i-p-r-f.org
International Pharmaceutical Regulators Forum

**Gene Therapy Working Group**

## Meeting Summary

**Meeting Date:** 16-17 May 2015

**Meeting Location:** New Orleans, Louisiana, U.S.A.

**Participating Regions:**
Brazil- ANVISA
Canada-Health Canada
Chinese Taipei- Taiwan FDA
European Union- European Medicines Agency
Japan- Ministry of Health, Labour and Welfare, Pharmaceutical and Medical Devices Agency
South Korea- Ministry of Food and Drug Safety
Singapore- Health Sciences Authority
Switzerland- Swissmedic
Thailand- Thai FDA
United States- U.S. FDA

**Meeting Title:** Assessment of Biodistribution Data in the Development of Gene Therapy Products

**Meeting Objectives**: The goal of this meeting was to understand the regulatory requirements and approaches for the use of biodistribution data (BD) and the development of BD studies for gene therapy products in various regions. Assessment of the BD profile for a gene therapy (GT) product is an important consideration for preclinical programs and can inform on the selection clinical dose, dosing schedule, and the clinical monitoring plan. In addition, the BD data can help guide the design of the definitive preclinical safety studies.[1,2] The GTWG selected this topic for discussion because a large amount of BD data currently exists and a harmonized approach among regulatory bodies could help facilitate GT product development.

**Meeting Summary:** This meeting was held at the end of the 18th Annual Meeting of American Society for Gene and Cell Therapies (ASGCT). Members of the IPRF GTWG participated in presentations and served on discussion panels.

[1] Guidance for Industry: Preclinical Assessment of Investigational Cellular and Gene Therapy Products, FDA November 2013.
[2] Draft Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products, EMA March 2015

Participants in the GTWG meeting included 22 representatives of 10 regions. The meeting began with overviews of the regulatory considerations for preclinical BD studies in Canada, the EU, South Korea, Switzerland and the U.S., followed by four group discussion sessions. Topics for these sessions included the following: 1) How does BD data inform the clinical trial design?; 2) BD assay methods, 3) How are BD data used to evaluate product safety in a clinical trial?; 4) Preclinical data sharing.

Key Points from the discussion sessions are as follows.

- The approaches for BD studies are similar between the EU and U.S., but vary in the other regions
- There are regional differences with regards to the timing of BD studies during clinical development.
- Some GT products may be similar enough to each other in a vector class that BD studies may not be required prior to first-in-human (FIH) clinical studies.
- Sponsors might use the same BD data for a virus/vector product that expresses a different transgene for different clinical indications.
- For multicenter clinical studies sponsors might apply with the same BD data package in the various regions.
- With regards to methodology/assays used in BD studies,
    - qPCR is a reliable assay.
    - Imaging technologies may be useful for understanding relative tissue distribution but may lack sensitivity.
- Sharing of BD data would be very useful however; issues with data quality and sharing of confidential data submitted to regulatory authorities needs to be resolved.
- A database for BD data is needed but how to establish a database and who could be responsible for maintaining it needs further discussion.

**Expected Outcomes:** Proposals for follow-up activities as a result of the information gathered at this meeting include: a discussion of general principles and expectations to be shared via journal article in ASGCT's journal *Molecular Therapy*, and/or developing a guide for clinical study design and follow-up.