# MEDPACE

## **GLOBAL REGULATORY AFFAIRS SERVICES** INTEGRATED SUMMARY OF IMMUNOGENICITY (ISI)



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## AN OFTEN OVERLOOKED, YET CRUCIAL COMPONENT OF BIOLOGICAL DEVELOPMENT PROGRAMS

- Facilitate the review and alignment of manufacturing, nonclinical, and clinical aspects of the immunogenicity profile of a biologic therapy
- Understand immunogenicity risks to inform clinical monitoring and regulatory strategy
- Enable alignment with regulators to advance biotherapeutic development throughout the lifecycle of the product

## WHO SHOULD SUBMIT AN ISI?

• Sponsors developing biological therapeutic proteins and other therapeutic classes with a potential to produce immunogenic responses.

## WHERE SHOULD IT BE SUBMITTED?

• The full summary should be included in eCTD Module 5.3.5.3 (Reports of Analyses of Data from More than One Study), and briefly outlined in Module 2.7.2.4 (Special Studies: Immunogenicity).

## WHEN SHOULD IT BE SUBMITTED?

- While typically submitted for marketing authorization, the US FDA and EMA recommend generating ISIs early in product development.
- Submission and discussion of ISIs at key milestones (eg, IND/CTA submission and End-of-Phase 2 Meetings) offer considerable strategic advantage for informing and supporting risk management strategies and ensuring alignment with regulatory agencies.

## HOW IS IT STRUCTURED?

### Analysis of Risk Factors

A risk assessment of the product's immunogenic potential under the proposed treatment conditions. This includes intrinsic factors for the product/product class, additional concerns due to the dosing regimen (eg, dosing frequency, formulation, and route of administration), and any patient or disease-related factors.

### Assay Strategy & Clinical Approach

A detailed description of specific tiered and phase-dependent bioanalytical approach(es) used. An overview of the clinical study designs and sampling approaches should also be included.

#### **Immunogenicity Results**

An overview of the results from each study, including incidence, titers, and persistence of anti-drug antibodies (and neutralizing antibodies), as well as any impact they may have had on pharmacokinetics, pharmacodynamics, efficacy, and safety.

### **Conclusions & Risk Mitigation Strategies**

A critical evaluation of the impact of immunogenicity on clinical benefit and risk, with appropriate recommendations for risk mitigation strategies.

## WHAT KEY GUIDANCE DOCUMENTS COVER THE ISI?

- US Food and Drug Administration. Final guidance for industry: immunogenicity testing of therapeutic protein products - developing and validating assays for anti-drug antibody detection. 2019.
- US Food and Drug Administration. Final guidance for industry: immunogenicity assessment for therapeutic protein products. 2014.
- Committee for Medicinal Products for Human Use. Guideline on immunogenicity assessment of therapeutic proteins. EMEA/CHMP/BMWP/ 14327/2006 Rev 1. 2017.

FOR MORE INFORMATION ON ISI AND OTHER SERVICES, PLEASE CONTACT MEDPACE BUSINESS DEVELOPMENT.

