CenterWatch Weekly

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FDA Proposes Three New Guidelines for Gene Therapy Trials

The FDA last week released its first disease-specific guidances for gene therapy products, focusing on clinical trials for the treatment of rare diseases, hemophilia and retinal disorders.

Because most rare diseases manifest early in life, the FDA urges sponsors to be extra cautious about ethical issues when designing pediatric trials. It also says that if the disease is caused by a genetic defect, sponsors "should perform genetic tests" on all clinical trial participants.

The rare disease guidance also makes detailed recommendations on study design, including alternatives to a randomized control trial to help sponsors deal with the scarcity of patients and the diversity of disease presentation. If a disease is caused by a genetic defect, for instance, sponsors are urged to perform genetic tests on subjects. Regulators also urge sponsors to be extra cautious about ethical guidelines when designing pediatric trials.

The three disease-specific guidances were issued on July 12 and comments are due October 10. The FDA at the same time issued three guidances on CMCs for gene therapy products.

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—Daniel Kavanagh, senior scientific advisor for gene therapy, WCG

The FDA's guidance on hemophilia trials focuses on efficacy endpoints. Daniel Kavanagh, senior scientific advisor for gene therapy at WCG, says he can see the question of surrogate endpoints becoming controversial.

Kavanagh also says there are likely to be questions about the hemophilia draft guidance's impact on efficacy—how long after a patient uses gene therapy for hemophilia can he or she expect it to work—and also on patient eligibility for future trials.

For retinal disorders, the FDA says that understanding a disease's natural history may well be a key to clinical trial design. It also suggests that sponsors use a randomized, concurrent parallel control group "whenever possible." A patient's other eye can be considered a control, but it's "generally not recommended" because eyes may be at different stages of disease and it can also cloud results when two different drugs are being tested in two different eyes.

WCG's Kavanagh says the retinal diseases draft guidance has a much more intricate conversation on clinical trials. The guidance warns of ethical concerns over injecting placebos into patient's retinas during clinical trials, particularly for pediatric subjects. The guidance points out that carefully designed dose finding studies can serve as an alternative control.

The FDA's guidances are available here. www.fdanews.com/07-11-18-GeneTherapy.pdf.