

Pediatric Exclusivity Provisions of the
Food and Drug Administration Modernization Act

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FDA/Generic Trades Discussion
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GPIA Comments

Section 111(b) – “may produce health benefits”

“May” makes this a very broad statement and it is unlikely that this was the intent. The list should be developed on a much firmer basis, e.g., nature of the indications for the drug, prevalence of these indications in pediatrics, available alternatives for pediatrics, off-label experience with the drug or recognized therapeutic alternatives (both with respect to safety and efficacy), specific safety/efficacy concerns with use of the drug or therapeutic class in pediatrics, feasibility of pediatric administration, etc.

Section 111(d) – “submitting studies”/“filing of an application or supplement”

From past experience, it is understood (rightly or wrongly) that, in general, the submission of studies forms the basis for a change (addition, deletion) in labeling language whereas the filing of an application or supplement is the basis for a change in indication. The latter has a much more significant impact on the sponsor in terms of effort, but also in terms of the ability to actively promote the product for the indication and the resultant financial rewards. Whether or not “studies” would suffice depends on previous experience with the drug in the pediatric population.

Section 111(g) – “pharmacokinetic studies”

If pharmacokinetic studies are to be seen as an adequate substitute for clinical studies, it would seem that a full cadre of such studies should be done. Given differences in liver and kidney function between adults and children, at the least an oral vs i.v. study would be needed to fully characterize relevant parameters. If, then, there is a difference between adults and the pediatric population with respect to fraction excreted unchanged and fraction metabolized, additional studies in liver or renal impairment may be needed. Pro-drugs or drugs with active metabolites would especially have to undergo such scrutiny. It may be important to look at the possibility of dose-dependent kinetics depending on relative first-pass metabolism between adults and pediatrics and the relative expected doses. A pharmacodynamic/pharmacokinetic study may also be indicated unless one can unequivocally state that the correlation between plasma levels and pharmacodynamic effect is the same in adults and pediatrics. Depending on the age group, it would seem that a meaningful set of pharmacokinetic studies would be less feasible than one or two well-designed clinical studies.

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Section 111(h) – “drug”

Confused as to what this section is saying. It appears to allow a 6-month exclusivity for pediatric studies plus a 3-year plus another 6-month exclusivity if later a supplement is filed. Correct? Can't quite see what the relevance of the definition of “drug” is here. What is of more concern is what additional data does the supplement contain? Is it based on any data already submitted for the first period of exclusivity?

Section 111(a) and (c) – “written request”

Written request should include a timeframe as noted in the Act. It should also outline the nature of the studies felt to be necessary, the size of the studies, the exact pediatric population in which the data are needed. There should be background and rationale for the request, including epidemiological data documenting the need.

Section 111(d)(1) – “written agreement”

The written agreement should be detailed and in line with the written request. Timeframe, study design, final report requirements, etc. should be included.

Section 111(d)(3) – “commonly accepted scientific principles and protocols”

Commonly accepted scientific principles and protocols should be those accepted for studies which would meet the requirements for submissions such as NDAs and support of new drug labeling language. Statistical design, sample size, endpoint measurement, etc. must meet the same standards as required for any regulatory submission.

Section 111(i) – “other requirements”

It would seem that “other requirements” encompasses all requirements of the section, including written request, written agreement, limitations, etc.

Section 111(g) – “anticipation of use”

For already marketed drugs, pediatric and family physicians should be the source of off-label use information which would then give some scope of anticipated use. For all drug, new and marketed, the nature of the disease, its prevalence in a particular age group, the availability of alternative therapies, its inherent safety/efficacy profile, ease of administration, etc. etc. must all be pooled to determine some probability of use.