U.S. FOOD & DRUG ADMINISTRATION

General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products

Final Guidance for Industry

What Is Covered in This Guidance?

This final guidance addresses the clinical pharmacology considerations for any planned studies in neonates submitted in new drug applications (NDAs), biologics license applications (BLAs), and supplements.

Why Is This Guidance Important?

- Neonates present unique absorption, distribution, metabolism, and excretion (ADME) characteristics.
- Many drugs administered in neonatal intensive care units (NICUs) are used in an off-label capacity.
- Pharmacokinetics (PK) and pharmacodynamics (PD) are affected by multiple factors in the neonatal population (e.g., size, growth and physiologic maturation, underlying illnesses, and concomitant medications) and may differ between neonates and older children and adults.
- Pharmacogenomics has not been extensively studied in the neonatal population.

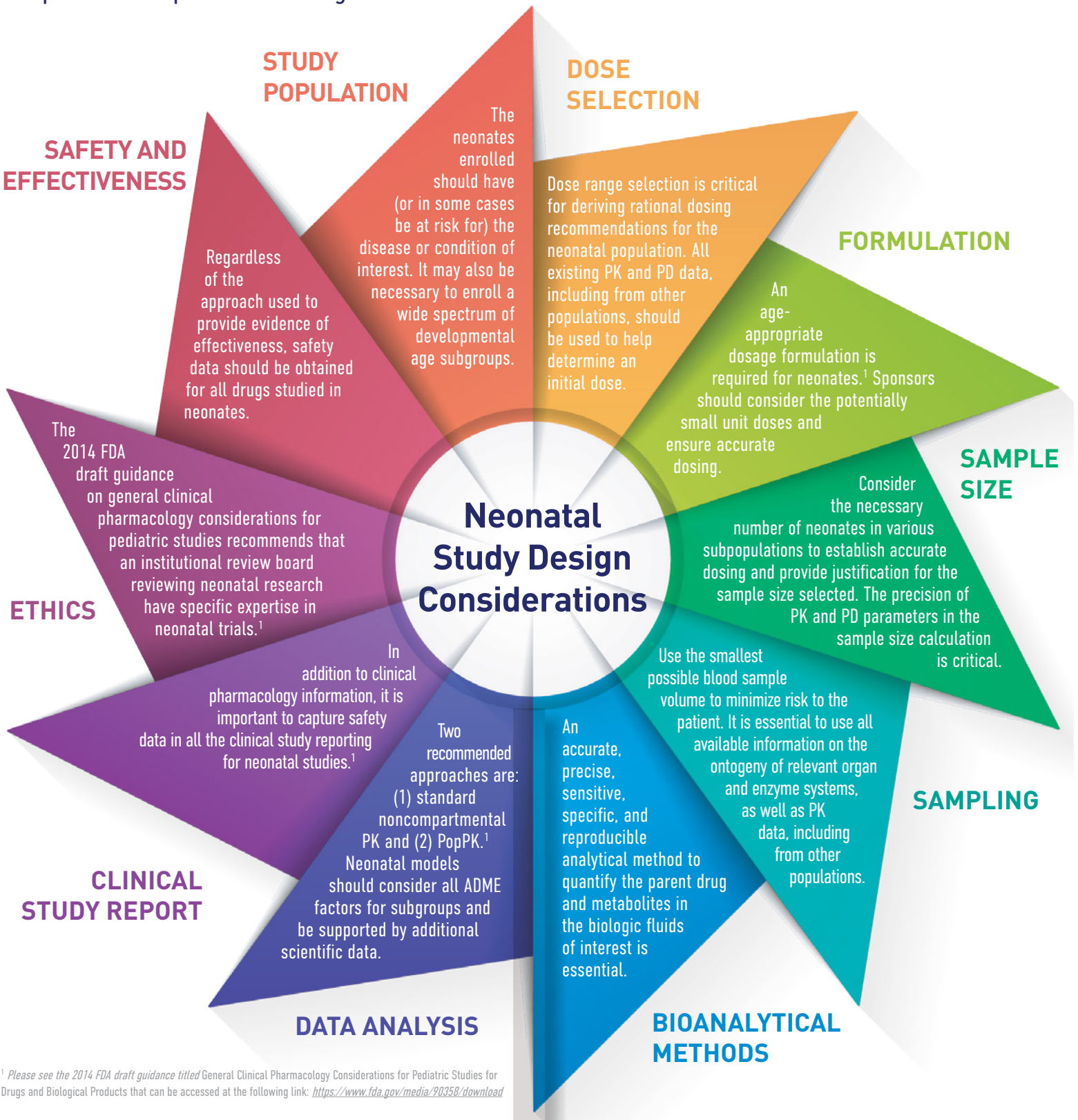
What Is the Age Range for Neonates?

This guidance defines the neonatal period for the term and post-term newborn as the day of birth plus 27 days, and for the preterm newborn as the day of birth through the expected date of delivery plus 27 days. When designing studies, it is important to consider stratifying the neonatal population to decrease variability. While neonates can be grouped by gestational age and/or weight at birth, postnatal age is another important variable to consider for stratification, as it can significantly affect ADME.

Guidance Snapshots are a communication tool and are not a substitute for the guidance document.
To learn more about general clinical pharmacology considerations for neonatal studies, read the guidance:
https://www.fda.gov/media/129532/download

Prior to Neonatal Study Initiation:

Sponsors should assess the available scientific information regarding the neonatal condition, mechanism of action, PK, PD, and the ontogeny of any organs and tissues that are involved in the predicted response to the drug and or its metabolites.



[1] *Please see the 2014 FDA draft guidance titled* General Clinical Pharmacology Considerations for Pediatric Studies for Drugs and Biological Products that can be accessed at the following link: *https://www.fda.gov/media/90358/download*

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Background About the Guidance

This guidance supplements the FDA draft guidance titled General Clinical Pharmacology Considerations for Pediatric Studies for Drugs and Biological Products (December 2014). The agency issued this guidance as part of an ongoing effort to support sponsors and investigators who are planning neonatal trials. Currently, many drugs are used off-label in NICUs, and there have been cases where adult drugs have been ineffective or even harmful to neonates. The FDA would like to spread the message that therapies designed specifically for neonates need to be developed, and neonates can be protected through clinical research.

Guidance Recommendations Apply Throughout the Drug Development Timeline

This guidance provides recommendations for neonatal clinical pharmacology studies. Before initiating neonatal clinical pharmacology studies, the sponsor should assess the available scientific information regarding the mechanism of action and PK of the drug, as well as the ontogeny of any organs and tissues that are involved in the predicted response to the drug or its metabolites. This scientific information can be derived from several sources, including applicable animal models, in vitro studies, and other potentially relevant clinical studies. This guidance does not discuss the timing to initiate neonatal studies. Sponsors should direct questions on the initiation of neonatal studies with the relevant FDA review division.

Guidance Recap Podcast – Hear Highlights Straight From FDA Staff

Speakers: Elimika Pfuma Fletcher, PhD, policy lead for the Office of Clinical Pharmacology, Gerri Baer, MD, team lead for pharmacovigilance and neonatology in the FDA's Office of Pediatric Therapeutics (OPT)

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To learn more about the general clinical pharmacology considerations for neonatal studies for drugs and biological products, read the guidance: https://www.fda.gov/media/129532/download

To see additional Guidance Snapshots, check out the pilot program: https://www.fda.gov/drugs/guidances-drugs/guidance-snapshot-pilot