Guidance for Industry

Recommendations for Complying With the Pediatric Rule (21 CFR 314.55(a) and 601.27(a))

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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
November 2000

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11/27/00

TABLE OF CONTENTS

I. INTRODUCTION 1

I. BACKGROUND 1

II. OVERVIEW —WHAT AM I REQUIRED TO DO UNDER THE PEDIATRIC RULE? 2

A. GENERAL REQUIREMENTS 2
B. POSTMARKETING REQUIREMENTS 2

III. PEDIATRIC ASSESSMENTS 3

A. WHAT IS A PEDIATRIC ASSESSMENT? 3
B. WHEN MUST MY APPLICATION CONTAIN PEDIATRIC ASSESSMENTS? 3
C. WHEN DO I SUBMIT MY PEDIATRIC ASSESSMENT? 3
D. WHAT TYPES OF STUDIES SHOULD I SUBMIT AS PART OF MY PEDIATRIC ASSESSMENT? 4
E. WHEN SHOULD I INITIATE PEDIATRIC STUDIES? 4

IV. THE PEDIATRIC PLAN 5

A. WHEN SHOULD I DEVELOP A PEDIATRIC PLAN? 5
B. WHAT AGES SHOULD I COVER IN MY PEDIATRIC PLAN? 6
C. DO I HAVE TO DEVELOP A PEDIATRIC FORMULATION? 6

V. WAIVERS AND DEFERRALS 7

A. WHAT IS A WAIVER? 7
B. HOW DO I GET A WAIVER? 7
C. WHAT IS A DEFERRAL? 10
D. HOW DO I GET A DEFERRAL? 10

VI. COMPLIANCE WITH THE PEDIATRIC RULE — WHAT HAPPENS IF I DON'T DO A PEDIATRIC ASSESSMENT? 11

VII. EXCLUSIVITY AND THE PEDIATRIC RULE 12

A. HOW WILL THE RULE AND EXCLUSIVITY INTERACT? 12
B. IF I SATISFY THE REQUIREMENTS OF THE RULE, WILL I QUALIFY FOR EXCLUSIVITY? 12

VIII. THE PEDIATRIC ADVISORY SUBCOMMITTEE OF THE ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE — WHAT IS ITS ROLE? 13

IX. ADDITIONAL INFORMATION 13

A. WHERE CAN I GET MORE INFORMATION ABOUT COMPLYING WITH THE PEDIATRIC RULE? 13
B. WHERE CAN I GET MORE INFORMATION ON PEDIATRIC EXCLUSIVITY? 14

ATTACHMENT A — REQUEST FOR WAIVER OF PEDIATRIC STUDIES 15

ATTACHMENT B — REQUEST FOR DEFERRAL OF PEDIATRIC STUDIES 16

Draft – Not for Implementation

GUIDANCE FOR INDUSTRY[1]

Recommendations for Complying With the Pediatric Rule (21 CFR 314.55(a) and 601.27(a))

This draft guidance, when finalized, will represent the Food and Drug Administration's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. INTRODUCTION

This draft guidance provides recommendations for sponsors of new drug applications (NDAs) and biologics license applications (BLAs) on how to meet the requirements of the final Pediatric Rule.[2] Areas covered include pediatric assessments, pediatric plans, waivers and deferrals, compliance issues, pediatric exclusivity, and the role of the Pediatric Advisory Subcommittee.

I. BACKGROUND

On December 2, 1998, the Food and Drug Administration published in the *Federal Register* the final Pediatric Rule. Under the Pediatric Rule, applications for new active ingredients, new indications, new dosage forms, new dosing regimens, and new routes of administration must contain a pediatric assessment unless the sponsor has obtained a waiver or deferral of pediatric studies (21 CFR 314.55(a) and 601.27(a)).

The rule became effective on April 1, 1999. Under the compliance dates in the final rule, pediatric assessments must be included in applications after December 2, 2000, for (1) NDAs, (2) BLAs, and (3) abbreviated new drug applications (ANDAs) that are based on suitability petitions for a change in active ingredient, dosage form, or route of administration.[3]

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[1] This guidance has been prepared by the Pediatric Implementation Team in the Center for Drug Evaluation and Research (CDER) in consultation with the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] "Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drugs and Biological Products in Pediatric Patients," 63 FR 66632, December 2, 1998.

[3] On November 4, 1999, FDA received a citizen petition raising issues associated with the relationship between the Pediatric Rule and abbreviated new drug application suitability petitions. The issues raised in the petition are still under consideration by the Agency. Therefore, this guidance does not address pediatric studies associated with suitability petitions.

II. OVERVIEW —WHAT AM I REQUIRED TO DO UNDER THE PEDIATRIC RULE?

A. General Requirements

The Pediatric Rule requires that every application (drug or biologic) for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration, contain a pediatric assessment or a deferral or waiver of the requirement for this assessment (see section IV.B). FDA can also require pediatric studies of marketed drugs and biological products (1) that are used in a substantial number[4] of pediatric patients for the claimed indications and where inadequate labeling could pose significant risks, or (2) that would provide a meaningful therapeutic benefit[5] over existing treatments for pediatric patients and where inadequate labeling could pose significant risks (21 CFR 201.23).

In general, the Pediatric Rule pertains to those diseases and/or conditions that occur in both the adult and pediatric populations. Products intended for pediatric-specific indications will be subject to the requirements of the rule only if they are developed for a subset of the relevant pediatric population. The Pediatric Rule does not require pediatric studies for the pediatric use of a drug for indications for which the sponsor has not obtained, or does not seek, approval.

B. Postmarketing Requirements

The Pediatric Rule requires manufacturers to include in their annual postmarketing reports a summary of any new information pertaining to pediatrics. Specifically, the summary must list whether labeling supplements for pediatric use have been submitted and whether new studies in the pediatric population have been initiated (21 CFR 314.81 for NDAs, 601.27 for BLAs). Where possible, an estimate of patient exposure to the drug product, with special reference to the pediatric population (neonates, infants, children, adolescents) must be provided, including dosage form (21 CFR 314.81 for NDAs and 601.27 for BLAs).

1. Products to Which the Rule Does Not Apply

- Orphan Drugs

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[4] FDA considers the term *substantial number of patients* to mean 50,000 pediatric patients in the U.S. with the disease or condition for which the drug or biological product is indicated.

[5] The term *meaningful therapeutic benefit* is defined as a significant improvement in the treatment, diagnosis, or prevention of a disease, compared to marketed products adequately labeled for that use in the relevant pediatric population. Examples of how improvement might be demonstrated include evidence of increased effectiveness in treatment, prevention, or diagnosis of disease, elimination or substantial reduction of a treatment-limiting drug reaction; documented enhancement of compliance; or evidence of safety and effectiveness in a new subpopulation; or the drug or biological product is in a class of products or for an indication or indications for which there is a need for additional therapeutic options.

If a product has been granted orphan designation for an indication or indications under section 526 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bb), submission of pediatric data is not required for applications to market the product for the orphan-designated indications and a waiver is not needed (21 CFR 314.55(d) for NDAs and 601.27(d) for BLAs).

- Generic Drugs Under 505(j)

The rule does not impose any pediatric study requirements on applications for generic copies of approved drugs (see section 505(j) of the Act). Applications for drugs that are not duplicates of already approved products are required to comply with the rule. This includes applications submitted under 505(j)(2)(C) suitability petitions for changes in dosage form, active ingredient, or route of administration.

III. PEDIATRIC ASSESSMENTS

A. What is a Pediatric Assessment?

A pediatric assessment is the data set (results of studies) adequate to characterize the safety and effectiveness of a drug or biological product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective (21 CFR 314.55(a) for NDAs, 601.27(a) for BLAs).

B. When Must My Application Contain Pediatric Assessments?

After December 2, 2000, all applications must contain a pediatric assessment to be in compliance with the rule, unless the applicant has obtained a waiver or a deferral of pediatric studies (21 CFR 314.55(a); 601.27(a)). In situations where the pediatric plan has been discussed during a meeting with the Agency, and a decision to defer or waive pediatric studies has been mutually agreed upon, the minutes of the meeting will serve to document the decision.

C. When Do I Submit My Pediatric Assessment?

A pediatric assessment must be submitted at the time an application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration is submitted to the Agency, unless the requirement for the assessment has been deferred or waived (21 CFR 314.55; 601.27). If a deferral has been granted, the pediatric assessment will be due by the date specified by the Agency. If the studies submitted in response to the pediatric rule are also the studies for which you may be requesting pediatric exclusivity, refer to the guidance for industry on *Qualifying for Pediatric Exclusivity Under Section 505A*

of the Federal Food, Drug, and Cosmetic Act. As noted in that guidance, you should obtain your written request before submitting your studies.

D. What Types of Studies Should I Submit as Part of My Pediatric Assessment?

The pediatric data submitted in each case under the rule will depend on the nature of the application, what is known about the product in pediatric populations, and the underlying disease or condition being treated. In certain cases where the course of the disease and the drug's effects are expected to be similar in adults and pediatric patients, the Agency may find that pediatric effectiveness can be extrapolated from adult data, and, therefore, adequate and well-controlled trials of clinical effectiveness in the pediatric population will not be needed. However, additional information, such as dosing, pharmacokinetic, and safety data in pediatric patients may be important to support pediatric labeling. Further, if extrapolation from adult effectiveness data is inappropriate, adequate and well-controlled efficacy studies in the pediatric population will need to be conducted (see section 505 of the Act; 21 CFR 314.55; 601.27)). The rule does not require manufacturers to conduct separate studies in pediatric patients in every case. The Agency may determine that sufficient data can be obtained by including pediatric patients and adults in the original studies conducted on a product.

Pediatric studies in more than one age group may be necessary, depending on expected therapeutic benefit and use in each age group, and on whether safety and effectiveness data from one age group can be extrapolated to other age groups. FDA may conclude that it is not necessary to conduct studies in each age group if pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults or other pediatric age groups, and the extrapolation is supplemented with data to define dosing and safety for the relevant age groups. Although the complex medical state of neonates and infants make it critical to evaluate drugs that will be used for them, FDA recognizes that studies in these populations raise special ethical issues. Studies in these patients may be waived or may be deferred until additional experience with the drug or biological product has been gained. However, there will be cases in which the drug or biologic is an important advancement and it is anticipated that it will be used in these age groups. In such cases, studies will be required (21 CFR 314.55; 601.27), unless the applicant obtains a partial waiver (see section V.B.2).

You should contact the appropriate review division to discuss the type of pediatric studies needed to complete your pediatric assessment.

E. When Should I Initiate Pediatric Studies?

The Agency expects that most sponsors will initiate pediatric studies of drugs and biologics for life-threatening diseases for which adequate treatment is not available earlier in development than would be appropriate for less serious

diseases. In some cases, pediatric studies of a drug or biological product for life-threatening diseases may begin as early as phase 1 or phase 2 when the initial safety data in adults become available. The medical need for these products may justify early pediatric trials despite a paucity of safety and effectiveness data.

In general, products with a narrow therapeutic index that do not fulfill an urgent need should be studied in pediatric patients later in drug development.

In certain cases, the Agency recognizes that scientific and ethical considerations will determine that pediatric studies should not begin until after approval of the drug or biological product for use by adults. For example, where a product has not shown any benefit over other adequately labeled products in the class, the therapeutic need is likely to be low, and the risks of exposing pediatric patients to the new product may not be justified until after the product's safety profile is well established in adults after initial marketing. To encourage use of properly labeled drugs in pediatric patients, the Agency may require that products carry labeling statements recommending preferential use in pediatric patients of products that are already adequately labeled.

IV. THE PEDIATRIC PLAN

A. When Should I Develop a Pediatric Plan?

Sponsors are encouraged to submit to the Agency their development plans for assessing pediatric safety and effectiveness as early as possible. Sponsors should be prepared to discuss their plans for pediatric studies with the Agency at critical points in the drug development process for a particular product.

1. Products Intended for Life-Threatening or Severely Debilitating Illnesses

- Pre-investigational new drug application meetings should include plans for studying the drug product in pediatric populations.

- End-of-phase 1 meetings consist of reviewing and reaching agreement on the design of phase 2 controlled clinical trials. For these products a possible goal of phase 2 testing is to provide sufficient data on the drug's safety and effectiveness to support a decision on its approvability for marketing (21 CFR 312.82). The need for, as well as the design and time of, studies of the drug in pediatric patients should also be discussed at end-of-phase 1 meetings for these products. For drugs for life-threatening diseases, the Agency will provide its best judgment at the end-of-phase 1 meetings whether pediatric studies will be required and whether the submission will be deferred until after approval. The minutes of the meetings should reflect whether pediatric studies are likely to be required,

waived, or deferred. If deferral of studies is granted at the time of the meeting, a projected date for submission should be included.

2. *Other Products*

- End-of-phase 2 meetings should be used to determine whether it is safe to proceed to phase 3, to evaluate the phase 3 plan, protocols, the adequacy of current studies, and plans to assess pediatric safety and effectiveness. At least 1 month prior to an end-of-phase 2 meeting, the sponsor should submit background information for the meeting. The background package should include plans for pediatric studies, including a time line for protocol finalization, enrollment, completion, and data analysis. Alternatively, information to support any planned request for waiver or deferral of pediatric studies should be submitted. The review division will provide its best judgment of the pediatric assessment that will be required for the drug product, and whether its submission can be deferred. In addition, there should be a discussion of the applicant's intent to qualify for and studies needed for pediatric exclusivity.

  The minutes of the meeting should indicate whether pediatric studies are likely to be required, waived, or deferred. If a deferral of studies is granted at the time of the meeting, a projected date for submission should be included.

- Pre-NDA or pre-BLA meetings should include a discussion of any major unresolved problems and whether ongoing or recommended studies are adequate to assess pediatric safety and effectiveness.

B. What Ages Should I Cover in My Pediatric Plan?

In general, the age range of the pediatric population is considered to be birth to 16 years. The Pediatric Rule requires the assessment of safety in each age group in which the drug or biological product will provide a meaningful therapeutic benefit or will be used in a substantial number of pediatric patients for the indications claimed. Age groups should be defined flexibly, depending on the pharmacology of the drug or biological product, the manifestations of the disease in various age groups, and the ability to measure the response to therapy.

C. Do I Have to Develop a Pediatric Formulation?

Under the Pediatric Rule you may be required to produce a pediatric formulation if one is necessary, particularly in cases where a new drug or biological product provides a meaningful therapeutic benefit over existing treatments and the required pediatric studies are to be conducted in the age groups needing the pediatric formulation. You must use appropriate formulations for each age group for which the assessment is required (21 CFR 314.55(a); 601.27(a)). It is usually

prudent to begin the development of a pediatric formulation before initiation of pediatric clinical trials.

FDA can waive the requirement for pediatric studies in age groups requiring a pediatric formulation if the manufacturer provides sufficient evidence that reasonable attempts to produce a pediatric formulation have failed. The manufacturer should provide evidence that unusually difficult technological problems prevented the development of a pediatric formulation. FDA will consider the potential importance of the product for pediatric patients when determining whether those problems were severe enough to warrant a waiver of pediatric studies. In certain cases the Agency may also take to an appropriate advisory committee or other external expert body questions about whether a waiver should be granted in light of the technical difficulties in producing pediatric formulations. For additional information on waivers, see section V.

V. WAIVERS AND DEFERRALS

A. What is a waiver?

A waiver removes the requirements for conducting a pediatric assessment for part or all of the pediatric population for a particular application. The Pediatric Rule allows FDA to waive the pediatric study requirement, based on established criteria, for some or all pediatric age groups. FDA can grant a full or partial waiver of the pediatric study requirements on its own initiative or at the request of a sponsor. If a sponsor requests a waiver, it is the sponsor's responsibility to provide adequate justification in writing for the waiver.

B. How Do I Get a Waiver?

Discussions with FDA should occur early in the drug development process, as described in section V.A. A sponsor can request a full waiver of all pediatric studies if one or more of the following criteria for a waiver apply to the pediatric population as a whole.

1. Full Waiver

A full waiver may be granted if the applicant provides evidence that:

- The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used in a substantial number of pediatric patients; or

- Necessary studies are impossible or highly impractical because the number of patients is so small or geographically dispersed; or

- There is evidence strongly suggesting that the drug product would be ineffective or unsafe in all pediatric age groups.

Disease-Specific Waivers

FDA has developed a list of diseases that have extremely limited applicability to pediatric patients in that the signs and symptoms of these diseases occur for the most part in the adult population. Thus, products being developed for the treatment of these conditions in adults are likely to be granted a waiver. These include the following:

- Alzheimer's disease
- Age-related macular degeneration
- Prostate cancer
- Breast cancer
- Non-germ cell ovarian cancer
- Renal cell cancer
- Hairy cell leukemia
- Uterine cancer
- Small cell and non-small cell lung cancer
- Squamous cell cancers of the oropharynx
- Pancreatic cancer
- Basal cell and squamous cell cancer
- Endometrial cancer
- Osteoarthritis
- Parkinson's disease
- Amyotrophic lateral sclerosis
- Arteriosclerosis
- Infertility
- Symptoms of menopause

2. *Partial Waiver*

A partial waiver excusing the sponsor from carrying out studies in particular age groups can be requested if one or more of the grounds for waiver apply to one or more pediatric age groups. In addition, FDA can grant a partial waiver for those age groups for which a pediatric formulation is essential to the conduct of studies if reasonable attempts to produce a pediatric formulation have failed. However, if a waiver is granted on the grounds that it was not possible to develop a pediatric formulation, the waiver would cover only those pediatric age groups needing a pediatric formulation. A partial waiver can be granted for a specific age group if the applicant provides evidence that:

- The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients in that age group, and is not likely to be used in a substantial number of patients in that age group; or

- Necessary studies are impossible or highly impractical because the number of patients in that age group is so small or geographically dispersed; or

- There is evidence strongly suggesting that the drug product would be ineffective or unsafe in that age group; or

- The applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

3. Information in a Waiver Request

FDA has developed a sample waiver request and included it in this guidance as Attachment A. To request a waiver, a sponsor should provide:

- Product name and indication
- Age groups included in waiver request
- Reason for waiving pediatric studies
- Justification for waiving pediatric studies

4. Waiver Decision

FDA will grant a waiver request if there is a reasonable basis on which to conclude that any of the grounds for a waiver have been met. If a full or partial waiver is granted because there is evidence that the product would be ineffective or unsafe in pediatric populations, this information must be included in the product's labeling (21 CFR 314.55(c); 601.27(c)).

For waivers agreed to at the end-of-phase 2 or pre-NDA/pre-BLA meetings, the meeting minutes will document the waiver of pediatric studies. Full or partial waiver documentation should be submitted in an NDA or BLA in the Pediatric Use part of item 8, the Clinical Data Section of the application (Form FDA-356h), and also under item 20, Other. In the latter item, the sponsor should identify the location (volume and page number) of the waiver in the NDA or BLA submission. Decisions to waive the requirement for pediatric studies that are made early in the pre-approval development period (e.g., end-of-phase 1 or end-of-phase 2 meetings) reflect the Agency's best judgment at that time. If, prior to approval, the Agency becomes aware of new or additional scientific information that affects the criteria on which the waiver decision was based, the Agency may reconsider its earlier decision. A

waiver decision becomes final once issued in the NDA or supplemental NDA approval letter.

Ordinarily, a discussion on waiving pediatric studies should take place at the end-of-phase 2 or pre-NDA/pre-BLA meeting, and this discussion should be reflected in the minutes of the meeting. If this did not occur, and a sponsor wishes to obtain a waiver, the waiver request should be submitted to the Agency at least 60 days prior to the application submission.

C. What is a Deferral?

A deferral permits the sponsor to submit the pediatric assessment after the submission of an NDA, BLA, or supplemental NDA or BLA. FDA has the authority, on its own initiative or at the request of the applicant, to defer the submission of some or all of the required pediatric data until after approval of the product for adult use (21 CFR 314.55(b); 601.27(b)).

D. How Do I Get a Deferral?

1. Information in a Deferral Request

FDA has developed a sample deferral request and included it in this guidance as Attachment B. To request a deferral, a sponsor should provide:

- Product name and indication
- Age groups included in deferral request
- Reason for not including entire pediatric population
- Reason for deferring the studies
- Description of planned or ongoing studies
- Evidence that planned or ongoing studies are proceeding
- Projected date until which submission of studies would be deferred (deferral date)

2. Deferral Decision

The decision to defer and the date when pediatric data are to be submitted will be determined on a case-by-case basis. FDA can grant a deferral if, among other reasons, the drug is ready for approval in adults before studies in pediatric patients are complete (21 CFR 314.55(b)(1); 601.27(b)(1)). Additional factors that will be considered are the need for the drug or biologic in pediatric patients, the availability of sufficient safety data to initiate pediatric trials, the nature and extent of pediatric data needed to support pediatric labeling, the existence of substantiated difficulties in enrolling patients, and evidence of technical problems in developing pediatric formulations.

If the FDA agrees to defer the submission of pediatric studies and the application is otherwise approvable, the Agency would approve the product if the applicant agrees to submit the pediatric studies within a specific time period (i.e., deferral date) after approval. The deferral date should specify the date on which pediatric data should be submitted in an application, not the date when the studies are to be initiated. For a deferral granted during the pre-approval development period, the Agency can reevaluate the length of the deferral, taking into account any new information on other drugs in the class approved for use in the pediatric population during the time the product was in development and information reviewed in the NDA or BLA. FDA will review the development of pediatric studies and information as required in the annual reports to determine whether pediatric assessments are being conducted with due diligence.

Ordinarily, a discussion of deferral of pediatric studies should take place at the end-of-phase 2 or pre-NDA/pre-BLA meetings, and this discussion should be reflected in the minutes of the meeting. If this did not occur, and a sponsor wishes to obtain a deferral, the deferral request should be submitted to the Agency at least 60 days prior to the application submission.

VI. COMPLIANCE WITH THE PEDIATRIC RULE — WHAT HAPPENS IF I DON'T DO A PEDIATRIC ASSESSMENT?

If pediatric studies to evaluate safety and effectiveness are not submitted by a manufacturer in the time allowed, the drug product may be considered misbranded or an unapproved new drug or unlicensed biologic (21 CFR 201.23(d)). When a product is misbranded or an unapproved new drug, sections 302, 303, and 304 of the Act (21 U.S.C. 332, 333, 334) authorize injunction, prosecution, or seizure. The Agency can also seek an injunction or bring prosecution under the Public Health Service Act. FDA can bring an enforcement action for injunctive relief for failure to submit a required assessment of pediatric safety or effectiveness. Violation of the injunction could result in a contempt proceeding or such other penalties as a court orders (e.g., fines). However, FDA does not intend to deny or withdraw approval of a product for failure to conduct pediatric studies except in rare cases, because removal of a product from the marketplace could deprive other patients of the benefits of a useful medical product.

To determine whether pediatric assessments are needed or are being carried out with due diligence, FDA amended 21 CFR 314.81(b)(2) for NDAs and 601.27 for BLAs (annual postmarketing reports) to require that the annual reports filed by the manufacturer contain information on labeling changes that have been initiated in response to new pediatric data, analysis of clinical data that have been gathered on pediatric use, assessment of data needed to ensure appropriate labeling for the pediatric population, and information on the status of ongoing pediatric studies. The annual report also must contain an estimate of patient exposure to the drug product, with special reference to the pediatric population if possible (21 CFR 314.81(b)(2)(i); 601.27(a)). If a manufacturer fails to conduct required

pediatric studies, FDA can bring issues related to progress of the pediatric studies before a panel of experts, and can use other forms of publicity to provide the public with information about the status of required pediatric studies, in addition to the enforcement actions discussed above.

VII. EXCLUSIVITY AND THE PEDIATRIC RULE

A. How Will the Rule and Exclusivity Interact?

Under the Pediatric Rule, and as described in section III of this guidance, FDA has the authority to require a pediatric assessment of safety and effectiveness of certain drugs or biological products. In contrast, the pediatric exclusivity provisions of the Modernization Act provide incentives to conduct studies, but do not require them (see the guidance for industry on *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act*).

1. Already Marketed Drugs

FDA believes that with respect to already marketed drugs eligible for exclusivity under the Modernization Act, the availability of pediatric exclusivity may decrease the Agency's need to exercise its authority to require studies. The Agency will allow manufacturers of marketed products ample opportunity to voluntarily obtain a Written Request and submit studies identified in the Written Request for already marketed drugs and biologics. If the Agency finds that after such an opportunity there still remains a need for studies on certain drugs or biologics, the Agency can exercise its authority under the rule to require studies. In addition, FDA can exercise its authority to require studies on marketed drugs and biologics that are not eligible for exclusivity under the Modernization Act. The Agency will restrict its authority to require studies of marketed drugs and biologics to the compelling circumstances described in 21 CFR 201.23.

2. New Drugs

New drugs for which the sponsor is required to conduct a pediatric assessment of safety and effectiveness under the rule may also qualify for exclusivity. To qualify for pediatric exclusivity, the sponsor must obtain a Written Request from the FDA and satisfy the other requirements of section 111 of the Modernization Act (see the guidance for industry on *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act*).

B. If I Satisfy the Requirements of the Rule, Will I Qualify for Exclusivity?

To qualify for pediatric exclusivity, studies conducted to satisfy the requirements of the Pediatric Rule must also satisfy the requirements for pediatric exclusivity

(see section 505A(i) of the Act). For pediatric exclusivity, FDA issues a Written Request for studies on the use of an active moiety for all indications that occur in pediatric populations. Under the Pediatric Rule, FDA requires studies only on those indications included in the application subject to the Rule. To ensure eligibility for pediatric exclusivity, sponsors should follow the procedures outlined in the guidance for industry on *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act*.

VIII. THE PEDIATRIC ADVISORY SUBCOMMITTEE OF THE ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE — WHAT IS ITS ROLE?

The Pediatric Advisory Subcommittee was formed as part of the Anti-Infective Advisory Committee to provide advice and expertise on the implementation of the Pediatric Rule for all drugs and indications. Specifically, the subcommittee may:

- Provide annual assessment of the implementation of the rule
- Review the Agency's record of granting waivers and deferrals
- Discuss ethical issues raised by clinical trials in pediatric patients
- Review the need for additional therapeutic options
- Recommend specific marketed drugs and biological products that should be studied in pediatric patients
- Monitor the timeliness or progress of studies
- Review trials design and data analysis (often in conjunction with other advisory committees or with specific disease experts from those committees as part of the pediatric subcommittee)

IX. ADDITIONAL INFORMATION

A. Where Can I Get More Information About Complying With the Pediatric Rule?

You can get general information about complying with the pediatric rule from the Pediatric Implementation Team (PdIT), 301-594-7337, e-mail pdit@cder.fda.gov. Additional pediatric information is available at http://www.fda.gov/cder/pediatrics.

You can get specific information about the types of pediatric studies that should be conducted for your drug product from the appropriate review division. You can also refer to the pediatric rule (21 CFR 314.55) and the preamble to the pediatric rule (63 FR 66632; December 2, 1998).

B. Where Can I Get More Information on Pediatric Exclusivity?

You can get general information and the latest statistical information regarding pediatric exclusivity at http://www.fda.gov/cder/pediatrics. You can also refer to the guidance for industry on *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act*.

ATTACHMENT A — REQUEST FOR WAIVER OF PEDIATRIC STUDIES

IND/NDA/BLA number (as applicable)
Sponsor:
Indications(s):

1. What age ranges are included in your waiver request?

2. Reasons for waiving pediatric studies:

   (a) No meaningful therapeutic benefit over existing treatments **and** is unlikely to be used in a substantial number of pediatric patients
   (b) Studies are impossible or highly impractical because the number of patients is so small or geographically dispersed
   (c) The product would be ineffective or unsafe in all pediatric age groups
   (d) Attempts to develop a pediatric formulation for a specific age group have failed
   (e) Disease-specific waiver indicated for the treatment of the condition in adults (please check)

_____ Alzheimer's disease
_____ Prostate Cancer
_____ Renal cell cancer
_____ Hairy cell cancer
_____ Osteoarthritis
_____ Uterine cancer
_____ Endometrial cancer
_____ Parkinson's disease
_____ Arteriosclerosis
_____ Infertility
_____ Age-related macular degeneration
_____ Breast cancer
_____ Non-germ cell ovarian cancer
_____ Pancreatic cancer, colorectal cancer
_____ Squamous cell cancers of the oropharynx
_____ Basal cell and squamous cell cancer
_____ Small cell and non-small cell lung cancer
_____ Amyotrophic lateral sclerosis
_____ Symptoms of menopause
_____ Other (please state and justify)

3. Justification for waiver (not necessary if category 2(e) is checked):

ATTACHMENT B — REQUEST FOR DEFERRAL OF PEDIATRIC STUDIES

IND/NDA/BLA number (as applicable)
Sponsor:
Indications(s):

(NOTE: If more than one indication, address the following for each indication.)

(a) Is the indication for a life-threatening condition that occurs in the pediatric population? Yes _____ No

(b) If yes, are there approved therapies labeled for use in the pediatric population? Yes _____ No

(c) If yes, list the approved therapies and labeled pediatric age groups(s) of approval.

1. What ages are included in your deferral request?

   Reason for not including the entire pediatric population in the studies or in the deferral request:

   (a) Adequate pediatric labeling _____
   (b) Studies Completed in Ages _____
   (c) Requesting a waiver
   (d) Other
   (e) Currently conducting pediatric studies that will be submitted with application

2. Reason(s) for deferring pediatric studies:

   (a) Adult studies completed and ready for approval
   (b) Additional postmarketing safety data needed
   (c) Technological problems with development of a pediatric formulation (provide documentation)
   (d) Difficulty in enrolling pediatric patients (provide documentation)
   (e) Other (specify)

3. Have pediatric drug development plans been submitted to the Agency?
   Yes _____ No

   If yes, date submitted

   If no, projected date pediatric plan is to be submitted

4. Suggested deferred date for submission of studies