European Bioanalysis Forum vzw
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Subject: European Bioanalysis Forum Call for a Science-Aligned IVDR Interpretation in Early Drug Development with focus on Pharmacokinetic, Immunogenicity and Biomarker assays.

To whom it may concern

The European Bioanalysis Forum (EBF vzw, EBF) is a non-profit, science-driven organisation representing more than 80 pharmaceutical companies, CROs, and academic groups engaged in regulated bioanalysis across Europe and globally (www.e-b-f.eu). Founded in 2006, the EBF aims to promote scientific excellence, regulatory dialogue, and best practices in support of patient-focused drug development.

The IVDR was established to provide a clear regulatory framework for in vitro diagnostics that support healthcare decision-making and patient management.

The EBF supports the IVDR's goal of strengthening quality and oversight for diagnostic devices in the EU. Its intent and scope were never designed to encompass the scientific, exploratory assays used in understanding drug behaviour during development. However, as a bioanalytical community, we have observed assays being placed into the scope of the IVDR where we believe this was/is not the intention of the IVDR, i.e. during drug development and its clinical development stages the majority of the Pharmacokinetic (PK), Immunogenicity (ADA) and Biomarker (BM) assays are used to understand the biology and drug mechanism. These assays serve no other use than collect relevant scientific data including defining the right drug dosage. We believe the IVDR was not designed for PK, ADA or BM assays supporting early clinical development, and its diagnostic framework does not reflect the scientific, operational or regulatory reality of bioanalysis. They appear to have been inadvertently brought into IVDR scope due to misinterpretation of the regulation's intent by both industry and regulators

These assays are not diagnostic devices; they cannot be taken "off the shelf" as commercial kits, nor are they used to evaluate patient health or guide clinical decisions. They are study-specific analytical procedures, developed and validated individually to address scientific questions relevant to PK/PD, ADA assessments, drug–drug interactions, or biological characterisation. No universal kit can capture the unique structure, pharmacology, or matrix behaviour of a new investigational drug.

Moreover, their performance is already governed by a stringent and globally harmonised scientific and regulatory environment, including but not limited to the ICH M10 guidance, EMA scientific review expectations, GLP / GCLP / GxP frameworks, EMA and FDA guidelines on ADA, CoU principles applied to BM assays and study audits, sponsor QA oversight, and health authority inspections.

Above mentioned guideline and systems provide extensive scrutiny on method development, validation, sample handling (shipment, storage, analysis), data integrity, and reporting. In early phases of clinical development, these assays are used to generate scientific insight for cohort-level decisions (dose selection, PK modelling, stopping rules for the programme) rather than individual patient management. They are non-interventional: their results do not guide diagnosis, individual safety assessment, or real-time treatment decisions, and therefore do not influence patient care or clinical risk.

Imposing full IVDR compliance on these assays would require notified-body involvement, diagnostic-level documentation, and quality-system structures that are disproportionate to their actual risk and incompatible with the scientific nature of study-specific bioanalysis. Such requirements would not improve patient safety, already ensured through GCP, protocol-driven safety monitoring, and established clinical trial governance, but would significantly delay early development, disrupt operational feasibility, increase cost, and reduce Europe's competitiveness in innovative research.

For these reasons, the EBF recommends a proportionate, risk-based and science-aligned interpretation of the IVDR based on the intended use of an assay. PK, ADA and biomarker assays used in clinical trials to generate scientific insight, not to diagnose, select or manage individual patients, should not fall within IVDR scope, regardless of the development phase in which they are applied.

We further recommend that the IVDR, or its associated guidance, provide a clearer framework that explicitly excludes assays whose purpose is limited to cohort-level interpretation, dose understanding, pharmacology and programme decision-making, and that have no role in patient management or in the marketed label. These assays should remain governed by the established global scientific-validation principles, which already ensure quality, reliability and patient safety, while avoiding the unintended consequence of applying a diagnostic regulatory pathway to tools that are fundamentally non-diagnostic in purpose and design.

The EBF is available to engage further, share our collective experience, and support a proportionate and scientifically grounded interpretation of the IVDR

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References:

- *Finding our way in the In Vitro Diagnostic Medical Devices Regulation: a discussion paper from the European Bioanalysis Forum, Bioanalysis. 2024 Feb;16(3):117-120.*
- *Navigating IVDR challenges for pharmacokinetic, anti-drug antibodies, and biomarker assays in early clinical research: a recommendation from the European Bioanalysis Forum, Bioanalysis. 2025 Jul;17(14):889-892.*
- *Link to EBF Roadshows: https://e-b-f.eu/conferences/past-conferences-2/*