Pediatric Drug Development: Regulatory Updates to Know

All applications for marketing authorization for new medicines must include the results of studies in children as described in the pediatric plan, unless the medicine is exempt because of a deferral or waiver. Pediatric legislation internationally has led to better medicines for children, but gaps still exist that regulatory agencies want to close.

How will pediatric drug development requirements impact sponsors?

In August 2017, the United States passed the FDA Reauthorization Act and with it the Research to Accelerate Cures and Equity for Children Act (RACE). RACE will eliminate exemptions and improve opportunities for cancer drugs development for children by:

- Requiring companies to do PREA studies in children when the molecular target of their drug is relevant to children's cancer
- Ending exemption of PREA obligations for cancer drugs with orphan designations if the molecular target of the drug is relevant to children's cancer

In August 2018, the FDA will publish a list of molecular targets substantially relevant to growth and progression of pediatric cancer. It will also publish a list of molecular targets for which pediatric study requirements will be automatically waived.

Other recent actions include:

- Congress reauthorized through 2020 the Rare Pediatric Disease Priority Review Voucher program in the 21st Century Cures legislation.
- In the EU, the Commission report on 10 years EU Pediatric Regulation (October 26, 2017) showed encouraging impact of the Pediatric Regulation overall, though the regulation appears most effective when adult and pediatric needs overlap.

Global Progress Continues

Fewer advances have been made in diseases that are unique to children. While some instances of over- or under-compensating drug developers with financial rewards exist, overall benefits seem to outweigh costs.

Therefore, the European Commission does not currently recommend re-opening the legislation. It will evaluate pediatric and orphan regulations to better understand why rewards do not seem to be driving development for rare diseases. Findings are expected to be delivered in 2019, enabling the next Commission to make informed decisions about policy options.

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Meanwhile, the European Commission and EMA have started to streamline application and implementation of the regulation, including making changes to deferrals and revisiting PIP processes and other aspects.

A revised and revoked class waivers list will be effective in July 2018. Applications for new medicines or variations of marketing authorizations will be validated against it. Waivers, specifically in oncology, will no longer be automatic. Regulators will expect companies to have considered product mechanism of action and pediatric needs prior to decision.

Regarding multi-stakeholder discussion of pediatric needs, the EU Commission and EMA held a workshop with patients, academia, healthcare professionals, and industry on March 20, 2018. Potential improvements to implementing the regulation were discussed. An action plan addressing challenges will be published mid-2018. The EMA, EU Commission, and stakeholders will need to commit to implementation within two years.

ICH E11 (R1) "Clinical Investigation of Medicinal Products in the Pediatric Population," enforced in February 2018, aims to advance pediatric research globally. Addendum R1 reflects latest technical, scientific, and regulatory approaches and recognizes topics where consensus had not been achieved, including:

- Ethical considerations
- Age classification and pediatric subgroups
- Pediatric formulations
- Common scientific approaches to aid discussions in different regions
- Pediatric extrapolation and introduction of modeling and simulation
- Practicalities in design and execution of trials, including feasibility, outcome assessments, and long-term clinical aspects.

We expect global progress to continue. ICH E11 A "Pediatric Extrapolation Guideline," discussed at the ICH meeting in Geneva (November 2017), is expected to reach Step 2a by November 2020. ICH S11 "Safety Testing in Support of Development of Pediatric Medicines" is expected to reach final stage, Step 4, in June 2019.

These are important updates to know and promising steps toward making better medicines available to treat children. PV

Editor's Note: Dr. Martine Dehlinger-Kremer is an observing member of the Coordinating Group of Enpr-EMA, the European Network of Pediatric Research at the European Medicines Agency, and is a member of Working Parties of Enpr-EMA. She is also President of EUCROF, the European CRO Federation, and a Board Member of EFGCP. Contact Synteract at +1 760-268-8200 to leverage its three decades of pediatric experience to advance your clinical trial.

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Three of our experts will be attending upcoming industry events and we'd like you to meet them.

DIA

Dr. Martine Dehlinger-Kremer, Vice President, Pediatric Development

With 30 years of experience in the CRO and pharma industries. Martine shares insights she knows from 100+ NDAs/MAAs and numerous clinical studies. She is Chair of both EUCROF's Pediatric Working Group and the European Forum for GCP Children's Medicines Working Party as well as a member of the European Network of Pediatric Research at EMA. She is a PharmaVoice 100 recipient for her dedication to the littlest patients.

ASCO

Etienne Drouet, Vice President, Oncology Development

Etienne has spent 25 years focused on curing cancer, working on the forefront of innovation using data-based evidence, genomic information and personalized and precision therapies. He is a PharmaVoice 100 recipient for the way he educates and inspires his teams, and helps our clients with trial strategies and planning.

DIA

Linda Rawlings, Vice President, Neuro Degenerative Development

Linda has deep knowledge and an ability to see the big picture while also paying attention to details, having spent 27 years coming up through the ranks in the CRO, pharma and medical device sectors after earning her MS degree in Chemical Analysis. Her keen focus on implementing strategies delivers excellence at the local, international and global levels through her thorough understanding of challenges facing clients.

Improving the quality of human lives – it's why we are all in this industry

Synteract recently announced formal establishment of our new Centers of Therapeutic Development in four key and complex areas in the biopharma industry:

- Oncology, including leading-edge immunotherapy studies
- Neuro degenerative disorders
- Pediatrics
- Rare and orphan disease

By aligning our operational excellence, deep therapeutic expertise, and supportive technology in these focused centers of development, Synteract is perfectly positioned to help clients advance innovative therapies in these and other complex areas. Our enhanced focus reinforces our core capabilities, and displays our passion around the work we do for our clients each day, because patients are waiting.

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