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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.

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