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FDA provides guidance on assessing growth, pubertal development in pediatric clinical trials

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The Food and Drug Administration (FDA) has issued draft guidance (https://bit.ly/3iKaMfN) describing methods for measuring and recording growth and evaluating pubertal development to assess safety for pediatric participants in clinical trials.

If an investigational drug has the potential to affect growth or pubertal development, clinical trials generally should include accurate, serial measurements and recordings of weight, linear growth and, when appropriate, head circumference and sexual maturity rating for pediatric participants.

The guidance provides general considerations for growth measurements. It highlights the importance of collecting and recording measurements for a minimum of 12 months, ensuring measurements are collected by trained personnel using properly calibrated instruments and performing measurements at the same time of day to address diurnal variations in height and weight.

Determining age

The FDA provides specific parameters to consider when making age determinations to ensure growth is

documented accurately. The guidance specifies when to record age based on weeks, months, years or a combination depending on the participant's age. For example, age should be calculated based on completed weeks for participants younger than 3 months born at term. The guidance also provides direction for determining gestational age at birth and establishing both chronologic and corrected age for participants born preterm.

Using standardized growth charts

The guidance calls for use of appropriate standardized growth charts for the trial population. For U.S. trials involving participants born at term, Centers for Disease Control and Prevention growth charts are recommended for participants 2 years and older and World Health Organization growth charts for participants younger than 2 years.

The guidance references specific preterm infant growth charts for participants born prematurely and encourages use of disease-specific growth charts, when available.

Assessing weight, linear growth, head circumference

The guidance describes important factors to consider when obtaining and recording weight, linear growth and head circumference, including the type of measurement tools to use for various age groups and situations, how to address factors that may influence accurate measurements (e.g., devices and assistive technologies, edema, diapers and clothing) and which decimal to record. Following are examples of recommendations provided in the guidance.

When measuring weight:

- Record to the nearest 0.1 kilograms (kg) for participants weighing 5 kg or more.
- Record to the nearest 10 grams for neonates weighing less than 5 kg.
- Use a standing scale for participants who can stand still independently. The guidance also offers
- techniques to measure weight of participants who cannot stand independently.

When assessing linear growth:

- Measure recumbent length in participants younger than 2 years using a length board.
- Measure standing height in participants 2 years and older using a stadiometer.
- Measure recumbent length and standing height during the transition from 2 to 3 years.
- Measure to the nearest 0.1 centimeter (cm).
- Record three measurements per visit and use the mean for analyses.

When measuring head circumference in participants younger than 2 years (and when clinically appropriate),

use a nonelastic tape measure at the maximum diameter of the head to the nearest 0.1 cm. Record three measurements per visit and use the mean for analyses.

Evaluating pubertal development

The guidance recommends using a sexual maturity rating (e.g., Tanner staging) at trial entry and at regular intervals based on the potential safety concerns associated with the drug and the participant's pubertal development stage. The guidance emphasizes that trained personnel should complete ratings based on both breast and pubic hair changes in females and on both genital and pubic hair changes in males, including assessment of testicular volume using an orchidometer.

Finally, the guidance provides considerations and tools for other measurements, such as assessing skeletal age and evaluating bone mineral density.

The FDA's Office of Pediatric Therapeutics and Office of New Drug's Division of Pediatrics and Maternal Health contributed to this article.

Resources

"Measuring Growth and Evaluating Pubertal Development in Pediatric Clinical Trials Draft Guidance for Industry," https://bit.ly/3iKaMfN