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Extrapolating data can accelerate drug development for children

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The Food and Drug Administration (FDA) has issued draft guidance (https://bit.ly/3LUnh2P) to aid drug companies and regulators in using pediatric extrapolation during drug development. When applied appropriately, pediatric extrapolation can accelerate the approval and availability of safe and effective medicines for use in children.

"Finding ways to make new treatment options available for children sooner is a high priority for the FDA," said Dionna Green, M.D., director of the FDA's Office of Pediatric Therapeutics. "This draft guidance will help drug companies improve the efficiency of developing certain medicines for children. It also will help to ensure children only participate in clinical trials when necessary to further the scientific understanding of a medical product's use in children."

The FDA generally requires adequate and well-controlled clinical studies to establish a drug's safety and effectiveness before granting approval. In some cases, drug developers can use pediatric extrapolation to limit the need for conducting large, randomized, controlled clinical trials in the pediatric population, Dr. Green said.

Pediatric extrapolation can be used when it can be assumed that the disease course and expected response to the drug would be sufficiently similar in the target pediatric population and a reference (adult or other pediatric) population.

"We've been using pediatric extrapolation for many years and have gained valuable experience that has been included in this draft guidance," said Lynne Yao, M.D., director of the FDA's Division of Pediatrics and Maternal Health. "The use of pediatric extrapolation has evolved from a 'yes or no' approach to an iterative process that requires review of existing data to support the degree to which extrapolation is acceptable and to identify gaps in knowledge that must be filled in order to support the efficacy and safety of a drug when used in a pediatric population."

One recent example of the use of pediatric extrapolation is in the development of antipsychotic drugs for adolescents with schizophrenia. The 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 (Kalaria S, et al. *J Clin Pharmacol*. 2020;60:848-859).

The FDA concluded that pediatric extrapolation from adults to adolescents could be considered for antipsychotic drugs with similar mechanisms of action to treat schizophrenia. This means that 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 large randomized, controlled trials. Hopefully, this will lead to earlier approvals of newer antipsychotic drugs for adolescents with schizophrenia.

Drs. Yao and Green participated in the expert working group that developed the draft guidance, working under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (https://www.ich.org/). The council works to ensure medicines are developed efficiently worldwide by preventing unnecessary, duplicative clinical trials.