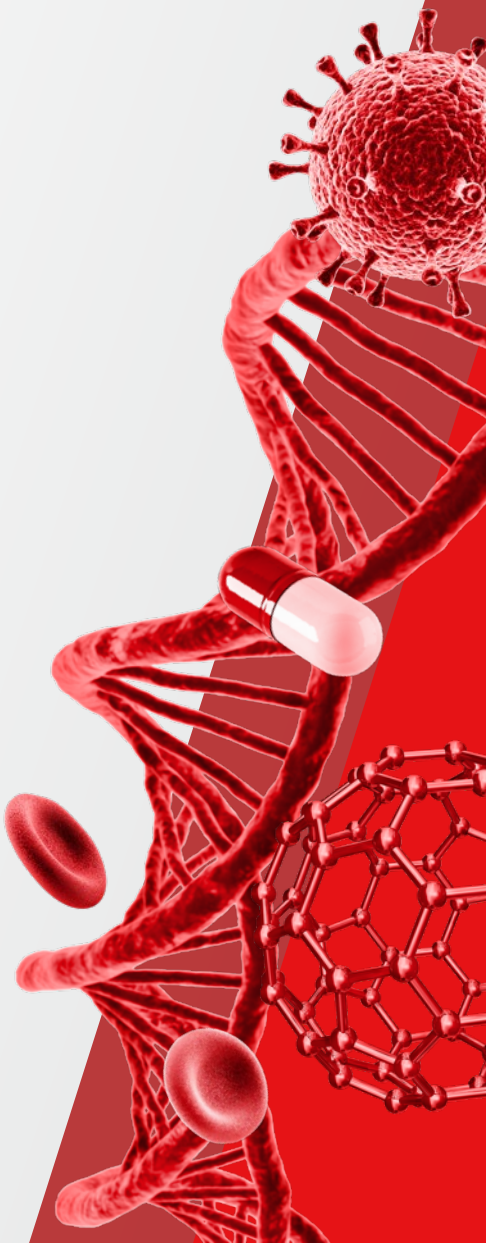
A change is gonna come; the road to sustained clinical adoption of novel IVD tests

Ste Harding

July 18th 2025



The world leader in serving science

The Binding Site Journey

Established brand and strong track record of innovating and successfully bringing its innovations to market

1960s: Department of Immunology at Birmingham University active in researching the use of sheep to develop antisera reagents

1960

1970s: Antisera collaboration ongoing with Unilever

1970

TBS established

1983

Launch of IgG subclass commercial testing kits

1984

Tolerisation technology developed

1996

First Freelite™ publication highlighting clinical significance, as well as FDA approval

Antisera farm established in Vermont (US)

2001

2006

Mayo clinic recommends Freelite™ as a routine Multiple Myeloma screening test

2008

SPAplus launched

2009

Hevylite™ product launched in European market

The AutoImmune (AI) product group is sold to Werfen

2010

Freelite™ receives Japanese approval

2011

Hevylite™ patents granted

Binding Site acquired by the Sponsors

NORDIC CAPITAL Five Arrows Principal Investments

2012

Completed move into state-of-the-art HQ & manufacturing facility

2014

Revised IMWG guidelines recommend Freelite for SMM[1]

Extended farm facilities in Vermont (US)

2015

Optilite launch

2016

iSTOPMM Trial commences

Mass Spec licensing agreement signed with Mayo Clinic

2017

New Warehouse/Distribution Centre opened and operational – Sovereign Road

Mass Spec Laboratory opened in Rochester MN

2019

Mass Spec α-sites planned and initiated

2022

Acquired by Thermo Fisher Scientific

2023

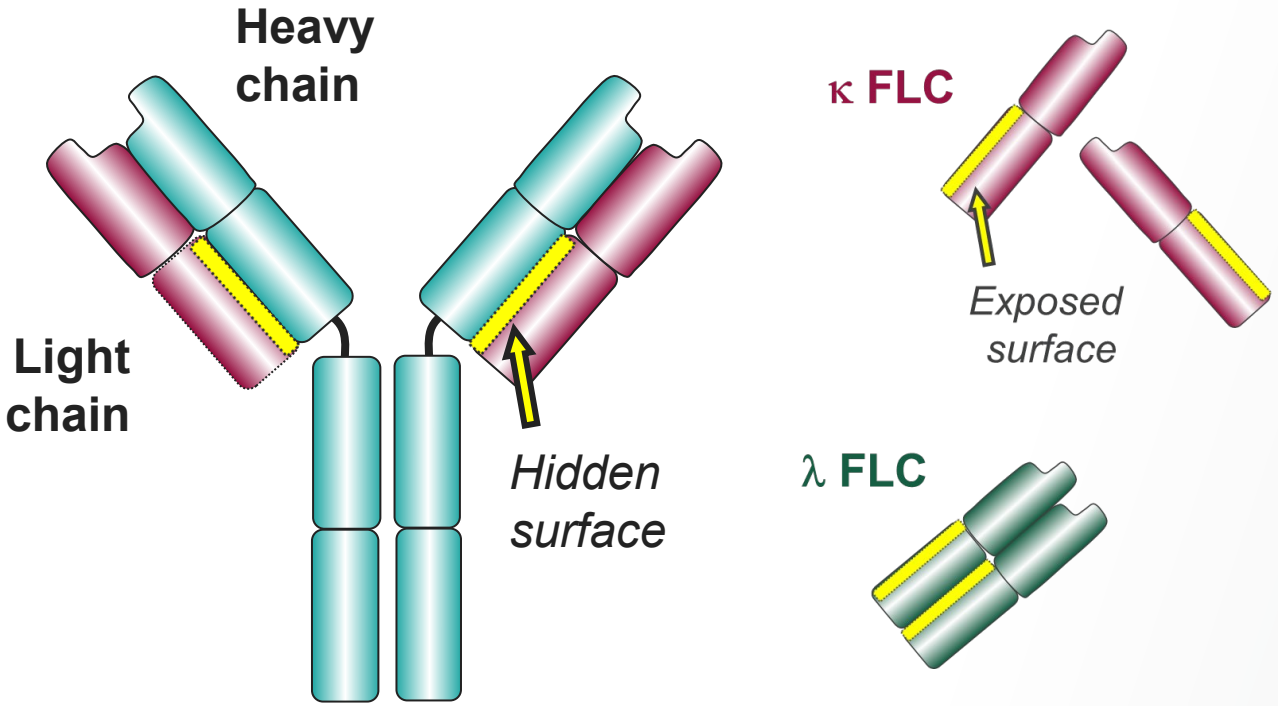
EXENT IVDR launch

2025

SUBSIDIARIES / REP. OFFICES FOUNDED

1983 · 1988 · 1993 · 1996 · 2008 · 2010 · 2013 · 2014 · 2015 · 2017 · 2018 · 2019

Serum Free Light Chain



Clinical Chemistry 47:4
673–680 (2001)

Enzymes and Protein Markers

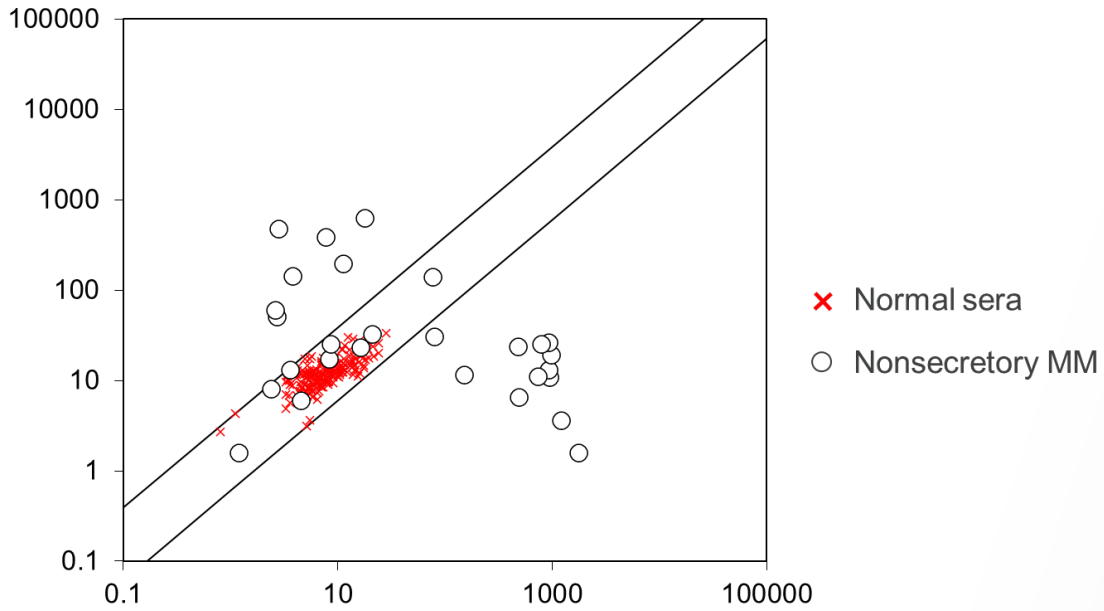
Highly Sensitive, Automated Immunoassay for Immunoglobulin Free Light Chains in Serum and Urine

Arthur R. Bradwell,[1*] Hugh D. Carr-Smith,[2] Graham P. Mead,[2] Lian X. Tang,[2] Paul J. Showell,[2] Mark T. Drayson,[1] and Roger Drew[2]

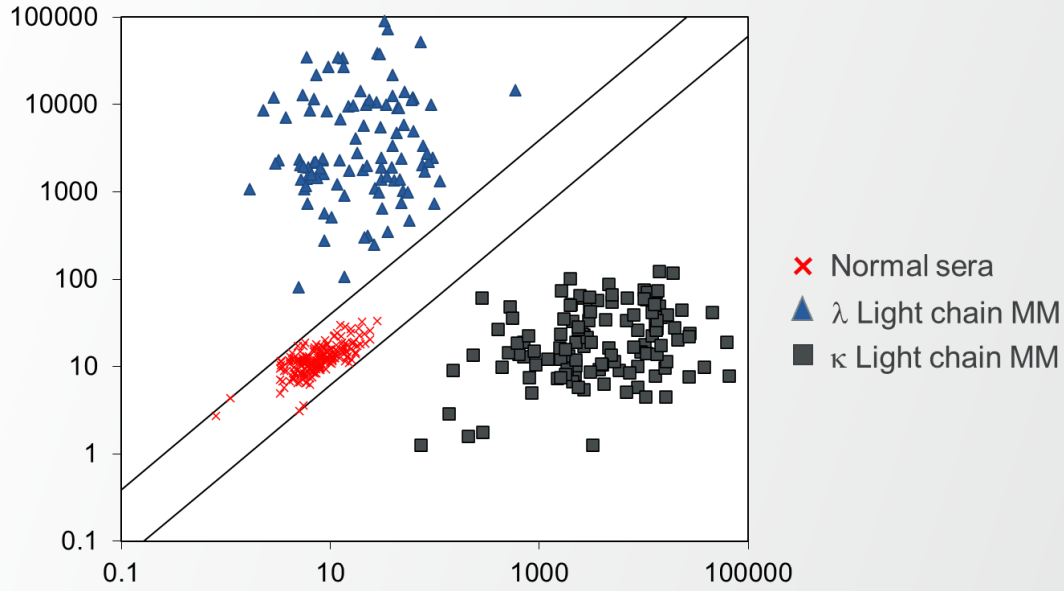
We agree that sensitive and accurate immunoassays for FLCs can be useful in clinical laboratories for studying the renal handling of polyclonal FLCs in various conditions. **We do not agree, however, that this type of assay can be used to detect Bence Jones protein (BJP) in serum or urine.**

Maria Stella Graziani[1*]
Giampaolo Merlini[2]

Serum Free Chain, Evidence Generation

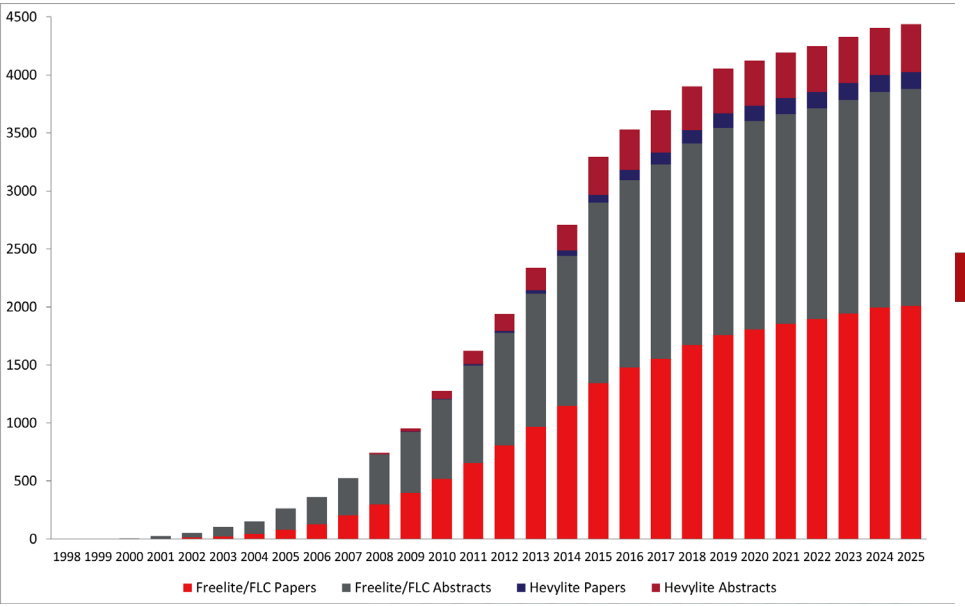


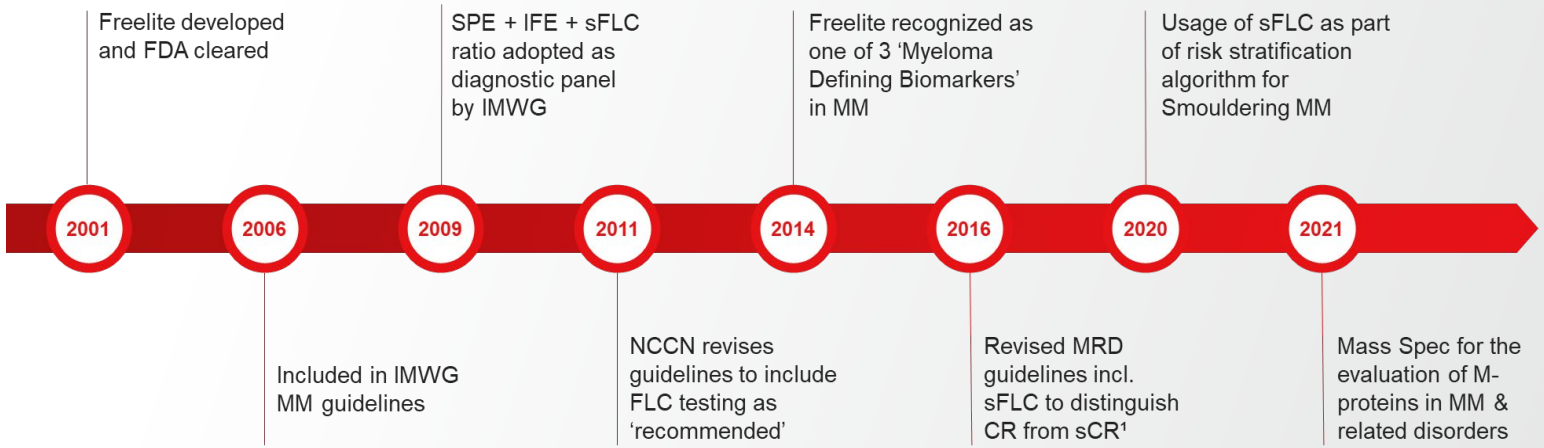
Drayson Blood 2001;97:2900–02



Bradwell Lancet 2003;361:489–91

Publication to Guidelines





A Breakthrough in Monoclonal Gammopathy Assessment

The EXENT® System is an automated solution that enables M-protein identification and measurement in serum with enhanced sensitivity beyond conventional methods

The EXENT® Analyser

The EXENT® Analyser consists of three integrated modules, **automating the mass spectrometry workflow.**

EXENT® Analyser

Prepare

Automatically isolate immunoglobulins using isotype-specific paramagnetic reagents

Analyze

Rapidly analyze samples by MALDI-TOF mass spectrometry with load and click technology

Data review

Easily review and release quantitative results using simple intuitive interface

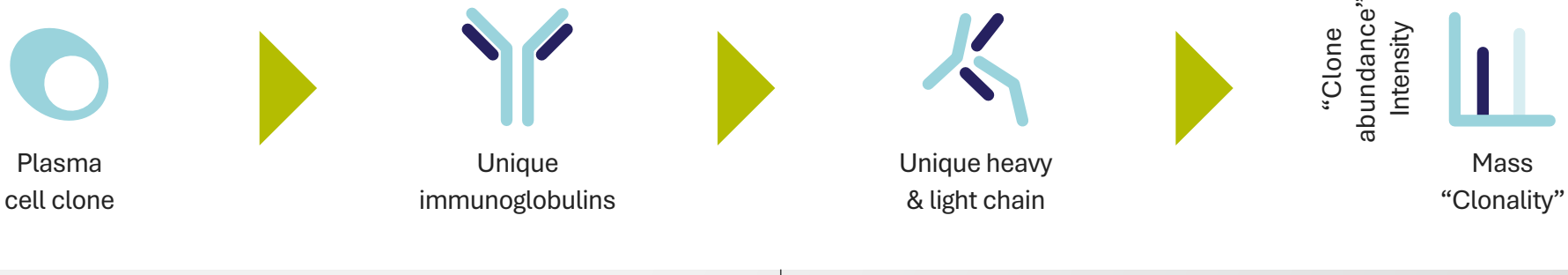
Integration for quantification

Optilite® Analyser*

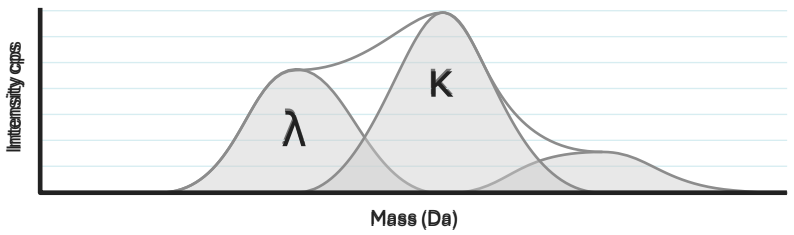
*Optilite® Analyser is not part of the EXENT® Analyser

A New Paradigm for the Detection and Quantification of M-proteins

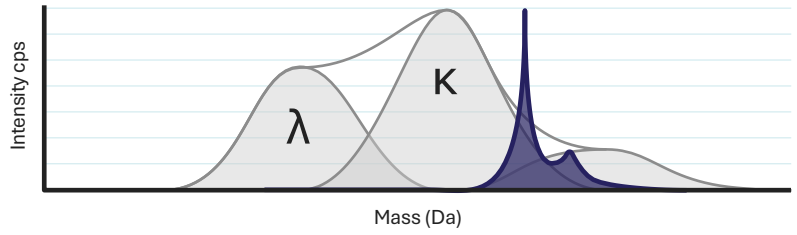
The EXENT® System identifies monoclonal proteins by their unique molecular mass



A: In a healthy individual light chains reduced from immunoglobulins are normally distributed



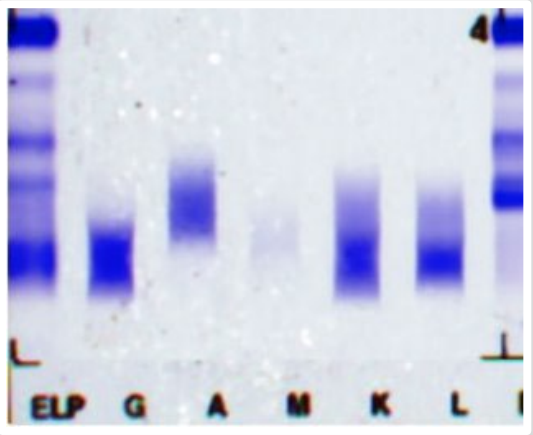
B: Presence of monoclonal proteins is indicated by sharp peaks in the reduced light chain distribution



Some monoclonal gammopathies can be difficult to diagnose due to low M-protein concentrations.[1-3]

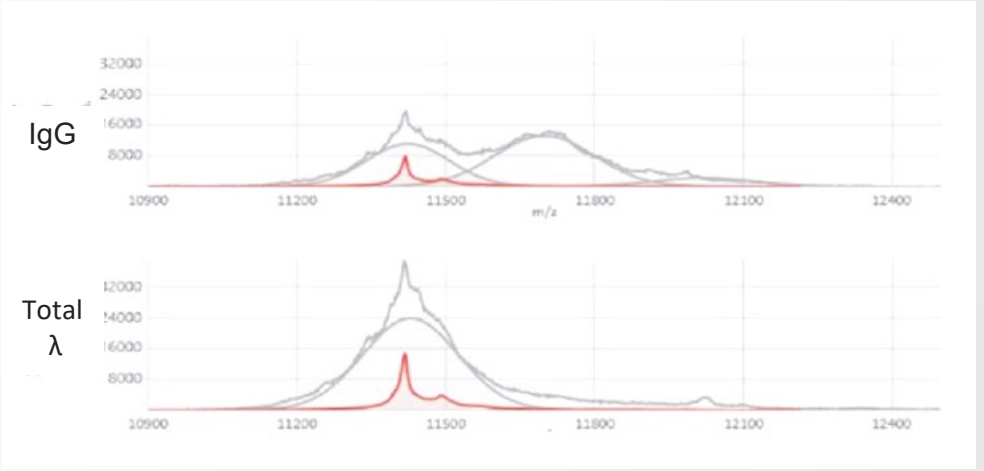
A patient with a confirmed diagnosis for AL amyloidosis was found to be negative by all measures of M-protein in the serum and urine.

Their original diagnosis was confirmed by a tissue biopsy and Congo red stain.



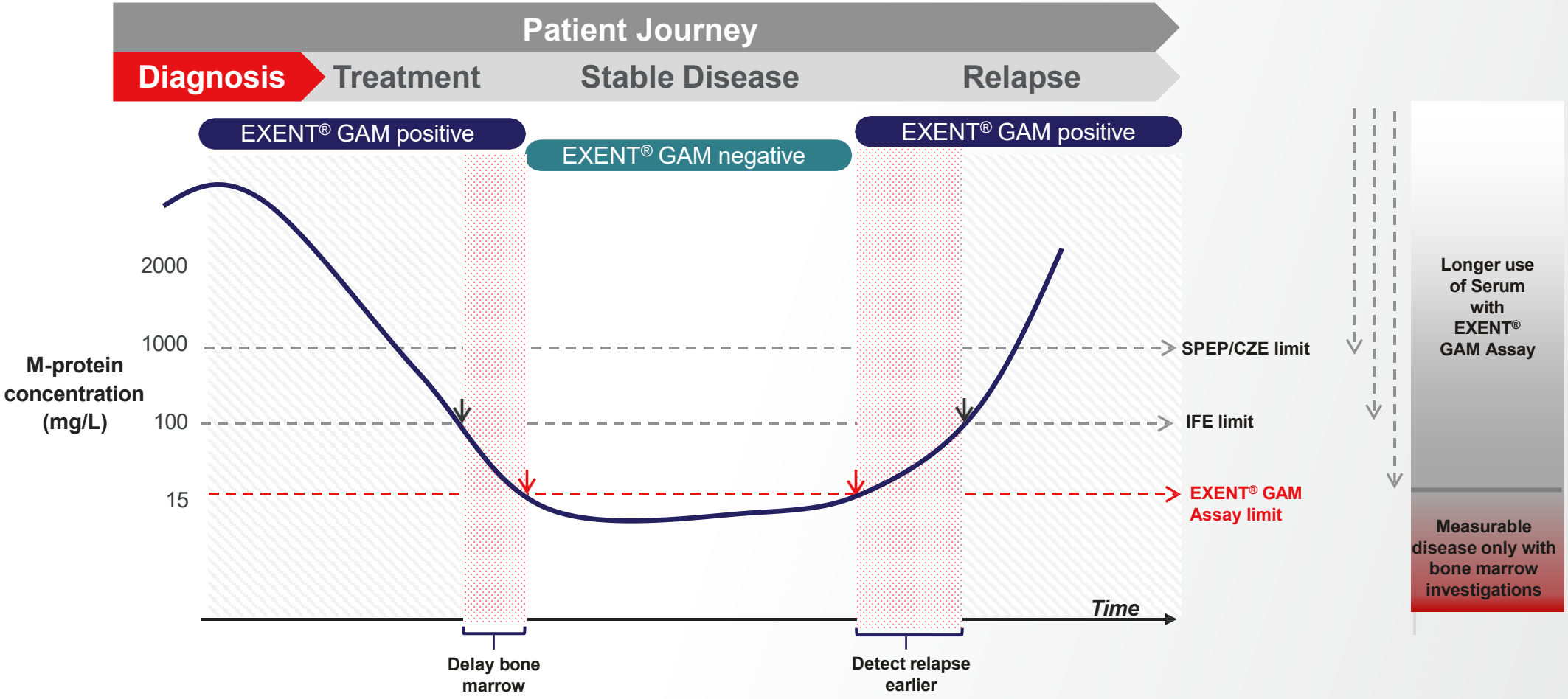
Serum IFE was negative for M-protein

The EXENT GAM assay identified an IgGλ M-protein at a concentration of 2.42 g/L



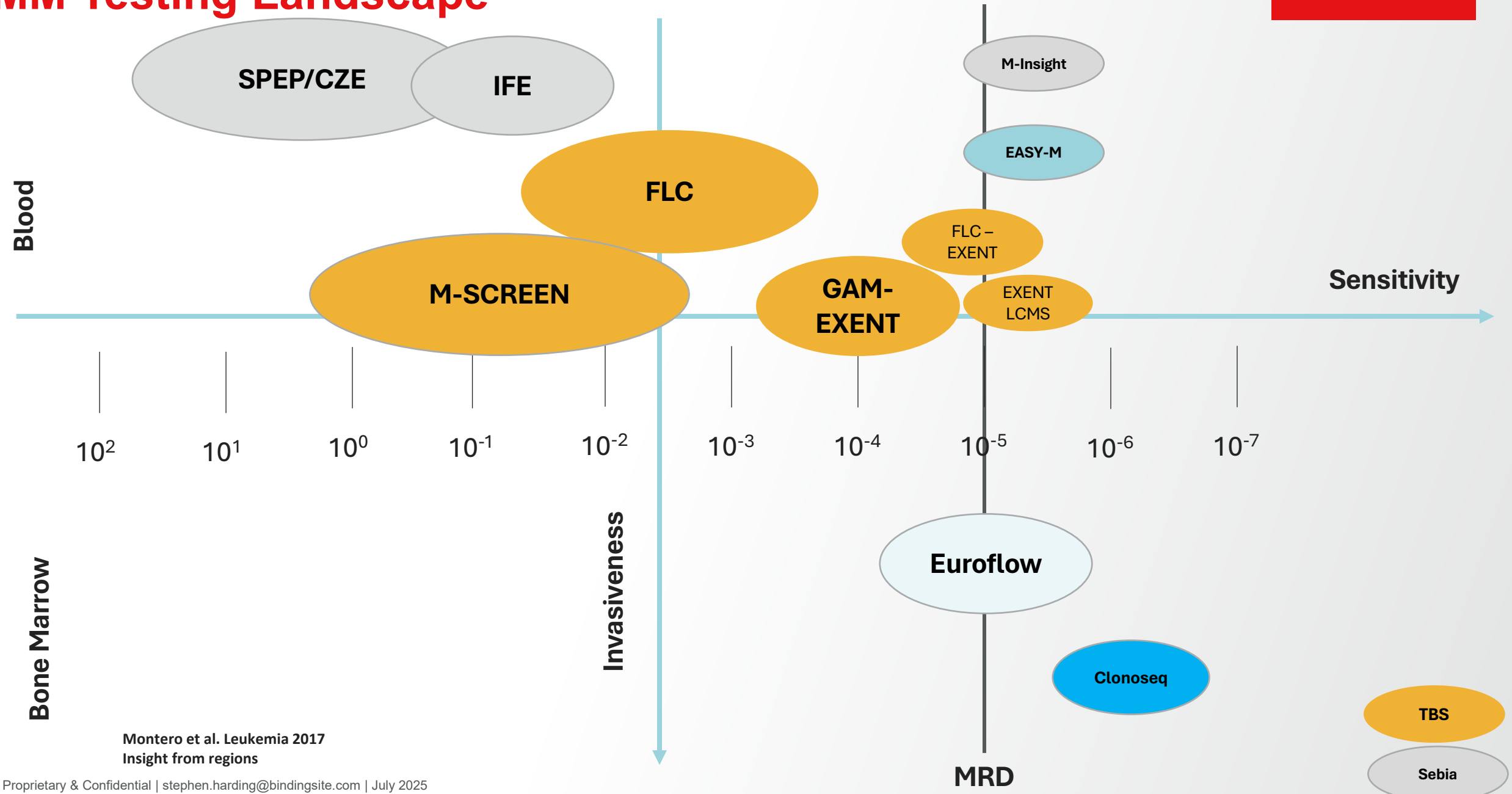
1. Elsayed, et al. J Hematol. 2021, 10(4): 147-161; 2. Roque, et al. BMJ Case Rep. 2021, 14(4): e240404; 3. Dupuis, et al. Onco Targets Ther. 2016, 9: 7583-7590

Value in Routine Use



~6-12 Immunoglobulin isotype tests per year depending on place in the patient journey

MM Testing Landscape

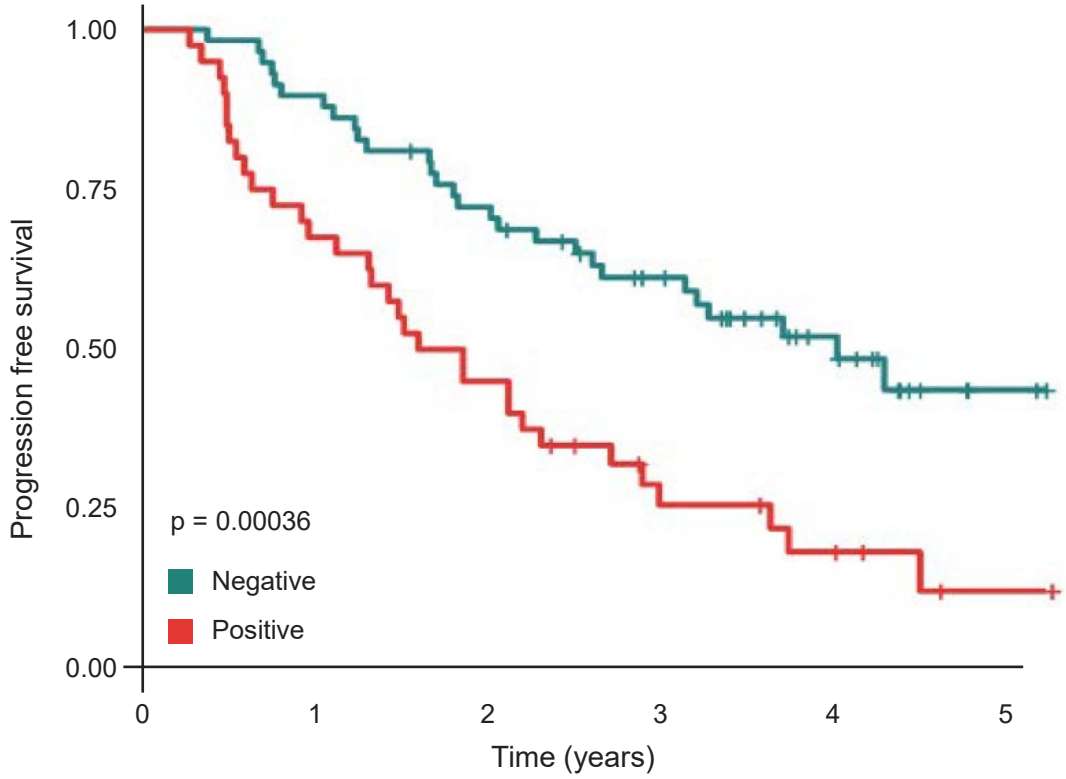


Montero et al. Leukemia 2017
Insight from regions

Is identifying residual M-protein beyond CR meaningful?

EXENT identified M-proteins in 41% (40/98) of patients that had been assigned CR by conventional methods.

Patients assigned CR and MS positive had a median progression free survival (PFS) to maintenance of 1.7 years compared with 3.3 years in patients who were assigned CR and MS negative.



In this study it was determined that patients who achieve CR and are EXENT negative have better PFS than those who achieve CR and are EXENT positive.

Mai EK, et al. Blood Cancer Journal 2023; 13:1-9

A Breakthrough in M-Protein Assessment

Guidelines

MALDI-ToF MS technology endorsed by IMWG-MS committee for clinical practice as an alternative to IFE [1]

M-protein precise identification

Easily differentiates known therapeutic monoclonal antibodies from patient's monoclonal protein[2, 3]

The EXENT GAM Assay offers insights into M-protein light chain glycosylation[4]

Measuring serum M-protein beyond IFE

Accurate diagnosis for patients with low level of M-protein[5]

Higher sensitivity compared to IFE across MM patient treatment journey[6]

Detect residual disease in samples from patients assigned CR[2,6,7]

Identifies different risks of progression in MM patients when IFE and CR status did not[6]

Enable Kinetics of response

A non-invasive strategy for evaluations of the kinetics of response [6]

Kinetics of response identify different patient outcome in term of PFS[6]

Sustained negativity or conversion to negativity associated to longer PFS[6]

During maintenance, the conversion to positivity is associated to an imminent clinical progression[6]

Early biochemical relapse detection: Detects relapse over 5 months before SPE[8]

Cost-saving

The higher sensitivity of EXENT GAM compared to sIFE leads to a significant reduction in premature MRD tests and may be cost-saving for testing patients with MM in France. [9]

Potential to guide the appropriate timing of MRD tests based on BM aspirations.[6,10]

*The EXENT System consists of the following CE marked products: EXENT Analyser, IE800 (IVDR Class A, nonsterile); Immunoglobulin isotypes (GAM) for the EXENT Analyser - MSR801.M (IVDR Class C)
EXENT Immunoglobulin Isotypes (GAM) Control Pack - MSQ801.M (IVDR Class C)
**Only in countries where the product is launched. MM, Multiple Myeloma

[1]Murray et al., Blood Cancer J 2021, [2] Eveillard et al., Clin Chim Acta 2021, [3]Barnidge et al., JALM 2024, , [4] CST031_1124_EXENT Case Study - New perspectives on monoclonal proteins, [5] CST029_1124_EXENT Case Study - Accurate diagnoses for patients with low-level M-protein, [6]Puig et al., Blood 2024, [7]EXENT GAM Assay IFU (instruction for use), [8]Li et al., ASH 2022, [9]Siegfried C. and al, ClinicoEconomics and Outcomes Research 2025:17 107–114, [10]Puig et al., Haematologica 2024.

Market Access, Value & Evidence (MAVE)

Drivers that shape the demand for MAVE capabilities

External: Stakeholder Demand for Value

- Accelerating demand for evidence to demonstrate value from healthcare stakeholders
- The value of our products is increasingly measured in terms of clinical utility and economic impact rather than technical performance alone
- Decisions by purchasers and prescribers will be made in the context of evidence of value relative to alternatives

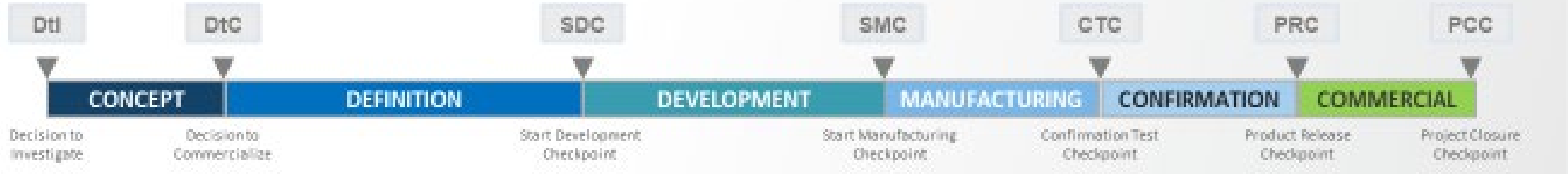
Internal: Portfolio Dynamics and Competitive Advantage

- Range of disease areas and clinical applications (e.g., screening vs. diagnosis vs. monitoring)
- Launching novel Dx content may require significant evidence investment vs. what is needed for established biomarkers
- Demonstrating success in deploying MAVE capabilities to secure incremental payment over competitive tests to capture unique value

Key Considerations

- Delivering value requires a deep **understanding of stakeholder evidence needs** and priorities
- Demonstrating value will require a robust **understanding of care pathways** to identify unmet needs, develop value propositions, and supporting evidence
- Need to understand **when clinical and economic evidence can support differentiated value**, is required to match competitors, or when it may not make a difference at all
- Routinely **assessing "Evidence ROI" upstream** will be an essential MAVE capability
- To build a holistic value story for a diagnostic test, we must consider both clinical and non-clinical values, including validity, utility, and often health economics
- Integrated evidence planning embeds holistic evidence thinking and requires a detailed roadmap developed upstream that supports **value assessment, value demonstration, and value communication beyond regulators and lab providers**

MAVE Considerations Must be Embedded Routinely in Product Development to Inform Strategy and go/no-go Decisions



Value Assessment | **Value Demonstration** | **Value Communication**

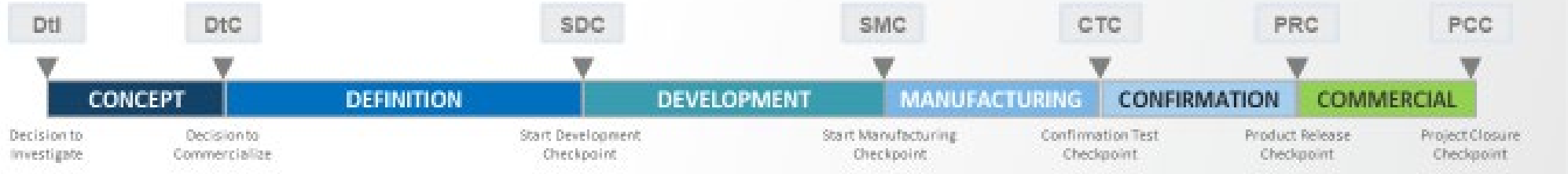
High-level MAVE activities	*Identify value and access challenges and opportunities*	*Establish evidence-based value proposition potential*	*Formalize MAVE strategy and build into clinical and marketing plans*	*Reassess and update strategy and prepare supportive publications*	*Evaluate market experience and invest in new evidence to anticipate demand*

Upstream
- Understand / monitor unmet needs, evidence, and policy context
- Assess evidence needs, gaps, and build a value-demonstration plan

Downstream:
- Coordinate efforts to demonstrate and communicate value supported by evidence

MAVE activities should be aligned with innovation, development, and commercialization processes to optimize reimbursement

MAVE Considerations Must be Embedded Routinely in Product Development to Inform Strategy and go/no-go Decisions



Value Assessment → **Value Demonstration** → **Value Communication**

Example Upstream Activities:

- Clinical Pathway / Unmet Needs Analysis
- Policy Monitoring (Access, Regulatory)
- Scientific / Medical Advisory Board
- Evidence Needs Assessment
- TPP MAVE Input
- Market Access Landscape and Strategy
- HEOR Landscape and Strategy
- Regulatory Landscape and Strategy
- Integrated Evidence Planning

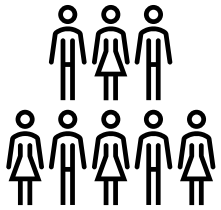
Example Downstream Activities:

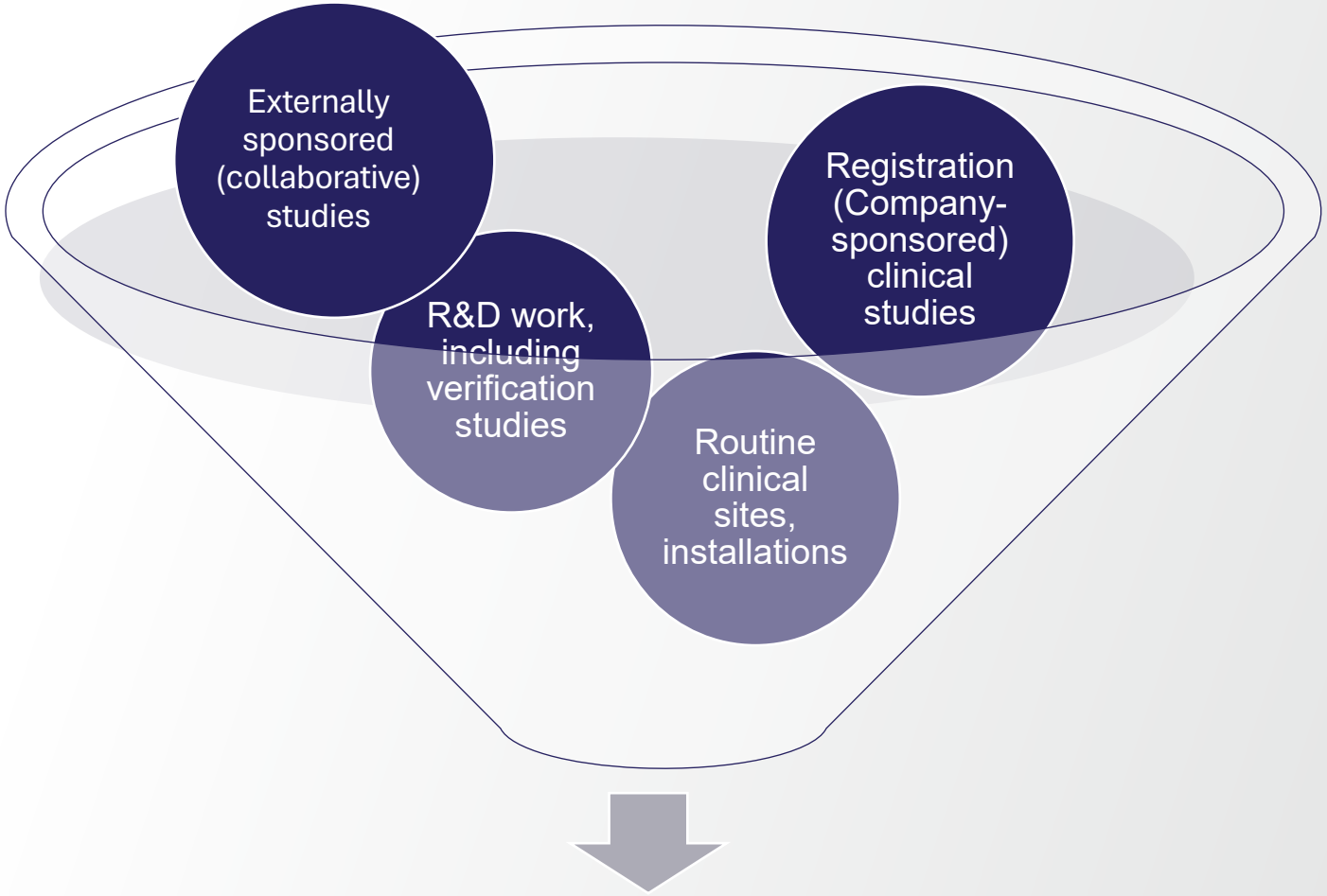
- Study Execution
- Regulatory Submission
- Sustaining: Claims Extension, RWE
- Guidelines Inclusion Strategy
- Patient Advocacy
- MedSci and Value Communication + Tools (HE Models, Value Dossiers, Manuscripts, etc.)
- HTA and Payor Engagement

MAVE activities should be aligned with innovation, development, and commercialization processes to optimize reimbursement

Evidence Generation

- **Scientific evidence support:**
  - Value proposition
  - Positioning
  - Laboratory adoption and clinical adoption
  - Market access, reimbursement
- **Resources Required**
  - R&D Scientists
  - Medical Affairs Specialists (Global Medical and Scientific Affairs)
  - Medical Science Liaisons (Field MSLs)
  - Medical Writer
- **Collaborators & Customers**





Peer reviewed publications, posters

Final Thoughts

- Historically, new technologies could be launched on their innovation and clinical impact alone
- IVDR, FDA and other regulatory bodies are looking to robust clinical evidence rather than predication to support registrations, especially in the absence of international standards
- IVD innovation, alongside an agile approach to MAVE is increasingly required to help establish new tests
- Access to well characterised samples, key opinion leaders, healthcare economics are now part of our upfront planning
- Despite headwinds, there has never been a greater need for IVD innovation


The road ahead is hard,
so is it worth it?

YES

Thank You