FDA STATEMENT

FDA Takes Steps to Provide Clarity on Developing New Drug Products in the Age of Individualized Medicine

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Statement From:

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Advances in scientific knowledge and drug development technology have provided an opportunity for new approaches to drug development, including the development of drugs for the treatment of rare diseases. These advances have contributed to an increase in development and approval of drugs for the treatment of rare diseases in recent years. In fact, in the past eight years, the U.S. Food and Drug Administration has approved more than twice as many drugs for rare diseases, often referred to as orphan drugs, as in the previous eight years.

For genetic diseases, recent approaches to testing and molecular diagnosis have allowed us to pinpoint, in some cases, the exact cause of a patient's disease. For a patient with a very rare genetic disease, development of a drug product that is tailored to that patient's specific genetic variant may be possible. This is an important advance in treatment for those with very rare genetic diseases, especially those for which there are no adequate therapies available to treat the disease. Often, these very rare diseases are rapidly progressing, debilitating, and in many cases, can lead to premature death if left untreated.

Developing these products – also referred to as "n of 1" therapies by some because they are designed for a patient population of one person – brings a set of challenges and considerations not seen with the typical drug development process. First, as noted above, the disease is often rapidly progressing, requiring prompt medical intervention. Therefore, development needs to proceed very quickly to have a chance at helping the individual. Second, drug discovery and development for these drug products may be carried out by academic investigators, rather than by biopharmaceutical or pharmaceutical companies. These investigators may be less familiar with FDA's regulations, policies and practices, and less experienced in interacting with the FDA.

At this time, development of individualized genetic drug products is most advanced for antisense oligonucleotide (ASO) products. Therefore, we are taking the first steps in bringing clarity to this emerging area of individualized drug development by releasing a new draft guidance (/regulatory-information/search-fda-guidance-documents/ind-submissions-individualized-antisense-oligonucleotide-drug-products-administrative-and-procedural) on investigational new drug (IND) submissions for individualized ASO drug products.

The guidance was developed to advise those developing ASO products on an approach to interacting with, and making regulatory submissions to, the FDA. The guidance addresses the following points:

- The approach to obtaining feedback from the FDA,
- The expectations and process for making regulatory submissions to the FDA,
- Recommendations about the requirement for Institutional Review Board (IRB) review of the protocols within, and
- How to obtain informed consent.

As also discussed in a *New England Journal of Medicine* (https://www.nejm.org/doi/full/10.1056/NEJMe1911295) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) editorial in October 2019, we are fully aware that this new drug-discovery paradigm raises many ethical and societal issues that will need to be addressed throughout the process. For example, in these situations, the individuals and their families often function more like drug development collaborators than traditional trial participants. Therefore, it is important to discuss with the individual and family members how effectiveness will be measured. It is also important to ensure that the individual and family members understand the parameters for continuing administration of the investigational drug product before emotions influence decisions, and to recognize that some investigational drug products may fail, or worse, lead to unforeseen side effects.

The FDA understands that we'll need to work together with the developers of these drug products to bring them safely to patients, and we are willing to engage as needed to address the challenges. For example, for those developing these drug products, it will be important to further understand the required data and information that must be submitted to the FDA so that clinical testing can begin. The FDA is continuing to consider and further develop policy to address some of these issues.

We also are optimistic that development of these individualized drug products may spur gene sequencing that leads to the development of additional individualized drug products for the same disease (though perhaps caused by a different mutation). For this approach to drug development, we need to determine – collectively – how to effectively bring these drug products to all who need them. If we have the scientific ability to develop drug products for these rare

diseases, we need to find a way to bring them to patients while ensuring there is the right balance of risk to benefit. This guidance, which provides clarity on the early development and IND submission process, is the FDA's first step in working with those who are developing these individualized drug products.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Related Information

- Guidance: IND Submissions for Individualized Antisense Oligonucleotide Drug Products: Administrative and Procedural Recommendations Guidance for Sponsor-Investigators (/regulatory-information/search-fda-guidance-documents/ind-submissions-individualized-antisense-oligonucleotide-drug-products-administrative-and-procedural)

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