Diagnostics Readiness Levels

A Multi-Dimensional Framework for Diagnostic and Biomarker Development

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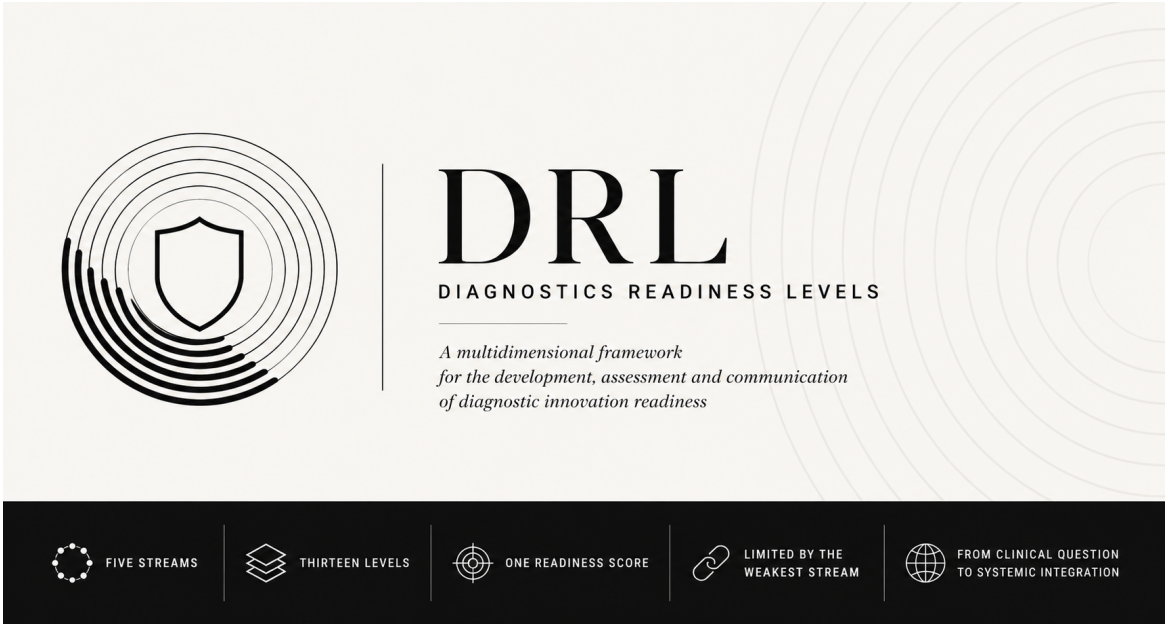

Status: Working proposal. The DRL framework is grounded in practitioner experience and draws on established frameworks; it has not yet been subject to formal empirical validation. It is offered as a structured tool for development teams, investors, and evaluators, and as a basis for community refinement.

Who this is for

Developers and founders: DRL shows you which dimensions of your programme are behind, before they become crises. It changes how you plan, how you fundraise, and what you build next.

Funders, grant panels, and TTOs: DRL gives you a structured, reproducible grid for assessing readiness across all five development dimensions - not just the science. It makes disagreements between evaluators productive rather than irresolvable.

Investors: DRL makes the gap between a project's claimed TRL and its actual readiness explicit, across all five streams. It tells you not just where a project is, but what closing the gaps will cost.

Abstract

The Technology Readiness Level (TRL) scale, and its biomarker-specific adaptations, cannot capture the full complexity of diagnostic development. A project that is technically mature may simultaneously lack a regulatory strategy, a viable business model, or a path to reimbursement - and the single-number TRL score hides those gaps until it is too late. Arguably, technology readiness should be independent from all the other dimensions, but not explicitly pushing them in parallel creates both dead ends of technologies with no viable path to market, and illusions of maturity.

The Diagnostics Readiness Level (DRL) framework addresses this by assessing readiness across five parallel streams - Scientific & Technical, Clinical, Regulatory & Quality, Commercial & Market, and Strategic & Systemic - on a thirteen-level scale organised into four phases. A single headline DRL is reported using a weakest-stream rule: a project's overall DRL is the lowest level at which all five stream gates are passed. This makes imbalances explicit rather than averaged away. The framework is designed for three primary uses: self-assessment by development teams, evaluation by funders and technology transfer offices, and investment/grant due diligence. It draws on TRL, which it parallels, BMK Tools, ACCE, and REASSURED, while extending into the commercial and strategic dimensions none of them reach.

1. The Problem: Why One Number Is Not Enough

1.1 The Scientist/Entrepreneur's Problem

For a scientist or entrepreneur building a new diagnostic, the development journey rarely fails on the science. It fails on the coordination of five parallel tracks that must all advance simultaneously - technical, clinical, regulatory, commercial, and strategic - each with its own logic, its own timeline, and its own capital requirements. But all

informing each other: if that coordination happens early, the typical pitfalls of the diagnostics journey are avoided.

The TRL scale offers a single number that implies a single track. In practice, a project can be at TRL-7 technically while sitting at TRL-3 commercially, and the single number hides that gap until it becomes a crisis. A team that has completed analytical validation may have no freedom-to-operate assessment, no business model decision, and no clinical partner capable of running a study to the evidence standard required for adoption. Each of those gaps is a separate development problem requiring separate investment, separate expertise, and a separate timeline. None of them are visible in the TRL score - but all must inform the technology development.

What developers need is not a simpler map but an honest one: a framework that shows where each dimension stands, where the gaps are, and where the next investment should go - and, more importantly, what cannot be left behind at each stage of development. Building such a framework was one of the driving motivations behind writing Precision Diagnostics: A Founder's Journey. The DRLs are the manifestation of its conclusions.

1.2 The Investor's Problem

Investors in diagnostics face a version of the same problem from the opposite direction. Most diagnostic development companies present their progress in TRL terms - a single number that conflates technical maturity with commercial readiness and regulatory status. A company at "TRL-7" may have strong clinical evidence but no regulatory strategy, no distribution model, and no health economics data. The investment required to bridge those gaps is orders of magnitude larger than the number implies.

The DRL framework was designed to make that gap explicit - to give investors a multi-dimensional profile that reveals not just where a project is, but where the bottlenecks are and what resolving them will cost. The stream profile matters as much as the headline number: a project at DRL-6 on all other streams but with a Commercial & Market stream at DRL-3 has a fundamentally different risk profile, and a different capital requirement, than a project at DRL-6 across all streams.

1.3 The Evaluator's Problem

Grant panels, technology transfer offices, accelerator programmes, and public funders face a structural challenge: they must assess the readiness of diagnostic projects using criteria designed for either basic research or pharmaceutical development. Neither fits.

Biomarker-specific frameworks like BMK Tools (Aviesan/EIT Health) and the ACCE model provide useful checklists for the scientific and regulatory dimensions, but they were not designed as multi-dimensional assessment tools. The result is that evaluators systematically overweight technical maturity and underweight commercial and strategic readiness, potentially rewarding projects that have strong science but no viable path to adoption. In addition, grant evaluators and TTOs must resort to variable intuition or experience in grading the maturity of each project, lacking objective tools. The DRL framework provides a structured assessment grid that covers all five dimensions, enabling evaluators to identify not just where a project is strong, but where it will face specific challenges.

2. What Existing Frameworks Get Right - and Where They Fall Short

Several frameworks have been developed to structure the assessment of diagnostic and biomarker development. Each addresses a real problem and does so well within its scope. The DRL framework is not a rejection of these tools - some of which, like the TRLs and the BMK Tools, I have used repeatedly over the years - but an extension of them into territory they were not designed to cover. Understanding where each falls short is necessary for understanding why a new framework is needed.

2.1 Technology Readiness Level (TRL)

Developed by NASA in the 1970s to track the maturity of space and defence technologies, TRL was adapted for EU research and innovation funding through the Horizon programme and has since become the default language for technology readiness across sectors, including health.

What it gets right: TRL provides a shared vocabulary for technology maturity that is legible across disciplines and funding contexts. Its nine-level scale from basic

principles (TRL-1) to proven system in operational environment (TRL-9) captures the arc from concept to deployment in a form that non-specialists can follow. For purely technical development - materials, engineering, software - it works extremely well.

Where it falls short for diagnostics: TRL was never designed for regulated, evidence-based industries. It has no concept of clinical evidence, regulatory pathway, business model, or reimbursement. A diagnostic that has completed analytical validation (TRL-5 or 6 by most mappings) may be years and millions of euros away from clinical adoption - but TRL does not make that visible, as it concentrates on the technology in the absence of other dimensions. If those dimensions are not tackled from day one, informing technology-related choices and milestones, the technology development itself is less likely to succeed in terms of widespread adoption. More critically, TRL implies a single track: technical maturity advances and everything else follows. In diagnostics, clinical, regulatory, commercial, and strategic dimensions must advance in parallel and are not downstream consequences of technical maturity.

2.2 BMK Tools (Aviesan / EIT Health)

Developed by Aviesan in collaboration with EIT Health, BMK Tools is the most serious attempt to adapt TRL to the specific requirements of biomarker and diagnostic development. It maps biomarker development stages against TRL levels and introduces a structured checklist approach to evidence requirements.

What it gets right: BMK Tools correctly identifies that biomarker development has a distinct logic from generic technology development. It introduces clinical validation stages, regulatory considerations, and some attention to the evidence requirements of health technology assessment. For academic and early-stage biomarker programmes in the EU context, it provides a useful structure that TRL alone cannot offer.

Where it falls short: BMK Tools remains primarily scientific and regulatory in scope. It does not address business model selection, cost-of-goods, logistics, distribution, or reimbursement as development dimensions requiring active management. The commercial and strategic tracks - which account for the majority of late-stage diagnostic failures - are outside its architecture. It also does not extend to the systemic integration phase. Finally, BMK Tools is structured as a sequential checklist rather than a parallel multi-stream framework, which means it does not

surface the imbalances between dimensions that are the most common cause of development failure.

2.3 ACCE

Developed by the CDC Office of Public Health Genomics, ACCE provides a structured framework for evaluating genomic and genetic tests across four domains: Analytic validity, Clinical validity, Clinical utility, and Ethical/legal/social implications.

What it gets right: ACCE is the most rigorous framework available for clinical evidence evaluation in diagnostics. Its four-domain structure correctly identifies that analytical validity and clinical validity are necessary but not sufficient - clinical utility is the standard that health systems actually require. The inclusion of ethical, legal, and social implications is forward-looking and relevant, particularly for genomic testing.

Where it falls short: ACCE is an evaluation framework, not a development framework. It tells you how to assess a test's evidence base; it does not tell you how to build one, in what sequence, at what cost, or with what regulatory and commercial infrastructure. It has no concept of readiness stages, development phases, or the parallel tracks that must advance simultaneously.

2.4 REASSURED

REASSURED (Real-time connectivity, Ease of specimen collection, Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free or simple, Environmentally friendly, Deliverable to end-users) was developed by WHO and FIND as an extension of the earlier ASSURED criteria, specifically for point-of-care diagnostics in low- and middle-income country settings.

What it gets right: REASSURED correctly identifies that diagnostics deployed at the point of care in resource-limited settings have fundamentally different requirements from laboratory-based tests in high-income health systems. It is one of the few frameworks that takes end-user context seriously as a development constraint rather than a deployment afterthought.

Where it falls short: REASSURED is a product specification framework, not a development readiness framework. It defines what a good point-of-care diagnostic should look like; it does not provide a structure for tracking whether a development

programme is on track to produce one. Its scope is also limited to point-of-care diagnostics.

2.5 BRLa and P-IRL

BRLa represents an adaptation of TRL specifically to biomarker development, with an emphasis on the analytical and pre-clinical validation stages. It provides finer resolution than TRL in the early stages but does not address clinical validation, regulatory pathway, commercial development, or strategic positioning - in effect, a more detailed TRL-1 through TRL-5 for biomarkers. P-IRL frameworks have been developed for specific diagnostic platforms. Platform-specific frameworks correctly recognise that development logic varies by platform, but by definition cannot serve as a general readiness framework, and share the broader limitation of TRL-derived tools: they omit the commercial and strategic tracks.

2.6 The Consistent Gap

The gap is consistent across all existing frameworks: none addresses the commercial and strategic dimensions as first-class development tracks that must be actively managed, evidenced, and gated alongside the scientific and regulatory work. Figure 1 maps this coverage landscape. Figure 2 shows how the stage structures of the different frameworks align across the four DRL phases.

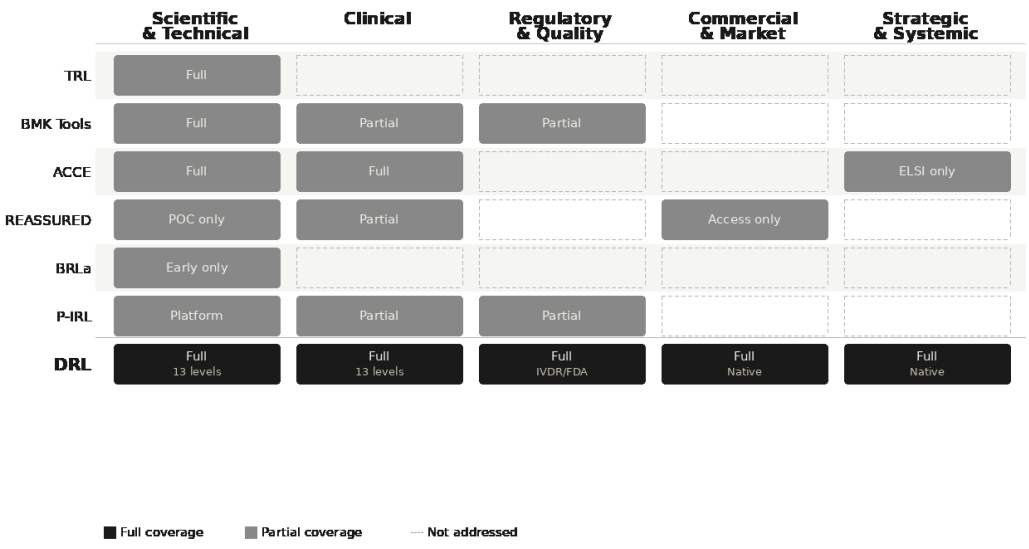

Figure 1. Framework coverage comparison. DRL extends existing frameworks into the commercial and strategic dimensions none of them address.

Framework	Primary scope	Key strengths	Key gaps
TRL	Technology maturity	Universal vocabulary, cross-sector legibility	No clinical, regulatory, commercial, or strategic dimension
BMK Tools	Biomarker science + regulatory	Diagnostic-specific, EU-aligned, evidence checklist	No business model, reimbursement, or systemic integration
ACCE	Clinical evidence evaluation	Rigorous clinical validity framework, includes ELSI	Evaluation only; no commercial or strategic dimension
REASSURED	POC product specification	End-user context, LMIC applicability	Not a development framework; limited to POC
BRLa	Early biomarker stages	Fine-grained early-stage structure	Stops at pre-clinical; no clinical, commercial, or strategic dimension
P-IRL	Platform-specific IVD	Platform-appropriate requirements	Not generalisable; lacks commercial and strategic streams
DRL	Full development journey	Five parallel streams, 13 levels, weakest-stream rule	Empirical calibration pending

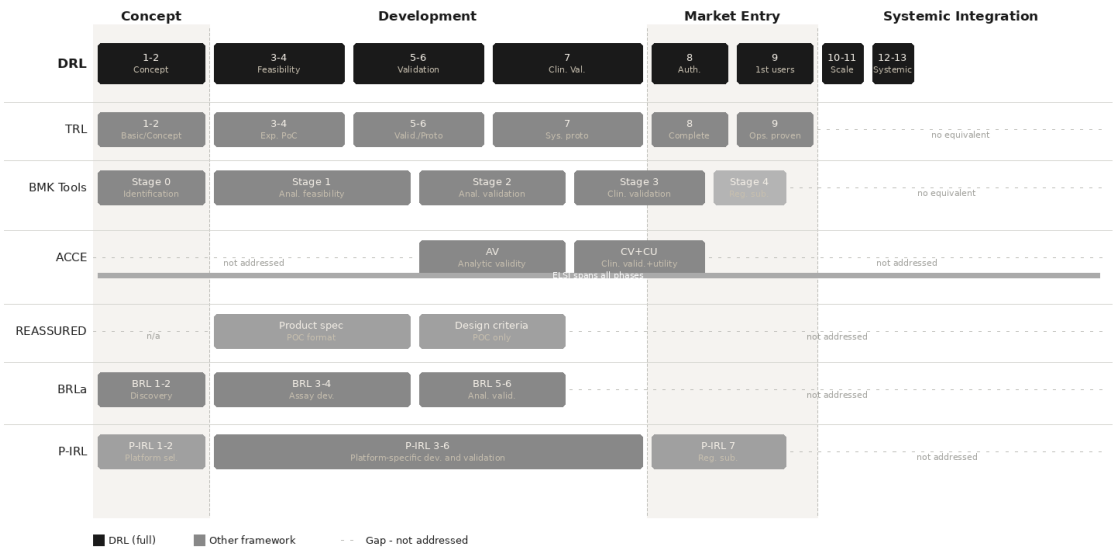

Figure 2. Framework level mapping across four development phases. Dashed lines indicate stages not addressed by a given framework. DRL is the only framework covering all four phases across all five dimensions.

3. How and Why the DRL Framework Was Built

The DRL framework did not begin as a framework, but as my attempt to deal with a recurrent problem.

Over more than a decade of building diagnostic programmes - from early biomarker discovery through clinical validation, regulatory submission, and commercial deployment - the same pattern appeared repeatedly. Projects that looked strong on the science stalled at the regulatory filing. Projects with solid clinical evidence collapsed at the business model decision. Programmes that had navigated all of that successfully discovered, at the point of market entry, that the reimbursement pathway had never been mapped and the distribution infrastructure did not exist. In each case, the failure was not a scientific failure. It was a coordination failure across dimensions that no existing framework made simultaneously visible.

The most formative of these lessons came from a context where the stakes made the failure impossible to overlook. I had previously taken a liquid biopsy test to market successfully - a test that was essentially a better implementation of something that already existed and did not fundamentally change clinical decision pathways. That

experience gave me a false sense of what clinical evidence was required. When we developed a diagnostic for liver transplantation selection in hepatocellular carcinoma, the clinical and evidentiary bar was entirely different. This was not a test that informed a marginal decision; it was a test that determined who received a liver and who did not. Every clinician we spoke to told us what we were building was important and needed. It took years - and our first serious attempts at selling - to understand that important and needed were not the same as adoptable. The evidence level required for a decision of that gravity, involving the life of the transplant candidate and the life of the patient who did not receive the same organ, was categorically higher than anything we had planned for. We had not set the evidence level early enough. In retrospect, I have to admit we had not set it at all when we started, moving forward with a mix of intuitive validaiton strategy, conditioned by sample availability and opportunistic collaborations. We should have done it at DRL-2, which would have focused on the important collaborations, and less on the ones that did not move the project forward.

A parallel lesson came from a different direction. Earlier, we had built a clinical NGS sequencing service at a time when next-generation sequencing was not yet routine in clinical laboratories. The technology worked; the clinical value was real. What we discovered late - too late - was that the market required confirmation of variants by an orthogonal technology, typically Sanger sequencing. The demand seemed scientifically unnecessary to us – absurd, actually - but it was the real market objection, and it was not negotiable. Meeting it meant either acquiring Sanger sequencing equipment or subcontracting confirmation runs, with costs and timelines we had not anticipated. We learned this not from a framework, not from a literature review, but from the moment we first tried to sell. DRL-6 requires that attempt. We had been treating it as optional.

I’ve seen the same pattern recurrently in evaluation contexts. In grant panels, technically strong projects generated irresolvable arguments between commercially-oriented and clinically-oriented evaluators - not because either was wrong, but because they lacked a shared language for naming the specific weakness each was identifying. In investment due diligence roles, the gaps became sharper. I assessed one company with genuinely impressive technology and a seemingly complete path to market - strong IP, regulatory strategy documented, distribution conversations underway - but on closer inspection their clinical evidence standard was incompatible

with the intended application, and the sample type their claimed TRL assumed was almost never collected in routine clinical practice. The maturity they were reporting was real in the scientific stream and fictional in the clinical one.

Another company I evaluated had a different profile: an established international distributor network, OEM contracts in place, and a strong commercial narrative. The underlying technology had never progressed past an early prototype. Their path to market was highly regulated, and their regulatory strategy consisted of having 'a regulatory person' on their team. A third case remains the most instructive: a liquid biopsy programme with genuinely exceptional analytical performance - sensitivity and specificity that were rare in the field - and a large, well-characterised validation cohort. But the technology they had built was expensive, appropriate for research settings, and incompatible with the early detection and screening application they were targeting. They had never validated their intended commercial price point with anyone who made financial decisions. The whole programme eventually required a complete pivot to a clinical application compatible with their cost structure, losing years and millions of investment in an application that had never really existed as a viable market.

These experiences, not a theoretical analysis, are what drove the construction of the DRL framework. The structured review of existing frameworks described in Section 2 confirmed what practice had already taught: the commercial and strategic dimensions were either absent from existing tools or treated as downstream consequences of technical maturity. The retrospective application of the five-stream architecture to completed programmes - mapping where each project actually stood at the time of key decisions - revealed imbalances that the TRL score had hidden, and those imbalances predicted where the project subsequently struggled. The gate structure was written, tested against these cases, and revised until each gate answered a question that a practitioner with real capital at risk would actually need to answer before proceeding.

The result is a framework that is practice-grounded in a specific sense: not that it has been empirically validated across a large sample of programmes, but that every gate in it corresponds to a real decision point that I have encountered, made, or seen fail to be made in actual diagnostic development. The limitations of that origin are acknowledged explicitly in Section 8.

4. Framework Architecture

4.1 The Five Streams

The DRL framework assesses readiness across five parallel streams. Each stream has its own gate at every level; all five must be passed for a level to be claimed.

Stream 1 - Scientific & Technical: Covers biomarker identification and characterisation, assay development, analytical validation, technology transfer, manufacturing validation, and post-market technical surveillance. This is the dimension that existing frameworks address most thoroughly; DRL integrates it with little modification and maintains a full mapping to the TRL scale.

Stream 2 - Clinical: Covers clinical partnership, evidence generation, clinical validation at the appropriate evidence level, clinical utility demonstration, real-world outcomes, and guideline inclusion. The evidence level requirement - whether Level I, II, or III evidence is needed for adoption in the target indication - is determined at DRL-2 and treated as a binding constraint throughout the development programme. This prevents the common failure mode of generating the wrong type of evidence for the target clinical setting.

Stream 3 - Regulatory & Quality: Covers documentation practices, regulatory pathway identification and confirmation, quality management system implementation, regulatory submission and authorisation, post-market surveillance, and multi-geography regulatory sequencing. Post-market surveillance is treated as a regulatory dimension, not a standalone phase - it is integrated from DRL-8 onward.

Stream 4 - Commercial & Market: Covers business model selection and commitment, cost-of-goods estimation, logistics mapping, distribution model development, reimbursement pathway navigation, health technology assessment, and multi-geography commercial scaling. The business model decision - service, kit, laboratory-developed test, or hybrid - is locked as a binding commitment at DRL-5, with its regulatory, manufacturing, distribution, and capital implications explicitly acknowledged.

Stream 5 - Strategic & Systemic: Covers stakeholder mapping, funding landscape navigation, investor narrative development, partnership strategy, institutional and sovereign procurement, supply chain resilience, and policy influence. This stream has

no equivalent in existing frameworks. It captures the dimensions that determine whether a diagnostically and commercially validated product actually reaches patients at scale - the difference between a product that works and a product that is used.

4.2 The Thirteen Levels and Four Phases

Thirteen levels are organised into four phases, each corresponding to a distinct development logic and capital profile.

Phase	Levels	Core question
Phase 1 - Concept	DRL 1-2	Is the hypothesis sound and the landscape understood?
Phase 2 - Development	DRL 3-7	Can the test be built, validated, and prepared for authorisation?
Phase 3 - Market Entry	DRL 8-9	Can the test be authorised, sold, and used in routine care?
Phase 4 - Systemic Integration	DRL 10-13	Can the test scale, sustain, and contribute to a diagnostics value chain?

4.3 The Weakest-Stream Rule

A project's overall DRL is the lowest level at which all five stream gates are passed. A project with Scientific & Technical at DRL-7, Clinical at DRL-6, Regulatory & Quality at DRL-5, Commercial & Market at DRL-3, and Strategic & Systemic at DRL-4 has an overall DRL of 3 - not an average of 5, not the highest stream at 7.

This rule is intentional and non-negotiable. It makes imbalances visible rather than averaging them away. The stream profile - which streams are ahead, which are behind - is as diagnostically valuable as the headline number. A project at DRL-6 with all streams aligned is fundamentally different from a project at DRL-6 with a Commercial & Market stream two levels behind, even though both report the same headline number under other frameworks.

Partial passes within a level do not contribute to the overall DRL score, but they identify where the next investment should go.

4.4 The Pass Criterion

A gate is passed when the required evidence artefact already exists - not when the work has been started, not when it is planned, but when the evidence has been produced and verified. The DRL framework proposes specific artefacts as evidence for gate crossing. This demand prevents the reporting of aspiration as progress, which is the most common source of DRL inflation in practice.

Each gate specifies not only the question to be answered but the artefact that must exist in each stream: a document, a dataset, a signed agreement, a certificate, a record. The artefact standard makes assessment reproducible across evaluators and over time. It further helps developers close steps of development instead of opening new avenues that do not advance the maturity of the product.

4.5 A DRL Profile in Practice

The following profile illustrates how the framework operates on a real development situation. The project is anonymised and changed from the original to make it untraceable; the profile is representative of a type of programme I have encountered and assessed directly.

A molecular diagnostic test for a defined oncology indication, developed over several years within an academic laboratory using standing research funding. The founding team has done substantial work. The assay has been developed from research-grade reagents, the assembly protocol standardised, a fill-and-finish process established, and cost-of-goods estimated. Analytical validation has been completed internally, characterising sensitivity, specificity, and reproducibility across multiple operators within the team, but without external independent validation by a third-party laboratory. Two retrospective clinical cohorts exist, one of 120 patients and one of 77, from two independent clinical sites, both showing strong and consistent correlation with clinical outcome. The team has thought carefully about clinical evidence: they have determined that a prospective-retrospective study will be required for broad adoption, but that a defined niche market could support first sales on the strength of

the retrospective data alone. They have not yet identified prospective-retrospective sample sources.

The programme has never applied for a specific development grant - it grew from standing academic funding. It has won two small innovation prizes, which brought visibility and external validation of the scientific concept. Now, for the first time, the team is attempting to establish a company and raise an investment round. They have mapped the investor landscape, identified suitable investors, and are in active early-stage conversations. They present the programme at TRL-6, noting demonstrated performance in a relevant clinical environment across two independent sites. That claim is defensible. It is also, in the most important sense, incomplete.

A DRL assessment produces the following profile:

Stream	DRL reached	Key Blocker
Scientific & Technical	DRL-4	External independent validation absent; final assay format undefined pending business model decision
Clinical	DRL-3	Evidence level defined with two-tier strategy; niche first-sales track data-rich; main validation track blocked by absence of identified prospective-retrospective sample sources
Regulatory & Quality	DRL-3	Regulatory pathway unconfirmed; no QMS initiated; pre-company means no regulatory infrastructure yet exists
Commercial & Market	DRL-3	COGS estimated; business model undecided; no first sales attempt made

Strategic & Systemic	DRL-3	Investor landscape mapped; suitable investors engaged; innovation prizes as credibility markers; capital not yet confirmed
Overall DRL	DRL-3	All five streams reach DRL-3; multiple DRL-4 gates blocked across all streams

TRL claimed: TRL-6. DRL assessed: DRL-3.

The gap between these two numbers is not a sign of a failed project. It is a sign of a project that has been developed in a specific context - academic, pre-company, prize-validated - that systematically rewards scientific progress and defers the decisions that commercial readiness requires. Innovation prizes are awarded on scientific merit and potential; they do not require a regulatory pathway, a business model, or a confirmed sample source. Grant applications, which this team never made for this programme, force the articulation of milestones, capital requirements, and development logic that the DRL gates require. The absence of that discipline is visible across every stream.

What the DRL profile reveals is not that the team has done the wrong work. It is that five parallel streams are all sitting at the same level, all blocked by the same cluster of decisions: business model and final format lock, which would unblock both the Scientific and Regulatory streams; prospective-retrospective sample source identification, which would unblock the Clinical stream; and company formation with a structured seed round, which would create the infrastructure the Commercial and Regulatory streams require. These are coordination and decision problems, not scientific ones, and they are all addressable, some of them in weeks, at minimal cost.

The round this team is raising needs to be designed to make those decisions, not simply to continue the science. A round sized and structured around TRL-6, assuming technically mature, nearly ready for clinical deployment, will be severely undersized and mis-sequenced for a programme that is actually at DRL-3: coherent, well-founded, and requiring a specific set of parallel decisions before the next phase of development can begin. That mismatch between the TRL framing and the DRL reality is precisely what an investor, a TTO, or an accelerator programme needs to see before committing capital, not to reject the programme, but to structure the investment correctly.

5. The Gate Structure in Summary

The full gate structure - 13 levels x 5 streams = 65 gates, each with a binary pass/fail question and a required evidence artefact - is provided in the companion scoring instrument (DRL Scoring Instrument v1.0). Below is a phase-level summary of what each phase requires and what it produces.

Phase 1 - Concept (DRL 1-2)

At DRL-1, a project must demonstrate that a biological parameter has been named and linked to a clinical gap, that a clinician has confirmed the gap exists, that documentation has been initiated, that the commercial use case is plausible, and that the stakeholder landscape has been mapped. These are the minimum conditions for avoiding the most common early-stage failure modes - pursuing a biomarker with no clinical champion or real need, building for a market that does not exist, or developing in a regulatory vacuum.

At DRL-2, the characterisation deepens. The evidence level decision at DRL-2 is the most important single decision in the development programme: it determines the study design, the sample size, the timeline, and the capital requirement for the entire clinical evidence generation process.

Phase 2 - Development (DRL 3-7)

Phase 2 spans first detection (DRL-3) through regulatory-ready clinical validation (DRL-7). The five streams advance in parallel, with gates at each level designed to ensure that no stream falls so far behind that it becomes a programme-ending bottleneck. Key transitions: DRL-3 to DRL-4 moves from first detection to reproducible performance across real samples; DRL-4 to DRL-5 from reproducibility to full analytical validation with business model locked; DRL-5 to DRL-6 from analytical validation to clinical proof of concept; DRL-6 to DRL-7 from clinical PoC to multi-centre validation and regulatory technical file preparation.

The business model lock at DRL-5 is particularly important. The choice of service, kit, LDT, or hybrid is a technical, regulatory, and capital architecture decision - more than

a commercial preference. Making it late, or leaving it provisional, generates costly rework across all five streams.

Phase 3 - Market Entry (DRL 8-9)

At DRL-8, the project crosses the authorisation threshold: market authorisation is obtained, manufacturing is validated under ISO 13485, distribution is operational, and institutional procurement conversations have begun. This is the phase where the commercial and strategic streams become load-bearing: a product can be technically excellent and clinically proven but fail to reach patients because reimbursement is not secured, distribution partners are not trained, or the institutional buyers have not been engaged.

At DRL-9, the test is in routine clinical use - beyond research or grant-funded collaborations - in real care settings, ordered by real clinicians, paid for by real payers.

Phase 4 - Systemic Integration (DRL 10-13)

Phase 4 addresses dimensions that no existing framework reaches. At DRL-10 the business is generating positive unit economics and scaling. At DRL-11 manufacturing is scaling without quality degradation and reimbursement is secured or in final-stage application. At DRL-12 the test is commercially available in three or more geographies, embedded in procurement frameworks, and no longer dependent on the founding team for business development. At DRL-13 the test is standard of care in at least one national clinical pathway, the company is contributing to a local diagnostics value chain, and policy influence is documented.

DRL-13 is explicitly a sovereignty and systemic contribution level. It captures the difference between a product that is sold in a market and a product that is part of the diagnostic infrastructure of a health system.

6. Capital Intensity Across Phases

One of the practical uses of the DRL framework is capital planning. The four phases have radically different capital profiles, and misalignment between a project's stated DRL and its actual burn rate is a reliable warning sign.

The ranges below are indicative and will vary by diagnostic category and ambition, geography, regulatory pathway, and business model. They are meant to illustrate the shape of the capital journey, not to provide normative budgets.

Phase	Typical capital range	Primary cost drivers
Phase 1 (DRL 1-2)	EUR 50K-250K	Personnel, IP assessment, feasibility studies
Phase 2 (DRL 3-7)	EUR 3M-10M	Clinical studies, analytical validation, QMS build, regulatory advisory
Phase 3 (DRL 8-9)	EUR 5M-20M	Manufacturing scale-up, regulatory submissions, distribution infrastructure, market access, COGS
Phase 4 (DRL 10-13)	EUR 10M-75M+	Multi-geography expansion, reimbursement, KOL programmes, supply chain resilience

The DRL stream profile, not the headline number alone, determines which cost drivers are active at any given stage. From Phase 3 onwards, cost of goods (COGS) becomes a relevant and growing component of total expenditure.

7. Relationship to Regulatory and HTA Frameworks

The DRL framework is designed to be compatible with, not to replace, the regulatory and HTA (Health Technology Assessment) structures that govern diagnostic development in major markets. It is not itself an HTA method, a regulatory pathway, or a costing tool. Three specific anchor points illustrate the alignment:

- DRL-5 is where IVDR-grade analytical validation is completed in the final assay format - the threshold at which the Regulatory & Quality stream transitions from development documentation to regulatory technical file preparation, and where ISO 13485 QMS implementation is formally initiated.
- DRL-7 is where the clinical evidence package for CE-IVD, FDA De Novo, or PMA is largely complete, and where the health economics model required for HTA bodies is in place.
- DRL-7 and DRL-11 are the natural anchor points for EU Joint Clinical Assessment (JCA) evidence requirements and national HTA dossiers respectively.

IVDR (EU In Vitro Diagnostic Regulation): The Regulatory & Quality stream gates are aligned with the IVDR evidence requirements for Class B, C, and D IVDs. The transition from development documentation to regulatory technical file occurs at DRL-4 to DRL-5. ISO 13485 QMS implementation is initiated at DRL-5 and required for market authorisation at DRL-8.

FDA (510(k), De Novo, PMA): The framework accommodates FDA regulatory pathways through the Regulatory & Quality stream gates; the specific pathway determines the evidence standard required at DRL-5 to DRL-7.

HTA and reimbursement: The reimbursement pathway mapping gate at DRL-7 and the HTA dossier gate at DRL-11 are aligned with the Joint Clinical Assessment (JCA) process under EU HTA Regulation 2021/2282. The health economics model required at DRL-7 is designed to be compatible with NICE, HAS, IQWiG, and equivalent bodies' evidence standards.

8. Limitations and Future Work

The DRL framework is a working proposal, not yet a validated scale. Several limitations are present.

Calibration: The gate thresholds - particularly the quantitative artefact standards (20 or more samples at DRL-4, 50 or more subjects at DRL-6, two or more

independent sites at DRL-7) - are grounded in practitioner experience and regulatory precedent, not in empirical analysis of development outcomes. They are offered only as indicative ranges.

Diagnostic category variation: The framework is designed to be applicable across IVD categories - molecular, immunoassay, point-of-care, companion diagnostic, screening. However, evidence standards and capital profiles differ substantially across categories. A companion diagnostic for an oncology drug has a fundamentally different clinical evidence requirement than a population screening test. Future versions should incorporate category-specific guidance.

Geography: The regulatory and reimbursement gates are written primarily with EU and US frameworks in mind. Application in the GCC, Africa, Southeast Asia, and other markets requires adaptation. This is an active area of development.

Weighting: The weakest-stream rule treats all five streams as equally important. A weighted version - in which stream importance is calibrated to project type and development stage - is a logical next step but introduces subjectivity that the current binary architecture avoids.

Empirical validation: The framework has been developed in parallel to a number of diagnostic development programmes, including the development of CE-marked liver cancer diagnostics at Ophiomics, and is used regularly in due diligence work for investors and in grant evaluations. It has not been subject to prospective validation, inter-rater reliability testing, or formal comparison with development outcomes.

What DRL is not: The framework is not an HTA method, a regulatory pathway, or a costing tool. It does not replace the IVDR technical file, the HTA dossier, or the business plan. It is a readiness assessment instrument - a structured way to ask whether the evidence that those processes require is being built in the right sequence, at the right time, across all five dimensions simultaneously.

The DRL framework is offered in the spirit of a working instrument: useful now, improvable with use. Groups with retrospective portfolios of diagnostic development programmes, incubators, technology transfer offices, and HTA bodies interested in stress-testing and calibrating DRL are explicitly invited to collaborate. Near-term priorities include retrospective application to completed programmes across at least two independent evaluators, and an inter-rater reliability study to test whether the

gate structure produces consistent assessments across practitioners with different backgrounds.

9. Conclusion

The diagnostic development journey fails most often not on the science but on the coordination of parallel tracks that existing frameworks do not make visible. The DRL framework addresses this by providing a structured, multi-dimensional assessment across five streams and thirteen levels, with a weakest-stream rule that makes imbalances explicit and a pass criterion grounded in evidence existence rather than progress claims.

It is not a checklist. It is a map - one that shows where each dimension of a development programme stands, where the gaps are, and where the next investment should go. Used well, it changes the conversations that matter: between founders and investors, between development teams and TTOs, between companies and regulators, and between diagnostics developers and the health systems they are trying to serve.

References and Related Resources

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- ACCE Model for evaluation of genomic tests. CDC Office of Public Health Genomics.
- REASSURED criteria for point-of-care diagnostics. WHO/FIND.
- EU HTA Regulation 2021/2282 (Joint Clinical Assessment).
- IVDR (EU) 2017/746 - In Vitro Diagnostic Medical Devices Regulation.

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Full scoring instrument: DRL Scoring Instrument v1.0 (companion document)

Download and resources: pereiraleal.com/drl