MD squared
Growing Medtech Together

EPIC
EUROPEAN PHOTONICS INDUSTRY CONSORTIUM

Clinical Evaluation

What does it take to bring your innovation to market under MDR?

EPIC Meeting on Photonics assisted Cancer Pathology & Surgery

University Hospital Antwerp
Claus Schaffrath, MD MSc
30-11-2023

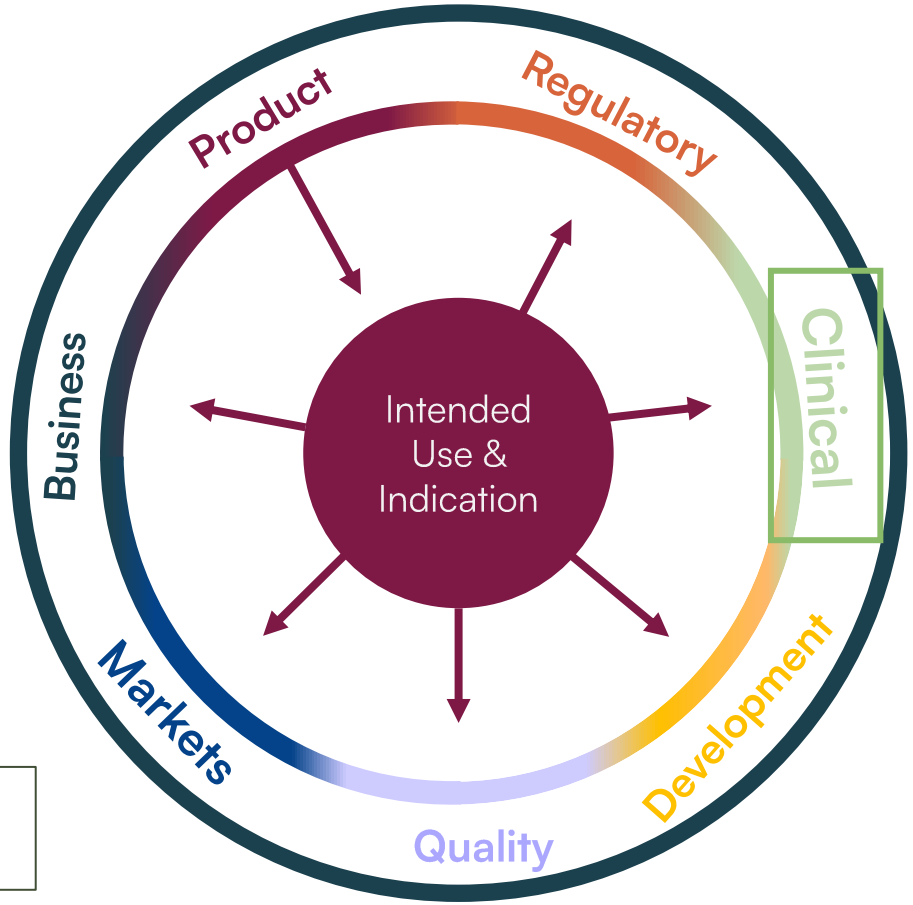
For a Medical Device Clinical Evaluation it starts with:

"What does your technology do exactly?"
(Intended Purpose)

AND

"What happens today without your device?"
(Applicable Standard of Care or
Treatment Alternative)

Product Definition & Intended Purpose are the Cornerstones for your Clinical Evaluation and Regulatory Approach



e.g. Classification, regulatory pathway

e.g. Addressable market, Competition, GTM

e.g. Study requirements, Clinical Dev. Plan

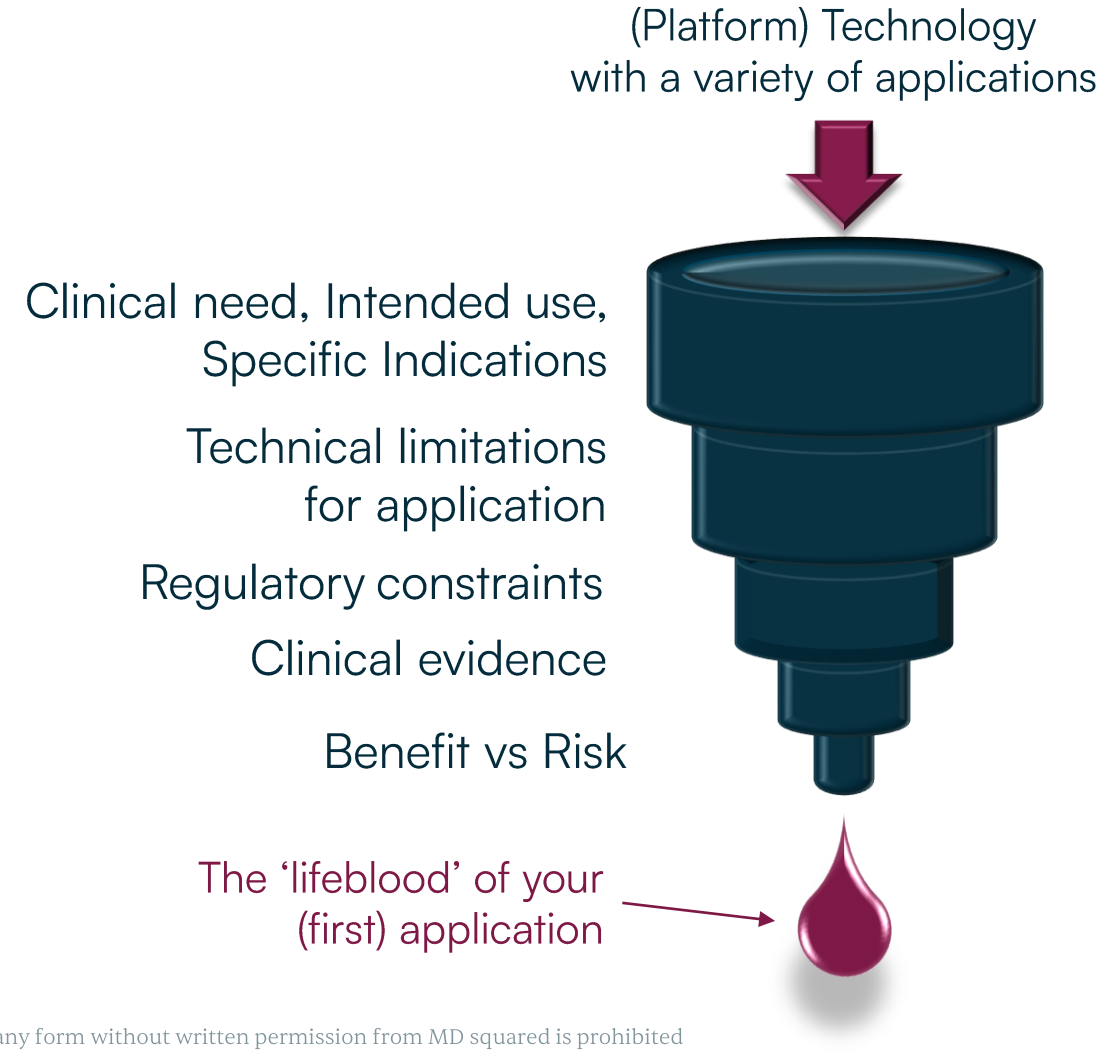
e.g. Reimbursement codes, local SoC

e.g. Specific requirements

e.g. Risk-analysis, QMS/ supplier management

From Technology to '*Product definition*'

A stepwise approach to define **what the product does** and by **whom it will be used for what.**



MD Squared - Expert Insight

Make the intended use as broad as possible & the indication for use specific

What are the Rules on Clinical Data for a Regulatory Purpose?

Clinical Evaluation (incl. Clinical Investigation)

Clinical Evaluation & Clinical Investigation

MDR - Art. 61 & 62ff. – Annex XIV and XV

- Clinical Evaluation

CHAPTER VI

CLINICAL EVALUATION AND CLINICAL INVESTIGATIONS

Article 61

Clinical evaluation

1. Confirmation of conformity with relevant general safety and performance requirements set out in Annex I under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit-risk- ratio referred to in Sections 1 and 8 of Annex I, shall be based on clinical data providing sufficient clinical evidence, including where applicable relevant data as referred to in Annex III.

Clinical Evaluation & Clinical Investigation

Art. 61 & 62ff – Annex XIV and XV

Clinical Evaluation

3. A clinical evaluation shall follow a defined and methodologically sound procedure based on the following:

(a) a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device, where the following conditions are satisfied:

— it is demonstrated that the device subject to clinical evaluation for the intended purpose is equivalent to the device to which the data relate, in accordance with Section 3 of Annex XIV, and

— the data adequately demonstrate compliance with the relevant general safety and performance requirements;

(b) a critical evaluation of the results of all available clinical investigations, taking duly into consideration whether the investigations were performed under Articles 62 to 80, any acts adopted pursuant to Article 81, and Annex XV; and

(c) a consideration of currently available alternative treatment options for that purpose, if any.

Clinical Investigation
Art. 62 – 81 - Annex XV

Clinical Investigation

Clinical Data from a Clinical Investigation for the device needs to be provided unless

- Substantial equivalence (Technical, Biological and Clinical) with an already marketed device can be demonstrated for which adequate clinical data is available.
- The manufacturer has access to this data and its continuous updates.

- For implantable and Class III devices (with some exemptions) a Clinical Investigation is **mandatory** unless adequate data is available on an earlier not significantly modified (i.e. substantial equivalent) version of the device.

…. In God we Trust All Others Must Bring Data *(W. Edwards Deming)*

Clinical Evaluation & Clinical Investigation

Art. 61 & 62ff – Annex XIV and XV

A potential loophole for low-risk devices?

10. Without prejudice to paragraph 4, where the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception shall be given based on the results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performance intended and the claims of the manufacturer. In such a case, the manufacturer shall duly substantiate in the technical documentation referred to in Annex II why it considers a demonstration of conformity with general safety and performance requirements that is based on the results of non-clinical testing methods alone, including performance evaluation, bench testing and pre-clinical evaluation, to be adequate.

What Clinical Data do I need?

Clinical data

"If we can't avoid a clinical study before CE, let's make it 30 patients... That should be sufficient"

The **required clinical data** is not the same for each medical device,
it depends on:

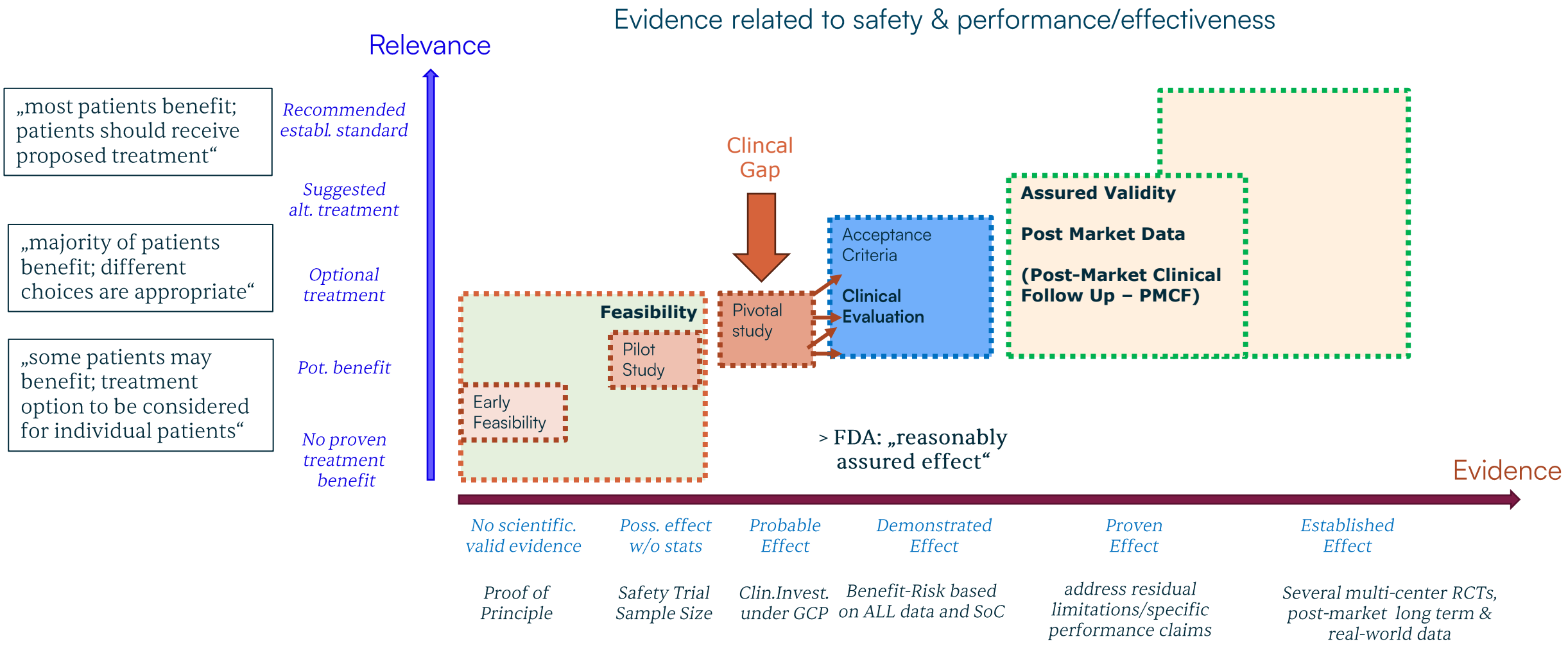
- **Its intended use & indication**
- **Its Risk Classification**
- **Its safety & performance profile** in relation to the applicable **Standard of Care or Alternative Treatments**

Clinical data - Claim substantiation

type of (clinical) data	costs	strength	time
anecdotal (KOL) statement	$		
survey data, case report	$$		
bench test, simulations, pilot study	$$		
cohort study/ observational study	$$$		
comparative study (RCT), meta analysis	$$$$		
multi-center RCT	$$$$$		
post-market clinical follow-up	$$$		
post-market real world data	$$		

**acceptable clinical threshold for regulatory*

Clinical data – Level of evidence



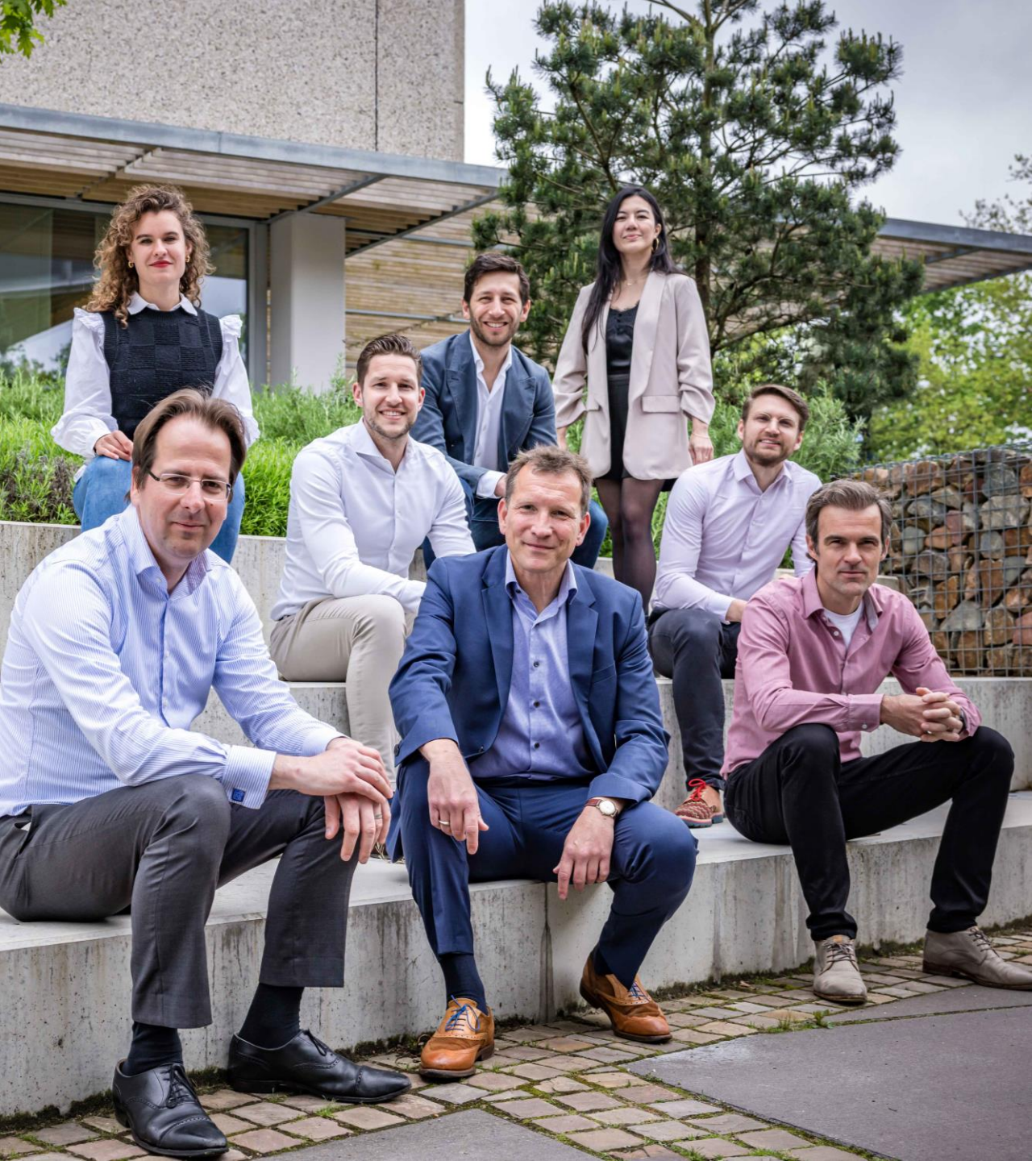
Conclusion

- All **Cinical Evaluations** hinge on
  - the Intended Purpose of the Medical Device,
  - the inherent Risks of its application and
  - the applicable **Standard Of Care** or Alternative Treatment

- Based on the available own data and literature on the device and alternatives a **Clinical Data Gap** needs to be determined.
- This data gap then needs to be covered with a pre-market **Clinical Investigation** to establish the safety & performance of the Medical Device and its Benefit-Risk Profile for **Market Access.**

- The Study design hinge on the Intended Purpose, the Comparator (SoC) and the detectability of desired and undesired effects.
- For Market Acceptance further in Post-Market Clinical Follow-Up (PMCF) Studies are needed to confirm the safety profile of the Device, and to potentially demonstrate specific claims.


What can we do for you?



MD squared B.V.

Competence • Curiosity • Care

Our aspiration is a world where meaningful MedTech innovations reach patients in time.

Growing MedTech Together is our contribution in helping our clients making informed choices in the complex and regulated MedTech environment, and in executing them towards market success.

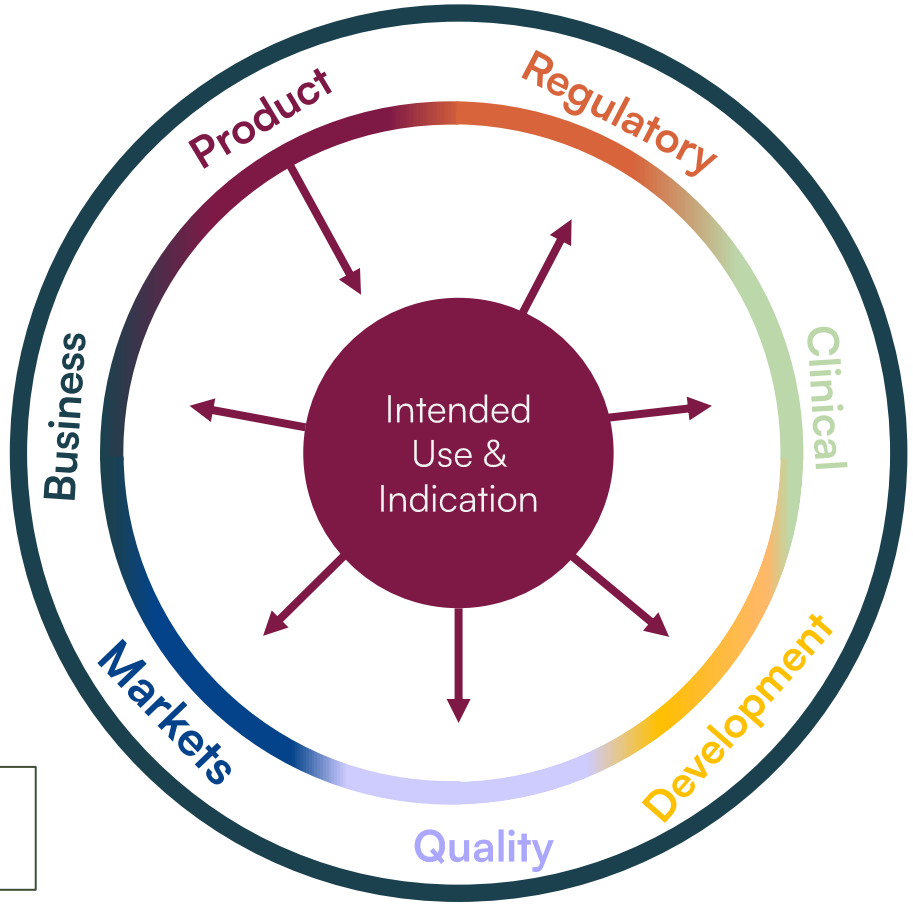
We firmly believe in our multi-disciplinary approach of problem solving and decision making. Every MedTech innovation brings business, product, clinical, regulatory and technical challenges, which are intertwined and require holistic insights.

With over a 100 years of hands-on MedTech experience together in our fields of expertise, we still love to continuously learn from each other and our clients in developing fit-for-purpose support to their needs.

Founded in 2017 we have our offices in Eindhoven & Rijswijk, The Netherlands.


What can you do for us?

If you have a tough nut to crack in getting your Innovation to the Market, we like to take on the challenge :)



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We support our customers in making
informed decisions to successfully bring
their innovations to market

Seasoned professionals in MedTech

We have experience in the fields of Regulatory, Quality, Clinical, Research & Development, Business strategy, Marketing & Sales

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Office Manager

Abel Swaan, PhD
Clinical Consultant

Nancy Zhang, MSc RCA
Regulatory Affairs Consultant

Our services

QuickExam™

"A fast and structured assessment of the core of the innovation proposition from different angles."

- Product: definition, intended use, claims and classification
- Regulatory: Regulatory requirements and applicable standards (MDR/IVDR, FDA and SFDA)
- Clinical Data Analyssi: Clinical Evaluation, Clinical Studies and PMCF
- Development & Manufacturing: Technical Documentation, Adequate Product Design and Validation
- Quality: Risk-based QMS according to ISO13485:2016
- Market: Evaluating the addressable market, SoC and treatment alternatives
- Business Strategy: Viability of business case & differentiation

Venture Support

"Support and guide Start- & Scale-Ups towards Market Access and Market Acceptance."

- Reimbursement: strategic positioning for EU & US reimbursement & pricing
- Regulatory Support: Communication with Competent Authorities and Notified Bodies throughout market access process in EU, US, UK, China.
- Clinical Planning: Clinical Investigational Study Design, Clinical Evaluation, Post-Market Clinical Follow-Up
- Development support: Regulatory insights required for development (e.g. GSPR-based product requirements)
- QMS: build and implement an ISO13485:2016 quality management system
- Strategic Review/Audit: Develop Scenarios & Assess Impact

‘A key role in the Medtech industry’

‘We performed QuickExam for the current state of our development with MD squared. This provided us with a very solid stepping stone to also plan activities, timelines and budget for our quality & regulatory infrastructure, and for the efforts necessary towards introduction into the clinic’

Jeroen Kodde, CEO — Kaminari Medical

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