2021 BPCA and PREA report to Congress. It is not clear why there were relatively few noncompliance letters issued in 2022 and 2023, but this may reflect an increase in deferral extensions in those years (see Table 3) because of COVID-19 pandemic-related operational difficulties that sponsors were reporting.

[24] See http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm343203.htm and https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/prea-non-compliance-letters.

Figure 4: PREA Noncompliance Letters Issued by FDA by Calendar Year April 2013 through December 2024*



* Data for 2025 are not included. As of June 30, 2025, FDA had issued 9 PREA noncompliance letters in 2025.

In addition, FDA has been considering whether the issuance of noncompliance letters has had an impact on ensuring compliance with the completion of pediatric studies required under PREA. Therefore, FDA conducted additional analyses of sponsors who have received more than one noncompliance letter. During the current reporting period (July 1, 2020, to June 30, 2025), of the 67 sponsors who received a noncompliance letter, 20 (30%) have more than one noncompliance letter. For those sponsors who have received more than one noncompliance letter, the majority (16 of 20) received them for different PREA Post Marketing Requirements (PMRs). However, four sponsors (20%) received a second noncompliance letter for the same PREA PMR for which they had previously received a noncompliance letter. These data suggest that a substantial number of sponsors have not regarded these noncompliance letters as a deterrent for delays in completing PREA PMR studies in a timely manner. Table 4 includes a list of sponsors who have received more than one noncompliance letter for more than one drug.

Table 4: Sponsors Receiving PREA Noncompliance Letters for Different Drugs

Sponsor	Product
Azurity	Qbrelis (lisinopril) oral solution
Azurity	Katerzia (amlodipine besylate USP; amlodipine benzoate) suspension
Azurity	Edarbi (azilsartan medoxomil) tablets

Sponsor	Product
CMP Development LLC	CaroSpir (spironolactone) oral suspension
CMP Development LLC	potassium phosphates injection
Currax	Treximet (sumatriptan and naproxen sodium) tablets
Currax	Onzetra Xsail (sumatriptan nasal powder)
Gilead Sciences, Inc.	Sovaldi (sofosbuvir) tablets
Gilead Sciences, Inc.	Harvoni (ledipasvir; sofosbuvir) tablets
Heron Therapeutics, Inc.	Zynrelef (bupivacaine and meloxicam) extended-release solution
Heron Therapeutics, Inc.	Cinvanti (aprepitant) injectable emulsion
Hikma Pharmaceuticals USA, Inc.	codeine sulfate tablet and oral solution
Hikma Pharmaceuticals USA, Inc.	phenylephrine hydrochloride injection
Hikma Pharmaceuticals USA, Inc.	morphine sulfate oral solution and tablets
Neos Therapeutics, Inc.	Adzenys XR-ODT (amphetamine) extended-release orally disintegrating tablets
Neos Therapeutics, Inc	Cotempla XR-ODT (methylphenidate) extended-release orally disintegrating tablets
Primus Pharmaceuticals, Inc.	Sernivo (betamethasone dipropionate) topical spray
Primus Pharmaceuticals, Inc.	Impoyz (clobetasol propionate) cream
Salix Pharmaceuticals, Inc.	Trulance (plecanatide) tablets
Salix Pharmaceuticals, Inc.	Xifaxan (rifaximin) tablets
Rockwell Medical, Inc.	Triferic (ferric pyrophosphate citrate) solution
Rockwell Medical, Inc.	Triferic AVNU (ferric pyrophosphate citrate) injection

Under section 508(b)(13) of FDASIA, as amended by FDARA, FDA is required to report the number of sponsors who received pediatric exclusivity for studies completed and

submitted after they had received a noncompliance letter. There are no sponsors who received pediatric exclusivity for studies completed and submitted after they had received a noncompliance letter that was issued between July 1, 2020, and June 30, 2025. Overall, these data demonstrate that qualifying for pediatric exclusivity under BPCA after receiving a noncompliance letter for the completion of these studies under PREA remains a relatively uncommon occurrence overall. However, the data appear to demonstrate that noncompliance letters may be increasing.

Evaluation of Compliance with PREA Pediatric Study Deadlines

In accordance with amendments made by the 2026 Appropriations Act, under section 508(b)(11) of FDASIA, FDA is required to provide an evaluation of compliance with pediatric study deadlines provided for in deferrals and deferral extensions. As noted above, the number of deferral extension requests has been increasing over time. This suggests that sponsors are increasingly requesting to extend the deadlines to obtain more time to complete deferred pediatric studies. In addition, the number of noncompliance letters issued appears to be increasing over time, which may suggest that sponsors are increasingly failing to fulfill required deferred pediatric studies within the specified deadlines. Furthermore, there are also sponsors who have received more than one noncompliance letter, which may suggest a pattern of noncompliance. In the next section of this report focused on timeliness of pediatric study planning, the impact and potential cause of these and other factors that affect pediatric study timelines is discussed. These data are troubling and may signal the need to consider other measures to ensure that sponsors conduct their required pediatrics studies with due diligence. The Agency is currently examining the new authority granted by the 2026 Appropriations Act to take enforcement action, under certain limited circumstances, for PREA noncompliance occurring on or after August 2, 2026.

3. Timeliness of Pediatric Study Planning and Conduct Under BPCA and PREA

In the 2021 BPCA and PREA report to Congress, FDA highlighted the notable shift toward earlier integration of pediatric study planning in drug development in the era since BPCA and PREA were enacted. This section addresses reporting requirements related to timeliness of pediatric studies, and FDA's continuing efforts to address delays in pediatric study completion.

a. Time From the Application's Approval to Inclusion of Pediatric Information in the Approved Product's Labeling

Under section 508(b)(12)(A) of FDASIA, as amended by FDARA, FDA is required to report on the average length of time after the approval of an application under section 505(b)(1) of the FD&C Act or section 351(a) of the Public Health Service Act (PHS Act) before studies conducted pursuant to either section 505A or 505B of the FD&C Act or

section 351(m) of the PHS Act are completed, submitted, and incorporated into the labeling.

From July 1, 2020, to June 30, 2025, the average length of time between approval of an application under section 505(b)(1) of the FD&C Act or section 351(a) of the PHS Act and the inclusion of any pediatric use information in the approved product's labeling was approximately five years. For products regulated by CDER, the average time between original approval and the inclusion of any pediatric use information was 5.5 years (range 0.7-23.4 years). Notably, of the 218 CDER pediatric approvals identified in this analysis, 45 products included any pediatric use information as part of the original approval. This is improved compared to the prior reporting period, when only 6 products included pediatric use information as part of the original approval. In addition, three products (not included in this analysis) had studies waived because the drug was considered to be either unsafe or ineffective in pediatric patients, and this information was included in labeling at the time of the original approval. For products regulated by CBER, the average time between original approval and the inclusion of any pediatric use information was 5.0 years (range 0.7-18.8 years). Notably, 40.8% (29/71) of original CBER applications approved during this period included pediatric-specific use information for all or part of the intended pediatric age range at the time of the original approval.

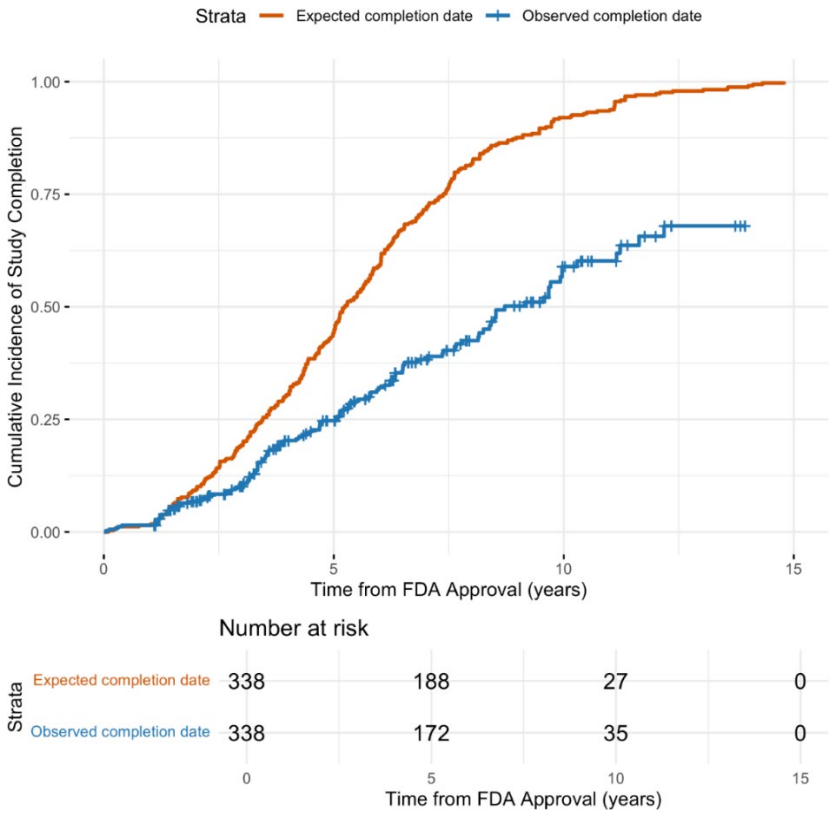
The overall time difference of five years for this reporting period is slightly lower than the time difference of six years reported for the period from July 1, 2017, to June 30, 2020. Given the delays in completion of some pediatric clinical trials related to the COVID-19 pandemic, the 5-year time difference does suggest some progress toward shortening the delay to inclusion of pediatric use information in labeling. While a precise analysis to determine the reason for the decreased time difference is not feasible, it may be that measures to help decrease this lag, such as the requirement in section 505B(e)(2) of the FD&C Act to submit iPSPs no later than 60 days after an end-of-Phase 2 meeting, as well as the evolution of regulatory and scientific advances to improve pediatric drug development (e.g., use of extrapolation, innovative study designs, and modeling and simulation), have contributed to earlier pediatric study planning and more efficient pediatric drug development programs.

It should be noted that in the above analysis, the length of time between approval and inclusion of any pediatric information was based on identifying submissions that added pediatric use information to labeling during the reporting period (July 1, 2020, to June 30, 2025) and comparing this to the date of the original approval date. This methodology was used because it is the same methodology used for the prior reporting period, making it reasonable to compare these data with the prior report. However, this analysis methodology does not account for labeling approvals that were not completed

during the current review period. Thus, it is likely that this analysis underestimates the time to complete pediatric labeling that has been cited in the literature.[25,26]

In a recent retrospective analysis of all novel drugs approved by FDA from 2011 to 2023 with at least one PREA PMR (n=166 drugs; 338 PREA PMRs), the authors found the mean time to pediatric approval was 5.7 years (SD 2.6), whereas labeling reflecting lack of pediatric safety or efficacy took an average of 8.3 years (SD 3.3) ($p < 0.001$).[27] The authors found that, while 90.4% of drugs were expected to have all pediatric studies completed by 10 years, only 52.8% had any labeling changes reflecting data from the PREA-mandated studies at that time (see Figure 5).

Figure 5: Time to Completion of Pediatric Studies Required for Novel Drugs



Reprinted with permission from McGonigle R, Naci H, Siebert M, et al. (2025) Pediatric studies and labeling additions required by the U.S. FDA for novel drugs approved from 2011 to 2023: A retrospective cohort study. PLOS Medicine. DOI:10.1371/journal.pmed.1004651.

[25] Price A, Simmons H, Gehring E, et al. (2024) Significant delays exist in industry-sponsored pediatric clinical drug trial start-up and enrollment processes. Contemporary Clinical Trials. DOI: 10.1016/j.cct.2024.107701

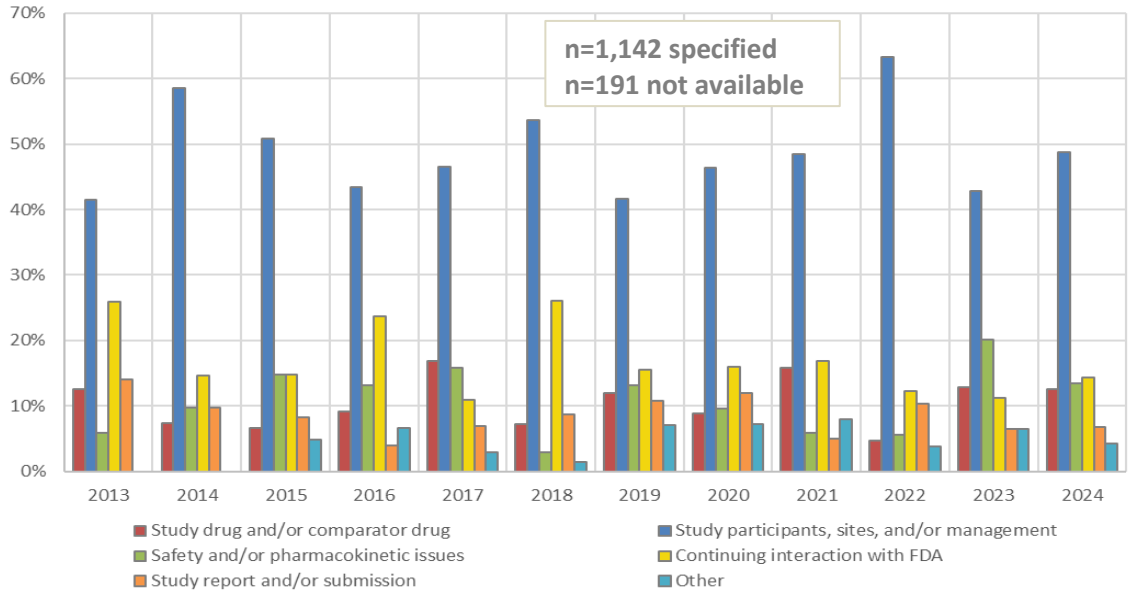
[26] McGonigle R, Naci H, Siebert M, et al. (2025) Pediatric studies and labeling additions required by the U.S. FDA for novel drugs approved from 2011 to 2023: A retrospective cohort study. PLOS Medicine. DOI:10.1371/journal.pmed.1004651

[27] Id.

In their analysis, the authors also found that over half (56.8%) of PREA PMRs were granted extensions of original timelines, by an average of 2.9 years (SD 2.0).

As stated above, FDA also has identified an increase in the number of DE requests over time. Pediatric assessments or investigations may be delayed for various reasons, including but not limited to, unexpected difficulties with enrollment, unexpected delays in reaching agreement with FDA on protocols for the pediatric clinical studies, or an unanticipated need for additional safety or effectiveness data before proceeding with studies in children. Review of sponsor-stated reasons for DE requests from 2013 through 2024 shows that issues with study enrollment and site management account for nearly half of all DE requests (see Figure 6).

Figure 6: Sponsor-Stated Rationale for Deferral Extension Requests (% of total per year, 2013-2024)



*DE requests may specify more than one rationale

These challenges with study enrollment and site management raise questions regarding whether there has been sufficient investment in pediatric clinical trial infrastructure to support timely pediatric assessments.

b. FDA's Progress Addressing Timeliness of Pediatric Study Planning and Conduct Under BPCA and PREA

Overall, FDA has made some progress toward the timely completion of pediatric assessments under BPCA and PREA despite the effect of the COVID-19 pandemic causing delays in completion of some pediatric clinical research. The PeRC continues to provide consultation on all PPSRs, WRs, and pediatric study plans submitted in accordance with BPCA and PREA and to review all DE requests for PREA studies, with

both actions aimed at ensuring the proposed pediatric study timelines are reasonable. In addition, FDA continues to engage with sponsors during the early planning stages of a drug development program, for example, during meetings prior to an initial Investigational New Drug (IND) application and during the iPSP review process at the end of phase 2, to ensure planning for pediatric assessments occurs at the early stages of development.

The Division of Pediatrics and Maternal Health (DPMH) plays an important role in fostering pediatric drug development. In addition to coordinating the PeRC review activities, DPMH has two teams of pediatricians who serve as a resource to help with questions about pediatric drug development. For challenging pediatric issues, DPMH has arranged workshops with external experts on particular diseases or through research projects described in later sections of this report.

One of FDA's key efforts has been issuing draft guidance to assist industry in understanding select regulatory, clinical, scientific, and ethical issues surrounding pediatric drug development to help sponsors more efficiently obtain the information needed to support approval of products in pediatric populations (see Section II.E). The draft guidances, "Pediatric Drug Development: Regulatory Considerations – Complying with PREA and Qualifying for Pediatric Exclusivity Under the BPCA" and "Pediatric Drug Development Under the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act: Scientific Considerations" include sections that provide information about obtaining a Written Request, developing pediatric formulations, and submission of pediatric study plans.[28]

FDA also has issued several guidances that discuss development programs in children for specific indications. Examples of such guidances include "Drugs for Treatment of Partial Onset Seizures: Extrapolation of Efficacy from Adults to Pediatric Patients 1 Month of Age and Older," "Development of Anti-Infective Drug Products for the Pediatric Population," and the draft guidance on "Obesity and Overweight: Developing Drugs and Biological Products for Weight Reduction" (which, when final, will reflect the Agency's current thinking). These guidances directly address pediatric considerations for development of drug products for these indications, or include pediatric considerations as part of the guidance provided for drug development in adults. FDA has consolidated a listing of such guidances that provide advice on pediatric drug development on its guidance search website.[29]

One guidance in particular that has had an impact on the feasibility and timeliness of pediatric drug development pertains to the use of pediatric extrapolation. Pediatric extrapolation is defined as, "an approach to providing evidence in support of effective and safe use of drugs in the pediatric population when it can be assumed that the course of the disease and the expected response to a medicinal product would be

[28] When final, these guidances will reflect the Agency's current thinking on these topics.

[29] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents and select "Pediatric Product Development" from the "Topic" filter drop-down menu.

sufficiently similar in the pediatric [target] and reference (adult or other pediatric) population."[30] FDA led efforts to develop and publish internationally harmonized guidance on this topic. When pediatric extrapolation is justified and can be incorporated into a pediatric drug development program, it can decrease the amount and types of data needed to support approval in pediatric populations. One recent example of the use of pediatric extrapolation is in the development of antipsychotic drugs for adolescents with schizophrenia. FDA reviewed data from several second-generation antipsychotic drug development programs and found that the drug exposure-response and efficacy data were similar between adult and adolescent patients.[31] FDA concluded that pediatric extrapolation from adults to adolescents could be considered for antipsychotic drugs with similar mechanisms of action to treat schizophrenia. Therefore, efficacy for certain antipsychotic drugs used to treat adolescents with schizophrenia could rely on open-label pharmacokinetic studies with additional longer-term safety data rather than large randomized, controlled trials.

FDA also considers regulatory science research and engagement with all interested parties as an important mechanism to advance specific pediatric drug development programs that have encountered challenges (see Section III.A). Scientific and regulatory advances over the decades since the laws were enacted have helped to improve the efficiency of pediatric drug development programs. For example, Veklury (remdesivir) was approved for use in pediatric patients, including neonates, for the treatment of COVID-19 about three years after approval for use in adults and adolescents. The public health emergency, unmet medical need, and existing data for remdesivir contributed to the timeliness of the pediatric approvals, but advances in pediatric extrapolation and pharmacokinetic modeling and simulation also played an important role.[32]

B. Special Populations: Children with Cancer, Children with Rare Diseases, and Neonates

1. Pediatric Cancer: Advances in Research and Labeling of Cancer Drugs

Despite recent progress leading to the approval of new oncology drugs for pediatric indications, cancer remains the most common cause of death from disease in children and adolescents one to 14 years of age in the United States, second in total deaths only

[30] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e11a-pediatric-extrapolation.

[31] Kalaria S, Farchione T, Mathis M, et. al. (2020) Assessment of similarity in antipsychotic exposure-response relationships in clinical trials between adults and adolescents with acute exacerbation of schizophrenia. J Clin Pharmacol. 60:848-859. DOI: 10.1002/jcph.1580.

[32] Chan-Tack K, Sampson M, Earp J, et al. (2022) Considerations and challenges in the remdesivir COVID-19 pediatric development program. J Clin Pharmacol. 63(2):259-265. DOI: 10.1002/jcph.2158.

to accidents. In 2025, an estimated 9,550 pediatric patients up to 14 years of age will be diagnosed with cancer, and approximately 1,050 children are expected to die from their disease.[33] There is an urgent need for additional focused and dedicated pediatric oncology drug development to improve outcomes in pediatric patients with cancer. Over the course of the past decade and a half, advances in the understanding of the molecular etiology and genetic epidemiology of human cancers have transformed the paradigm of cancer drug development; molecularly targeted drugs have advanced the concept of precision medicine in oncology, resulting in dramatic improvements in the outcome of patients with cancers such as melanoma[34] and non-small lung cancer.[35] However, extension of these scientific advances to pediatric cancers has been both delayed and limited, in part because the requirements for pediatric assessments of new cancer drugs under PREA were historically based on the adult indications under development (which typically do not occur in pediatric patients or occur so rarely as to make studies infeasible) and due to orphan exemption of requirements under PREA.

Section 504 of FDARA, commonly known as the Research to Accelerate Cures and Equity (RACE) for Children Act, amended PREA to grant FDA the authority to require sponsors to submit reports to FDA on pediatric investigations for certain new drugs directed at a molecular target determined to be substantially relevant to the growth or progression of one or more pediatric cancers, including drugs with orphan designation. These provisions (often referred to as the FDARA or RACE Act amendments to PREA), which went into effect on August 18, 2020, also directed FDA to establish, publish, and regularly update a list of molecular targets considered to be substantially relevant to the growth or progression of a pediatric cancer, and that may trigger requirements to conduct molecularly targeted cancer investigations (sometimes termed "The Relevant Molecular Target List"). FDA also publishes a list of targets that are considered not substantially relevant to the growth or progression of pediatric cancers, and would warrant a waiver of molecularly targeted pediatric cancer investigation requirements (sometimes termed "The Non-Relevant Molecular Target List"). These lists were first published in September 2021, and have been updated twice during the reporting period (the relevant and non-relevant molecular target lists were updated in September 2022, and the non-relevant molecular list was again updated in April 2023).[36] In May 2021, FDA issued a final guidance document titled "FDARA Implementation Guidance for

[33] National Cancer Institute. Childhood Cancers: National Cancer Institute. Updated September 29, 2023. https://www.cancer.gov/types/childhood-cancers.

[34] van Not O, van den Eertwegh A, Haanen J, et al. 2024. Improving survival in advanced melanoma patients: a trend analysis from 2013 to 2021. eClinicalMedicine. 69:102485. DOI:10.1016/j.eclinm.2024.102485.

[35] Howlader N, Forjaz G, Mooradian MJ, et. al. 2020. The effect of advances in lung-cancer treatment on population mortality. N. Engl. J. Med. 383 (640-649). DOI:10.1056/NEJMoa1916623.

[36] See https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-archives.

Pediatric Studies of Molecularly Targeted Oncology Drugs: Amendments to Sec. 505B of the FD&C Act."[37]

FDA encourages early engagement between sponsors and subject matter experts in the Oncology Center of Excellence (OCE) Pediatric Oncology Program. Type F meetings, also known as Early Advice Meetings, provide an opportunity for sponsors to discuss their pediatric development plans early in their drug development process. Specifically, Type F meetings have provided an opportunity for sponsors to discuss the Agency's current thinking about the relevance of a specific molecular target, and FDA's expectations for early investigation in the pediatric population unless there is appropriate justification for a waiver or deferral, and high-level concepts related to the design of a planned pediatric investigation, as warranted. These meetings are required to be granted and scheduled to occur within 30 days of the request. Between July 2020 and June 2025, 39 Type F meetings were requested and granted to discuss 39 distinct new molecularly targeted drugs under development for an adult cancer. These meetings were conducted by the FDA OCE Pediatric Oncology Program within the 30-day timeline in collaboration with the appropriate oncology review division or office in CDER or CBER and members of the FDA Oncology Subcommittee of the Pediatric Review Committee (OCE PeRC). Additionally, with sponsor permission, EMA representatives were invited to attend as observers to help facilitate harmonized international pediatric oncology drug development. Out of the 39 meetings granted and scheduled, 14 (36%) were cancelled by the sponsor prior to the scheduled meeting as they were satisfied with the preliminary FDA written responses to their questions.

The OCE Pediatric Oncology Program continues to work proactively with the clinical review divisions in CDER's Office of Oncologic Diseases and CBER's Office of Therapeutic Products to support communication of timely and appropriate advice to sponsors regarding pediatric drug development programs to facilitate early investigation of new targeted drugs and biological products that have the potential to provide an advantage over existing therapies for pediatric patients. Recently, sponsors have shown heightened interest in confirming that they meet FDARA expectations during pivotal PDUFA milestones meetings and have sought Type D meetings when needed to obtain comprehensive advice regarding aspects of pediatric drug development that require input from specific review disciplines.

During this reporting period, FDA held several Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (ODAC) meetings to discuss FDARA implementation, its impact on pediatric cancer drug development, and ways to optimally leverage FDARA to facilitate product development for pediatric cancers. On May 11, 2022, the subcommittee discussed development of a conceptual framework to inform FDA's decision-making on sponsor plans and requests for waivers of early pediatric investigations of molecularly-targeted cancer drugs and biologics when multiple same-in-class products are approved or in development, recognizing that the rarity of pediatric

[37] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fdara-implementation-guidance-pediatric-studies-molecularly-targeted-oncology-drugs-amendments-sec.

cancers may preclude the feasibility of investigations of multiple products. The subcommittee discussed several important factors that should be considered, including the disease context, product attributes, and comparative efficacy and toxicity data.[38]

On June 16, 2023, the Pediatric Subcommittee of ODAC convened to discuss considerations related to dosage optimization of new drug and biological products for pediatric patients with cancer. Dosage optimization is an integral aspect of oncology drug development and is important to maximizing the safety, efficacy, and tolerability of new drugs for pediatric cancers. Unique considerations associated with dosage selection and optimization in pediatric oncology include variability in pharmacokinetic and pharmacodynamic parameters by age and size, the need for age-appropriate formulations, potential for toxicities associated with long-term use, and the rarity of pediatric cancers.[39]

On May 22, 2024, the Pediatric Subcommittee of ODAC convened to discuss FDA's approach to implementing FDARA. The subcommittee discussed the positive effects, including increased attention and development of drugs for pediatric patients with cancer, potentially leading to more available clinical trials, and increased communication among stakeholders. In addition, the subcommittee discussed important issues that needed continued attention including the need to prioritize which drugs to study given the rarity of pediatric cancers and in some cases, the presence of multiple drugs directed against the same molecular target and greater transparency among all stakeholders in the development and progress of pediatric cancer trials. The role of nonclinical proof of concept studies and approaches to increase collaboration among stakeholders were also discussed.[40]

We note that on February 3, 2026, the Mikaela Naylon Give Kids a Chance Act (GKCA) was enacted as part of the 2026 Appropriations Act. The GKCA further amended section 505B of the FD&C Act to expand the Agency's authority to require dosing, safety, and preliminary efficacy studies of certain oncology drugs in pediatric cancers. This new authority will allow FDA to require molecularly targeted pediatric cancer investigations of certain molecularly targeted oncology drugs in combination with certain other oncology drugs, reflecting the reality that treatment of pediatric cancer generally necessitates a multi-therapy approach. These changes to the law occurred outside the reporting period, and thus will not be discussed here, but the Agency looks forward to implementing this new authority to help spur development of multi-drug approaches to pediatric cancer treatment.

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[38] See https://web.archive.org/web/20230326222702/https://www.fda.gov/advisory-committees/advisory-committee-calendar/may-11-12-2022-pediatric-oncology-subcommittee-oncologic-drugs-advisory-committee-meeting.

[39] See June 16, 2023: Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee Meeting Announcement - 06/16/2023 | FDA

[40] See https://www.fda.gov/advisory-committees/advisory-committee-calendar/may-22-2024-meeting-pediatric-oncology-subcommittee-oncologic-drugs-advisory-committee-meeting.

a. Impact of FDARA on Sponsors' Conduct of Pediatric Cancer Research

Since August 18, 2020,[41] sponsors with oncology development programs subject to FDARA must include in the agreed iPSP a description of their plans to meet the requirement to submit reports of a molecularly targeted pediatric cancer investigation, or plans to request a full waiver, partial waiver, or deferral, with appropriate justification.

In compliance with FDARA provisions, the U.S. Government Accountability Office (GAO) conducted a comprehensive assessment of FDA implementation of the RACE Act amendments to PREA for the period from the onset of its implementation (August 18, 2020), through August 18, 2022; the GAO published the results of this assessment on January 31, 2023.[42] In this report, the GAO concluded that early evidence indicates that the RACE Act has contributed to an increase in the number of planned studies to test certain adult cancer drugs in pediatric patients; however, the GAO also noted that it was too soon to determine if the RACE Act will increase the number of drugs approved to treat pediatric cancers.

Additional experience acquired since publication of the GAO report continues to point to favorable effects of the RACE Act on sponsors' timely consideration and initiation of appropriate studies of molecularly targeted cancer drugs that would historically have gone unstudied in children. During this reporting period, FDA reached agreement on 141 iPSPs for new molecularly targeted oncology products subject to FDARA requirements between June 30, 2020, and July 1, 2025. A total of 81 (57%) of these 141 agreed iPSPs contained a plan to conduct a pediatric investigation of their product in one or more pediatric age groups.

Table 5 provides an assessment of the impact of FDARA over the past 5 years by comparing the number of planned pediatric studies required under the RACE Act with what would have been required for these same products prior to RACE Act implementation. Of the 81 molecularly targeted products with agreed iPSPs that included a plan to conduct pediatric studies under the RACE Act, original applications for 30 (37%) of these products were subsequently approved by FDA during the reporting period and 51 (63%) remained under development at the end of this reporting period. As summarized in Table 5, of the 81 products, 65 (80%) would have qualified for a PREA exemption or waiver and only 16 (20%) could have been subject to the requirement to conduct a pediatric assessment under PREA prior to RACE Act implementation.

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[41] The requirement for sponsors to comply with the amended PREA provisions requiring them to submit reports on the molecularly targeted pediatric cancer investigation for certain molecularly targeted cancer drugs became effective on August 18, 2020 (which was 3 years after enactment of the legislation).

[42] See https://www.gao.gov/products/gao-23-105947.

Table 5: Products with Planned Pediatric Studies under the RACE Act versus Pre-RACE Act (July 1, 2020, through June 30, 2025)

	Products with planned pediatric studies under RACE (n)	Products with planned pediatric studies that would have been exempted or waived pre-RACE (n)[a]	Products with planned pediatric studies that could have been required pre-RACE (n)
Total	**81**	**65[b]**	**16**

Abbreviations: n: number; RACE: Research to Accelerate Cures and Equity Act

[a] Under section 505B(k)(1) of the FD&C Act, requirements to conduct pediatric assessments do not apply to any drug for an indication for which orphan designation has been granted under 21 U.S.C. 360bb (i.e., "orphan drugs"). See 21 U.S.C. § 355c(k)(1). However, orphan drugs are not exempt from the requirement to conduct molecularly targeted pediatric cancer investigations. See 21 U.S.C. § 355c(k)(2).

[b] 25 (31%) of the planned studies under the RACE Act amendments to PREA are for drugs that have orphan status, and 40 (49%) were for a condition that rarely or never occurs in the pediatric population, and for which a pediatric study would be impossible or highly impracticable.

Another way to evaluate the impact of FDARA is through assessment of PMRs. Over the 5-year reporting period, FDA issued PMRs for deferred pediatric studies under PREA for 27 unique oncology products, including PREA PMRs issued for 3 supplemental marketing applications subject to the original PREA provisions and 24 original marketing applications subject to FDARA provisions of PREA. Prior to the passage of FDARA, 21 of the 24 (88%) molecularly targeted products with PMRs for a pediatric investigation under FDARA would have been exempt from PREA due to orphan product designation, or would have qualified for a waiver of pediatric assessment requirements due to the rarity of the adult indication in pediatric patients, rendering a study impossible or highly impracticable. This analysis indicates that FDARA is responsible for a substantial increase in the number of required pediatric studies of molecularly targeted oncology products.

Of the 27 products with PREA PMRs, 4 subsequently received approval for pediatric indications based on data generated in response to PREA PMRs, including 2 during this reporting period: Tafinlar (dabrafenib) and Mekinist (trametinib) in combination for the treatment of pediatric patients ages one year and older with BRAFV600 mutation positive low-grade glioma based on data submitted to fulfill postmarketing requirements under the original PREA provisions under 505B(a)(1)(A) of the FD&C Act. After this reporting period, Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs) was approved for the treatment of adult and pediatric patients ages 12 years and older with unresectable or metastatic alveolar soft part sarcoma (ASPS) and Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) was approved for the treatment of pediatric patients ages 12 years and older with unresectable or metastatic melanoma or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal

cancer.[43] The latter two approvals were based on data generated by studies conducted by sponsors of applications subject to FDARA. In general, because the scope of pediatric studies that FDA has the authority to require under FDARA is limited (i.e., studies intended to provide information on dosing, safety, and preliminary efficacy rather than to establish safety and effectiveness), it is generally expected that additional studies to support approval in pediatric patients with cancer will be needed following conduct of FDARA post-marketing studies.

Product labeling was also updated to inform providers of negative data from studies conducted to fulfill requirements under FDARA for two products: tremelimumab and tisotumab vedotin-tftv. Given the significant risks associated with use of most oncology products, labeling information describing negative results of trials conducted to fulfill PREA PMRs has important health benefits because this information can enhance decision-making by physicians, families, and patients, who often contemplate off-label use of drugs in the absence of satisfactory standard of care.

Prior to and during this reporting period, the FDA also has worked to maximally leverage the incentives under BPCA to encourage timely investigation of oncology products that have a prospect to benefit pediatric patients with cancer. For drugs approved prior to August 18, 2020, that have molecular targets determined to be substantially relevant to the growth or progression of a pediatric cancer and that would have been subject to FDARA amendments to PREA[44] had the application been filed later, FDA has issued 12 WRs. In addition, FDA issued two WRs for molecularly targeted products after August 18, 2020, that are subject to FDARA requirements.

b. Advances in Labeling Drugs for Pediatric Cancer

During this reporting period, the following 29 oncology drugs have been approved and labeled for use in the pediatric population:

Table 6: Oncology Products Approved for Pediatric Use between July 1, 2020, through June 30, 2025 (n=29)

Asparaginase Erwinia chrysanthemi (recombinant)-rywn**	**Lutetium Lu 177 dotatate**
Atezolizumab	**Naxitamab-gqgk**
Azacitidine	**Nivolumab***
Belzutifan	Nivolumab and Relatlimab-rmbw
Blinatumomab	Pembrolizumab*

[43] To facilitate an assessment of the early impact of FDARA on pediatric cancer research, the report includes information for pediatric oncology approvals beyond the reporting period.

[44] Requirements under section 505B(a)(1)(B) of the FD&C Act

Bosutinib	Pralsetinib*
Brentuximab vedotin	Repotrectinib
Cabozantinib*	Revumenib**
Crizotinib*	Rituximab
Dabrafenib*	**Selpercatinib***
Daunorubicin and cytarabine liposome	**Tovorafenib**
Eflornithine	**Trametinib***
Entrectinib	Treosulfan*
Inotuzumab ozogamicin	Vorasidenib**
Ipilimumab*	--

* Drug received approval for more than 1 indication
** Original applications subject to FDARA requirements
NB: In some cases, approvals were supplemental approvals of previously approved products

Thirteen (45%) of the 29 oncology drugs approved for use in pediatric patients with cancer include product labeling supported by studies conducted pursuant to BPCA (bolded in the table above), and two of these oncology drugs (dabrafenib and trametinib, discussed above) received supplemental approvals also based on data from trials conducted to fulfill a PREA requirement. Additionally, two of the 29 pediatric approvals listed in Table 6 were supported by data submitted with original applications that addressed FDARA requirements for a pediatric investigation in one or more pediatric age groups without the need for a deferral.

c. FDA External Engagement to Promote Development of Products for Pediatric Patients with Cancer

The OCE Pediatric Oncology Program proactively works with numerous stakeholders to advance product development and enhance effective communication and collaboration between FDA, international regulatory agencies, patients and advocates, physician scientists at the National Cancer Institute and other academic centers, and industry. Examples include speaking engagements in public workshops and meetings such as the ACCELERATE Pediatric Platform annual meetings and strategy forums. OCE representatives also participate in multistakeholder working groups such as the ongoing international working group coordinated by the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard seeking to develop guidelines and tools to encourage use of innovative study designs such as platform trials in pediatric oncology. Under the auspices of a confidentiality agreement, OCE also has regular discussions with representatives from the European Medicines Agency to promote harmonization of regulatory advice regarding international pediatric cancer drug development programs.

OCE has also organized and conducted multiple external workshops and meetings related to pediatric cancer drug development including the 2024 FDA Oncology Center of Excellence Pediatric Advocacy Forum, which drew over 250 participants including

pediatric oncology patient advocates, clinician scientists, and pharmaceutical company representatives.[45] OCE also co-organizes quarterly meetings with the Children's Oncology Group to informally discuss important issues related to pediatric cancer drug development, such as dose-finding for antibody-drug conjugates and pragmatic study designs including decentralized clinical trials.

2. Rare Pediatric Diseases: Successes and Limitations in Drug Development

Section 508(b)(10) of FDASIA requires that FDA provide an assessment of the successes of and limitations to studying drugs for rare diseases under BPCA and PREA. In addition to BPCA and PREA, other laws impact the study of drugs intended to treat rare pediatric diseases, such as sections 526 and 527 of the FD&C Act (which authorize orphan-drug designation and orphan-drug exclusivity per the Orphan Drug Act[46]) and section 529 of the FD&C Act (which authorizes the rare pediatric disease (RPD) priority review voucher (PRV) program).

The Orphan Drug Act, enacted in 1983, was established to encourage the development of drugs for rare diseases. However, the provisions of the Orphan Drug Act (and subsequent legislative amendments to relevant statutes) do not require pharmaceutical industry sponsors to evaluate drugs with orphan-drug designation in any specific populations affected by a rare disease. Section 505 of FDARA required FDA to report on the lack of pediatric use information in the labeling of drugs for indications that have received an orphan-drug designation. As described in the 2019 report to Congress on the pediatric labeling of orphan drugs, there is a public health need for additional pediatric information in the labeling for over one-third of approved orphan indications that are relevant to the pediatric population. In some cases, there is no pediatric information at all in the labeling, and in other cases, the labeling does not address the full age range of the affected pediatric patients.[47]

PREA does not apply to drugs for an indication for which orphan-drug designation has been granted under section 526 of the FD&C Act, except for certain molecularly targeted cancer drugs.[48] As such, PREA does not serve to ensure the evaluation in the pediatric population of such drugs subject to this "orphan exemption." Notably, the impact of the RACE Act, which requires pediatric studies of certain oncology drugs regardless of orphan-drug designation, appears promising. As described above, evidence suggests that the RACE Act has had a favorable impact on the timely

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[45] See https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/2024-fda-oncology-center-excellence-pediatric-advocacy-forum-10152024.

[46] Public Law 97-414, as amended, codified at sections 525-528 of the FD&C Act (21 U.S.C. 360aa-360dd).

[47] See https://www.fda.gov/media/130060/download.

[48] See section 505B(k) of the FD&C Act.

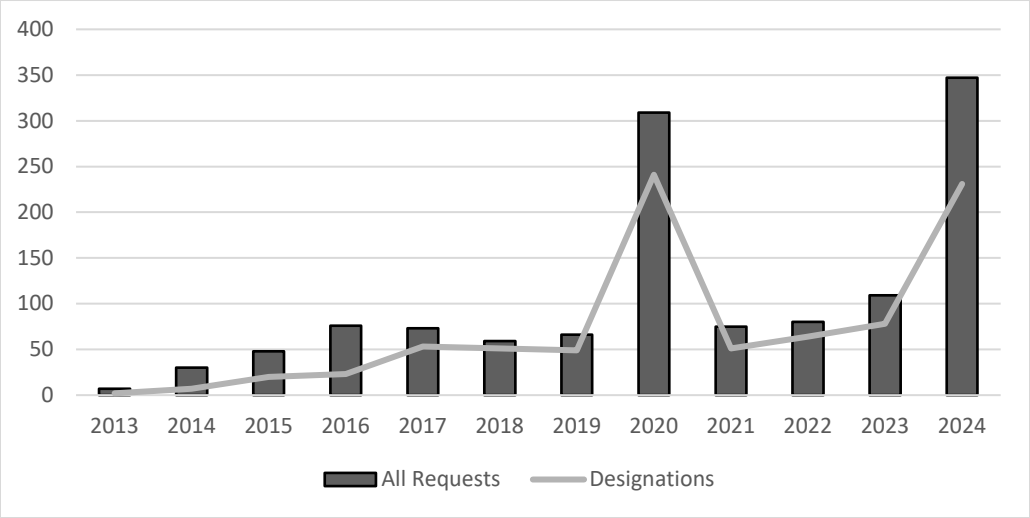
consideration and initiation of studies of appropriate molecularly targeted cancer drugs that would previously have not been required and that would historically have gone unstudied in children.

a. Rare Pediatric Disease Priority Review Voucher Program

The RPD PRV program was established in 2012 under FDASIA to encourage development of new drug and biological products for the prevention and treatment of rare pediatric diseases.[49] It was reauthorized in 2016, 2020, and 2026.[50] Products may be designated as a "drug for a rare pediatric disease" under this program. To be a "rare pediatric disease," a disease must be (1) a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and (2) a rare disease or condition within the meaning of section 526 of the FD&C Act.

The high level of interest in this program has been demonstrated by significant surges in the number of requests for RPD designation received by FDA in the years of the scheduled sunsets in 2020 and 2024 (see Figure 7).

Figure 7: Annual RPD Requests and Designations by Calendar Year (2013-2024)



As of June 30, 2025, FDA has granted 917 rare pediatric disease designations for over 300 unique rare pediatric diseases and has awarded 61 RPD PRVs since the RPD PRV program's inception in 2012 (See Appendix B). Importantly, the requirements to qualify for an RPD PRV generally exclude drugs containing a previously-approved active moiety or active ingredient. Approximately 70% (43/61) of approved products that

[49] FDASIA, Pub. L. 112-144. 126 Stat 993 (July 9, 2012).

[50] As of February 2026, the RPD PRV program has been reauthorized until September 30, 2029. After September 30, 2029, FDA may not award any RPD PRVs.

qualified for an RPD PRV were the first approved therapy for the disease. Most products receiving RPD PRVs treat the underlying disease rather than a specific disease symptom, representing significant progress in developing disease-modifying therapies for diseases for which such therapies had not been available.

In the current reporting period, there were 39 RPD PRV's awarded from July 1, 2020, through June 30, 2025. Approved disease-modifying products receiving an RPD PRV in the current reporting period include the first ever FDA-approved CRISPR/Cas9-based gene-editing therapy: Casgevy (exagamglogene autotemcel) for sickle cell disease, and the first cell-based gene therapy for treatment of adult and pediatric patients with beta-thalassemia who require regular red blood cell transfusions: Zynteglo (betibeglogene autotemcel). Other notable RPD PRV products include targeted therapies for the treatment of spinal muscular atrophy and Duchenne muscular dystrophy.

We note that the 2026 Appropriations Act extended FDA's authority to award RPD PRVs through September 30, 2029. As it currently exists, however, the RPD PRV program must be renewed periodically by legislative action. This need for continued reauthorization creates unpredictability in long-term planning and resource allocation for companies developing these drugs and biologics. FDA supports making the RPD PRV program permanent, as reflected in legislative proposals included in the FY2027 FDA budget.

3. Challenges and Progress in Developing Drugs for Neonates

a. The Current State of Neonatal Drug Development Under BPCA and PREA

Over the past nearly 25 years since passage of BPCA and PREA, the vital progress in labeling updates for the general pediatric population has not been observed in the neonatal subpopulation. Of the 1,364 pediatric labeling changes pursuant to BPCA and PREA, only 12% included information for neonates. Of the 137 drugs granted a new indication in neonates, approximately 40% relied on data from older pediatric patients and/or adults rather than clinical studies conducted in neonates (see Figure 8). Additionally, the current paradigm for drug development under BPCA and PREA generally has not resulted in a significant increase in research addressing conditions solely affecting the neonatal population. For example, only two drugs (aflibercept for retinopathy of prematurity and phenobarbital for neonatal seizures) were studied and approved for a neonatal-specific condition during the current reporting period.

Figure 8: Labeling Changes for Neonates Pursuant to the Pediatric Rule, BPCA, and PREA from April 1999 through June 2025



Multiple factors contribute to the suboptimal pace of neonatal therapeutics development under BPCA and PREA. Drugs under development for adult conditions may not be relevant to neonates, in which case studies in accordance with BPCA and PREA may not be appropriate. PREA does not provide an incentive for the pharmaceutical industry to develop drugs that specifically address conditions characterized by unique neonatal pathophysiology. Although FDA has the authority to request studies of drugs for a different indication pertinent to the neonatal population by issuing WRs under BPCA, completion of studies in a WR is voluntary and current incentive structures may not be sufficient to support development.

In accordance with FDASIA, any WR that does not request studies in neonates must include a statement describing the rationale for not requesting studies in neonates. From passage of FDASIA on July 9, 2012, through June 30, 2025, we reviewed the inclusion of neonates in WRs that resulted in the granting of Pediatric Exclusivity (PE). Of the 95 moieties granted PE, only 19% (18/95) included the neonatal population in the requested studies. The reasons cited for why the vast majority of WR did not require studies in neonates included that (1) the disease did not occur in or could not be diagnosed in the neonatal population (n=50), (2) the neonatal population with the given indication was too small to study (n=19), (3) it was unsafe to conduct the studies in neonates (n=5), or (4) the drug was already approved in neonates or offered no therapeutic benefit over existing therapies (n=3).

Ultimately, the limited impact of PREA and BPCA on neonatal drug development, coupled with numerous other challenges, result in an unmet medical need for neonates. As noted above, only two drugs were approved in the current five-year reporting period for a neonatal-specific condition and there are no FDA-approved drugs indicated to treat or prevent some of the major diseases afflicting neonates, such as prematurity-associated chronic lung disease, necrotizing enterocolitis, and hypoxic ischemic encephalopathy.

Most neonatal conditions are considered rare and, therefore, may benefit from incentive programs designed to promote product development for rare diseases. At the same time, drugs receiving orphan drug designation are currently exempted from pediatric study requirements under PREA. Similar to the shift in the regulatory landscape for pediatric cancer drug development that occurred following implementation of the RACE

Act, elimination of the PREA exemption for orphan designated drugs that would offer therapeutic benefit to neonates would be expected to have a favorable impact on neonatal drug development.

b. FDA Efforts to Promote Medical Product Development for Neonates

Section 508(b)(7) of FDASIA requires that FDA report on efforts made by the Agency to increase the number of studies conducted in the neonatal population and the results of these efforts. Despite the challenges noted above, some progress has been made in neonatal drug development during the reporting period. Since the 2021 report to Congress, under BPCA and PREA, the labeling for 61[51] drugs has been updated to include the drug's dosing, safety, and/or efficacy for neonates. Of note, this represents an approximately 30% increase in the number of neonatal labeling changes that occurred during the prior reporting period (n=47).[52] The labeling changes have provided important information to support neonatal use for a selection of drug products, particularly antivirals and other anti-infectives, that would historically have gone unlabeled in the neonatal population.

FDA continues to encourage and support the conduct of studies in neonates by (1) providing reviewers across the Agency with expert neonatal-perinatal consultation services, (2) encouraging drug development in neonates through engagement and outreach with internal and external interested parties, (3) coordinating cross-cutting programs relevant to neonates, and (4) developing guidance documents to facilitate neonatal studies. In addition, FDA has been working to overcome the obstacles to advancing neonatal regulatory science, recognizing the importance of establishing a strong scientific foundation to support drug development for neonates.

Considerable strides have been made since FDA's neonatology program was developed within the Office of Pediatric Therapeutics (OPT). This program has seen steady growth of its neonatal-perinatal medicine consultation service, which provides expertise to reviewers across the Agency in the development and use of FDA-regulated products that benefit neonates. FDA now has three neonatologists on staff in OPT dedicated to support these consultation services. Value of the neonatology consultation service is evidenced by its increased utilization over time, with consult requests increasing by nearly three-fold from inception to current and originating from all product development centers as well as the Human Foods Program (HFP). FDA's neonatology staff also remain active on the PeRC, as required by section 505C of the FD&C Act, and

[51] Labeling updates resulted from the 409I program (12 drugs), PREA (44 drugs), BPCA (4 drugs), and BPCA plus PREA (1 drug).

[52] FDA periodically reviews the approach to data collection, as well as the completeness and accuracy of its pediatric clinical trial database, which can lead to shifts in the reported data. After a recent review of the database, FDA identified a discrepancy in the number of neonatal labeling changes reported for the last reporting period from July 1, 2015, through June 30, 2020. There were 47, rather than the previously reported 22, neonatal labeling changes during that period.

are integral in fostering drug development in neonates by addressing the unique challenges of evaluating products in this population during PeRC discussions.

FDA's neonatology staff remain engaged with various interested parties to promote product development in neonates. In partnership with the International Neonatal Consortium (INC), FDA supported development of tools to facilitate safety monitoring in neonatal clinical trials. FDA's neonatology program also organized several public meetings to foster discussions on addressing challenges in neonatal clinical trials and advancing medical product development in areas of unmet need relevant to neonates (see Section III.A).

Participation in cross-cutting initiatives across the agency and HHS is a cornerstone of the neonatology program's efforts. For example, FDA neonatology support and expertise was provided to the HFP response to the 2022 infant formula shortage, the Necrotizing Enterocolitis (NEC) in Preterm Infants Working Group of the National Advisory Council of Child Health and Human Development (NACHHD),[53] and the Operation Stork Speed initiative.

Guidance development to support the conduct of studies in neonates remains a core initiative for FDA's neonatology program. In July 2022, FDA finalized the guidance document titled "General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products" to address the clinical pharmacology considerations for any planned studies in neonatal populations.[54] In addition, FDA issued as draft in February 2023, and later finalized in October 2024, the guidance "Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development."[55]

c. Advancing Regulatory Science in the Conduct of Studies in Neonates

FDA recognizes that advancing the science to support regulatory decision-making in the development of drugs to treat conditions affecting neonates is of utmost importance and involves collaboration with internal and external stakeholders. FDA continues to support and contribute to efforts to further the science and to develop tools to streamline drug development programs. For example:

- FDA collaborated in a consensus process with the INC to develop the neonatal adverse event severity scale (NAESS). Use of a neonatal-specific standardized

[53] See https://www.nichd.nih.gov/about/advisory/council/NEC-working-group-of-council.

[54] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-clinical-pharmacology-considerations-neonatal-studies-drugs-and-biological-products-guidance.

[55] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-long-term-clinical-neurodevelopmental-safety-studies-neonatal-product-development.

severity scale will improve the quality and consistency of safety evaluations during the conduct of neonatal clinical trials. Current efforts to expand the scale and develop a digital tool will promote further dissemination of the NAESS across multinational clinical trials.

- FDA awarded a multi-year grant to INC and the Critical Path Institute (C-Path) to advance standards and methodologies to generate real-world evidence from existing real-world data within neonatal datasets and electronic health records through a neonatal data pilot project. The INC/C-Path team has obtained over 300,000 data points from neonatal electronic health records and clinical trial data. This pilot project has generated real-world evidence to define normal and abnormal laboratory values to guide safety assessments in clinical trials.

- FDA used the Broad Agency Announcement process[56] to fund the following projects:

    - To study actigraphy as a potential endpoint in clinical trials involving pediatric patients with pulmonary arterial hypertension beginning from birth. The published results of this study[57] supported the feasibility of an actigraphy-based endpoint that has potential to reduce sample sizes needed for future clinical trials.

    - To evaluate the health and long-term neurodevelopmental outcomes of children with intrauterine opioid exposure. The project will use electronic health records that incorporate maternal, neonatal, and pediatric data to assess whether abnormal neurodevelopment may be associated with pharmacologic treatment for neonatal withdrawal. These data will help provide a better understanding of the outcomes of children with intrauterine opioid exposure and the impact of treatment during the neonatal period.

    - To develop a perinatal COVID registry to link clinical data in maternal-fetal dyads, biospecimens and outcomes to better understand the impact of the COVID-19 pandemic on maternal/fetal/neonatal outcomes. This project established methods to link data across various sources including electronic health records from hospitals, state Department of Health records, Census-based Geographic Information Systems and hospital biobanks that can be

[56] This process is a specialized contract mechanism that makes it possible for the Agency to solicit innovative ideas and approaches to developing and evaluating FDA-regulated products by tapping into external knowledge and infrastructure in areas where FDA has limited expertise or capacities. The proposals solicited from industry, academia, and other government agencies enable FDA to better understand the breadth of innovative scientific and technical solutions available to solve difficult regulatory science problems.

[57] Sun H, Stockbridge N, Ivy D, et al. 2025. Actigraphy Study Endpoints to Reduce Sample Size and Facilitate Drug Development for Pediatric Pulmonary Arterial Hypertension. J Pediatr. 277:114383.

leveraged to investigate other diseases that impact pregnant women and their offspring.

- FDA funded a project to identify high-quality clinical outcome assessments (COAs) and endpoints for measuring acute pain in neonates and infants from birth to two years of age. Given the historical challenge assessing pain in this age group, these tools can help open the door for new pain medications to be developed and approved for young children, including neonates.

C. Achievements of the BPCA/409I Program

Section 409I of the PHS Act, which was created by the Best Pharmaceuticals for Children Act of 2002, requires NIH, in consultation with FDA and experts in pediatric research, to create a pediatric drug development program (the "BPCA/409I program") to study medications that no longer have patent status (off-patent) and that are prescribed to children but still need improvements in the dosing, safety, and/or efficacy labeling information for children. Among other things, section 409I specifically mandates NIH to (1) identify and prioritize drugs and therapeutics that need further study in pediatric populations, (2) sponsor clinical trials and support research for prioritized drugs and therapeutic areas, (3) submit data from these trials to FDA, which will determine if labeling changes are appropriate, (4) disseminate sponsored research from the BPCA/409I program to researchers and the public, and (5) sponsor training programs in the field of pediatric pharmacology.

The early achievements of the BPCA/409I program have been described in detail in past reports.

1. Prioritizing Drugs and Therapeutics for Further Study

One of the primary responsibilities of the BPCA/409I program involves identifying and prioritizing needs in pediatric therapeutics. The prioritization process, first established in 2010, refined in 2017, and restructured in 2024, includes structured and frequent outreach to various stakeholders involved in pediatric drug development. Based on the prioritization process, more than 160 drugs/therapeutics and 40 conditions/indications have been prioritized for further study over the history of the BPCA/409I program. Due to limitations in fit, feasibility, and financial infrastructure, all prioritized drugs cannot be studied under the BPCA/409I program; however, the BPCA priority list serves as a foundation for the pediatric drug development program at NIH as well as a beacon of needs that remain in the pediatric population.[58] NIH has highlighted the BPCA priority list as a resource in funding opportunity announcements to encourage investigator-initiated research in these areas outside of the BPCA/409I program (e.g., PAR-25-110

[58] See https://www.nichd.nih.gov/research/supported/bpca/prioritizing-pediatric-therapies.

"Translational Research in Maternal and Pediatric Pharmacology and Therapeutics (R01 Clinical Trial Optional))."

2. Clinical Trials of Prioritized Drugs

Prior to 2010, the BPCA/409I program sponsored prioritized clinical trials based on Written Requests (WR) received from FDA and subsequently conducted and/or co-funded 14 pediatric clinical trials for conditions such as bipolar disease, status epilepticus, hypertension, and cancer.

The program's current success can be attributed largely to work done by the Pediatric Trials Network (PTN) which serves as the infrastructure for protocol design and implementation and pharmacology expertise, as well as serving as the Clinical Coordinating Center. The concomitant Data Coordinating Center provides data management, statistical, and regulatory expertise, and both entities have been vital to the success of the BPCA/409I program. The PTN, originally funded in 2010 and funded again in 2017 and 2025, has developed and implemented over 50 pediatric clinical trials that include evaluation of more than 160 drug molecules across more than 300 clinical sites to improve the knowledge of medicines used in children. As of June 30, 2025, NIH has submitted 39 clinical study reports to FDA for labeling change considerations to improve knowledge and close labeling gaps in medications used in children.

3. Labeling Changes Under the BPCA/409I Program

The primary goal of the BPCA/409I program is to update pediatric labeling for medications prescribed to children off-label that no longer have patent protection. As of June 30, 2025, clinical trials supported by the BPCA/409I program have led to a total of 26 labeling changes, two of which are for medical devices.[59] Of the 26 labeling changes, 21 occurred through the established process for the BPCA/409I program.[60]

Between 2002 and 2016, FDA approved labeling for three drugs through this program. In the 2020 report to Congress, FDA highlighted that the number of drugs with approved labeling changes had more than tripled, with FDA approving the labeling for seven additional drugs. Since that report, FDA has approved pediatric labeling changes for 11 additional drugs, demonstrating considerable gains with each reporting period. Stemming from the BPCA/409I program, FDA has approved a change to the labeling of the following products to provide details related to the product's use in pediatric patients:

- Acyclovir for the treatment of neonatal herpes simplex virus

[59] See https://www.nichd.nih.gov/research/supported/bpca/accomplishments.

[60] See https://www.fda.gov/drugs/development-resources/nih-funded-pediatric-labeling-changes-drugs-studied-under-409i-process.

- Ampicillin for the treatment of sepsis and/or meningitis
- Bactrim for the treatment of infections per Standard of Care
- Caffeine Citrate for the short-term treatment of apnea of prematurity
- Clindamycin for the treatment of serious infections
- Clindamycin for the treatment of intra-abdominal infections
- Diazepam for the treatment of status epilepticus
- Doxycycline for the treatment of life-threatening infectious diseases
- Fluconazole for patients on extracorporeal membrane oxygenation
- Furosemide for bronchopulmonary dysplasia (BPD)
- Levetiracetam for juvenile myoclonic epilepsy disorder in obese patients
- Lithium for the treatment of bipolar disorder
- Lisinopril for the treatment of hypertension in kidney transplant recipients
- Lorazepam for the treatment of status epilepticus
- Meropenem for injection for the treatment of intra-abdominal infections
- Metronidazole for the treatment of the intra-abdominal infections
- Ondansetron for the treatment of nausea and vomiting
- Oxcarbazepine for the treatment of partial onset seizures in obese patients
- Oxycodone for the treatment of infant exposure to medications
- Rifampin for the treatment of MRSA, various infections and tuberculosis
- Propylthiouracil for the treatment of hyperthyroidism (the labeling was changed for safety and dosing)
- Pralidoxime for use in organophosphate poisoning
- Sodium Nitroprusside for the treatment of blood pressure in the perioperative environment
- Mercy TAPE to estimate body weight based on measurements of arm length and upper arm circumference
- Mercy BabyTAPE to estimate body weight of infants from birth to 90 days of age
- Topiramate for the treatment of complex partial epileptic seizure (disorder) in obese patients

The pediatric labeling changes under the BPCA/409I program include: improving dosing ranges for antibiotics used for various infectious disease indications in children and neonates, including pre-term neonates (acyclovir, ampicillin, bactrim, clindamycin, doxycycline, fluconazole, meropenem, and rifampin); providing tolerance, and long-term

safety and effectiveness for psychotherapies (lithium); providing novel dose pharmacokinetic modeling matched with use of real world evidence (RWE) for medications used in pre-term and term neonates (ampicillin, caffeine, fluconazole, and furosemide); as well as important updates in various medications used for specific indications (lorazepam, diazepam, and levetiracetam for seizures, sodium nitroprusside and lisinopril for hypertension, and dosing of medications based on body mass index including oxcarbazepine and topiramate). In addition to drug studies, PTN also has submitted data to FDA for pediatric labeling changes for medical devices used for weight estimation (Mercy Tape and Baby Tape). These devices are used to aid with the timely determination of pediatric weight in trauma and/or emergency situations and help guide appropriate treatment dosing.

Several drugs also have had improvements in their drug labeling based on research supported by the BPCA/409I program, including propylthiouracil and pralidoxime. In recent years, PTN has also embarked upon improving data on medications used by mothers during breastfeeding. There has been a longstanding need to provide data related to the transfer of medications into breast milk. Programs such as the Drugs and Lactation Database (LactMed®), supported by the National Library of Medicine (NLM), have been vital in providing objective data from published literature. In 2024, PTN became trailblazers in this drug development ecosystem by characterizing the pharmacokinetics and safety profile of commonly used medications in breastmilk (oxycodone, ondansetron) resulting in FDA approved labeling updates.

4. Dissemination of Information Obtained from BPCA/409I Research

Data from NIH-funded studies pursuant to the BPCA/409I program are published in an FDA public docket for all labeling changes, in peer-reviewed journals for scientific advancements, and on the National Institute of Child Health and Human Development's (NICHD's) Data and Specimen Hub (DASH) for investigators to access the datasets publicly. To date, clinical study data from the BPCA/409I program and the PTN have resulted in 26 drug labeling changes and contributed more than 200 peer-reviewed publications to the scientific literature. NIH-funded BPCA study findings are available as two-page study summaries and as full datasets on the DASH website for researchers; in addition, lay summaries of clinical trial findings that are geared toward families and participants are provided on the PTN website.[61] The summaries also link to FDA's drug labeling, PubMed, the NLM Bookshelf, and NICHD's DASH.

In addition to the study data being made available to interested researchers and stakeholders, the NIH BPCA/409I program leadership worked with investigators in the field of pediatric pharmacology and therapeutics to develop a comprehensive online collection of resources for those involved in pediatric drug development research, the

[61] Summaries are available at https://www.nichd.nih.gov/research/supported/bpca/resources/study-summaries, https://dash.nichd.nih.gov/, and https://pediatrictrials.org/.

"BPCA Framework to Enable Pediatric Drug Development," which is also available on the NIH's website.

5. NIH-Sponsored Training Programs

The NIH has sponsored several programs aimed at training pediatric investigators, including the Pediatric Clinical and Developmental Pharmacology Network (CPTN) and the Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub.

The CPTN was formed in response to the requirements in section 409I of the PHS Act for NIH to consider the adequacy of the infrastructure necessary to conduct pediatric pharmacological research, including research networks and trained pediatric investigators. The training goals of the CPTN continue to expand to foster more entry points for aspiring clinician-scientists, cultivate early intellectual curiosity, and maintain continuity, thus promoting and sustaining career development. The CPTN provides both didactic and hands-on experience in clinical pharmacology, and has instructed more than 300 trainees across the U.S. since its inception.

The MPRINT Hub is an initiative that was formed in 2021 and is partially funded by the BPCA/409I program.[62] This program supports the advancement of fundamental pediatric pharmacology principles and promotes their integration into clinical trials by providing expertise and consultation in pharmacology and therapeutics to investigators. The MPRINT Hub provides a bridge between translational research and clinical research and serves as a scientific service center and a platform for improved dissemination and training in the respective pharmacology fields. The goal of the MPRINT Hub is to provide a hub of knowledge and expertise in maternal and pediatric therapeutics to the scientific community with the goal to catalyze and accelerate maternal and pediatric therapeutics towards precision medicine using the most current scientific approaches and knowledge.

D. PAC Activities: Evaluation of FDA's Post-Marketing Pediatric Safety Reviews and Other Matters in Pediatric Product Development and Use

FDA continues to implement the congressionally mandated pediatric-focused post-marketing safety review process of drugs and biologics covering the 18-month period after a pediatric labeling change pursuant to BPCA and PREA and to facilitate the sharing of these reviews with the PAC.

FDA analyses have consistently shown that fixed-schedule post-marketing safety reviews provide minimal added value compared to ongoing, risk-based

[62] See https://www.nichd.nih.gov/about/org/der/branches/opptb/mprint.

pharmacovigilance systems.[63] An FDA retrospective analysis examined all post-marketing pediatric-focused safety reviews conducted over a 6-year period from October 1, 2013, through September 30, 2019. Among 163 products reviewed following pediatric labeling changes, new safety signals were identified for only 5 products, contributing to less than 1% of the 585 safety-related labeling changes for these products during the study period. None were specific to the pediatric population.[64]

These findings have been confirmed in the current reporting period. Since the 2021 report to Congress, FDA has reviewed 184 products for post-marketing pediatric safety after labeling changes pursuant to BPCA and PREA. In this reporting period, FDA's post-marketing pediatric-focused safety reviews, together with evaluations by the PAC, have confirmed the safety profiles of products under review and have not identified new pediatric-specific safety signals requiring labeling changes.

In contrast, FDA's routine pharmacovigilance consistently identifies a greater number of safety signals relevant to the adult and pediatric populations compared to the fixed 18-month review process. For example, FDA issued a safety labeling change notification within 6 months of approval of Beyfortus (nirsevimab-alip), a monoclonal antibody indicated for RSV respiratory disease prevention in infants and certain high-risk young children, based on adverse event reports of serious hypersensitivity reactions identified during routine pharmacovigilance. This action occurred well before the 18-month pediatric-focused safety reviews were due. In June 2025, FDA warned of the risks of heat-related complications with use of the antinausea patch Transderm Scōp (scopolamine transdermal system) and added this risk and other information to the product's labeling after cases of hyperthermia, mostly in children 17 years and younger and in adults 60 years and older, were identified through FDA's routine pharmacovigilance.[65] Transderm Scōp is not approved in pediatric patients and therefore not subject to the 18-month pediatric safety review process. This case illustrates that FDA's routine pharmacovigilance is robust and able to identify pediatric-related safety signals even for products used off-label.

Collectively, these findings demonstrate that the 18-month post-marketing pediatric-focused safety review requirement provides minimal public health benefit beyond FDA's existing, comprehensive pharmacovigilance and medical product safety monitoring framework. Although the mandated reviews have identified a small number of safety signals, the resources required represent a significant opportunity cost, diverting pharmacovigilance expertise from risk-based surveillance activities. Reliance on a

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[63] Sekine S, Pinnow EE, Wu E, et al. 2016. Assessment of the impact of scheduled postmarketing safety summary analyses on regulatory actions. Clin Pharmacol Ther. 100(1):102-8. doi: 10.1002/cpt.346. PMID: 26853718; PMCID: PMC4943082.

[64] Mohamoud M, Cheng C, Ryan D, et al. 2023. Assessment of the impact of mandated postmarketing pediatric-focused safety reviews on safety-related regulatory actions 2013-2019. Clin Pharmacol Ther. 113(6): 1368-77. doi: 10.1002/cpt.2900. PMID: 37021630.

[65] See https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-warning-about-serious-risk-heat-related-complications-antinausea-patch-transderm-scop.

standardized, time-based schedule does not represent the most effective or efficient strategy for detecting safety signals.

FDA previously faced similar challenges with time-based post-marketing safety reviews required under FDAAA, which mandated reviews (not limited to the pediatric population) 18 months after drug approval or after use of the drug by 10,000 individuals, whichever was later. Like the current pediatric-focused reviews, an FDA analysis found these scheduled reviews provided minimal value compared to ongoing, risk-based pharmacovigilance. Subsequently, the Cures Act (Pub. L. 114-255)[66] eliminated this requirement, and FDA implemented a risk-based framework for post-marketing safety surveillance of human drug and biological products, including pediatric safety surveillance. The risk-based safety surveillance considers the product's pharmacological characteristics, clinical use patterns, and overall risk profile to inform the timing, scope, and methodology of safety assessments.[67] This modernized, risk-informed model streamlines safety signal detection while maintaining robust protections for pediatric populations.

1. Strategies for Optimal Utilization of PAC Expertise

To maximize the impact of the PAC, FDA is exploring strategies to more effectively align PAC activities with emerging pediatric priorities. Given the breadth and complexity of pediatric-focused post-marketing safety surveillance, PAC meetings could be structured to focus on the highest-risk safety concerns and complex pediatric product development challenges. This targeted approach would ensure that PAC expertise is directed toward areas where its input can add the greatest value, such as safety concerns with significant public health implications, evolving therapeutic areas, and topics requiring nuanced clinical and scientific perspectives, as demonstrated by previous PAC discussions on artificial womb technologies for management of extremely premature infants,[68] neuropsychiatric risks with montelukast,[69] and opioid analgesic use in children.[70] These strategies would optimize PAC contributions, ensuring their expertise is used where it will have the most meaningful impact on pediatric safety and product development.

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[66] Section 3075 of the Cures Act (Pub. L. 114-255) amended section 505(r)(2)(D) of the FD&C Act.

[67] See Best Practices for FDA Staff in the Postmarketing Safety Surveillance of Human Drug and Biological Products (January 2024) at https://www.fda.gov/media/130216/download.

[68] See https://www.fda.gov/advisory-committees/advisory-committee-calendar/pediatric-advisory-committee-meeting-announcement-09192023.

[69] See https://www.fda.gov/advisory-committees/advisory-committee-calendar/september-27-2019-meeting-pediatric-and-drug-safety-and-risk-management-committees-09272019.

[70] See https://www.fda.gov/advisory-committees/advisory-committee-calendar/september-11-2017-pediatric-advisory-committee-meeting-announcement-09102017.

E. Guidance Documents

FDA has issued many guidance documents since the 2021 BPCA and PREA report to Congress related to implementation of the pediatric statutes and conduct of pediatric research, including the following draft and final guidance documents that are relevant to this report:

- Final Guidance Document – *E11A Pediatric Extrapolation* (December 2024)[71]

  This guidance document finalized the draft guidance of the same title that was issued in August 2022.

- Final Guidance Document – *Considerations for Long-Term Clinical Neurodevelopmental Safety Studies in Neonatal Product Development* (October 2024)[72]

  This guidance document finalized the draft guidance of the same title that was issued in February 2023.

- Final Guidance Document – *Rare Diseases: Considerations for the Development of Drugs and Biological Products* (December 2023)[73]

  This guidance document finalized the draft guidance entitled, "Rare Diseases: Common Issues in Drug Development" that was issued in February 2019.

- Draft Guidance Document – *Pediatric Drug Development Under the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act: Scientific Considerations* (May 2023)[74]

  When final, this guidance document will represent the Agency's current thinking on this topic.

- Draft Guidance Document – *Pediatric Drug Development: Regulatory Considerations — Complying With the Pediatric Research Equity Act and*

[71] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e11a-pediatric-extrapolation.

[72] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-long-term-clinical-neurodevelopmental-safety-studies-neonatal-product-development

[73] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/rare-diseases-considerations-development-drugs-and-biological-products.

[74] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-under-pediatric-research-equity-act-and-best-pharmaceuticals-children-act.

Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act (May 2023)[75]

When final, this guidance document will represent the Agency's current thinking on this topic.

- Draft Guidance Document – *Measuring Growth and Evaluating Pubertal Development in Pediatric Clinical Trials* (October 2022)

  When final, this guidance document will represent the Agency's current thinking on this topic.

- Draft Guidance Document – *Ethical Considerations for Clinical Investigations of Medical Products Involving Children* (September 2022)[76]

  When final, this guidance document will represent the Agency's current thinking on this topic.

- Draft Guidance Document – *General Clinical Pharmacology Considerations for Pediatric Studies of Drugs, Including Biological Products* (September 2022)[77]

  When final, this guidance document will represent the Agency's current thinking on this topic.

- Final Guidance Document — *General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products* (July 2022)[78]

  This guidance document was required under section 505(d)(2) of FDARA and addresses the clinical pharmacology considerations for any planned studies in neonatal populations. This guidance document finalized the draft guidance of the same title that was issued in August 2019.

- Final Guidance Document – *Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics* (March 2022)[79]

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[75] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-regulatory-considerations-complying-pediatric-research-equity-act-and.

[76] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ethical-considerations-clinical-investigations-medical-products-involving-children.

[77] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-clinical-pharmacology-considerations-pediatric-studies-drugs-including-biological-products.

[78] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-clinical-pharmacology-considerations-neonatal-studies-drugs-and-biological-products-guidance.

[79] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/master-protocols-efficient-clinical-trial-design-strategies-expedite-development-oncology-drugs-and.

This guidance document finalized the draft guidance of the same title that was issued in October 2018.

- Final Guidance Document — *FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs: Amendments to Sec. 505B of the FD&C Act* (May 2021) [80]

  This guidance document addresses early planning for the pediatric evaluation of certain molecularly targeted cancer drugs. This guidance document finalized the draft guidance entitled "FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs" that was issued in December 2019 and finalized certain recommendations related to FDA's implementation of FDARA that were included in the January 2020 draft guidance document entitled "Pediatric Study Plans for Oncology Drugs: Questions and Answers."

- Final Guidance Document — *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Initial Pediatric Study Plans* (July 2020)[81]

  This guidance document provides recommendations regarding the submission of iPSPs and amendments to an iPSP. This guidance document was required under section 505B(e)(7) of the FD&C Act, added by section 506 of FDASIA. After issuing two draft guidance documents, in July 2013 and March 2016, FDA finalized this guidance document in July 2020 after incorporating comments received on those drafts. FDA continues the process of developing a proposed rule regarding iPSPs in accordance with section 505B(e)(7) of the FD&C Act.

- Final Guidance Document – *Cancer Clinical Trial Eligibility Criteria: Minimum Age Considerations for Inclusion of Pediatric Patients* (July 2020)[82]

  This guidance document finalized the draft guidance of the same title that was issued in March 2019.

[80] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fdara-implementation-guidance-pediatric-studies-molecularly-targeted-oncology-drugs-amendments-sec.

[81] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-study-plans-content-and-process-submitting-initial-pediatric-study-plans-and-amended.

[82] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cancer-clinical-trial-eligibility-criteria-minimum-age-considerations-inclusion-pediatric-patients.

III. Impact of Pediatric Statutes: Beyond the Mandates

The pediatric statutes have stimulated scientific growth and innovation in the way drugs are developed for children and have spurred robust international collaboration to ensure pediatric studies are well designed to meet global regulatory standards.

A. Advancing Regulatory Science and Enhancing Collaboration for Pediatric Drug Development

1. Advancing Pediatric Regulatory Science Research

FDA engages in regulatory science research to support regulatory policies and scientific advancements that impact pediatric drug development. The outcomes from FDA-funded research contribute to improving strategies for optimizing clinical trials in pediatric patients, facilitating timely access to therapies.

Over the past five years, FDA engaged in several collaborative research projects spanning a wide range of pediatric research topics including pediatric dose selection, extrapolation of data, analysis of negative pediatric trials, inclusion of pediatric patients in adult trials, bridging efficacy and safety to the obese, innovative approaches to analgesic drug development in pediatric patients, fetal pharmacology, and pharmacokinetic modeling. These regulatory research projects have resulted in several peer-reviewed publications, demonstrating the scientific rigor and impact of FDA's pediatric research initiatives. Most projects were conducted in collaboration with the Office of New Drugs review divisions and fostered cross-center and cross-disciplinary collaboration to ensure research findings directly inform regulatory decision-making. The research outcomes have informed FDA's policy on developing products in pediatric patients, providing an evidence-based foundation for regulatory guidance and decision-making processes. Some notable examples of pediatric regulatory science research conducted between 2020 and 2025 are included below:

- **Pediatric Hypertension**: FDA's systematic review of pediatric hypertension trials established a new regulatory framework that streamlined development of angiotensin receptor blockers in pediatric patients by requiring only pharmacokinetic data collection/analysis and long-term safety studies rather than controlled efficacy trials. This evidence-based approach supported the regulatory approval of valsartan for patients ages one to 6 years through extrapolation from older pediatric data, significantly reducing development burden and expanding treatment options for young children with hypertension.

- **Pediatric Heart Failure**: FDA leveraged its unique access to pooled adult heart failure trial data to support the use of N-terminal pro-B-type natriuretic peptide (NT-proBNP) as a bridging biomarker for efficacy extrapolation from adults to

children. This research enabled feasible pediatric heart failure trial designs using NT-proBNP as the primary efficacy endpoint for some drugs, transforming previously impractical development programs and currently supporting ongoing pediatric trials with this streamlined approach.

- **Pediatric Major Depressive Disorders**: FDA's project PARADOX's comprehensive analysis of over 30,000 patients across pediatric and adult antidepressant trials identified critical factors contributing to pediatric trial failures, including baseline disease severity differences between age groups. The research demonstrated that pediatric patients present with lower baseline severity compared to adults, establishing preliminary evidence for baseline severity as a potential trial enrichment strategy that could improve the probability of success for pediatric major depressive disorders trials and ultimately improve the rigor and interpretability of pediatric trials for children and adolescents with depression.

FDA also has awarded several grants to support pediatric research and development. These grants help fund activities ranging from bench research to pediatric clinical trials.[83]

Additionally, FDA trained multiple ORISE fellows, fellows from Walter Reed Army Institute of Research, as well as pediatric medical fellows under Individual Personnel Agreements, further strengthening the agency's capacity to conduct high-quality pediatric research and develop the next generation of regulatory scientists.

2. Enhancing Collaboration for Pediatric Drug Development

FDA recognizes that encouraging the timely completion of pediatric studies necessitates the cooperation of all pediatric stakeholders involved in the drug development process. FDA has created opportunities for interested parties to meet to discuss feasible development approaches in areas of unmet need and in areas in which development has been historically difficult. Since 2020, FDA has hosted numerous workshops to examine ways to optimize pediatric drug development. Table 7 provides a listing of select pediatric-focused workshops convened by FDA during the reporting period.

Such workshops have been well-received by external stakeholders and have led to specific meaningful changes that have created pathways to drug approval in pediatric populations. For example, in 2023, FDA participated in a meeting hosted by the Kidney Health Initiative and NephCure to review challenges in the development of sodium-glucose cotransporter-2 (SGLT2) inhibitors for pediatric chronic kidney disease. Industry

[83] For examples of FDA-awarded grants, visit usaspending.gov or visit FDA websites such as https://www.fda.gov/about-fda/oncology-center-excellence/oce-funded-active-extramural-research-projects and https://www.fda.gov/industry/orphan-products-grants-program/orphan-products-grants-awarded.

representatives, academic researchers, clinicians, patient advocates, caregivers, and other governmental authorities gathered to discuss strategies to overcome challenges in this area. The result of this workshop was the development of a pathway for drug developers to conduct feasible, timely pediatric trials of SGLT2 inhibitors in pediatric chronic kidney disease. The meeting proceedings were published in 2025.[84]

Table 7: Select Pediatric Workshops Hosted by FDA (July 2020 – June 2025)

Workshop Title	Date
FDA's Advancing the Development of Pediatric Therapeutics (ADEPT) Workshops	
Enhancing Diversity in Therapeutics Development for Pediatric Patients (ADEPT 9)	September 6, 2024
Drug Dosing in Pediatric Patients with Renal Impairment (ADEPT 8)	November 30 – December 1, 2023
Advancing the Development of Pediatric Therapeutics Complex Innovative Trial Design (ADEPT 7)	September 1-2, 2021
FDA and M-CERSI Co-Hosted Workshops	
Nonprescription Analgesic/Antipyretic Drug Development in Children 2 to Less Than 12 Years of Age	November 15, 2024
Evaluating Immunosuppressive Effects of In Utero Exposure to Drug and Biologic Products	July 11-12, 2024
Defining "Candy-Like" Nonprescription Drug Products	October 30, 2023
Analgesic Clinical Trial Designs, Extrapolation, and Endpoints in Patients from Birth to Under Age 2	October 13-14, 2021
Pediatric Dose Selection	October 22-23, 2020
FDA and Duke-Margolis Center for Health Policy Co-Hosted Meetings	
Advancing Drug Development for the Prevention of Spontaneous Preterm Birth	January 24, 2024

[84] Smoyer WE, Gillespie BS, Oni L, et. al. (2025) Strategies for the development of sodium-glucose cotransporter-2 inhibitors for kidney protection in pediatric chronic kidney disease: proceedings of a workshop meeting in July 2023. Kidney Int. S0085-2538(25)00747-1. DOI:10.1016/j.kint.2025.09.009.

FDA also continues to engage in various outreach activities with external stakeholders to facilitate an understanding of regulatory issues and to share updates on FDA's pediatric-focused efforts. FDA gives numerous pediatric-related presentations each year to external parties and collaborates in several consortia and working groups focused on advancing pediatric research and drug development. For example, FDA participates annually in a "Pediatric Liaison" meeting with BIO.

B. Global Alignment of Pediatric Research and Drug Development

FDA continues to engage with international stakeholders to help ensure children around the world participate in clinical trials that are well designed to meet international regulatory standards. FDA's international collaborative efforts have helped improve therapeutics development globally by increasing the efficiency of clinical trial enrollment for small populations, by expanding information and knowledge-sharing with global experts, and by aligning clinical trial designs to help ensure pediatric clinical trials are not needlessly repeated.

1. International Pediatric Cluster Conference Calls

FDA's Office of Pediatric Therapeutics (OPT) continues to coordinate monthly Pediatric Cluster conference calls with international regulatory agencies. Regulatory agencies included in the Pediatric Cluster include FDA (founding member, 2007), the European Medicines Agency (EMA) (founding member, 2007), Japan's Pharmaceuticals and Medical Devices Agency (PMDA) (joined 2009), Health Canada (joined 2010), Australia's Therapeutic Goods Administration (TGA) (joined 2014), and the Swiss Agency for Therapeutic Products (Swissmedic) (joined 2025). From July 1, 2020, to June 30, 2025, the Pediatric Cluster discussed 176 products proposed for pediatric study and 37 general topics related to pediatrics. Common issues discussed include the scope of pediatric drug development, safety, dosing, types of clinical trials, and trial design.

In 2012, FDA and EMA developed a process for sharing brief Common Commentary documents for certain topics discussed at the Pediatric Cluster. These documents convey high-level, unofficial comments from FDA and EMA to pharmaceutical industry sponsors. From July 2012 to June 2025, FDA issued 76 Common Commentaries spanning 13 therapeutic areas.

The Pediatric Cluster has been an important forum for collaboration with international regulatory agencies regarding pediatric cancer drug development, including attempting to align decision-making and advice to sponsors, particularly since implementation of

the RACE Act. From July 1, 2020, through June 30, 2025, 64 oncology products were the subject of discussion during 36 Pediatric Cluster calls. FDA and EMA aimed to provide coordinated advice to sponsors to facilitate global drug development for these oncology drugs. During this time, 22 Common Commentaries regarding 20 cancer drugs were issued confidentially to sponsors. In addition, one Common Commentary was issued publicly, titled "Common issues requested for discussion by the respective agency (EMA/PDCO and FDA) concerning paediatric oncology development plans (Paediatric Investigation Plans [PIPs] and initial Pediatric Study Plans [iPSPs])."[85]

2. Important Efforts to Encourage International Collaboration

Highlighted below are several activities and initiatives FDA has undertaken to encourage international collaboration in pediatric drug development:

- FDA and EMA exchange pediatric committee discussion meeting minutes. On a monthly basis, EMA shares with FDA the most recent Paediatric Committee (PDCO) discussion minutes. Similarly, FDA shares with EMA the most recent PeRC and Oncology Subcommittee of PeRC discussion minutes.
- FDA participates with EMA in work conducted by the ACCELERATE Platform, an international, multi-stakeholder group focused on accelerating the development of new therapies for children with cancer. Given the rarity of cancer in children generally, which is further exacerbated by further subdivision of many pediatric cancer genomic characteristics, a coordinated international approach to pediatric cancer product development is particularly important.
- FDA serves on EMA's initiative for the European Network of Paediatric Research's working group on international cooperation, which is tasked with comparing the pre-market regulatory and ethical requirements for the conduct of pediatric clinical trials and for participation as a clinical trial site across the following five jurisdictions: United States, European Union, Canada, Japan, and Australia.[86]
- FDA participates on the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use's E11A Expert Working Group, which issued a final guideline on pediatric extrapolation in January 2025.
- FDA collaborates with Japan's Pharmaceuticals and Medical Devices Agency Asia Training Center on an annual international pediatric review workshop designed to further disseminate information on advances in scientific and technical knowledge for pediatric drug development. Over the 8 years since the

[85] See https://www.fda.gov/media/147197/download?attachment.

[86] See https://www.ema.europa.eu/en/partners-networks/networks/european-network-paediatric-research-european-medicines-agency-enpr-ema/enpr-ema-priority-activities#international-collaboration-11851.

workshop began, 226 international regulators from 34 countries have participated.

- FDA was a member of the World Health Organization (WHO) Paediatric Regulatory Network until early 2025. The Paediatric Regulatory Network serves as a forum for enabling dialogue and fostering development of international consensus on effective regulatory approaches for increasing the availability of pediatric medical products around the world.
- FDA serves on a working group with the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard which seeks to recommend harmonized approaches and tools to regulate and facilitate pediatric research worldwide.

IV. Interested Parties Input

In accordance with section 508 of FDASIA, FDA held a public meeting entitled, "Interested Parties Meeting: Implementation of the Best Pharmaceuticals for Children Act and Pediatric Research Equity Act" on September 15, 2025. This meeting was organized as a listening session to gather input from patient groups, consumer groups, regulated industry, academia, and other interested parties on any recommendations or information relevant to this BPCA and PREA report to Congress. The meeting information, materials, and webcast are available on FDA's website.[87]

In response to FDA's January 2025 Federal Register announcement of the interested parties meeting and request for comments,[88] interested parties from the pharmaceutical industry, academia, and a variety of advocacy organizations provided input on BPCA and PREA. FDA received a total of 20 written comments posted to the public docket, which was open from January 3, 2025, to September 30, 2025. At the September 15, 2025, interested parties meeting, a total of 25 interested parties provided comments during the scheduled sessions, and 6 speakers provided comments during the open public comment period. These various interested parties supported the continued implementation of BPCA and PREA in the development and labeling of drugs for pediatric populations and the continued research and development of pediatric therapeutics.

The following sections summarize key themes and recommendations that emerged from the interested parties' input and docket responses received, including key successes and challenges associated with BPCA and PREA.

A. Successes and Challenges Related to Implementation of BPCA and PREA

Interested parties highlighted numerous successes associated with BPCA and PREA, noting that these laws have fundamentally addressed the historical problem where children were considered "therapeutic orphans" with limited pediatric prescribing information and widespread off-label drug usage. Interested parties celebrated the over 1,000 medicines that now include evidence-based pediatric information in product labeling and highlighted the real-world impact.

During the interested parties meeting, youth patient representatives provided compelling testimonials about how proper pediatric dosing and safety monitoring for medications have enabled successful disease management and saved lives through effective, safe,

[87] See https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/interested-parties-meeting-implementation-best-pharmaceuticals-children-act-and-pediatric-research.

[88] FR Doc. 2024-31312 (published: Jan. 3, 2025).

and modern treatments. These youth patient representatives shared personal stories demonstrating how BPCA and PREA have directly improved their lives, with one stating that "having access to a medication like this has really been a game changer" and emphasizing the importance of "treatments that are safe and effective and really tailored to what we need." Another stated, “As a child cancer survivor, I’m very grateful for the treatments that saved my life, treatments that wouldn't have existed without pediatric legislation like the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act.” Finally, a third youth patient representative stated, “I can only hope future pediatric patients will be as fortunate as I was to receive such incredible care but it's dependent on continued funding.”

Other successes underscored by interested parties included changes in industry behavior to consider pediatric populations early in drug development, improvements in regulatory practices to establish systematic approaches for pediatric study plans and post-marketing requirements, acceleration of therapeutics development for pediatric cancers, and improvements in scientific innovation and infrastructure to support pediatric drug development. Interested parties also noted the influence of these laws on international pediatric drug development approaches, and the benefits of global alignment to support pediatric drug development programs.

Despite ongoing challenges identified by interested parties described herein, the overall consensus from the interested parties feedback reflects that BPCA and PREA have successfully established a robust foundation for pediatric drug development that continues to evolve and benefit children worldwide through systematic approaches to studying medicines for pediatric populations.

1. PREA Compliance and Enforcement Needs Strengthening

Interested parties recommended that FDA develop better tracking mechanisms and be granted stronger enforcement authority to ensure timely completion of pediatric studies under PREA, noting that nearly half of PREA studies are deferred and many companies seek repeated deferral extensions or ignore PREA required pediatric clinical studies. One speaker highlighted significant delays in study completion, citing an average of 2.5-year deferral extensions beyond original due dates and poor study completion rates, with only 54% of required PREA studies completed, and just 25% completed on time. Multiple parties emphasized that FDA lacks appropriate enforcement tools to ensure pediatric studies required under PREA are completed in a timely manner, and some noted their support for Congressional efforts to allow FDA to issue civil monetary penalties for PREA noncompliance while retaining the ability to extend deadlines when needed for companies acting in good faith.

2. Impact of the PREA Orphan Drug Exemption

Interested parties discussed continuing challenges related to the PREA exemption for orphan designated drugs. Interested parties emphasized that approximately 50-75% of rare diseases occur in pediatric populations, yet these drugs remain exempt from pediatric study requirements. One speaker noted that PREA exemptions for orphan designated drugs have become more common over time, citing data showing almost half (47%) of new drugs approved from 2015 to 2021 were exempt from PREA due to orphan designations, representing a dramatic increase from 15% from 1999 to 2003.[89] Several speakers noted that nearly 40% of orphan indications approved from 1999 to 2018 were incompletely labeled for pediatrics.

3. Funding for the BPCA/409I Program

Interested parties explained that funding for the BPCA/409I Program has remained at $25 million since inception, with no increase despite rising costs over time. This 'flat funding' has occurred since 2002, with purchasing power now only 56% of original capacity, and leads to less work being supported as costs increase over time. Several interested parties recommended that funding levels be increased, and even doubled to $50 million, for additional efficiency and effectiveness of the program. Interested parties suggested increased funds would allow the program to pursue needed Phase 3 studies.

4. Children Should Be Partners in Clinical Trial Design

The International Children's Advisory Network (iCAN) emphasized that children and families want to be involved and help guide decisions from the very beginning of clinical development and prefer interviews and storytelling over administered questionnaires. iCAN recommended that FDA include a formal requirement or incentive for incorporating pediatric patient group perspectives for feasibility assessments for all pediatric trials.

5. More and Earlier Pediatric Labeling Information is Needed

Interested parties noted that sometimes drug labeling contains unhelpful or contradictory information, and requested more practical, user-friendly information in labeling that helps pharmacists translate information to caregivers. Specific recommendations included providing consistent information about compounding and dosing options and specific instructions for dosing based on weight and height. Pharmacists and care providers also emphasized that earlier information in labeling for pediatric use would be helpful in the clinical care setting.

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[89] Liu ITT, Hwang TJ, Kesselheim AS. (2024) Testing of New Drugs Approved From 2015 to 2021 under the US Pediatric Research Equity Act. JAMA. 332(17):1482–1484.

6. Special Populations Require Tailored Approaches

Interested parties highlighted how different pediatric subpopulations face distinct challenges that require tailored regulatory and research approaches. Interested parties generally expressed broad support, when appropriate, for use of pediatric extrapolation, novel trial designs, real-world evidence, surrogate endpoints, and platform trials as key strategies to improve data generation efficiency in pediatric drug development.

7. Neonates Remain Therapeutic Orphans Despite BPCA and PREA

Interested parties discussed continuing challenges related to inclusion of neonates in clinical research. One speaker highlighted that up to 90% of medications used in neonatal intensive care units (NICUs) are off-label, with no drugs approved for major neonatal diseases like bronchopulmonary dysplasia or necrotizing enterocolitis in over 30 years. The speaker explained that "neonates are perhaps one of the hardest populations to study" and that BPCA and PREA have been helpful for developing more drugs for children, but “their impact hasn't really extended to neonates." Interested parties emphasized that neonatal diseases often have no adult counterparts, making use of pediatric extrapolation infeasible in many drug development programs, and requiring specialized approaches beyond traditional BPCA and PREA mechanisms.

8. Pediatric Oncology Drug Development Lags Behind Adult Programs

One speaker provided data showing dramatic improvements in some cancers (80% decline in Hodgkin lymphoma mortality) while others like bone cancers have "mortality higher today than it was in 2000." The speaker emphasized that "what childhood cancer researchers need" are "active new agents" and noted the challenge that "many agents developed for adult cancers entering the clinic today have little or no relevance for pediatric cancers." Another speaker emphasized that it takes an average of six years after adult trials start for pediatric drug development to begin, with limited progress in bone cancers and CNS tumors. The speaker called for requiring sponsors to submit initial Pediatric Study Plans earlier than the end of adult Phase 2 trials and for FDA to have authority to require full development of effective agents.

9. Diminishing Incentives for Pediatric Drug Development

Interested parties expressed a nuanced understanding of pharmaceutical business realities, accepting profit considerations as necessary drivers of drug development while seeking systemic reforms to better align industry profitability with children's medical needs. The consensus emphasized partnership between industry, regulators, and

advocates to create economically viable pathways that prioritize children's health outcomes alongside sustainable business models.

One speaker argued that the Inflation Reduction Act's (IRA's) Medicare/Medicaid drug price negotiation provisions (at 7- and 11- years post-approval) have inadvertently undermined BPCA by creating a disincentive for companies to pursue pediatric studies. The speaker explained that companies now avoid BPCA WRs for both unprofitable drugs (as before, when companies would pursue a WR if drugs were profitable enough to justify the investment) and now also for highly profitable drugs (due to fear of triggering price negotiations), leaving companies pursuing WRs only for moderately profitable drugs, thereby dramatically reducing the pool of drugs considered under BPCA. The speaker requested a Congressional carve-out exempting BPCA-studied drugs from IRA price negotiations, arguing that pediatric drug development serves a critical public health need, the exclusivity periods for pediatric studies should not be undermined by later price negotiations, and that this would restore the original economic incentive structure that made BPCA effective. In addition, the speaker advocated for requiring earlier deadlines for clinical trials conducted under BPCA to ensure companies conduct pediatric studies earlier in the drug lifecycle rather than waiting toward the end of market exclusivity to maximize earnings and avoid generic drug competition.

10. International Alignment is Essential for Pediatric Drug Development

Industry stakeholders called for harmonization of iPSPs and Pediatric Investigation Plans (PIPs) early in drug development. Industry representatives emphasized the need for expanding the scope of the Pediatric Cluster and Common Commentaries as one approach to help reduce duplicative efforts across regions. One speaker noted that, "we have often struggled with addressing different feedback between global agencies as we try to write global development programs for most assets" and urged for "a more established clear predictable process for dialogue" to "help facilitate achievement of a harmonized program." Industry representatives emphasized that varying global standards increase trial complexity and delay drug availability for children worldwide.

11. Maintaining Balance of Incentives and Requirements

Interested parties expressed varied views on balancing BPCA incentives with PREA requirements, with most advocating for complementary rather than competing approaches. Industry stakeholders emphasized the need for both "carrot and stick" mechanisms, arguing against viewing dual leverage as "double dipping" and raised

concerns about FDA's 2023 draft guidance[90] stating the agency does not expect to issue Written Requests solely for PREA-required studies. Pediatric advocacy groups strongly supported maintaining both frameworks while calling for enhanced enforcement of PREA requirements and earlier study deadlines, with some advocating for enhancing the BPCA incentives to help cover orphan designated drugs currently exempt from PREA. Healthcare providers and academic researchers emphasized that the frameworks should work synergistically to address different aspects of pediatric drug development, noting that BPCA's voluntary approach allows exploration of off-patent drugs and broader indications while PREA ensures systematic coverage of new approvals.

One theme that emerged from the presentations was that rather than choosing between voluntary incentives and mandatory requirements, the optimal approach involves strengthening both frameworks while improving their coordination, ensuring adequate FDA resources for implementation, and addressing specific gaps like neonatal populations and rare diseases where neither framework currently provides sufficient coverage. The speaker presentations generally aligned on the notion that the success of both programs depends on adequate funding, clear regulatory guidance, and recognition that different therapeutic areas may require different balances of incentives and requirements to achieve optimal pediatric drug development outcomes.

12. Need for Issuing or Updating FDA Guidance Documents and Greater Transparency in Regulatory Decision-Making

Interested parties emphasized the need for early and open dialogue with FDA and transparent regulatory decisions. Interested parties expressed broad consensus that comprehensive and current guidance is essential for effective pediatric drug development. One speaker noted that FDA needs to issue more guidance documents on key pediatric issues and update or finalize existing guidances, while also acknowledging FDA's progress in issuing over 80 pediatric-related guidance documents, including recent publications on scientific and regulatory considerations for PREA and BPCA, as well as guidance on pediatric extrapolation.

Another theme that emerged from the presentations was that while FDA has made significant progress in issuing pediatric guidance documents, there remains a critical need for more frequent updates to reflect evolving science, clearer implementation instructions that address real-world challenges, and guidance that better integrates the various pediatric regulatory frameworks to optimize drug development efficiency. Industry stakeholders called for clearer guidance on molecular target determinations

[90] See Draft Guidance Document "Pediatric Drug Development: Regulatory Considerations - Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act (May 2023) at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-regulatory-considerations-complying-pediatric-research-equity-act-and. When final, this guidance document will represent the Agency's current thinking on this topic.

under FDARA, more transparent processes for pediatric study plan reviews, and updated guidance addressing global harmonization challenges, with particular emphasis on guidance that facilitates early dialogue and flexible study designs for rare diseases.

One organization highlighted the need for updated guidance addressing practical issues, noting that current package insert requirements often run contrary to modern pediatric pharmacy practice and requesting guidance on combination antibiotics, excipient safety (particularly ethanol), and standardized concentration requirements. Healthcare providers and academic researchers emphasized the need for guidance on innovative trial designs, real-world evidence integration, and neonatal-specific considerations. Patient advocacy groups, including those representing rare diseases and cancer patients, requested guidance that facilitates earlier pediatric inclusion in clinical trials, addresses orphan drug exemption challenges, and provides clearer pathways for patient engagement in study design and feasibility assessments.

V. Program Improvements for Continued Advancement of Product Development for Children

While BPCA and PREA have been instrumental in improving pediatric research, product development, and labeling, FDA continues to evaluate strategies for further improvements, which are discussed in this section.

A. Impact of the Orphan Exemption Under PREA

On December 2, 1998, FDA published "Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drugs and Biological Products in Pediatric Patients" (63 FR 66632, December 2, 1998), often referred to as "the Pediatric Rule." That rulemaking,[91] which served as the template for PREA, contained a provision exempting applications for orphan-designated drugs and biological products from pediatric study requirements prior to marketing (see, e.g., id. at 66672). In the preamble to that rule, FDA explained that it believed this exemption for orphan-designated drugs and biological products was appropriate because the Orphan Drug Act (ODA) was enacted "to encourage the development of drugs for patient populations that are so small as to make the manufacture and sale of the drug[s] [otherwise] unprofitable" and the "[i]mposition of a pediatric study requirement . . . could conflict with the balance struck by the [ODA] by further raising the cost of marketing the[se] drug[s]" (id. at 66640). However, since the issuance of the Pediatric Rule and the enactment of PREA, changes in law[92] and science and the advent of new incentives to conduct pediatric studies[93] warrant a fresh look at the tools FDA has to help meet the drug development needs of children with rare diseases while continuing advancement of orphan product development and innovation.

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[91] The Pediatric Rule was invalidated in *Association of Am. Physicians & Surgeons, Inc. v. FDA*, 226 F. Supp. 2d 204, 222 (D.D.C. 2002).

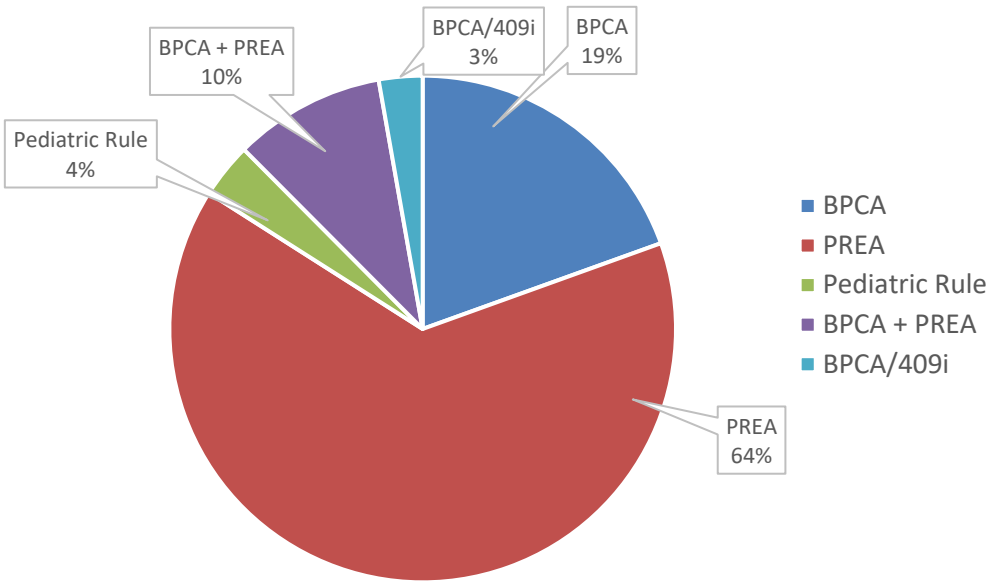
[92] See, e.g., section 504 of FDARA. These required studies may lead to full development programs and more approved treatments for pediatric populations with rare diseases or conditions.

[93] For example, the rare pediatric disease (RPD) priority review voucher (PRV) program, which was enacted after the enactment of PREA, changed the landscape for studying rare diseases and conditions in children. Under that program, a sponsor of a "rare pediatric disease product application" is eligible to receive, upon approval of that application, a voucher for priority review of a subsequent application that may be otherwise ineligible for priority review (*see* section 529 of the FD&C Act). These vouchers can be used on a subsequent application (e.g., for a non-rare disease drug with a large market) or sold to another sponsor who seeks a priority review for a blockbuster product; thus, this program provides a potentially significant financial incentive to develop drugs and biological products to prevent or treat certain rare pediatric diseases. Particularly because both the RPD PRV program (which was reauthorized in February 2026) and the pediatric exclusivity incentive under section 505A of the FD&C Act, are voluntary, removal of the orphan exemption would give FDA an important tool to require, where appropriate, the sponsor of an orphan-designated drug to explore the potential benefits of that drug to children of all ages in whom the drug is expected to be used.

The scientific and regulatory landscape has evolved since the passage of BPCA and PREA such that there has been substantial success in utilizing more efficient and innovative approaches for development of drugs and biological products in pediatric populations with rare diseases. For example, for rare and non-rare diseases alike, efficacy may, in some circumstances, be extrapolated from one population to another (see, e.g., section 505B(a)(2)(B) of the FD&C Act) – and since the enactment of PREA, better scientific understanding of certain diseases or conditions, along with novel approaches to data analysis (e.g., Bayesian methodology), have increased the number of circumstances in which the Agency is able to extrapolate efficacy. Thus, depending on the specifics of the development program, the pediatric studies required under section 505B of the FD&C Act may be reduced when compared to a historical development program (e.g., efficacy studies in children may not be needed if efficacy can be extrapolated, enabling PREA requirements to be satisfied with more streamlined approaches). In addition, for those development programs where randomized, controlled studies are needed, innovations in study design and analysis have better enabled the conduct of robust, informative studies using fewer participants. This is a particularly significant advance in pediatric rare disease therapeutics development, enabling sponsors to feasibly investigate, and FDA to appropriately assess, the benefits of new therapies in rare pediatric conditions.

FDA believes that requirements under PREA have driven the development of therapies for children. The majority of pediatric labeling changes have resulted from studies conducted under PREA, not BPCA (see Figure 9). These data demonstrate the importance of PREA in advancing the availability of approved therapies for pediatric patients.

Figure 9: Pediatric Labeling Changes From 1998 through June 2025 (n=1,364)



Advances in science that help improve the efficiency of pediatric drug development, along with the availability of incentive programs to encourage therapeutics development for rare pediatric diseases, should be taken into account as stakeholders consider how to balance getting necessary information on drugs for pediatric rare diseases with concerns about potential financial burdens if pediatric study requirements are applied to orphan-designated drugs. Furthermore, it is important to note that pediatric experts on the PeRC are able to consistently review development programs for rare diseases as presented in iPSPs to provide advice that would potentially improve the speed and efficiency of drug development in rare pediatric diseases, and to help determine when granting waivers under PREA may be appropriate. FDA has granted waivers under PREA, as appropriate, when a rare disease that is the subject of an application does not affect children.

FDA wants robust orphan product development and evidence for all relevant pediatric age groups with rare diseases and is evaluating potential strategies that further these goals.

B. Modernization of Pediatric Pharmacovigilance

Using a standardized time-based approach to review the safety of drugs with new pediatric use information is not the most effective or efficient approach for safety signal detection. The 18-month pediatric-focused safety reviews required by sections 505A(l) and 505B(i) of the FD&C Act are redundant with the Agency's established post-marketing safety surveillance. FDA has implemented risk-based rather than time-based frameworks as part of its overall post-marketing safety surveillance programs.[67]

FDA continues to develop and implement processes needed to support efficient and effective post-market safety surveillance, including for pediatric populations. This includes a post-market safety modernization initiative and technologies to proactively identify safety surveillance issues. An FDA legislative proposal is to modernize post-market safety monitoring of medical products used in children by removing the time-based requirement for post-market safety reviews under BPCA and PREA, allowing FDA to dedicate resources to real-time, risk-based surveillance activities conducted as safety signals emerge. FDA recommended removing this requirement in the legislative proposals included in the FY2027 budget. The Agency's existing, modern, risk-based approach to post-market safety surveillance already ensures that the purpose of these sections of BPCA and PREA, to fully and appropriately monitor the post-marketing safety of drugs and biological products in children, is achieved.

C. Enhancement of Product Development for Neonatal Conditions

Drugs under development for adult conditions may not be relevant to neonates, thereby limiting the impact of BPCA and PREA on advancing therapeutics development for the neonatal population. PREA does not provide an incentive for the pharmaceutical

industry to develop drugs that specifically address conditions characterized by unique neonatal pathophysiology, and voluntary BPCA incentive structures may not be sufficient to support needed product development. As such, the vital progress observed generally for the pediatric population since passage of BPCA and PREA has not been nearly as robust for the neonatal subpopulation, which continues to have substantial unmet medical needs.

Amply incentivizing the pharmaceutical industry to develop products that address the unique medical conditions affecting neonates, like bronchopulmonary dysplasia, necrotizing enterocolitis, and hypoxic ischemic encephalopathy, would be expected to have an immense impact on public health. While existing programs that incentivize drug development for rare diseases may be leveraged for many neonatal conditions, it does not appear that those programs have had a substantial impact and there are no programs specifically designed to expedite or incentivize drug development for the neonatal population. FDA is continuing to leverage its authorities to encourage or require studies and assessments in neonates, when appropriate, under BPCA and PREA, and is continuing to advance regulatory science research, stakeholder collaboration, and guidance development to provide the critical foundation for advancing neonatal therapeutics development.

D. More Timely Pediatric Product Development

1. PREA Compliance

Section 505B(d)(1) provides that the consequence to a sponsor of a failure to comply with PREA obligations is the receipt, and public posting, of a noncompliance letter from FDA, along with the sponsor's response. Although such failure to comply with PREA obligations may result in the drug being considered misbranded (see section 505B(d)(2) of the FD&C Act), the law has, until recently, prohibited such noncompliance from being the basis of imposing penalties for misbranding under section 303 of the FD&C Act (21 U.S.C. 333), and also prohibited such noncompliance from being the basis of withdrawing approval or licensure of the corresponding NDA or BLA (see section 505B(d)(2) of the FD&C Act). Thus, in effect, the penalty for failure to comply with PREA requirements historically has been no penalty at all.

The 2026 Appropriations Act authorized the Agency to take enforcement action, under certain limited circumstances, for PREA noncompliance occurring on or after August 2, 2026. Although this new authority was provided after the time period covered by this report, we mention it here to note that the Agency is working to develop policy around implementation of this new authority.

2. *International Alignment*

Aligning development plans across global regulatory authorities presents an important opportunity to increase the efficiency and success of pediatric drug development. Substantial progress has occurred in this area, including the use of the Pediatric Cluster, the development of internationally harmonized guidance, and the convening of workshops and meetings with global partners. Another potential approach is the ability to convene product-specific discussions that include more than one regulatory body at the meeting. While there is no prohibition for such a meeting currently in place, highlighting the utility of such a meeting through the creation of a specific meeting type to allow for discussion of pediatric drug development plans early in overall drug development could be considered.

3. *Balance of Incentives and Requirements*

FDA continues to consider strategies and approaches to increase the efficiency and timeliness of pediatric drug development programs. Clearly a balance between incentives and requirements can play an important role in advancing drug development in children, as exemplified by the success of BPCA and PREA. One area of "rebalancing" that FDA has recently considered has been outlined in recent draft guidance.[94] In this draft guidance, FDA described its intent, once the guidance is finalized, to issue Written Requests that include studies or planned studies not limited to those already required under PREA but will also need to include additional indications or populations. If there are no additional studies for indications or populations that may produce health benefits in the pediatric populations beyond the studies or planned studies required under PREA, then FDA does not expect to issue a Written Request for that drug. This proposed modification of current policy was based on an evaluation conducted by FDA that identified that 63% of pediatric-specific labeling changes were based on studies conducted under PREA alone, while only 21% were based on studies conducted under BPCA alone. FDA expects to provide a final decision about this proposed policy when the guidance is finalized. Other opportunities to rebalance incentives and requirements are also being considered, with the specific goal of more timely access to approved treatments for children.

[94] See Draft Guidance Document "Pediatric Drug Development: Regulatory Considerations - Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act (May 2023) at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pediatric-drug-development-regulatory-considerations-complying-pediatric-research-equity-act-and. When final, the guidance will reflect the Agency's current thinking on this topic.

VI. Conclusion

Implementation of BPCA and PREA has fundamentally transformed the landscape of pediatric drug development, delivering substantial benefits to children and families across the United States and globally. Since their enactment, these landmark statutes have generated over 1,364 pediatric labeling changes, providing evidence-based prescribing information for conditions ranging from common childhood ailments to rare diseases and pediatric cancers. The personal testimonials from young patients during FDA's interested parties meeting powerfully illustrate the real-world impact of these laws.

The data presented in this report demonstrate remarkable progress in several key areas. The RACE Act provisions have resulted in important progress for pediatric cancer drug development. Eighty-one of 141 new molecularly targeted oncology products subject to FDARA with agreed iPSPs issued during the current reporting period now include planned pediatric investigations, 65 of which would have previously qualified for exemptions or waivers. FDA's regulatory science advances have enhanced the efficiency of pediatric drug development through innovations such as pediatric extrapolation, while international collaboration efforts have facilitated global alignment that helps reduce duplicative studies and accelerate access to pediatric therapies worldwide.

The average time between adult approval and pediatric labeling incorporation has decreased from six years in the previous reporting period to five years currently, suggesting some progress toward more timely pediatric drug development. However, this improvement must be viewed in the context of broader completion data showing that only 53% of drugs had any labeling changes reflecting data from PREA-mandated studies at 10 years post-approval. The increasing number of deferral extension requests and noncompliance letters further indicates that systemic barriers continue to challenge timely study completion. The number of deferral extension requests has risen substantially, particularly from 2022 through 2024, with approximately 20% higher annual requests compared to the previous reporting period. While the COVID-19 pandemic contributed to some of these increases, the data show that deferral extension requests have been steadily rising since 2015, suggesting underlying structural challenges in pediatric study conduct. Correspondingly, FDA has issued 97 noncompliance letters to 67 sponsors since the 2021 BPCA and PREA report to Congress, with 30% of these sponsors receiving multiple noncompliance letters, indicating that current enforcement mechanisms may not be providing sufficient deterrent for some companies.

FDA has implemented numerous enhancements to optimize pediatric drug development processes, demonstrating strong performance in key operational metrics. The Agency has maintained timely responses to Proposed Pediatric Study Requests, with 83% receiving responses within the required 120-day timeframe, and has shown its commitment to issuing feasible Written Requests, as evidenced by sponsors accepting

49 of the 50 Written Requests issued during the reporting period. FDA has developed over 80 guidance documents that provide specific advice on pediatric drug development, including critical guidance on pediatric extrapolation that enables sponsors to leverage adult data when scientifically appropriate, thereby reducing the burden of pediatric studies while maintaining safety standards. The Agency has actively worked with sponsors to identify opportunities for extrapolation and innovative study designs that can generate necessary pediatric data more efficiently.

FDA's commitment to regulatory science research and stakeholder engagement is demonstrated through publishing numerous peer-reviewed manuscripts and hosting several workshops, including the Advancing the Development of Pediatric Therapeutics (ADEPT) series and other collaborative meetings, that bring together industry, academia, patient advocates, and regulatory experts to identify practical solutions to pediatric drug development challenges. Such regulatory science research and collaborative meetings have informed FDA's policies on developing products in pediatric patients, providing an evidence-based foundation for regulatory guidance and decision-making processes. FDA’s regulatory science research programs have been highly successful in identifying areas to advance drug development for children where development has been difficult, including pediatric hypertension, pediatric heart failure, and pediatric major depressive disorder.

Particularly concerning gaps remain in neonatal therapeutics development, where the vital progress observed for the general pediatric population has not extended to this vulnerable subpopulation. Of the 1,364 pediatric labeling changes pursuant to BPCA and PREA, only 12% included information for neonates and there remains a persistent unmet medical need for conditions such as prematurity-associated chronic lung disease, necrotizing enterocolitis, and hypoxic ischemic encephalopathy. The limited impact of BPCA and PREA on neonatal drug development reflects the reality that drugs under development for adult conditions may not be relevant to neonates, and these laws do not provide sufficient incentive for pharmaceutical companies to develop drugs specifically addressing conditions characterized by unique neonatal pathophysiology.

As drugs that treat rare diseases represent an increasing proportion of novel drug approvals, more drugs are subject to the PREA exemption for orphan-designated drugs. The impact of the RACE Act, which removed the orphan exemption for certain molecularly targeted cancer drugs, demonstrates a potential impact of changes to the PREA exemption for orphan-designated drugs.

The BPCA/409I program at NIH has demonstrated remarkable productivity, generating 26 labeling changes for off-patent products through the Pediatric Trials Network infrastructure. These achievements include critical dosing improvements for antibiotics used in neonates, safety and efficacy data for psychotherapeutic agents, and innovative pharmacokinetic modeling approaches. Looking forward, the program seeks to prioritize optimizing data collection methodologies to support evidence-based pediatric use of medications currently prescribed off-label to children and foster improvements in pediatric research infrastructure.

The achievements documented in this report underscore that BPCA and PREA have been highly successfully in increasing the availability of approved drugs and biological products for children. However, addressing persistent challenges in rare disease and neonatal therapeutics development, improving compliance with PREA requirements, and enhancing international alignment will require continued collaboration among all stakeholders. As we look toward the future, the foundation established by BPCA and PREA provides a strong platform for continued innovation in pediatric therapeutics, with the ultimate goal of ensuring safe, effective, and appropriately studied medications for all children who need them.

Appendix A: Pediatric Labeling Changes Under BPCA and PREA Since the 2021 Report to Congress (Covering July 1, 2020, Through June 30, 2025)

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
6/27/2025	Spritam tablets	levetiracetam	Partial-onset seizures	PREA Only
6/27/2025	Gammagard liquid ERC	immune globulin infusion (human)	Primary humoral immunodeficiency	PREA Only
6/20/2025	Enflonsia injection	clesrovimab-cfor	Prevention of RSV lower respiratory tract disease	PREA Only
6/20/2025	Descovy tablets	emtricitabine/ tenofovir alafenamide	HIV – 1 infection	PREA Only
6/20/2025	Tybost tablets	cobicistat	HIV – 1 infection	PREA Only
6/20/2025	Benlysta injection	belimumab	Lupus nephritis	PREA Only
6/18/2025	Yeztugo injection	lenacapavir	HIV – 1 infection	PREA Only
6/12/2025	Steqeyma injection	ustekinumab-stba	Plaque psoriasis	PREA Only
6/11/2025	Hectorol capsules	doxercalciferol	Secondary hyperparathyroidism due to chronic kidney disease	PREA Only
6/10/2025	Mavyret tablet/coated pellet	glecaprevir/ pibrentasvir	Acute hepatitis C virus infection	PREA Only
5/30/2025	Xenoview for oral inhalation	xenon Xe 129 hyperpolarized	Evaluation of lung ventilation with magnetic resonance imaging	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
5/30/2025	mNexspike injection	COVID-19 Vaccine, mRNA	Active immunization to prevent COVID-19	PREA Only
5/23/2025	MenQuadfi injection	Meningococcal (Groups A, C, Y, W) Conjugate Vaccine	Active immunization for the prevention of invasive meningococcal disease caused by Neisseria meningitidis	PREA Only
5/22/2025	Zoryve foam	roflumilast	Plaque psoriasis	PREA Only
5/22/2025	Kalydeco tablets	ivacaftor	Cystic fibrosis	BPCA Only
5/22/2025	Prolia injection	denosumab	Glucocorticoid-induced osteoporosis	PREA Only
5/22/2025	Kyprolis for injection	carfilzomib	Acute lymphoblastic leukemia (ALL)	BPCA Only
5/16/2025	Nuvaxovid injection	COVID-19 Vaccine, Adjuvanted	Active immunization to prevent COVID-19	PREA Only
5/14/2025	Welireg tablets	belzutifan	Pheochromocytoma	PREA Only
5/9/2025	Rexulti tablets	brexpiprazole	Schizophrenia	PREA Only
4/29/2025	Releuko injection	filgrastim-ayow	Hematopoietic Syndrome of Acute Radiation Syndrome	PREA Only
4/23/2025	Fylnetra injection	pegfilgrastim-pbbk	Hematopoietic Syndrome of Acute Radiation Syndrome	PREA Only
4/17/2025	Dupixent injection	dupilumab	Chronic spontaneous urticaria	PREA Only
4/17/2025	Eliquis tablets	apixaban	Venous thromboembolism	BPCA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
4/15/2025	Mezofy oral soluble film	aripiprazole	Schizophrenia	PREA Only
4/8/2025	Opdivo injection	nivolumab	Colorectal cancer	PREA Only
4/8/2025	Yervoy injection	ipilimumab	Colorectal cancer	PREA Only
4/7/2025	Cyramza injection	ramucirumab	Solid tumors	BPCA Only
4/7/2025	Dextenza ophthalmic insert	dexamethasone	Ocular inflammation and pain after surgery, and ocular itching associated with allergic conjunctivitis	PREA Only
4/4/2025	Sivextro tablets	tedizolid phosphate	Acute bacterial skin and skin structure infections	PREA Only
3/31/2025	Flublok injection	Influenza Vaccine	Influenza A and B virus immunization	PREA Only
3/26/2025	Cabometyx tablets	cabozantinib	Neuroendocrine tumors	PREA Only
3/25/2025	Blujepa tablets	gepotidacin	Uncomplicated urinary tract infections	PREA Only
3/25/2025	Conexxence injection	Denosumab-bnht	Osteogenesis imperfecta	PREA Only
3/21/2025	Otulfi injection	ustekinumab-aauz	Plaque psoriasis	PREA Only
3/21/2025	Prezcobix tablets	darunavir/cobicistat	HIV – 1 infection	PREA Only
3/17/2025	Baqsimi nasal powder	glucagon	Hypoglycemia in Type 1 diabetes mellitus	PREA Only
3/14/2025	Metronidazole injection	metronidazole	Intraabdominal infections	409i(BPCA)

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
3/13/2025	Arbli oral suspension	losartan potassium	Hypertension	PREA Only
3/12/2025	Topamax tablets	topiramate	Partial-onset seizures	409i(BPCA)
3/12/2025	Qudexy XR extended-release capsules	topiramate	Partial-onset seizures	409i(BPCA)
3/10/2025	Trokendi XR extended-release capsules	topiramate	Partial-onset seizures	409i(BPCA)
3/5/2025	Neffy Nasal Spray	epinephrine nasal spray	Type I allergic reactions, including anaphylaxis	PREA Only
2/28/2025	Stoboclo injection	Denosumab-bmwo	Glucocorticoid-induced osteoporosis	PREA Only
2/28/2025	Opsumit tablets	macitentan	Pulmonary arterial hypertension (PAH)	BPCA Only
2/27/2025	Odactra sublingual	House Dust Mite	House dust mite-induced allergic rhinitis	PREA Only
2/21/2025	Xeljanz tablets	tofacitinib citrate	Systemic Juvenile Idiopathic Arthritis (SJIA) and Polyarticular Course Juvenile Idiopathic Arthritis (PcJIA)	BPCA Only
2/19/2025	Odefsey tablets	emtricitabine/ rilpivirine/ tenofovir alafenamide	HIV – 1 infection	PREA Only
2/14/2025	Penmenvy injection	Meningococcal Groups A, B, C, W, and Y Vaccine	Active immunization to prevent invasive disease caused by Neisseria meningitidis	PREA Only
2/14/2025	Vimkunya injection	Chikungunya Vaccine, Recombinant	Prevention of disease caused by chikungunya virus	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
2/14/2025	Merilog and Merilog Solostar injection	insulin aspart-szjj	Type 1 diabetes mellitus	PREA Only
2/14/2025	Simlandi injection	adalimumab-ryvk	Polyarticular juvenile idiopathic arthritis (pJIA) and Crohn's disease	PREA Only
2/14/2025	Ospomyv injection	Denosumab-dssb	Giant cell tumor of bone	PREA Only
2/12/2025	Selarsdi injection	ustekinumab-aekn	Crohn's disease and ulcerative colitis	PREA Only
1/28/2025	Inzirqo for oral suspension	Hydro-chlorothiazide	Hypertension and edema associated with congestive heart failure, hepatic cirrhosis, and renal disease, including the nephrotic syndrome	PREA Only
12/23/2024	Arixtra injection	fondaparinux sodium	Prophylaxis of deep vein thrombosis	PREA Only
12/19/2024	Xofluza tablets	marboxil baloxavir	Influenza	PREA Only
12/19/2024	Harvoni pellets	ledipasvir/ sofosbuvir	Hepatitis C virus infection	PREA Only
12/18/2024	Invokamet XR extended-release tablets	canagliflozin/ metformin hydrochloride	Type 2 diabetes mellitus	BPCA + PREA
12/18/2024	Invokamet tablets	canagliflozin/ metformin hydrochloride	Type 2 diabetes mellitus	BPCA + PREA
12/18/2024	Invokana tablets	canagliflozin	Type 2 diabetes mellitus	BPCA + PREA
12/13/2024	Orkambi tablets	lumacaftor/ ivacaftor	Cystic fibrosis	BPCA Only
12/12/2024	Bridion injection	sugammadex	Reversal of neuromuscular blockade	BPCA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
11/27/2024	Wegovy injection	semaglutide	Obesity	PREA Only
11/27/2024	Iomervu injection	iomeprol	Contrast agent	PREA Only
11/22/2024	Imkeldi oral solution	imatinib	Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML)	PREA Only
11/15/2024	Epysqli injection	eculizumab-aagh	Generalized myasthenia gravis	PREA Only
11/15/2024	Revuforj tablets	revumenib	Relapsed or refractory acute leukemia with a KMT2A translocation	PREA Only
10/22/2024	Zarxio injection	filgrastim-sndz	Hematopoietic Syndrome of Acute Radiation Syndrome	PREA Only
10/11/2024	Onglyza tablets	saxagliptin	Type 2 diabetes mellitus	PREA Only
10/11/2024	Kombiglyze XR extended-release tablets	saxagliptin/ metformin hydrochloride	Type 2 diabetes mellitus	PREA Only
10/10/2024	Imuldosa injection	ustekinumab-srlf	Plaque psoriasis	PREA Only
10/1/2024	Furosemide injection	furosemide	Diuresis	409i(BPCA)
9/27/2024	Vistaseal injection	Fibrin Sealant (Human)	Adjunct to hemostasis for mild to moderate bleeding	PREA Only
9/20/2024	Cabenuva extended-release injectable suspension	cabotegravir/ rilpivirine	HIV – 1 infection (prevention of transmission and treatment)	PREA Only
9/20/2024	Vocabria tablets	cabotegravir	HIV – 1 infection (prevention of transmission and treatment)	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
9/20/2024	Apretude extended-release suspension injection	cabotegravir	HIV – 1 infection (prevention of transmission and treatment)	PREA Only
9/13/2024	Ebglyss injection	lebrikizumab-lbkz	Atopic dermatitis	PREA Only
9/13/2024	Cimzia injection	certolizumab pegol	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
8/29/2024	ACAM2000 injection	Smallpox and Mpox (Vaccinia) Vaccine, Live for scarification suspension	Active immunization for the prevention of smallpox and mpox disease	PREA Only
8/26/2024	Roszet tablets	rosuvastatin/ ezetimibe	Homozygous familial hypercholesterolemia	PREA Only
8/12/2024	Protonix IV for injection	pantoprazole sodium	Gastroesophageal reflux disease	PREA Only
8/9/2024	Neffy nasal spray	epinephrine	Type I allergic reactions, including anaphylaxis,	PREA Only
8/7/2024	Zurnai Autoinjector	nalmefene hydrochloride	Opioid overdose	PREA Only
7/31/2024	Fibryga Injection	Fibrinogen (Human)	Bleeding patients with acquired fibrinogen deficiency	PREA Only
7/26/2024	Palforzia Peanut Allergen Powder	Peanut (Arachis hypogaea) Allergen Powder-dnfp	Peanut allergy	PREA Only
7/24/2024	Imjudo for intravenous infusion	tremelimumab-actl	Solid tumors	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
7/22/2024	Opipza oral film	aripiprazole	Schizophrenia, irritability associated with Autistic disorder, and Tourette's disorder	PREA Only
7/22/2024	Femlyv orally disintegrating tablets	norethindrone acetate/ethinyl estradiol	Contraception	PREA Only
7/18/2024	Xembify injection	immune globulin subcutaneous, human – klhw	Primary humoral immunodeficiency	PREA Only
7/16/2024	Inlyta Tablets	axitinib	Solid tumors	BPCA + PREA
7/9/2024	Zoryve cream	roflumilast	Plaque psoriasis	PREA Only
7/1/2024	Velphoro chewable tablets	sucroferric oxyhydroxide	Control of serum phosphorus levels with chronic kidney disease on dialysis	PREA Only
6/18/2024	Sofdra topical gel	sofpironium	Primary axillary hyperhidrosis	PREA Only
6/18/2024	Ofev capsules	nintedanib	Fibrosing interstitial lung diseases	BPCA Only
6/14/2024	Nucynta ER tablets	tapentadol	Moderate to severe acute pain	BPCA Only
6/13/2024	Yimmugo Injection	immune globulin intravenous, human-dira	Primary humoral immunodeficiency	PREA Only
6/12/2024	Farxiga tablets	dapagliflozin	Type 2 diabetes mellitus	BPCA + PREA
6/12/2024	Xigduo XR extended-release tablets	dapagliflozin/ metformin hydrochloride	Type 2 diabetes mellitus	BPCA Only
6/10/2024	Kevzara injection	sarilumab	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
5/31/2024	Cefazolin in Dextrose Injection	cefazolin	Perioperative infection prophylaxis	PREA Only
5/24/2024	Onyda XR extended-release oral suspension	clonidine hydrochloride	ADHD	PREA Only
5/16/2024	Benlysta injection	belimumab	Systemic lupus erythematosus (SLE)	PREA Only
5/8/2024	Monodox capsules	doxycycline monohydrate	Infection - bacterial	409i(BPCA)
5/7/2024	Rexulti tablets	brexpiprazole	Major depressive disorder	BPCA Only
5/1/2024	Myhibbin oral suspension	mycophenolate mofetil	Prophylaxis of organ rejection after allogeneic kidney, heart or liver transplants	PREA Only
4/30/2024	Mircera injection	methoxy polyethylene glycol-epoetin beta	Anemia associated with CKD	PREA Only
4/26/2024	Rinvoq extended-release tablets	upadacitinib	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
4/25/2024	Otezla tablets	apremilast	Plaque psoriasis	PREA Only
4/23/2024	Lutathera	lutetium Lu 177 dotatate	Neuroendocrine tumors	BPCA Only
4/19/2024	Rezenopy nasal spray	naloxone hydrochloride	Opioid overdose	PREA Only
4/19/2024	Percodan tablets	aspirin/ oxycodone	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)
4/19/2024	Oxycodone Hydrochloride Oral Solution	Oxycodone Hydrochloride	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
4/19/2024	Roxicodone tablets	oxycodone hydrochloride	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)
4/19/2024	Oxycodone hydrochloride capsules	oxycodone hydrochloride	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)
4/19/2024	Oxycodone hydrochloride oral solution	oxycodone hydrochloride	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)
4/19/2024	RoxyBond tablets	oxycodone hydrochloride	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)
4/19/2024	Oxaydo tablets	oxycodone hydrochloride	Safety of breastfeeding for lactating women receiving oxycodone for postpartum pain management	409i(BPCA)
4/16/2024	Selarsdi injection	ustekinumab-aekn	Psoriatic Arthritis	PREA Only
4/12/2024	Entresto Sprinkle oral pellets and tablets	sacubitril/ valsartan	Heart failure	PREA Only
4/5/2024	Dovato tablet	dolutegravir and lamivudine	HIV – 1 infection	PREA Only
4/5/2024	FASENRA	benralizumab	Asthma	PREA Only
4/3/2024	Lenvima capsules	lenvatinib	Solid tumors	BPCA Only
4/3/2024	Zevtera for injection	ceftobiprole medocaril sodium	Community Acquired Bacterial Pneumonia	PREA Only
3/27/2024	Vemlidy tablets	tenoforvir alafenamide	Chronic hepatitis B infection	PREA Only
3/22/2024	Wilate Injection	von Willebrand Factor/Coagulation Factor VIII	von Willebrand disease	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
		Complex (Human)		
3/22/2024	Ixinity Injection	Coagulation Factor IX (Recombinant)	Hemophilia B	PREA Only
3/15/2024	Edurant 25 mg tablet	rilpivirine	HIV – 1 infection	BPCA Only
3/15/2024	Edurant Ped 2.5 mg tablet	rilpivirine	HIV – 1 infection	BPCA + PREA
3/8/2024	Praluent injection	alirocumab	Heterozygous familial hypercholesterolemia	PREA Only
3/5/2024	Tyenne injection	tocilizumab-aazg	Polyarticular juvenile idiopathic arthritis (pJIA) and Systemic Juvenile Idiopathic Arthritis (SJIA)	PREA Only
3/1/2024	Definity injectable suspension and Definity RT injectable	perflutren lipid microsphere	Contrast agent for echocardiogram	PREA Only
2/28/2024	Veklury injection	remdesivir	Coronavirus disease 2019 (COVID-19)	BPCA + PREA
2/28/2024	Ziextenzo injection	pegfilgrastim-bmez	Hematopoietic Syndrome of Acute Radiation Syndrome	PREA Only
2/16/2024	Xolair for injection	omalizumab	Reduction of type I allergic reactions, including anaphylaxis, that may occur with accidental exposure to one or more foods	PREA Only
2/13/2024	Legubeti for oral solution	acetylcysteine	Ingestion of a potentially hepatotoxic quantity of acetaminophen	PREA Only
2/12/2024	Diflucan	fluconazole	Invasive candidiasis	409i(BPCA)
1/26/2024	Avycaz for injection	ceftazidime/ avibactam	Complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
1/5/2024	Zelsuvmi topical gel	berdazimer	Molluscum contagiosum	PREA Only
1/5/2024	Idacio injection	adalimumab-aacf	Polyarticular juvenile idiopathic arthritis (pJIA) and Crohn's disease	PREA Only
12/22/2023	Udenyca injection	pegfilgrastim-cbqv	Chemotherapy induced neutropenia	PREA Only
12/22/2023	Abacavir and Lamivudine Tablets for Oral Suspension	Abacavir/ Lamivudine	HIV – 1 infection	PREA Only
12/15/2023	Zoryve Foam	roflumilast	Seborrheic dermatitis	PREA Only
12/14/2023	Adbry injection	tralokinumab-ldrm	Atopic dermatitis	PREA Only
12/8/2023	Cresemba capsules	Isavuconazo-nium sulfate	Aspergillis infections	BPCA Only
12/8/2023	Cresemba injection	Isavuconazo-nium sulfate	Aspergillis infections	BPCA + PREA
12/8/2023	Bivigam injection	Immune Globulin Intravenous (Human), 10% Liquid	Primary humoral immunodeficiency	PREA Only
12/1/2023	Wilate injection	Human coagulation F VIII and Von Willebrand Factor, von Willebrand Factor/Coag-	von Willebrand disease	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
		ulation F VIII Complex		
11/29/2023	Alvaiz tablets	eltrombopag	Immune thrombocytopenia (ITP)	PREA Only
10/30/2023	Orencia injection	abatacept	Psoriatic Arthritis	BPCA Only
10/20/2023	Rozlytrek oral pellets	entrectinib	Solid tumors	BPCA Only
10/20/2023	Cabtreo topical gel	clindamycin phosphate/ adapalene/ benzoyl peroxide	Acne vulgaris	PREA Only
10/20/2023	Coxanto capsule	oxaprozin	Juvenile rheumatoid arthritis (JRA)	PREA Only
10/20/2023	Penbraya for injection	Meningococcal Groups A, B, C, W, and Y Vaccine	Active immunization to prevent invasive disease caused by Neisseria meningitidis	PREA Only
10/18/2023	Savaysa tablets	edoxaban	Venous thromboembolism	PREA Only
10/18/2023	Enbrel injection	etanercept	Psoriatic Arthritis	PREA Only
10/13/2023	Opdivo injection	nivolumab	Melanoma	BPCA Only
10/5/2023	Zoryve cream	roflumilast	Plaque psoriasis	PREA Only
10/2/2023	Veltassa for oral suspension	patiromer	Hyperkalemia	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
9/29/2023	TECHNEGAS	Technetium Tc 99m-labeled carbon inhalation aerosol	Contrast for lung ventilation imaging	PREA Only
9/29/2023	Tofidence injection	tocilizumab-bavi	Systemic juvenile idiopathic arthritis (SJIA) and Polyarticular juvenile idiopathic arthritis (PJIA)	PREA Only
9/29/2023	Micafungin in Sodium Chloride Injection	micafungin	Candidemia	PREA Only
9/29/2023	Stimufend injection	pegfilgrastim-fpgk	Hematopoietic Syndrome of Acute Radiation Syndrome	PREA Only
9/26/2023	Bosulif tablets	bosutinib	Chronic myelogenous leukemia	BPCA Only
9/25/2023	Ryzumvi ophthalmic solution 0.75%	phentolamine	Pharmacologically-induced mydriasis	PREA Only
9/22/2023	Likmez oral suspension	metronidazole	Amebiasis infection	PREA Only
9/22/2023	Exxua extended-release tablets	gepirone	Major depressive disorder	BPCA + PREA
9/14/2023	Temodar capsules	temozolomide	Brain stem glioma and high-grade astrocytoma	PREA Only
9/11/2023	Comirnaty suspension for injection	COVID-19 Vaccine, mRNA	Active immunization to prevent COVID-19	PREA Only
9/11/2023	SPIKEVAX suspension for injection	COVID-19 Vaccine, mRNA	Active immunization to prevent COVID-19	PREA Only
8/31/2023	Spritam tablets for oral suspension	levetiracetam	Partial-onset seizures	409i(BPCA)

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
8/31/2023	Mekinist tablets	trametinib	Solid tumors	BPCA Only
8/31/2023	Keppra solution	levetiracetam	Partial-onset seizures	409i(BPCA)
8/23/2023	Trintellix tablets	vortioxetine	Major depressive disorder	BPCA + PREA
8/22/2023	Focinvez injection	fosaprepitant	Nausea and vomiting associated with chemotherapy	PREA Only
8/11/2023	Botox for injection	Onabotulinum-toxinA	Neurogenic detrusor overactivity	PREA Only
8/4/2023	Ezallor Sprinkle capsules	rosuvastatin	Heterozygous familial hypercholesterolemia	PREA Only
7/28/2023	RiVive nasal spray	naloxone hydrochloride	Opioid overdose	PREA Only
7/27/2023	Nesina and Kazano	alogliptin, alogliptin/ metformin hydrochloride	Type 2 diabetes mellitus	PREA Only
7/27/2023	Ervebo injection	Ebola Zaire Vaccine, Live	Immunization to prevent disease caused by Zaire ebolavirus	PREA Only
7/26/2023	Meropenem for Injection	meropenem	Bacterial meningitis	409i(BPCA)
7/21/2023	Ycanth topical solution	cantharidin	Molluscum contagiosum	PREA Only
7/17/2023	Beyfortus injection	nirsevimab-alip	Respiratory Syncytial Virus (RSV) infection	PREA Only
7/3/2023	Nucynta oral solution	tapentadol	Moderate to severe acute pain	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
7/3/2023	Nucynta tablet	tapentadol	Moderate to severe acute pain	PREA Only
6/30/2023	DENGVAXIA	DENGUE Tetravalent Vaccine, Live	Immunization against dengue infection	PREA Only
6/23/2023	Litfulo	ritlecitinib	Alopecia areata	PREA Only
6/20/2023	Jardiance tablets	empagliflozin	Type 2 diabetes mellitus	BPCA Only
6/20/2023	Blincyto for injection	blinatumomab	Acute lymphoblastic leukemia (ALL)	BPCA Only
6/20/2023	Jentadueto tablets and Jentadueto XR extended-release tablets	linagliptin/ metformin hydrochloride	Type 2 diabetes mellitus	BPCA + PREA
6/20/2023	Synjardy tablets and Synjardy extended-release tablets, Synjardy XR	empagliflozin/ metformin hydrochloride	Type 2 diabetes mellitus	BPCA Only
6/20/2023	Tradjenta tablets	linagliptin	Type 2 diabetes mellitus	BPCA + PREA
6/15/2023	Triumeq PD oral suspension and Triumeq tablets	abacavir/ dolutegravir/ lamivudine	HIV – 1 infection (prevention of transmission and treatment)	BPCA + PREA
6/12/2023	Linzess capsules	linaclotide	Functional constipation	BPCA + PREA
5/26/2023	Zinplava injection	bezlotoxumab	Reduce recurrence of Clostridioides difficile infection	BPCA + PREA

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
5/23/2023	Yuflyma injection	adalimumab-aaty	Polyarticular juvenile idiopathic arthritis (pJIA) and Crohn's disease	PREA Only
5/22/2023	Opvee nasal spray	nalmefene	Opioid overdose	BPCA + PREA
5/18/2023	Cyltezo injection	adalimumab-abdm	Juvenile rheumatoid arthritis (JRA)	PREA Only
5/12/2023	Lexapro	escitalopram	Generalized anxiety disorder	PREA Only
5/12/2023	Breo Ellipta inhalation powder	fluticasone furoate/ vilanterol	Asthma	BPCA Only
5/11/2023	Caldolor injection	ibuprofen	Mild to moderate acute pain	PREA Only
5/4/2023	Motpoly XR extended-release capsules	lacosamide	Partial-onset seizures	PREA Only
5/4/2023	Mydcombi ophthalmic spray	tropicamide/ phenylephrine hydrochloride	Mydriasis for diagnostic procedures	PREA Only
5/3/2023	Kalydeco granules	ivacaftor	Cystic fibrosis	BPCA Only
4/28/2023	Vimpat	lacosamide	Partial-onset seizures	PREA Only
4/27/2023	Prevnar 20	Pneumococcal 20-valent Conjugate Vaccine	Active immunization for prevention of invasive disease cause by Streptococcus pneumoniae	PREA Only
4/25/2023	Diazepam injection	diazepam	Partial-onset seizures	409i(BPCA)

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
4/14/2023	RizaFilm oral film	rizatriptan	Migraine	PREA Only
4/7/2023	HYQVIA	Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase	Primary immunodeficiency diseases	PREA Only
4/6/2023	Amjevita injection	adalimumab-atto	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
4/3/2023	Eucrisa	crisaborole	Atopic dermatitis	PREA Only
3/24/2023	Fetzima extended-release capsules	levomilnacipran	Major depressive disorder	PREA Only
3/20/2023	Hyrimoz Injection	adalimumab-adaz	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
3/16/2023	Tafinlar capsules	dabrafenib	Solid tumors	BPCA Only
3/10/2023	Daybue	trofinetide	Rett syndrome	BPCA Only
3/7/2023	Naloxone hydrochloride nasal spray	Naloxone hydrochloride	Opioid overdose	PREA Only
3/1/2023	Arnuity Ellipta Inhalation Powder	fluticasone furoate	Asthma	PREA Only
2/27/2023	Dapzura RT injection	daptomycin	Complicated skin and skin structure infections (cSSSI)	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
2/27/2023	M-M-R II	MMR Virus Vaccine	Active immunization for the prevention of measles, mumps and rubella	PREA Only
2/27/2023	PROQUAD	MMRV Virus Vaccine	Active immunization for the prevention of measles, mumps, rubella, and varicella	PREA Only
2/27/2023	Varivax	Varicella Virus Vaccine Live	Active immunization for the prevention of varicella	PREA Only
2/23/2023	Prevduo injection	neostigmine methylsulfate and glycopyrrolate	Reversal of the effects of nondepolarizing neuromuscular blocking agents	PREA Only
2/17/2023	Rifadin capsules and Rifadin injection	rifampin	Tuberculosis and asymptomatic carriers of Neisseria meningitidis infection	409i(BPCA)
2/15/2023	Opdivo	nivolumab	Melanoma	BPCA Only
2/9/2023	Cibinqo tablets	abrocitinib	Atopic dermatitis	PREA Only
2/8/2023	Eylea Injection	aflibercept	Retinopathy of Prematurity (ROP)	BPCA Only
2/3/2023	Takhzyro Injection	lanadelumab-flyo	Hereditary angioedema	BPCA Only
2/1/2023	Atorvaliq oral suspension	atorvastatin calcium	Heterozygous familial hypercholesterolemia	PREA Only
1/20/2023	ODACTRA	House Dust Mite (Dermato-phagoides farinae and Dermato-phagoides pteronyssinus) Allergen Extract	House dust mite-induced allergic rhinitis	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
1/10/2023	Airsupra inhalation aerosol	albuterol/budesonide	Asthma	PREA Only
1/9/2023	Adacel	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed	Immunization during the third trimester of pregnancy to prevent pertussis in infants	PREA Only
12/23/2022	Xenoview for oral inhalation	xenon Xe 129 hyperpolarized	Contrast to evaluate lung ventilation with MRI	PREA Only
12/23/2022	Wegovy injection	semaglutide	Obesity	PREA Only
12/22/2022	Cimzia Injection	certolizumab pegol	Crohn's Disease	PREA Only
12/20/2022	Avycaz for injection	ceftazidime/ avibactam	Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia	PREA Only
12/19/2022	Jakafi tablets	ruxolitinib	Hematologic malignancies	BPCA Only
12/16/2022	Precedex injection	Dexmedetomidine hydrochloride	Sedation	PREA Only
12/13/2022	Idacio injection	adalimumab-aacf	Polyarticular juvenile idiopathic arthritis (pJIA) and Crohn's disease	PREA Only
12/9/2022	Tecentriq injection	atezolizumab	Alveolar soft part sarcoma	BPCA Only
11/30/2022	Brexafemme injection	ibrexafungerp	Recurrent vulvovaginal candidiasis	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
11/22/2022	Sevenfact	Coagulation factor VIIa (recombinant)-jncw	Hemophilia A or B	PREA Only
11/17/2022	Trulicity injection	dulaglutide	Type 2 diabetes mellitus	BPCA Only
11/17/2022	IXINITY	Coagulation Factor IX (Recombinant)	Hemophilia B	PREA Only
11/10/2022	Erelzi Injection	etanercept-szzs	Systemic Juvenile Idiopathic Arthritis (SJIA) and Polyarticular Course Juvenile Idiopathic Arthritis (PcJIA)	PREA Only
11/10/2022	Adcetris for injection	brentuximab vedotin	Hodgkin lymphoma	BPCA Only
10/17/2022	Vemlidy tablets	tenofovir alafenamide	Chronic hepatitis B virus infection	PREA Only
10/14/2022	Lyumjev injection	insulin lispro-aabc	Type 1 diabetes mellitus	PREA Only
10/7/2022	Boostrix	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed	Active booster immunization against tetanus, diphtheria, and pertussis, including immunization during the third trimester of pregnancy to prevent pertussis in infants	PREA Only
9/21/2022	Elucirem injection	gadopiclenol	MRI Contrast agent	PREA Only
9/13/2022	Halaven Injection	eribulin mesylate	Solid tumors	BPCA Only
9/2/2022	Orkambi	lumacaftor/ ivacaftor	Cystic fibrosis	BPCA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
9/1/2022	Clindamycin Phosphate injection	clindamycin phosphate	Serious bacterial infections	409i(BPCA)
8/24/2022	Imbruvica	Ibrutinib	Chronic graft-versus-host disease	BPCA Only
8/23/2022	Comirnaty suspension for injection	COVID-19 Vaccine, mRNA	Immunization COVID-19	PREA Only
8/11/2022	Xofluza tablets	baloxavir marboxil	Influenza	PREA Only
7/29/2022	Abrilada	adalimumab-afzb	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
7/29/2022	Zoryve cream	roflumilast	Plaque psoriasis	PREA Only
7/29/2022	Stelara injection	ustekinumab	Plaque psoriasis	PREA Only
7/28/2022	Amjevita injection	adalimumab-atto	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
7/28/2022	Cotellic tablets	cobimetinib	Solid tumors	BPCA Only
7/26/2022	Benlysta for injection	belimumab	Active lupus nephritis	PREA Only
7/26/2022	Benlysta injection	belimumab	Active lupus nephritis	PREA Only
7/18/2022	Opzelura cream	ruxolitinib	Vitiligo	PREA Only
7/14/2022	Hulio injection	adalimumab-fkjp	Polyarticular juvenile idiopathic arthritis (pJIA) and Crohn’s disease	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
7/8/2022	Comirnaty suspension for injection	COVID-19 Vaccine, mRNA	Active immunization to prevent COVID-19	PREA Only
6/24/2022	Qsymia extended-release capsules	phentermine/ topiramate	Obesity	PREA Only
6/22/2022	Mekinist tablets	trametinib	Solid tumors	PREA Only
6/22/2022	Tafinlar capsules	dabrafenib	Solid tumors	BPCA Only
6/17/2022	VAXNEUVANCE injection	Pneumococcal 15-valent Conjugate Vaccine	Active immunization for the prevention of invasive disease caused by Streptococcus pneumoniae	PREA Only
6/17/2022	Hadlima injection	adalimumab-bwwd	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
6/16/2022	Zulresso injection	brexanolone	Postpartum depression	PREA Only
6/7/2022	Dupixent injection	dupilumab	Atopic dermatitis	PREA Only
6/6/2022	CellCept	mycophenolate mofetil	Prophylaxis of organ rejection	PREA Only
6/3/2022	PRIORIX	Combined Measles, Mumps, and Rubella (MMR) Live (Attenuated) Viral Vaccine	Active immunization for the prevention of measles, mumps, and rubella	PREA Only
5/19/2022	Prolia injection	denosumab	Severe osteogenesis imperfecta	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
5/9/2022	Brilinta tablets	ticagrelor	Vasoocclusive crises in sickle cell disease	BPCA Only
4/29/2022	Qelbree extended-release capsules	viloxazine	ADHD	PREA Only
4/25/2022	Veklury injection	remdesivir	COVID-19	PREA Only
4/21/2022	Zerbaxa for injection	ceftolozane/ tazobactam	Complicated intra-abdominal infections (cIAI)	PREA Only
4/7/2022	Gilotrif tablets	afatinib	Refractory solid tumors	BPCA Only
3/30/2022	Triumeq tablets	abacavir/ dolutegravir/ lamivudine	HIV – 1 infection	PREA Only
3/30/2022	Triumeq PD Suspension	abacavir sulfate/ dolutegravir/ lamivudine	HIV – 1 infection	PREA Only
3/29/2022	Edurant tablets	rilpivirine	HIV – 1 infection	BPCA + PREA
3/29/2022	Vocabria tablets	cabotegravir	HIV – 1 infection	PREA Only
3/29/2022	Cabenuva extended-release injectable suspension	cabotegravir/ rilpivirine	HIV – 1 infection	PREA Only
3/28/2022	Hyrimoz Injection	adalimumab-adaz	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
3/25/2022	Fintepla oral solution	fenfluramine hydrochloride	Lennox Gastaut syndrome	BPCA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
3/22/2022	Xelstrym transdermal system	dextroamphetamine	ADHD	PREA Only
3/22/2022	SMOFlipid	lipid injectable emulsion	Source of calories and essential fatty acids for parenteral nutrition	PREA Only
3/18/2022	Opdualag injection	nivolumab/ relatlimab-rmbw	Melanoma	PREA Only
3/10/2022	Methotrexate	Methotrexate	Acute lymphoblastic leukemia (ALL)	BPCA + PREA
2/28/2022	Naloxone Hydrochloride Autoinjector	naloxone hydrochloride	Opioid overdose	PREA Only
2/25/2022	ACUVUE Theravision with Ketotifen	etafilcon A drug-eluting contact lens/ketotifen	Allergic conjunctivitis	PREA Only
2/24/2022	Norliqva oral solution	amlodipine	Hypertension	PREA Only
2/18/2022	NephroScan Kit	Technetium Tc99m Succimer	Aid in scintigraphic evaluation of renal parenchymal disorders	PREA Only
2/4/2022	Fleqsuvy oral suspension	baclofen	Multiple sclerosis	PREA Only
1/28/2022	Geodon capsules	ziprasidone hydrochloride	Bipolar I disorder	PREA Only
1/27/2022	Pifeltro tablets	doravirine	HIV – 1 infection	PREA Only
1/27/2022	Delstrigo tablets	doravirine/lamivudine/tenofovir disoproxil fumarate	HIV – 1 infection	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
1/26/2022	Solosec oral granules	secnidazole	Bacterial vaginosis	PREA Only
1/26/2022	Solosec oral granules	secnidazole	Trichomoniasis infection	PREA Only
1/21/2022	Veklury injection	remdesivir	COVID-19	PREA Only
1/14/2022	Cibinqo tablets	abrocitinib	Atopic dermatitis	PREA Only
1/14/2022	Rinvoq extended-release tablets	upadacitinib	Atopic dermatitis	PREA Only
1/13/2022	Ryaltris nasal spray	olopatadine hydrochloride/ mometasone Furoate	Seasonal allergic rhinitis	PREA Only
1/7/2022	Genvoya tablets	elvitegravir/ cobicistat/ emtricitabine/ tenofovir alafenamide	HIV – 1 infection	BPCA + PREA
1/7/2022	Descovy tablets	emtricitabine/ tenofovir alafenamide	HIV – 1 infection	PREA Only
12/27/2021	Rexulti tablets	brexpiprazole	Schizophrenia	PREA Only
12/23/2021	Tascenso ODT orally disintegrating tablet	fingolimod	Multiple sclerosis	PREA Only
12/20/2021	Apretude extended-release injectable suspension	cabotegravir	HIV – 1 infection	BPCA + PREA

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
12/20/2021	Vocabria tablets	cabotegravir	HIV – 1 infection	BPCA + PREA
12/17/2021	Xarelto for oral suspension	rivaroxaban	Venous thromboembolism (VTE)	PREA Only
12/17/2021	Tezspire	tezepelumab-ekko	Asthma	PREA Only
12/17/2021	Yusimry	adalimumab-aqvh	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
12/17/2021	Rezvoglar injection	insulin glargine-aglr	Type 1 diabetes mellitus	PREA Only
12/9/2021	Zepatier tablets	elbasvir/ grazoprevir	Chronic hepatitis C infection	PREA Only
12/7/2021	Xaciato vaginal gel	clindamycin phosphate	Bacterial vaginosis	PREA Only
12/4/2021	Cleocin Phosphate injection	clindamycin phosphate	Serious infections	409i(BPCA)
11/22/2021	Lyvispah oral granules	baclofen	Multiple sclerosis	PREA Only
11/19/2021	Injectafer injection	ferric carboxymaltose	Anemia, iron deficiency	PREA Only
11/12/2021	Diazepam Injection	diazepam	Partial-onset seizures	409i(BPCA)
11/5/2021	Eprontia oral solution	topiramate	Epilepsy	PREA Only
11/4/2021	Byetta injection	exenatide	Type 2 diabetes mellitus	BPCA + PREA

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
11/4/2021	Dyanavel XR extended-release tablets	amphetamine	ADHD	PREA Only
10/22/2021	CUTAQUIG solution	Immune Globulin Subcutaneous (Human) - hipp	Primary humoral immunodeficiency	PREA Only
10/20/2021	Welchol	colesevelam hydrochloride	Type 2 diabetes mellitus	PREA Only
10/20/2021	Dupixent injection	dupilumab	Asthma	PREA Only
10/15/2021	Zimhi injection	naloxone hydrochloride	Opioid overdose	PREA Only
10/14/2021	FLUCELVAX QUADRIVALENT Suspension for Intramuscular Injection	Influenza Vaccine	Active immunization for the prevention of disease caused by Influenza A and B virus	PREA Only
10/14/2021	Vimpat	lacosamide	Partial-onset seizures	PREA Only
10/7/2021	Biktarvy tablets	bictegravir/ emtricitabine/ tenofovir alafenamide	HIV – 1 infection	PREA Only
10/7/2021	Topicort topical spray	desoximetasone	Plaque psoriasis	PREA Only
9/24/2021	Repatha injection	evolocumab	Heterozygous and homozygous familial hypercholesterolemia	PREA Only
9/21/2021	Opzelura cream	ruxolitinib	Atopic dermatitis	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
8/30/2021	Selenious Acid injection	selenious acid	Nutrition	PREA Only
8/27/2021	Briviact tablets, solution, and injection	brivaracetam	Partial-onset seizures	PREA Only
8/23/2021	Comirnaty suspension for injection	COVID-19 Vaccine, mRNA	Active immunization to prevent COVID-19	PREA Only
8/18/2021	Lexette topical foam	halobetasol propionate	Plaque psoriasis	BPCA + PREA
8/13/2021	TICOVAC Suspension for intramuscular injection	Tick-Borne Encephalitis Vaccine	Immunization to prevent tick-borne encephalitis	PREA Only
8/11/2021	Mirena intrauterine device	levonorgestrel-releasing intrauterine system	Contraception and heavy menstrual bleeding	PREA Only
7/30/2021	Adlyxin injection	lixisenatide	Type 2 diabetes mellitus	PREA Only
7/29/2021	Vyvanse	Lisdexamfet-amine dimesylate	ADHD	BPCA + PREA
7/28/2021	Semglee injection	insulin glargine-yfgn	Type 1 diabetes mellitus	PREA Only
7/26/2021	Twyneo cream	tretinoin/benzoyl peroxide	Acne vulgaris	PREA Only
7/22/2021	Bydureon injectable suspension	exenatide	Type 2 diabetes mellitus	BPCA + PREA

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
7/22/2021	Bydureon BCise injectable suspension	exenatide	Type 2 diabetes mellitus	BPCA + PREA
7/22/2021	Dalvance for injection	dalbavancin	Acute bacterial skin and skin structure infections	PREA Only
7/21/2021	Oxycodone hydrochloride	oxycodone hydrochloride	Moderate to severe acute pain	PREA Only
7/21/2021	Oxycodone hydrochloride	oxycodone hydrochloride	Moderate to severe acute pain	PREA Only
7/9/2021	ArmonAir RespiClick inhalation powder	fluticasone propionate	Asthma	BPCA + PREA
7/9/2021	AirDuo RespiClick; AirDuo Digihaler inhalation powder	fluticasone propionate/ salmeterol xinafoate	Asthma	BPCA + PREA
6/30/2021	Rylaze injection	asparaginase erwinia	Acute lymphoblastic leukemia (ALL)	PREA Only
6/30/2021	Multrys injection	trace elements	Source of zinc, copper, manganese, and selenium for parenteral nutrition	PREA Only
6/25/2021	Bridion injection	sugammadex	Reversal of neuromuscular blockade	PREA Only
6/24/2021	Austedo	Deutetra-benazine	Tourette Syndrome	BPCA Only
6/21/2021	Pradaxa capsules	dabigatran etexilate	Venous thromboembolic events	BPCA + PREA
6/21/2021	Pradaxa oral pellets	dabigatran etexilate	Venous thromboembolic events	BPCA + PREA
6/17/2021	Toviaz extended-release tablets	fesoterodine fumarate	Neurogenic detrusor overactivity	BPCA + PREA

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
6/15/2021	Cyramza	ramucirumab	Solid tumors	BPCA Only
6/10/2021	Mavyret	glecaprevir/ pibrentasvir	Chronic hepatitis C infection	BPCA + PREA
6/10/2021	Epclusa oral pellets	sofosbuvir/ velpatasvir	Chronic hepatitis C infection	BPCA + PREA
6/10/2021	Epclusa tablets	sofosbuvir/ velpatasvir	Chronic hepatitis C infection	BPCA + PREA
6/2/2021	Morphine sulfate	morphine sulfate	Moderate to severe acute pain	PREA Only
6/1/2021	Brexafemme tablets	ibrexafungerp	Vulvovaginal candidiasis	PREA Only
5/31/2021	Noxafil injection	posaconazole	Aspergillis and Candida infections	PREA Only
5/28/2021	Cosentyx for injection	secukinumab	Plaque psoriasis	PREA Only
5/25/2021	Zipsor capsules	diclofenac potassium	Mild to moderate acute pain	PREA Only
5/19/2021	Lymphoseek powder for injection	tilmanocept	MRI Contrast for lymphatic mapping	PREA Only
5/17/2021	KEDRAB solution	Rabies Immune Globulin (Human)	Passive, transient post-exposure prophylaxis of rabies infection	PREA Only
4/30/2021	Aubagio tablets	teriflunomide	Multiple sclerosis	BPCA + PREA
4/29/2021	Kloxxado nasal spray	naloxone	Opioid overdose	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
4/29/2021	Morphine sulfate injection	morphine sulfate	Moderate to severe acute pain	PREA Only
4/28/2021	Natroba topical suspension	spinosad	Scabies infestation	PREA Only
4/19/2021	Diovan tablets	valsartan	Hypertension	PREA Only
4/16/2021	Evekeo ODT orally disintegrating tablets	amphetamine sulfate	ADHD	PREA Only
4/16/2021	Ragwitek	Short Ragweed Pollen Allergen Extract	Short ragweed pollen-induced allergic rhinitis	PREA Only
4/15/2021	Nextstellis tablets	drospirenone/ estetrol	Contraception	PREA Only
4/2/2021	Qelbree extended-release capsules	viloxazine	ADHD	PREA Only
3/30/2021	Vyxeos Liposome injection	daunorubicin/ cytarabine	Acute myeloid leukemia	BPCA Only
3/25/2021	Myrbetriq granules	mirabegron	Neurogenic detrusor overactivity	BPCA + PREA
3/25/2021	Myrbetriq extended-release tablets	mirabegron	Neurogenic detrusor overactivity	BPCA + PREA
3/22/2021	Zegalogue injection	dasiglucagon	Severe hypoglycemia	PREA Only
3/22/2021	Exparel injection	bupivacaine liposome	Mild to moderate acute pain	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
3/3/2021	Flucelvax Quadrivalent	Influenza Vaccine	Active immunization for the prevention of influenza disease caused by influenza virus subtypes A and B	PREA Only
3/2/2021	Azstarys capsules	serdexmethylphenidate/ dexmethyl-phenidate	ADHD	PREA Only
2/25/2021	Octaplas	Pooled Plasma (Human), Solvent Detergent Treated	Replacement of multiple coagulation factors in patients with acquired deficiencies and thrombotic thrombocytopenic purpura	PREA Only
2/9/2021	Botox injection	Onabotulinum-toxinA	Neurogenic detrusor overactivity	PREA Only
1/28/2021	Rapivab injection	peramivir	Influenza virus infection	PREA Only
1/22/2021	Trintellix tablets	vortioxetine	Major depressive disorder	BPCA + PREA
12/23/2020	FIBRYNA	Fibrinogen (Human)	Congenital fibrinogen deficiency	PREA Only
12/23/2020	VAXCHORA	Cholera Vaccine, Live, Oral	Active immunization against disease caused by Vibrio cholerae	PREA Only
12/19/2020	ProHance Injection; ProHance Multipack Injection	gadoteridol	MRI Contrast to visualize lesions with abnormal blood-brain barrier and/or abnormal vascularity in the brain	PREA Only
12/18/2020	Xeomin injection	Incobotulinum-toxinA	Chronic sialorrhea	PREA Only
12/17/2020	RIABNI	rituximab-arrx	Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
12/4/2020	FLUAD QUAD	Influenza Virus Vaccine	Active immunization against influenza disease caused by influenza virus subtypes A and B	PREA Only
12/4/2020	Januvia tablets; Janumet tablets; Janumet XR tablets	sitagliptin; sitagliptin/metformin HCl	Type 2 diabetes mellitus	BPCA + PREA
12/4/2020	Saxenda injection	liraglutide	Obesity	PREA Only
11/23/2020	Cefazolin for Injection	cefazolin for Injection	Perioperative infection prophylaxis	PREA Only
11/23/2020	XOFLUZA for oral suspension	baloxavir marboxil	Influenza	PREA Only
11/20/2020	Pomalyst	pomalidomide	Melanoma	BPCA Only
11/16/2020	Vimpat	lacosamide	Epilepsy and partial-onset seizures	PREA Only
10/30/2020	Selzentry	maraviroc	HIV – 1 infection	BPCA Only
10/28/2020	Zinc Sulfate Injection	zinc sulfate	Nutrition	PREA Only
10/28/2020	FLUAD; FLUAD QUAD	Influenza Virus Vaccine	Active immunization for the prevention of disease caused by influenza virus subtypes A and B	PREA Only
10/22/2020	Veklury injection	remdesivir	COVID-19 infection	PREA Only
9/30/2020	Tecentriq injection	atezolizumab	Solid tumors	BPCA Only
9/29/2020	Simponi Aria injection	golimumab	Polyarticular juvenile idiopathic arthritis (pJIA) and psoriatic arthritis	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
9/25/2020	Xeljanz tablets	tofacitinib	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
9/25/2020	Xeljanz oral solution	tofacitinib	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
9/22/2020	Eraxis	anidulafungin	Candidemia	PREA Only
9/9/2020	Trelegy inhalation powder	fluticasone furoate/ umeclidinium/ vilanterol	Asthma	PREA Only
9/2/2020	Nityr tablets	nitisinone	Hereditary tyrosinemia type 1	PREA Only
8/27/2020	Ultravate lotion	halobetasol propionate	Plaque psoriasis	PREA Only
8/26/2020	Winlevi cream	clascoterone	Acne vulgaris	PREA Only
8/19/2020	Cystadrops ophthalmic solution	cysteamine	Cystinosis	PREA Only
8/18/2020	Xeomin injection	Incobotulinum-toxinA	Spasticity	PREA Only
8/13/2020	XYNTHA	Antihemophilic Factor (Recombinant), Plasma Albumin Free	Hemophilia A	PREA Only
8/10/2020	Septra tablets; Septra DS tablets	sulfamethoxazole/trimethoprim	Bacterial infection	409i(BPCA)
8/5/2020	Suprep Bowel Prep Kit oral solution	sodium sulfate/ potassium sulfate/	Colonoscopy preparation	PREA Only

Pediatric Labeling Date	Trade Name	Generic Name	Conditions Evaluated*	Pursuant to Statute
		magnesium sulfate		
7/31/2020	Prezcobix tablets	darunavir/ cobicistat	HIV – 1 infection (prevention of transmission and treatment)	PREA Only
7/31/2020	Evotaz tablets	atazanavir/ cobicistat	HIV – 1 infection (prevention of transmission and treatment)	PREA Only
7/29/2020	Stelara injection	ustekinumab	Plaque psoriasis	PREA Only
7/28/2020	Bactrim and Bactrim DS tablets	Sulfa-methoxazole/ trimethoprim	Bacterial infection	409i(BPCA)
7/28/2020	Bactrim Suspension and Bactrim Pediatric Suspension	Sulfa-methoxazole/ trimethoprim	Bacterial infection	409i(BPCA)
7/24/2020	Xeglyze lotion	abametapir	Lice infestation	PREA Only
7/17/2020	Vectical ointment	calcitriol	Plaque psoriasis	PREA Only
7/15/2020	Septra tablets; Septra DS tablets	Sulfa-methoxazole/ trimethoprim	Bacterial infection	409i(BPCA)
7/6/2020	Hulio injection	adalimumab-fkjp	Polyarticular juvenile idiopathic arthritis (pJIA)	PREA Only
7/2/2020	Tralement injection	trace elements	Nutrition	PREA Only

* Conditions provided in this table do not necessarily represent an approval in pediatric patients. In some cases, the condition may have been evaluated in pediatric patients and found to be ineffective or unsafe. Note that not all pediatric labeling changes have resulted from pediatric studies. In some cases, labeling may be updated based on other data sources such as pediatric extrapolation from adult data or the literature. For complete details regarding these labeling changes, please see https://www.fda.gov/science-research/pediatrics/pediatric-labeling-changes.

Appendix B: Rare Pediatric Disease Priority Review Vouchers Issued (February 2014 through June 2025)

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
4/28/2025	PRV BLA 125807	Prademagene zamikeracel (ZEVASKYN)	Abeona Therapeutics Inc.	Treatment of wounds in adult and pediatric patients with recessive dystrophic epidermolysis bullosa (RDEB)
2/11/2025	PRV NDA 219379	Mirdametinib (GOMEKLI)	SpringWorks Therapeutics, Inc.	Treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 with symptomatic plexiform neurofibromas not amenable to complete resection
12/20/2024	PRV BLA 761315	Concizumab-mtci (ALHEMO)	Novo Nordisk, Inc.	Routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A (congenital factor VIII deficiency) with FVIII inhibitors and hemophilia B (congenital factor IX deficiency) with FIX inhibitors
12/13/2024	PRV NDA 218808	Crinecerfont (CRENESSITY)	Neurocrine Biosciences, Inc.	Adjunctive treatment to glucocorticoid replacement to control androgens in adults and pediatric patients 4 years of age and older with classic congenital adrenal hyperplasia
11/13/2024	PRV BLA 125722/0	Eladocagene exuparvovec-tneq (KEBILIDI)	PTC Therapeutics	Treatment of adult and pediatric patients aromatic L-amino acid decarboxylase (AADC) deficiency
9/24/2024	PRV NDA 219132	Levacetylleucine (AQNEURSA)	IntraBio Inc.	Treatment of neurological manifestations of Niemann-Pick disease type C in adults and pediatric patients weighing ≥15 kg
9/20/2024	PRV NDA 214927	Arimoclomol (MIPLYFFA)	Zevra Denmark AS	Use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C in adult and pediatric patients 2 years of age and older
4/26/2024	PRV NDA 218709	Mavorixafor (XOLREMDI)	X4 Pharmaceuticals, Inc.	Treatment of WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome in patients 12 years of age and older to increase the number of circulating mature neutrophils and lymphocytes

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
4/23/2024	PRV NDA 217700	Tovorafenib (OJEMDA)	Day One Biopharmaceuticals, Inc.	Treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation
3/21/2024	PRV NDA 217865	Givinostat (DUVYZAT)	Italfarmaco S.p.A.	Treatment of Duchenne muscular dystrophy in patients 6 years of age and older
3/18/2024	PRV BLA 125758	Atidarsagene autotemcel (LENMELDY)	Orchard Therapeutics (Europe) Limited	Treatment of children with pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ) or early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD)
12/18/2023	PRV NDA 215064	Birch triterpenes (FILSUVEZ)	Amryt Pharmaceuticals	Treatment of wounds associated with dystrophic and junctional epidermolysis bullosa in adult and pediatric patients 6 months of age and older
12/8/2023	PRV BLA 125787	Exagamglogene autotemcel (Casgevy)	Vertex Pharmaceuticals Inc	Treatment of sickle cell disease (SCD) in patients 12 years and older with recurrent vaso-occlusive crises (VOCs)
11/9/2023	PRV BLA 125795	ADAMTS13, recombinant-krhn (ADZYNMA)	Takeda Pharmaceuticals U.S.A., Inc	Prophylactic or on-demand enzyme replacement therapy (ERT) in adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP)
8/18/2023	PRV BLA 761339	Pozelimab-bbfg (VEOPOZ)	Regeneron Pharmaceuticals, Inc.	Treatment of adult and pediatric patients 1 year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease
8/16/2023	PRV NDA 215559	Palovarotene (SOHONOS)	Ipsen Biopharmaceuticals, Inc.	Reduction in the volume of new heterotopic ossification in adults and pediatric patients (aged 8 years and older for females and 10 years and older for males) with fibrodysplasia ossificans progressiva
6/22/2023	PRV BLA 125781	Delandistrogene moxeparvovec-rokl (ELEVIDYS)	Sarepta Therapeutics, Inc	Treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene.
5/19/2023	PRV BLA 125774	Beremagene geperpavec-svdt (VYJUVEK)	Krystal Biotech, Inc.	Treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
3/24/2023	PRV NDA 217759	Leniolisib (JOENJA)	Pharming Technologies B.V.	Treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older
3/10/2023	PRV NDA 217026	Trofinetide (DAYBUE)	Acadia Pharmaceuticals, Inc.	Treatment of Rett Syndrome in adults and pediatric patients 2 years of age and older
2/28/2023	PRV NDA 216718	Omaveloxolone (SKYCLARYS)	Reata Pharmaceuticals, Inc.	Treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older
2/16/2023	PRV BLA 761278	velmanase alfa-tycv (LAMZEDE)	Chiesi Farmaceutici S.p.A.	Treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients
9/16/2022	PRV BLA 125755	Elivaldogene autotemcel (SKYSONA)	bluebird bio Inc.	To slow the progression of neurologic dysfunction in boys 4- 17 years of age with early, active cerebral adrenoleukodystrophy (CALD)
8/31/2022	PRV BLA 761261	olipudase alfa-rpcp (XENPOZYME)	Genzyme Corporation	Treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients
8/17/2022	PRV BLA 125717	Betibeglogene autotemcel (ZYNTEGLO)	bluebird bio Inc.	Treatment of adult and pediatric patients with ß-thalassemia who require regular red blood cell (RBC) transfusions
3/18/2022	PRV NDA 215904	Ganaxolone (ZTALMY)	Marinus Pharmaceuticals, Inc.	Treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder in patients 2 years of age and older
11/19/2021	PRV NDA 214938	Vosoritide (VOXZOGO)	BioMarin Pharmaceutical, Inc.	To increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses
10/8/2021	PRV BLA 125685	Allogeneic processed Thymus Tissue (RETHYMIC)	Enzyvant Therapeutics Inc.	Immune reconstitution in pediatric patients with congenital athymia
9/29/2021	PRV NDA 214662	Maralixibat (LIVMARLI)	Mirum Pharmaceuticals, Inc.	Treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
7/20/2021	PRV NDA 215498	Odevixibat (BYLVAY)	Albireo AB	Treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis
6/4/2021	PRV BLA 125659	Plasminogen, human-tvmh (RYPLAZIM)	Kedrion Biopharma Inc.	Treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia)
2/26/2021	PRV NDA 214018	Fosdenopterin (NULIBRY)	Origin Biosciences, Inc.	To reduce the risk of mortality in patients with Molybdenum Cofactor Deficiency Type A
2/25/2021	PRV NDA 213026	Casimersen (AMONDYS 45)	Sarepta Therapeutics Inc.	Treatment of Duchenne Muscular Dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping
11/25/2020	PRV NDA 213793	Setmelanotide (IMCIVREE)	Rhythm Pharmaceuticals, Inc.	Chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency
11/25/2020	PRV BLA 761171	Naxitamab-gqgk (DANYELZA)	Y-mAbs Therapeutics, Inc.	Treatment of pediatric patients 1 year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow
11/23/2020	PRV NDA 214103	Lumasiran (OXLUMO)	Alnylam Pharmaceuticals Inc.	Treatment of primary hyperoxaluria type 1 to lower urinary oxalate levels in pediatric and adult patients
11/20/2020	PRV NDA 213969	Lonafarnib (ZOKINVY)	Eiger BioPharmaceuticals, Inc.	Treatment in patients 12 months of age and older with a body surface area of 0.39 m2 and above to reduce the risk of mortality in Hutchinson-Gilford progeria syndrome and for treatment of processing-deficient progeroid laminopathies
8/12/2020	PRV NDA 212154	Viltolarsen (VILTEPSO)	Nippon Shinyaku Co., Ltd.	Treatment of Duchenne Muscular Dystrophy in patients who have a confirmed mutation in the DMD gene that is amenable to exon 53 Skipping
8/7/2020	PRV NDA 213535	Risdiplam (EVRYSDI)	Genentech Inc.	Treatment of spinal muscular atrophy in patients 2 months of age and older

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
4/10/2020	PRV NDA 213756	selumetinib, AZD6244 (KOSELUGO)	AstraZeneca Pharmaceuticals, LP	Treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 who have symptomatic, inoperable plexiform neurofibromas
12/12/2019	PRV NDA 211970	Golodirsen (VYONDYS 53)	Sarepta Therapeutics, Inc.	Treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping
10/21/2019	PRV NDA 212273	Elexacaftor/tezacaftor/ivacaftor (TRIKAFTA)	Vertex Pharmaceutical, Inc.	Treatment of cystic fibrosis in patients aged 12 years and older who have at least one F508del mutation in the CFTR gene
11/28/2018	PRV BLA 125694	Onasemnogene abeparvovec-xioi (ZOLGENSMA)	Novartis Gene Therapies, Inc. (formerly AveXis, Inc.)	Treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene
11/20/2018	PRV BLA 761107	Emapalumab-lzsg (GAMIFANT)	Novimmune S.A.	Treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy
10/5/2018	PRV BLA 761092	Elapegademase-lvlr (REVCOVI)	Leadiant Bioscience Inc.	Treatment of Adenosine Deaminase-Severe Combined Immunodeficiency (ADA-SCID) in pediatric and adult patients
6/25/2018	PRV NDA 210365	cannabidiol oral solution (EPIDIOLEX)	GW Research Ltd.	Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older
4/17/2018	PRV BLA 761068	Burosamab-twza (CRYSVITA)	Ultragenyx Pharmaceutical, Inc.	Treatment of X-linked hypophosphatemia in adult and pediatric patients 1 year of age and older
2/12/2018	PRV NDA 210491	Tezacaftor/ivacaftor (SYMDEKO)	Vertex Pharmaceutical, Inc.	Treatment of patients with cystic fibrosis aged 12 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor
12/19/2017	PRV BLA 125610	Voretigene Neparvovec (LUXTURNA)	Spark Therapeutics, Inc.	Treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
11/15/2017	PRV BLA 761047	Vestronidase alfa-vjbk (MEPSEVII)	Ultragenyx Pharmaceutical, Inc.	Treatment of Mucopolysaccharidosis type VII (MPS VII, Sly Syndrome) in pediatric and adult patients
8/30/2017	PRV BLA 125646	Tisagenlecleucel (KYMRIAH)	Novartis Pharmaceuticals Corporation	Treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse
4/27/2017	PRV BLA 761052	Cerliponase alfa (BRINEURA)	Biomarin Pharmaceuticals Inc.	To slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency
2/9/2017	PRV NDA 208684	Deflazacort (EMFLAZA)	Marathon Pharmaceuticals, LLC	Treatment of Duchenne Muscular Dystrophy in patients 5 years of age and older
12/23/2016	PRV NDA 209531	Nusinersen (SPINRAZA)	Biogen Inc.	Treatment of spinal muscular atrophy in pediatric and adult patients
9/19/2016	PRV NDA 206488	Eteplirsen (EXONDYS 51)	Sarepta Therapeutics	Treatment of Duchenne Muscular Dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping
12/8/2015	PRV BLA 125561	Sebelipase alfa (KANUMA)	Alexion Pharmaceuticals Inc.	Treatment of patients with a diagnosis of Lysosomal Acid Lipase deficiency
10/23/2015	PRV BLA 125513	Asfotase alfa (STRENSIQ)	Alexion Pharmaceuticals, Inc.	Treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)
9/4/2015	PRV NDA 208169	Uridine triacetate (XURIDEN)	Wellstat Therapeutics Corp.	Treatment of hereditary orotic aciduria
3/17/2015	PRV NDA 205750	Cholic acid (CHOLBAM)	Asklepion Pharmaceuticals, LLC	Treatment of bile acid synthesis disorders due to single enzyme defects and as adjunctive treatment of peroxisomal disorders, including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat soluble vitamin absorption

Date PRV Issued	Voucher Number	Product	Product Sponsor	Indication
3/10/2015	PRV BLA 125516	Dinutuximab (UNITUXIN)	United Therapeutics Corporation	Treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy
2/14/2014	PRV BLA 125460	Elosulfase alfa (VIMIZIM)	BioMarin Pharmaceutical, Inc.	Mucopolysaccharidosis type IVA (Morquio A syndrome)

This report was prepared by FDA's Office of Pediatric Therapeutics (OPT), Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), and Oncology Center of Excellence (OCE).

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