NoBoCap COMMUNITY

NOBOCAP COMMUNITY SUMMIT 2025

WEDNESDAY
OCTOBER 15 | 2025
BRUSSELS

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BRINGING TOGETHER EUROPE TO UNLOCK MEDICAL DEVICE REGULATIONS & THE AI ACT FOR INNOVATORS AND SMES IN EUROPE

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PRE-CONFERENCE WORKSHOPS

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Draft Guidance on Breakthrough devices under 2017/745 and 2017/746 versions 2.0 BtX

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Guidance Breakthrough

Scope

Guidance for manufacturers, expert panels and notified bodies on the process and regulatory considerations relevant for qualifying, assessing and certifying breakthrough medical devices and breakthrough IVDs.

This guidance also provides considerations on the clinical evaluation / performance evaluation of these **technologies.**

This guidance applies to all device risk classes.

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Guidance Breakthrough

Criteria – Under discussion

Technological

- The device introduces a high degree of novelty with respect to the device technology or the related clinical procedure,

AND

Clinical

- The device is expected to provide a significant positive clinical impact **on patient or public health**, for a life-threatening or irreversibly debilitating disease or condition, by either of the following:
  - Offering a significant positive clinical or health impact compared to available alternatives and the state of the art, OR
  - Fulfilling an unmet medical need where there is an absence or insufficiency of available alternative options for that purpose.

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Breakthrough (under discussion)

Table 1: Determining breakthrough devices based on technological and clinical criteria

Clinical impact on patient or public health for a life-threatening/irreversibly debilitating disease or condition **Degree of Novelty** Device or procedure related	**Minimal positive clinical impact** *Non-inferior but does not offer significant clinical benefit above alternatives/SOTA*	**Moderate positive clinical impact** *Offers significant clinical benefit to certain patients in a health area compared with alternatives/SOTA*	**Major positive clinical impact/New SOTA** *Redefines the SOTA by fulfilling an unmet medical need where no alternatives exist, or by offering a major clinical benefit above alternatives*
Minimal / Incremental *Minor/iterative change from alternative(s) / SOTA*	Next in class / "me too" device/IVD	Moderate incremental improvement	Major incremental improvement
Disruptive innovation *New design, manufacture, use, or procedural approach that significantly differs from alternatives/SOTA (e.g., first-in-class device)*	Non-breakthrough innovation	**Breakthrough device**	**Breakthrough device**
Paradigm shift *Disruptive innovation that represents a fundamental scientific, technological, or procedural change in a health area*	Non-breakthrough paradigm shift	**Breakthrough device**	**Breakthrough device**

As novelty increases, the uncertainty increases with respect to the safety or performance of the device and risks associated with the new technology. Three qualitative levels of uncertainty can be described:

Low level of uncertainty: Expected safety and performance well understood. Unlikely to have unidentified risks

Medium level of uncertainty: Possible that there are existing unidentified new/emerging risks

High level of uncertainty: Likely to have existing unidentified new/emerging risks

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Sections – Under discussion (1)

Breakthrough Definition (and acceptance rate)

Designation : By EMA – Expert PANELS

PART A : Clinical / Performance Evaluation Considerations

- Balance of pre- and post market data collection
- Role of non-clinical & pre-clinical
- Pre and post market trial design

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Appendix A.2 – Considerations on Clinical investigation designs for BtMD

Potential CI designs for high risk (Class III / implantable) breakthrough MD*					
	Initial/Early	**Pre-market confirmatory**	CE	**Post-market confirmatory**	**Long-term**
Preferred designs	Case report(s) of first use	Observations study (single arm with all consecutive patients)		RCT vs SOTA with blinded determination of clinical endpoints	Mandatory registry with clinical follow-up
	Planned comprehensive case series with prospective data collection	Comparative study with concurrent matched controls		Open label RCT Observational cohort study with concurrent matched controls	
Not advised	Retrospective review of individual cases	Comparative study with historical controls			Registry with unrepresentative recruitment

*Adapted from table developed by CORE-MD research consortium

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Sections – Under discussion (2)

- **PART B : PROCEDURAL**
    - Involvement expert panel
        - Designation, scientific advice, …
    - Role Notified Bodies
        - Prioritization and timelines
        - Access structured dialogue (-> more in-depth)
        - Consideration SME
        - Certification with specific provision
    - Role Competent Authorities
    - Funding program
        - Incl. EIC

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Guidance Breakthrough

Sections – Under discussion (3)

PART B : PROCEDURAL – CONSIDERATIONS SME

- Notified bodies should : (within framework) for example
  - Provide **tailored support and structured dialogue mechanisms** to help navigate regulatory expectations,
  - Establish and publish transparent fee structures that take into account the interest of micro, small, and medium enterprises,
  - Include SME-friendliness as a performance metric in internal quality management systems, which can be measured in terms of the NB's ability to appropriately address and support the needs and interests of SMEs, for example.

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Next Steps

Workshop : 21st May – EU4HS invited (EU4Health - Community)	
Update draft for consultation , Input by July 14	
Pre-pilot consideration	Input on Potential Case Example to align classification Which elements of value to have in guidance (general and specific SME)
Pilot (September)	Voluntary to test guidance
Guidance published by MDCG (End 2025)	
Interested to actively contribute	
(contact link to Nobocap : y.Verboven@eu4healthsolution.eu	

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Breakthrough Guidance

What is of highest value for MSE Innovators

- A. Structured Dialogues with NB
- B. Accelerated time : Obtain a Certification
- C. SME Concierge Services
- D. A financial support and investing in breakthrough innovation
- E. Trust Building of Payer community
- F. Prioritization of Breakthrough
- G.Designation by Committee
- H. Interplay with other initiatives towards an innovation enabling environment

EU 4 HEALTH SOLUTIONS

1.1 A key role for a Safe Harbor Structured Dialogues with NB for legal certainty , predictability and planning certainty. (1)

- The structured dialogue need to have the ability to exchange with NB content expert and obtain relevant information on predefined areas (at least those also covered in other jurisdictions)
  - as eg. Risk class, classification software -AI , address uncertainty terminology – applicability , intended purpose and intended use consideration. E**xchange and obtaining input on options for consideration on clinical (and non clinical) data requirements, accepted study design, data sources** for these novel (disruptive innovation/ paradigm shift) in technological innovation with an indication of acceptance of evidence (in pre-post market) over the lifecycle in conformity assessment.
- This exchange to take place within the safe harbor with legal provisions on confidentiality
- A clear mechanism of CA backing of NB on risk assessment and validating evidence acceptance i.e. a legal certainty, whereby also a mechanism of consistency in information provided amongst NB is installed.
  - As eg. Proposal by NB send to CA / MDCG with a period of ability to scrutinize by CA. If no input – accepted. If input to be addressed and a further review endorsed by no response or a by qualified majority,
  - Possibly the use of common specification for competitive product also receiving breakthrough designation with submission with in 1 year. Additional competitive product no breakthrough designation. Consistent mechanism of reporting along the lifecycle is de fined

EU 4 HEALTH SOLUTIONS

1.2 A key role for a Safe Harbor Structured Dialogues with NB for legal certainty , predictability and planning certainty. (2)

- A progressive information gathering. Ability for multiple structured dialogues that can take place.
- A structured dialogue need be able to take place in design and development phase, also to seek confirmation on NB available expertise and timeline agreement.

- **All point leading to predictability and planning certainty** in the conformity assessment process,

  this also leading to reducing risk of non-compliance and costs caused by it.

EU 4 HEALTH SOLUTIONS

1.3 A key role for a Safe Harbor Structured Dialogues with NB for legal certainty , predictability and planning certainty. (3)

- Ability to have additional to structured dialogues seeking advice on evidence expectations of expert panels and HTA community in Scientific advice expert panel or parallel advice part of Joint Scientific Consultations (JSC – HTAR)(if class III, IIb) with presence of NB.
- Prioritization obtained for breakthrough designated innovation.
  - (This to be benchmarked to FDA TAP program) (See FDA Direct https://www.youtube.com/watch?v=FaaQt1ql1u4).
- AIM : These inputs can inform an evidence generation program for SME (multiple specific trial, one adaptive trial, ….) but should **not impact the specific regulatory requirements for Breakthrough** as defined by NB.

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2.1 Accelerated time : Obtain a Certification of Conformity (CE Mark) (with provisions)

- By the ability of addressing the pre-market clinical investigation requirement more efficiently as part of an adaptive evidence generation in pre- and post market. A Conformity assessments (with provisions).
- The pre- and post evidence generation supported by applying latest regulatory science and data sources. (In Silico, RWD, …)
- The provisions to be specific to feasibility of evidence generation (eg for Orphan, Initial small targeted population …)
- More efficiently as compared to other jurisdictions (eg .US)

EU 4 HEALTH SOLUTIONS

2.2 Accelerated time : Fast track to enable European health systems accessibility of technologies having received a breakthrough designation in selected other jurisdiction

- Have an accelerate path (mutual reliance/recognition) to obtain e.g. a conformity assessment with provision. (for European SME driven innovation)

- A selective number of jurisdiction as e.g. US FDA, Japan, Australia

EU 4 HEALTH SOLUTIONS

3. Introduce for MSE/SME Innovators an SME Concierge Services for technologies with a Breakthrough Designation.

- The SME Breakthrough Concierge Service should include :
  - Provide a single point of contact to navigate the entire regulatory pathway. (all EU applicable regulations)
  - Offer proactive guidance on preparing for Structured Dialogues to ensure SMEs arrive prepared and the dialogues are efficient, since consultation can not be done .
  - Develop SME-specific templates and guidance documents for (proposed) clinical evidence generation plans pre- and post market
  - Ensure consistency in advice given by different regulatory entities (NBs, CAs, …) and formally document this advice to ensure it is guiding future assessments, addressing the need for 'validating evidence acceptance'."

EU 4 HEALTH SOLUTIONS

4.1 A financial support for MSE / SME should include

1. **Supportive fees** **:** A 50% supported fees to cover quality services for preparation of dossier, for NB regulatory fees for structured dialogues, and expert panel consultations, to be covered by a EU special Funding Scheme. (eg. extended EIC scope not limited to EIC Awardees but also for breakthrough) up to certain amount, complemented with National provisions (Innovation programs).

2. **Innovation Grants:** Automatic eligibility and NCA support for input and review on submission to dedicated EU innovation grants to support the generation of pre- and post-market clinical evidence required under the designation - which can be fitted with EC Funding Programs for SMEs/ RTD initiatives.(eg as HORIZON-HLTH-2025-03-IND-03 Multinational Clinical Studies for Breakthrough Devices)

3. **Supportive provisions from NB** : Clear timeline and accelerated review timelines but at standards cost. This to formalize the benefit as can be expected when expedited reviews offered by NB to MNE' and provides SMEs without requirement of extra cost with an equal opportunity and the predictability needed for business and investment planning."

EU 4 HEALTH SOLUTIONS

4.2 Foster an **alignment in breakthrough designation with other EU and national level initiatives selecting and investing in innovation**

1. Foster an **interplay in breakthrough designation with other EU and national level initiatives selecting and investing in innovation of value as by EIC, EU PCP, EIT-Health, Innovation procurement,** ..)
    1. Consideration (eg. streamline with technologies having obtained a seal of excellence, technologies co-created to address hospital need, integrated care need, …. and other EU prioritized areas of addressing health care needs and health emergency product needs.
    2. Create a link between Breakthrough Designated CE marked (possibly with provision) devices and National conditional reimbursement / innovation financing & innovation procurement pathways.

EU 4 HEALTH SOLUTIONS

5. Foster a **trust building** (and not a perception of lowering of evidence standards) with payers, patient, providers for use of breakthrough MD

1. Foster a **trust building** (and not a perception of lowering of standards) with payers, patient, providers, for the use of Breakthrough MD (disruptive novel technological innovation with expected **significant impact for patient/ health system)**.
    - To drive use - financing of innovation providing a significant benefit and size effect leading to high value care and avoidance of low value care.
    - Have clear guidance on a close monitoring by regulatory (NB, CA, EC) on breakthrough MD/IVD
    - An **EC supported overview with one stop shop on latest information on the breakthrough designated product and evidence generation** accessible to the hospital purchasers, group procurers, payer, … is installed
    - AIM to foster a prioritization of interest by payer, insurance, investor community to invest/ provide conditional reimbursement/innovation financing for breakthrough designated products responding to unmet healthcare needs.

EU 4 HEALTH SOLUTIONS

6. Enable to have the designation of breakthrough to be done by a committee.

1. A clear template of needed information to be available.
2. Info available on and when in lifecycle a (candidate for) a breakthrough designation can request to be reviewed. (What information of size effect benefit – risk, safety information)
3. The designation should not be limited to EMA Expert panel, but involving those entities to be able to appreciate the technological innovativeness and those to appreciate healthcare/ health system needs/ population needs. (to ensure adoption and use of breakthrough MD)
    - A stepwise approach might be considered, appreciating the technological innovativeness (NB), the country specific appreciation if it addresses an unmet healthcare need with final appreciation on the significant clinical size effect of benefit by expert panel.
        - The EC to make a final decision on designation.
        - Early value analysis of innovation might inform, with focus on unmet healthcare need (not limited to unmet medical need)

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7. Enable a **prioritization for European SME innovation and European hospital co-created innovative solution seeking certification**

1. E.g. Including technological innovation responding to a need developed in European supported PCP,
2. Consideration on prioritization for European SME driven innovation in

    (1) accessibility to NB,

    (2) timely/frequent interaction (structured dialogue) and

    (3) NB expertise build out in disease/technology area of interest and

    (4) to have a clear fixed proposed timeline

    e.g. have a maximum 90-day review period for conformity assessments. Even using a clock stop for Manufacturer responses.

    Guaranteed scheduling of a Structured Dialogue within 30 days of request.

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8.Ensure an interplay and capitalize on other regulatory initiatives with focus on breakthrough

Ensure an interplay and capitalize on other regulatory initiatives with focus on breakthrough – novel innovation and ensure a streamlined and seamless EU regulatory environment supporting an Innovation of value and partnership Medical and Digital Technology Access Pathways

- Consideration eg use on regulatory (AI) sandboxes, innovation procurement, innovation partnerships, Clinical trial joint ethics committees, Public procurement innovation lot provisions, HTA-R Emerging Health Technology evaluation, Joint scientific consultation, joint-voluntary clinical assessment for HTA, new environmental requirement application, orphan designation to establish an

EU regulatory environment supporting an Innovation of value and partnership Medical and Digital Technology Access Pathways. access-to-medical-technology-innovations-a-proposal-for-a-value-of-innovation-and-partnership-model.pdf

EU 4 HEALTH SOLUTIONS

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