Guide

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The Cost of a Late Start: IVDR Compliance for Laboratory-developed Tests

When a clinical trial relies on a diagnostic that has no CE-marked equivalent on the market, Article 5.5 of the IVDR provides a compliant route to developing an appropriate test.

This is certainly not a lighter version of the regulation; the scientific rigor is identical to full CE marking, even if the administrative path differs slightly.

For any program running trials at EU sites or relying on laboratory-developed tests (LDTs) that would otherwise require CE marking, Article 5.5 applies regardless of where the sponsor is based. Its reach extends beyond Europe so that any organization placing IVDs on the European market, or conducting a clinical study at EU sites, must comply, regardless of where they are based.





The process can be considered in five distinct phases:

1	Method development
2	Regulatory strategy
3	Design control
4	Method validation
5	Technical dossier

Each phase depends on the one before it. You cannot do design control well without solid method development, and you cannot validate against criteria that were never properly set.

Of these five phases, method development and design control carry the most weight. The quality of everything that follows, including validation, the technical dossier, and ultimately the data, depends on how well both are executed.

Method development

Method development is where the assay format is defined, critical reagents are identified, and the platform is established. It is also, in practice, where many programs make the most consequential mistakes.

The temptation is to treat method development as a technical starting point rather than a strategic one. In fact, it is both.

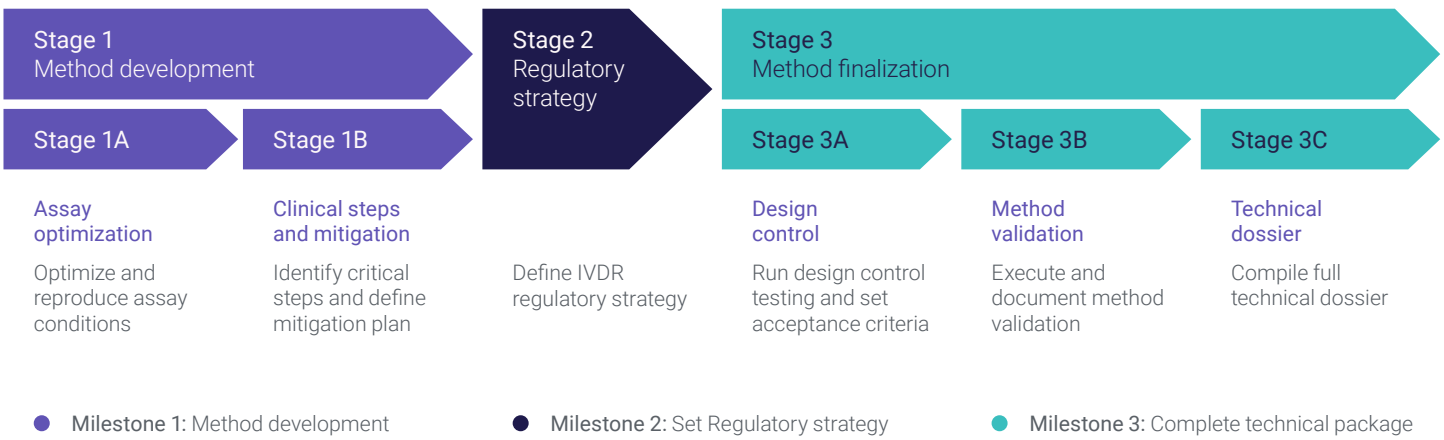
The platform and assay format selected at the outset determine whether the development that follows is iterative and controlled, or reactive and expensive. Starting with the wrong assay format or poorly sourced reagents creates problems that run through the entire development process.

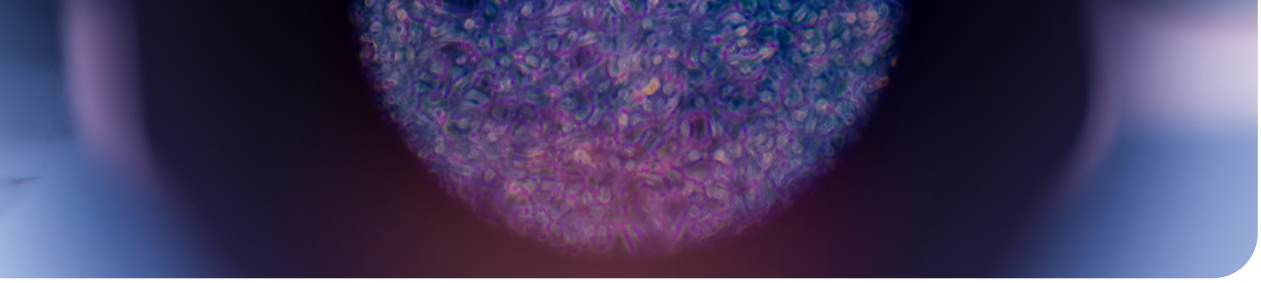
There is a practical consequence that is easy to underestimate. If the foundation is wrong, the program often needs a complete restart. Any development work that preceded the wrong decision is invalid, and the team goes back to the beginning. In a timeline already constrained by the pre-IND window, a restart is costly in both time and resource.

A program that begins with the right platform, the right assay format, and a clear picture of intended use builds iteratively. The investment in getting it right at the start makes the rest of the process more manageable and reduces the risk of costly rework.

This is also where the composition of the team matters. Scientific leads, regulatory affairs, quality assurance, project management, and the clinical team at the sponsor side all need to be aligned before running a single experiment.

IVDR context / Article 5.5 – process overview





Design control

Design control is the structured process that links the clinical purpose of the assay to the evidence required to demonstrate that it performs as intended. It begins with a question that should be answered before any experiment starts:

“Why does this assay exist, and what clinical question does it answer?”

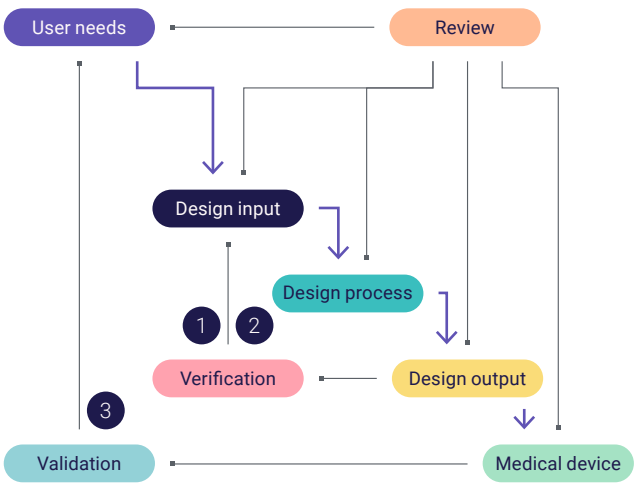
The design inputs are derived from the answer to that question: the patient need. They are translated into numbers, specific acceptance criteria, thresholds, and targets for every parameter the assay must meet. These must be defined before any experiment starts, so the validation tests the assay against a standard, not a description of its own results.

In practice, design control covers a significant body of work: blood sample collection conditions, critical reagent characterization across lots and suppliers, incubation parameter ranges, and the mitigation strategy for every foreseeable source of variability. Each feeds back into the analytical procedure, which is updated in parallel throughout. Good documentation practice allows a quick response if a reagent becomes unavailable, a lot fails qualification, or a question arises during submission.

Reagent sourcing deserves particular attention. If a critical reagent has only one supplier and that supplier fails, the options narrow quickly. Testing multiple suppliers and multiple lots during design control means a new reagent can be qualified and switched in. Without that data, finding an equivalent reagent later may require redesigning the assay format entirely.

The acceptance criteria set in this phase carry forward into method validation. If the design control data shows variability, that variability does not improve during validation. The assay goes back for further optimization.

Regulatory strategy Phase 2 and design control – design control loop



User needs	Initial design requirements: Intended purpose and user needs > Benefit of the IVD
Design input	
Design process	IVD development Pretesting phase with definition of the **acceptance criteria** (threshold and target)
Design output	Intended performance parameters Specifications, documentations, **acceptance criteria**
Verification	Targeted acceptance criteria 1 2
Validation	3
Review	Project milestone with paire’s review > Risk management ISO 14971

1 1: PEP

2 2: APR | CPR

3 3: PER

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Considerations before **phase I**

For a clinical development team, the decisions that matter most are made before phase 1 recruitment begins. By the time a trial is enrolling patients, the lab partner has been selected, the assay format is fixed, and the design control framework is either in place, or it is not. The decisions that determine whether the program runs cleanly have already been made.

The question worth asking of any lab partner is how they are integrating and approaching the Article 5.5 process. Is it a structured end-to-end program from the point at which method development begins, with regulatory strategy, design control, and documentation managed in parallel?

The 2030 deadline under Article 5.5 is not a deadline to stop using LDTs. It is a deadline to formally justify that no equivalent CE-marked test exists on the market. Programs that have not yet documented that justification need to know where they stand.



Interested in how we can shape your **laboratory strategy** for better outcomes?

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