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**Biosketch**

Dr. Mehta is currently a Medical Officer (clinical reviewer) for CDER-OND-ODE III-DGIEP (Division of Gastroenterology and Inborn errors of Metabolism). She reviews drug development programs for liver products, and inborn errors of metabolism products.

Previously, Dr. Mehta held various positions as follows:

- Locums: Georgia Regents University: Pediatric Gastroenterology
- Assistant Professor in Pediatric Gastroenterology, Nutrition and Hepatology: LeBonheur Children's Hospital and University of Tennessee
- Fellow Physician in Pediatric Transplant Hepatology: Children's health Care of Atlanta and Emory University, Atlanta, GA
- Fellow Physician in Pediatric Gastroenterology, Hepatology and Nutrition; Wayne State University; Detroit, MI

Dr. Mehta received he Bachelors of Medicine and Surgery (MBBS), in Rajasthan, India She completed her residency in pediatrics in 2007.

She speaks three languages - English, Hindi, and Urdu.

**Abstract: Recognizing, Assessing and Managing DILI: Challenges or FDA in NASH Development Programs**

In clinical trials of drugs being developed for treatment of non-alcoholic steatohepatitis (NASH), challenges exist in the ability to promptly identify drug-induced liver injury (DILI) in a study population in whom elevated liver biochemistries, including aminotransferases, total bilirubin, alkaline phosphatase and coagulation tests, are present at baseline. The current DILI guidance does not address how to recognize DILI in patients with pre-existing liver disease. Key knowledge gaps in the recognition of DILI in NASH patients include:

1. Limited available natural history data on the variability in liver biochemistries and the time course of progression of these changes in both pre-cirrhotic and cirrhotic NASH populations.
2. Limited available evidence upon which to establish biochemical criteria that will reliably detect DILI in these populations.

To address the current challenges in identifying DILI in NASH clinical trial participants, we hope to gather additional information on the following:

a. A better understanding of what constitutes normal variability vs. relevant changes in liver biochemistries and how such knowledge can provide guidance in determining the need for further evaluation and/or treatment modification.
b. Identification of the timing and number of values of individual biochemistries necessary to establish the

baseline level for trial inclusion.

c. Characterization of the normal variability to be expected in the baseline values of liver biochemistries in order to inform enrollment criteria for clinical trials in patients with NASH, such that enrollment of patients with deteriorating liver function will be prevented.
d. The usefulness of liver biochemistries as enrollment criteria and for identification of DILI in NASH patients with advanced cirrhosis, given that progressive depletion of hepatocyte mass may limit the applicability of the usual quantitative criteria for biochemical assessment.
e. Determining the frequency and timing of assessment of liver biochemistries to assess for DILI in clinical trials.
f. Defining criteria for establishing the patient's new "baseline" during the trial; if the investigational drug results in improvement of liver biochemistries, a new "baseline" is necessary for accurately evaluating any potential drug-related liver toxicity.