

# Artificial Pancreas Regulatory Guidance

## Accelerating Progress of the Artificial Pancreas: Bringing the Research Home

The Juvenile Diabetes Research Foundation (JDRF) is working to advance the development and delivery of an artificial pancreas to help people with type 1 diabetes better manage the disease and prevent its life-threatening complications. To prevent delays in the development of this transformational technology, JDRF has proposed that the Food and Drug Administration (FDA) adopt a “guidance document” so that outpatient artificial pancreas studies can proceed as soon as possible. This guidance will provide researchers, the public, and industry a defined pathway toward the development of these systems.

### How Was the Proposed FDA Guidance Developed?

JDRF has worked closely with FDA since the launch of its Artificial Pancreas Project (APP) in 2005. FDA, recognizing the importance of this initiative, placed it on its list of Critical Path opportunities in 2006, publicly stating it is a priority for the agency, and has since worked with the National Institutes of Health (NIH) as well as JDRF and its funded researchers to advance this critical technology.

By 2010, thanks to significant research advancements, outpatient clinical trials were on the horizon. To facilitate this next stage of artificial pancreas technologies, JDRF convened an expert advisory panel comprised of the leading authorities in the clinical management of type 1 diabetes, referred to as the Clinical Recommendations Panel on Closed

Loop Systems. This panel included world renowned experts in the care of people with type 1 diabetes, clinical trial design, and artificial pancreas systems. The panel came to a consensus on the key elements needed to ensure the safety of outpatient artificial pancreas studies, and presented its findings to FDA and other experts at a November 2010 FDA/NIH Public Workshop on the Clinical Development of the Artificial Pancreas. Because of the consensus achieved by the clinical panel and other experts at the November workshop, this is the optimum time to provide to researchers, the public, and industry a clear and defined regulatory pathway to foster further development.

JDRF has submitted a guidance document entitled “Draft Guidance for Industry and FDA Staff: Artificial Pancreas Systems – Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications,” for FDA’s consideration, to enable the next stage of clinical assessment and development – studies outside of the hospital – for this potentially transformative technology. This guidance document, once adopted by FDA, will serve as a roadmap for researchers and companies to develop safe and effective artificial pancreas devices.

### Summary of Guidance Content

The guidance JDRF has proposed to FDA is meant to cover several types of artificial pancreas systems. A large part of the guidance document addresses

the clinical assessment of such products. Within the clinical section, which is largely based on the recommendations of the panel JDRF convened, research studies and regulatory approval studies are addressed separately. The following provides an overview of the clinical recommendations.

- **Study Progression** – The guidance recommends that, in general, inpatient studies should be performed with an artificial pancreas system before outpatient studies. For research studies, a transition stage may be advisable where the patient operates the system independently with medical personnel in close proximity.
- **Study Design** – Inpatient studies will generally include a small study population, be of short duration, and may not include a control group. Early outpatient studies for research purposes may not be controlled, while pivotal outpatient studies should be randomized controlled trials. A staged approach is recommended, with the frequency of patient monitoring by study personnel decreasing with study progression and patient compliance.
- **Study Population** – Early research studies should include otherwise healthy patients with type 1 diabetes who have experience with components of an artificial pancreas (i.e., insulin pump and glucose sensor). As safety is demonstrated in that population, researchers may expand to other populations such as children and those prone to severe hypoglycemia. Studies for regulatory approval should enroll the intended patient population for the approved system.
- **Study Endpoints** – The guidance recommends a range of endpoints that may be acceptable depending on the design of the system and population under study, as well as the study design.

As an example, a safety endpoint could be no increase in severe hypoglycemia events, and an effectiveness endpoint could be an increase in the time spent in the target glucose range.

- **Safety Elements** – Importantly, several safety elements are recommended in the guidance to avoid complications such as hypoglycemia and hyperglycemia. These range from elements of the protocol, such as frequent contact with the patient early in a study, to elements of the design of the product, such as system alerts for the patient.

The document also covers other topics routinely included in guidance documents, such as: the device description, software information, preclinical testing, human factors testing, and labeling.

### Role of an FDA Guidance Document

A guidance document is a way that FDA can communicate with researchers and industry about their current thinking on a particular topic. They confer FDA's recommendations about how to fulfill regulatory requirements, but are not binding on the agency or the public.

Guidance documents are usually developed internally at FDA, sometimes with outside input from stakeholders. They are released for public comment before they are finalized (unless they address existing policy or minor changes to current regulatory interpretation). Guidance documents are often developed and released after a technology has been available for some time, is well understood, and has generally recognized standards associated with it. In a recent example of a patient group participating in guidance development, the Friends of Cancer Research proposed a guidance document to FDA, which the agency considered as they developed a draft guidance document for public comment.

## Artificial Pancreas Regulatory Guidance

Conversely, for innovative technology, there is often a lag in clear recommendations from FDA that can delay – and even stop – important advancements. Having clear and reasonable recommendations from FDA in a guidance document encourages innovation by providing researchers, innovators, industry, and investors a pathway to the patient.