

Pediatric Points to Consider

Over the past decade there has been a considerable effort to carefully study products in children, as appropriate. Two legislative initiatives in particular address pediatric product development. [The Best Pharmaceuticals for Children Act](#) (BPCA) is applicable to drugs and [The Pediatric Research Equity Act](#) (PREA) is applicable to both drugs and biologics. This document has been created as a helpful and optional adjunct (tool) for medical officer to use as they review pediatric protocols.

(This is not mandatory; therefore, this form does not require completion or entering into DFS.)

UNIQUE REVIEW CONCERNS FOR PEDIATRICS	NOTES
PRECLINICAL STUDIES	
Sufficient Chemistry, Manufacturing, and Controls (CMC) for human adult and comparative pediatric use	
CMC support for proposed pediatric formulation: e.g, oral suspension, solution, tablets, capsules, sprinkles, etc.	
Sufficient pre-clinical animal data for use in the proposed pediatric target population, as appropriate including juvenile animal models	
JUSTIFICATION FOR PEDIATRIC STUDIES E11 Clinical Investigation of Medicinal Products in the Pediatric Population ;	
— Can the scientific question only be answered by involving children in research	
— Clearly identify the scientific question that requires pediatric study	
— Preference for assenting children, if scientific considerations allow	
SCIENTIFIC/PUBLIC HEALTH/GENERAL	
— Briefly review safety and efficacy in Adult Population: Note any unusual features or pertinent safety concerns. Also note any pertinent clinical pharmacology (i.e. metabolism, drug-drug interactions, route of elimination)	
Evaluate need for product in children:	
— Information on children with condition of interest: e.g., epidemiology, incidence, prevalence, sex ratio, typical outcome, age at onset, geographic and racial distribution as applicable.	
— Available treatments; approved and or off-label use medication/s	
Number of children with condition proposed to be studied:	
— Consider number of patients with subtypes of the broad condition, if applicable.	
— Adequate representation of different age groups (i.e. substratification across age groups, as appropriate)	
Planned dose and dosage form:	
— Proposed study dose: dosing is typically by weight (mg/kg or body surface area) rather than by age alone, check the minimum and maximum dose at the extremes of any weight ranges used for dosing	
— Palatability and PK may differ by formulation	
o Administration: e.g., oral, nasal spray, topical patch, etc. and ease of use in pediatric patients across age groups	
STUDY DESIGN: Relevance to Pediatric Population E11 Clinical Investigation of Medicinal Products in the Pediatric Population ;	
— Review Proposed Pediatric Study Request Protocol, any Amendments, (if appropriate)	
— Review Written Request and any other WR amendments (For products that have WR's) (if appropriate)	
Broad Description of Protocol	
— Choice of controls	

UNIQUE REVIEW CONCERNS FOR PEDIATRICS	NOTES
– Inclusion criteria	
– Exclusion criteria	
– Concomitant medication	
– Duration of study	
– Endpoint Assessment	
– Length of post study evaluation	
– Total Blood Draw (see hyperlinks for limitations)	
<ul style="list-style-type: none"> ○ Volume: consider potential need to request proposed blood volume by weight (approx. 2.5 ml/kg) taking into consideration concurrent clinical testing. For examples see: Dr. Greene: How Much Blood is Too Much Guideline; Principles of Drawing from Newborns for Research; Maximum Blood Draw Amounts (PDF); 	
<ul style="list-style-type: none"> • Base schedule of PK blood draws on adult data to optimize use of pediatric blood draws. • Consider need for PK in different age groups 	
Safety	
– Proper Supervision of Trial (e.g. Pediatric Expertise)	
– Describe planned safety monitoring	
<ul style="list-style-type: none"> ○ Consider the need to Data Monitoring Committee (DMC) 	
– Are there potential effects that might be unique to pediatrics such as effects on growth or on puberty	
– Use of an appropriate toxicity grading scale for pediatric patients	
<ul style="list-style-type: none"> ○ Potential future safety risks; consider issues to be further evaluated in Phase 4 post-marketing investigations) 	
ETHICAL ISSUES: If scientific considerations permit then select children capable of assenting	
Specific Issues and References:	
– Procedures for obtaining informed consent/assent	
– Assent Process	
– Informed Parental Permission	
<ul style="list-style-type: none"> ○ One or both parent 	
– Compensation for Participation	
– Is payment only to cover expenses	
<ul style="list-style-type: none"> ○ If not, what amount is he/she compensated? Is the parent more than expenses (missed work, daycare for other children, travel costs, etc), what amount is she/he paid? 	
<ul style="list-style-type: none"> ○ Will child be compensated by money or gift? 	
– Institutional Review Board Composition (e.g. Pediatric Expertise)	
– Data Monitoring Committee Composition (e.g., Pediatric Expertise)	
General References:	
– Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations (AAP)	
– E11 Clinical Investigation of Medicinal Products in the Pediatric Population ;	
– FDA Ethics Consensus Statements – April 24, 2001 , September 11, 2000 , November 15, 1999	
– Subpart D regulations: Reviewers may want to keep these criteria in mind. Subpart D--Additional Protections for Children Involved in Clinical Trials	