

General Background Information

The Pediatric Market Exclusivity Incentive Program and Process

On January 4, 2002, President Bush signed into law the Best Pharmaceuticals for Children Act (BPCA). This legislation reauthorizes and amends the pediatric exclusivity incentive program – six months of additional marketing exclusivity that attaches to any existing exclusivity or patent protection for the drug [active moiety] studied - enacted originally under section 111 of Title I of the Food and Drug Administration Modernization Act of 1997, which created section 505A of the Federal Food, Drug, and Cosmetic Act. As reauthorized, section 505A continues to allow drugs to qualify for exclusivity if (1) the FDA determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, (2) the FDA makes a written request for pediatric studies (Written Request), (3) the reports on the requested pediatric studies are completed within the requested time, and (4) FDA determines the studies “fairly respond” to the Written Request.

Only those drugs with existing exclusivity or patent protection can benefit from pediatric exclusivity, which must attach to existing marketing exclusivity or patent protection (21 U.S.C. 355a(b) and (c)). If a drug has marketing exclusivity or patent protection, or it is expected to receive such protection upon approval, the sponsor of the drug or holder of an approved application can submit to FDA a Proposed Pediatric Study Request (PPSR) describing the studies the sponsor believes will provide information relating to the appropriate use of the drug in the pediatric population. If FDA issues a Written Request for pediatric studies, the sponsor or holder of an approved application has 180 days to respond to FDA that either (1) it agrees to initiate pediatric studies and indicates when the studies will be initiated or (2) it does not agree to conduct the requested studies (21 U.S.C. 355a(d)(4)(A)).

A Written Request is a specific legal document from FDA, signed by the applicable office director[s], and sent to the drug’s sponsor requesting the conduct of pediatric studies to obtain information on the use of a drug in the pediatric population. FDA can issue a Written Request at the request of an interested sponsor or on its own initiative. Issuance of a Written Request to a sponsor or holder of an approved application does not require the recipient to conduct the pediatric studies described in the Written Request. It is the recipient's decision whether to conduct the studies and possibly obtain pediatric exclusivity. The FDA considers the answers to the following three questions when developing and issuing a Written Request: 1) What is the public health benefit for using this product in children? 2) What other products are available/approved for this indication? 3) What studies should be done?

Generally, a Written Request seeks all applicable pediatric information for an active moiety. The Written Request addresses the following issues, as appropriate:

- Type and objective of studies to be performed
- Indications to be studied
- Number of patients to be studied
- Age groups in which the studies will be performed
- Study endpoints, including primary efficacy endpoints
- Timing of assessments
- Entry criteria
- Drug information
- Dosage form

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- Dosing regimens
- Route of administration
- Drug-specific safety concerns to be monitored or assessed
- Statistical information, including: power of the study, statistical analyses of data to be performed
- Labeling that may result from the studies
- Format of the report to be submitted to the FDA, including racial/ethnic minority information
- Time frame for submitting reports of the studies

If the sponsor or holder of an approved application does not respond or does not agree to conduct the requested pediatric studies specified in a Written Request within 180 days, and FDA determines that there is a continuing need for pediatric information, the Written Request will be referred to the Foundation for the National Institutes of Health for the conduct of pediatric studies (21 U.S.C. 355a(d)(4)(B)(i)). The name of the drug, the name of the manufacturer, and the indication(s) to be studied will be made public (21 U.S.C. 355a(d)(4)(B)(ii)).

Once requested studies are complete and an application is accepted for filing, the FDA will determine whether the studies “fairly respond” to the Written Request, and thus, qualify for pediatric exclusivity. This determination is not a full and complete review and analysis of the submitted data. FDA must make its assessment of the safety and efficacy of the product within 6 months (180 days) of submission of the studies (this required 180 day review clock is applicable only to supplements in response to Written Requests).. The exclusivity determination is a much briefer assessment that the elements requested in the written request have been submitted. A study is determined to “fairly respond” to the Written Request if data are obtained in a manner consistent with that specified in the Written Request. FDA will make its determination based upon whether the studies were conducted in accordance with (1) the Written Request, (2) any amendments, and (3) either a written agreement, if one existed, or commonly accepted scientific principles, if no written agreement existed. FDA will determine within a 90-day period after submission whether the studies “fairly respond” by comparing, on a point-by-point basis, the Written Request and any amendments and/or written agreements to the information submitted in the study reports.

FDA will not grant pediatric exclusivity to any product containing the active moiety studied in the Written Request until the all requested reports of studies on that active moiety have been submitted and the FDA has found that the studies respond fairly to the Written Request.

For all pediatric supplements submitted in response to a Written Request under the BPCA, the FDA is required to make available to the public (including by publication in the *Federal Register*) a summary of the medical and clinical pharmacology reviews of the pediatric studies conducted for the supplement. The summaries must be made available not later than 180 days after the report on the pediatric study is submitted to FDA (21 U.S.C. 355a(j)(1)). FDA will make such information publicly available consistent with section 301(j) of the Act, the Freedom of Information Act (5 U.S.C. 552), and the Trade Secrets Act (see 5 U.S.C. 552; and 21 CFR 20.61).