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Note of concern regarding the sources of scientific evidence used to justify the Reclassification of Non-Invasive Brain Stimulation (NIBS) Devices without an intended medical purpose into Class III

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Dear Editor,

The new European Medical Device Regulation (MDR), i.e. Regulation (EU) 2017/745, came into force in May 2021 and is being gradually implemented, with full compliance required for all medical devices on the EU market by May 2028. One key objective of the MDR is to regulate devices that, while technically being similar or even identical to medical devices, do not (yet) have an explicit clinical purpose. Under the previous regulatory framework, the Medical Device Directive (MDD), Non-Invasive Brain Stimulation (NIBS) devices with a medical purpose were classified as medical devices and subjected to regulatory control. However, when the same NIBS devices were used for non-medical purposes, such as cognitive enhancement in healthy individuals or experimental research on healthy participants, they were not regulated, despite posing the same risks. The new MDR aims to address this gap by extending regulatory control to such "*non-medical devices*", enhancing user safety through "more stringent" conformity assessment and post-market surveillance and ensuring that unsafe or non-compliant devices do not reach the public market.

Annex XVI of the MDR lists devices that fall under the scope of the law, even though they are lacking an intended medical purpose. The list includes: "*Equipment intended for brain stimulation that apply electrical currents or magnetic or electromagnetic fields that penetrate the cranium to modify neural activity in the brain.*" This category encompasses all forms of transcranial electrical stimulation (tES), including direct current, alternating current and random noise stimulation (tDCS, tACS, and tRNS) and transcranial magnetic stimulation (TMS). Notably, neither the list in Annex XVI nor their reclassification include more recently introduced technologies that employ other physical principles to non-invasively stimulate the human brain, such as transcranial ultrasonic stimulation (TUS) or photobiomodulation (PBM). While Annex XVI had listed the transcranial electrical and magnetic stimulation technologies in 2017, the risk classification for these devices, when being used for non-medical purposes, remained unspecified for several years. This left industry and researchers in limbo as they awaited final decisions from the EU.

Under the MDR, medical devices are classified into four classes following a risk-based classification scheme, which links the class of the device to the potential risk posed to the patient's health due to performance faults. All medical devices are classified as class I, IIa, IIb, or III, with class III being the highest risk class. Class III devices are per definition those where a malfunction or failure of the device could result in death or serious injury. These are primarily devices intended for invasive surgical procedures, such as deep brain stimulators or pacemakers. Guidance documents, published in 2021, clarified that NIBS technologies used for clinical or medical purposes (and thus covered by the core of the MDR rather than Annex XVI), were classified as Class IIa (i.e., TMS and low intensity tES) or Class IIb (see MDCG 2021-24).[3] It was therefore widely assumed that the classification of these types of NIBS devices would have the same or lower classification for non-medical use, as patients are generally considered to be at higher risk due to their overall health status, but this assumption proved incorrect, even the reverse came up.

While we agree that the risk-benefit ratio of NIBS devices may be higher and harder to control when used unsupervised by non-experts, the reclassification was based on the premise of "*increased risk*". This has led to widespread confusion in the brain stimulation field, slowing research, leaving clinicians uncertain, and frustrating patients [1,2].

The aim of this paper is i) to review the scientific evidence on the basis of which reclassification was implemented and provide the relevant scientific proof that was omitted; ii) to summarize our efforts how we have tried to act against the reclassification; iii) to present clear, evidence-based findings to address existing ambiguities in the regulatory NIBS field, providing the scientific community with reliable information to guide further research and application. This is relevant as any risk assessment and claims of possible side and adverse effects should be based on scientific empirical data rather than speculation. The "saga"

[3] https://health.ec.europa.eu/system/files/2021-10/mdcg_2021-24_en_0.pdf.

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until now was mainly about procedures and regulatory processes and thus, on formalities. What is missing is a scientific review of the concrete articles and evidence put forward by the reclassification committee to justify their revised risk assessment of NIBS. The current article is written by leading experts, scientists who evaluated this evidence and provide a pure scientific assessment of the data we have available today.

1. The timeflow of the reclassification

A detailed description related to the timeline of the introduction to of the MDR, the Reclassification and their effects in the NIBS field can be found elsewhere. [2]. In summary, in August 2022, the EU released the relevant draft legislation (active since December 2022 as Commission Implementing Regulation (EU) 2022/2347) that reclassified all forms of NIBS without an '*intended medical purpose'* as Class III devices, the highest risk category.[4] The reclassification of NIBS devices reflects concerns about their potential misuse when sold directly to individuals, as companies cannot guarantee proper usage. It is explicitly stated in the draft legislation: "*The suggested changes were discussed with national experts and considering the risks posed by these products on public safety, there was consensus to maintain them in class III"*. Although the EU claimed that research would remain unaffected and that only industry would be affected, this has not been the case in practice: many ethics committees have been misinformed, there have been significant delays in research projects, increased administrative burdens and delays in the start of clinical interventions, leaving patients unsatisfied [1–4].

The EU justified the reclassification of non-medical NIBS devices (Class III) versus medical NIBS devices (Class IIa) referring to recent scientific evidence suggesting that the risks of NIBS technologies are more significant than previously understood. The justification highlighted potential risks such as "*atypical brain development, abnormal patterns of brain activity, increased metabolic consumption, fatigue, anxiety, irritability, headaches, muscle twitches, tics, seizures, vertigo, skin irritation at the electrode site …* " (see below). The draft reclassification was open for feedback for four weeks during which several concerns were raised. It was questioned why the same device would have different risk classifications under the same regulation, depending on whether it is used in healthy individuals (e.g., for research) or clinical populations. Another point of criticism was the paradox of assigning a higher risk classification to healthy individuals than to patients.

In a meeting held on October 13th, 2022, the EU addressed complaints regarding the reclassification of brain stimulators, stating[5]: *"Contributions were also related to the reclassification of brain stimulators … For the brain stimulators, respondents compared Annex XVI products to analogous medical devices and noted that medical devices are classified as class IIb, sometimes also as IIa. Therefore, the suggestion was to classify brain stimulators without a medical purpose as class IIb. The suggested changes were discussed with national experts and considering the risks posed by these products on public safety, there was consensus to maintain them in class III"*. The list of "national experts" involved in these discussions was not made public. Feedback from the research community suggested that no safety experts in the field of NIBS were consulted to review the specific medical risks cited above or to assess how these risks are supported by scientific evidence.

The EU's response to the complaints failed to address the core contradiction in risk classification of NIBS devices. Identical devices are categorized differently based on the vague concept of "intended use". For example, a TMS stimulator used for diagnostic or therapeutic purposes is classified as a Class II device, but the same device, when used for research (e.g., studying cognitive functions), is reclassified into a Class III device. This leaves the field with unresolved questions about where to draw the line between medical and non-medical use, such as whether a clinical trial is considered medical or non-medical, or whether research into the pathophysiology of disease, which could lead to new treatments, qualifies as medical use.

Here, we review the scientific evidence on which this argument was based and provide the relevant scientific evidence that was omitted.

2. Sources used by the EU for reclassification of risk

In response to our request to the EU for an overview of the literature supporting the reclassification of NIBS technologies, we received the list of references that had been provided in the letter of the six member states to the European Commission that had requested the reclassification decision, covering all classes of technologies outlined in Annex XVI (Fig. 1). Subsequent communication confirmed that this is the complete list of evaluated sources.

Sources 1–5 do not deal with brain stimulation or safety aspects relevant to brain stimulation technology. From the remaining five sources that are relevant to NIBS devices (6–10), two are not original scientific papers, and only one is published in an international scientific peer-reviewed journal that focuses on brain stimulation. In the following sections, we will analyze each of the five sources related to brain stimulation (listed as 6 to 10) and discuss how each source contributed to the conclusions that prompted the reclassification.

(6) Maslen et al. 2014 is a peer-reviewed paper published in a law journal, exploring a regulatory framework for neuroenhancement devices. The authors present a case for extending existing medical device legislation to cover the use of neuroenhancement. The authors argue that regulation is necessary and propose that both medical and non-medical uses of NIBS devices should be subject to the same regulatory standards, as distinguishing between them is often challenging (e.g., is enhancing the memory of an elderly healthy individual considered a treatment for normal age-related memory decline or a form of neuroenhancement?). Consequently, the paper advocates for the classification of non-clinical tES use as Class II. The authors emphasize that both medical devices and neuroenhancement devices operate similarly and present comparable risks, necessitating consistent regulatory oversight. Thus, this source argues against the reclassification of NIBS devices as Class III and calls for uniform regulation regardless of whether these devices are used on patients or healthy individuals.

(7) Mind Machines 2014 is a policy paper published as a companion to the Maslen et al., 2014 article by the same authors, which is essentially a lay version of the same paper. They refer the reader to Maslen 2014 for a more academic review of the points made in the report, and make no new claims regarding safety. Therefore, in the context of risk classification it does not change the authors' position put forward in (6).

(8) Monte-Silva et al. 2013 is a highly regarded paper in the field of tES, published in a prominent peer-reviewed journal, with more than 800 citations to date. This foundational research investigates the metaplastic effects of tDCS on the motor cortex in healthy young participants, demonstrating that the outcomes of multiple tDCS sessions can be enhanced, abolished or reversed, depending on the interval between sessions and the duration of the sessions. However, this paper is irrelevant to the question at hand, i.e., the reclassification of NIBS devices. The study neither addressed the safety of tDCS nor reported any significant adverse effects. It is only stated that "*with the exception of a slight itching sensation under the tDCS electrodes mentioned by some participants during stimulation, no other side effects of tDCS or medication were reported.*" In summary, this source is just one among hundreds that explore the neurophysiology of low intensity tES and supports its safety without raising any major safety concerns. Therefore, this paper does not provide

[4] https://lne-gmed.com/news/implementing-regulation-eu-2022-2347-laying-down-rules-for-the-application-of-regulation-eu-2017-745-as-regards-reclassification-of-groups-of-certain-active-products-without-an-intended-medical-pu.

[5] Summary report from October 13 meeting by regulatory committee on medical devices. The meeting confirming the reclassification draft for all Annex XVI devices lasted from 14:30–17:30.https://www.ombudsman.europa.eu/en/decision/en/185531.

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7. Mind Machines, Oxford Marin Policy Paper
8. Induction of Late LTP-Like Plasticity in the Human Motor Cortex by Repeated Non-Invasive Brain Stimulation, Monte-Silva et al, Brain Stimulation 6 (2013)
9. Novel neurotechnologies: intervene in the brain, Nuffield Council on Bioethics
10. Would you be willing to zap your child's brain? Public perspectives on parental responsibilities and the ethics of enhancing children with transcranial direct current stimulation, Wagner et al, AJOB Empiral Bioethics, 2018

Fig. 1. List of references provided by the EU for "scientific evidence" regarding risks of Annex XVI devices the reclassification decision was based on.

evidence to justify reclassifying the non-medical use of NIBS devices as Class III.

(9) Laurie 2014 is a policy report that addresses all current and some emerging forms of neuromodulation, including stem cell therapies. While the primary focus of this publication is on the ethics of neuromodulation, safety aspects are only briefly discussed. Additionally, the authors conflate side effects and adverse effects associated with different NIBS techniques, despite their distinct modes of action. Ultimately, the report recommends that non-therapeutic neuromodulation should be a medical device with a therapeutic indication (i.e., Class II).

(10) Wagner et al. 2018 is the most recent source of information and examines the public attitudes towards a hypothetical scenario in which tDCS is used to enhance the cognitive capacities of children. This work neither evaluated the actual side-effect or adverse-effect profile of NIBS nor assessed the actual risks of pediatric or neuroenhancement use. Instead, it investigates which traits or abilities parents would be willing to enhance in their children using tDCS, while also discussing public perceptions of fairness regarding neuroenhancements such as mathematical abilities. The study reports that the surveyed group of 227 US respondents generally oppose making a neuroenhancement available to children and call for regulation of tDCS use to prevent its misuse. However, the article does not specify how such regulation should be implemented. The authors acknowledge that their study may not be suitable for informing policy development due to the necessary simplifications built in their experimental design.

3. General comments concerning the references provided for the reclassification

1 *The sources of evidence on which the reclassification was based on are insufficient:* It is noteworthy that there were over 7000 peer-reviewed publications on tDCS alone, and even more for TMS (more than 13,000 on PubMed) in 2020, when the work on reclassification supposedly started. Addressing such a vast field with only five sources, seems grossly inadequate. The decision making process apparently ignored a substantial body of recent data from several specific safety studies, meta-analyses and reviews, that would have been suitable for inclusion. Notably, the currently largest, and most relevant safety studies on tES, published in 2016 and 2017 [5,6], have not been considered. These publications were prompted after an international conference supported by the International Federation of Clinical Neurophysiology (IFCN) in Göttingen, Germany, specifically on this topic. These and other sources could have been easily identified by consulting almost any researcher in the field.

2 *The included five sources do not cover different NIBS technologies:* The 5 sources focus overwhelmingly on tDCS, with only minor references to rTMS and tACS. However, the conclusion affects all these and other technologies, by lumping them all together.

3 *Selective inclusion of the five sources do not comply with EU guidelines that require assessments to be based on the best available data:* The sources used for reclassification do not include safety reviews or reports on adverse or side effects from the past 10+ years. This omission is critical, given the rapid developments in the field. If the literature cited raises concerns from bioethicists or other experts, it is essential to investigate whether these concerns have been addressed in subsequent research. To comply with EU guidelines and offer a robust, informed assessment, a thorough review of the recent literature, particularly from the last decade—should have been conducted. This would have ensured the decision is based on the most up-to-date and relevant data.

4 *The inappropriate selection of sources led to a conflation of theoretical risks and actual observed risks:* The listed sources reflect the perspective of lawyers, bioethicists, and non-NIBS medical professionals, revealing a lack of expertise in NIBS. This becomes evident when speculative adverse effects, unsupported by references, are presented as real risks. For instance, Maslen 2014 claims on page 71:" *Particularly, if suboptimal tDCS devices are being used, or devices are being used incorrectly, there is a risk that undesirable changes to the user's brain and its functioning may become difficult to reverse".* This assertion is made without any supporting evidence, rendering the statement speculative rather than evidence-based. Similarly, Wagner et al. use alarmist language in their survey questions, without reference to actual observations of harm or mechanisms of risk: e.g., respondents are asked about the potential impact of a tDCS intervention that improves math skills, but might alter a child's sense of authenticity, remove beneficial adversity, or affect empathy. While these are valid and important ethical considerations, they do not relate to the current risk profile of NIBS technologies and are not relevant to the assessment of their safety.

5 *Duplicated data in two cited sources:* The policy paper "Mind Machines" and the peer-reviewed article by Maslen and colleagues (sources 6 and 7 on the list) are cited as separate sources but cover the same research and data. This redundancy exacerbates the lack of diversity of sources noted in the previous point.

6 *Incorrectly referral to cited sources:* The absence of a systematic search method highlights a significant flaw in the approach. The literature is not presented in a systematic reference style, making it more difficult than necessary to locate sources. Additionally, two reports are listed without a year of publication, which is crucial for assessing the state of research. With the exception of the paper by Monte-Silva, the reports and articles listed required very specific searches to be retrieved.

7 *Concerns regarding the explanations for reclassification:* The explanation of the reclassification states: " …. *The risks linked to the use of equipment intended for brain stimulation are: atypical brain development, abnormal patterns of brain activity, increased metabolic consumption, fatigue, anxiety, irritability, headaches, muscle twitches, tics, seizures, vertigo, skin irritation at the electrode site..".* This paragraph appears to be taken from a theoretical opinion paper, which was published in 2012, but the primary source was not cited: Cohen Kadosh et al. (2012), Current Biology, Vol 22, Nr 4, page R109 [7]. The original text states: *"For example, repeated stimulation of the parietal cortex to increase numerical competence during developmental stages when the prefrontal cortex is more important* [13] *might not only fail to give any improvement but it could even worsen performance and lead to atypical brain development. Like other types of atypical experience during sensitive periods [14], the stimulation of the wrong brain area might induce abnormal patterns of brain activity in this brain region and interconnected areas, and increase metabolic consumption in brain areas that are irrelevant to the specific psychological function.*" This paper is a theoretical essay on "*The neuroethics of non-invasive brain stimulation*", that speculates on the potential adverse effects of hypothetical future stimulation protocols, in particular on the developing brain in children, if safety issues are not carefully followed, and calls for "*more research into the safety and potential hazards*". It is therefore misleading and inappropriate to rely on speculative text as evidence of actual risks.

8 *Lack of support for reclassification from the sources.* Finally, even the listed sources, despite their pitfalls and misinterpretations, do not provide grounds for reclassification to Class III. On the contrary, Monte-Silva et al., 2013 supports safety, sources 6, 7, and 9 advocate for equal legal consideration for patients and healthy individuals.

In summary, it can be concluded that the entire field of non-medical NIBS and related industries is currently being regulated on the basis of an inappropriate and outdated selection of a few sources that neither provide a comprehensive review of the existing literature nor empirical data to substantiate or justify the reclassification.

Current knowledge on side effects and adverse events of NIBS technologies (last ten years, 5 most cited papers for tES and TMS).

According to the Common Terminology Criteria for Adverse Events (AEs)[6] adverse events are undesirable, uncomfortable, or harmful effects that are observed after a medical intervention that may or may not be causally related to it. Conversely, a side effect refers to a consequence that differs from the intended effect. While a side effect may be beneficial or adverse, an adverse event is by definition unfavorable. According to the recommendations of the International Council for Harmonisation (ICH) guidelines [8] (Food and Drug Administration, 2011), a mild adverse event (grade 1) is defined as mild symptoms that do not require medical treatment, such as skin redness or tingling sensation during tDCS. A moderate adverse event (grade 2) requires local or non-invasive treatment. Serious adverse events (grade 3) are serious or medically significant but not immediately life-threatening events, but include the need for inpatient hospitalization or prolongation of hospitalization. A life threatening serious adverse event is any event that puts life at risk (grade 4) or results in death from the SAE (grade 5).

In the justification text related to the reclassification it is stated[7]: "*According to the literature: …. The risks linked to the use of equipment intended for brain stimulation are: atypical brain development, abnormal patterns of brain activity, increased metabolic consumption, fatigue, anxiety, irritability, headaches, muscle twitches, tics, seizures, vertigo, skin irritation at the electrode site …* ".

There are several recent comprehensive reviews available based on a large number of empirical data from both healthy volunteers and patients to assess the true risk profile of NIBS technologies both with and without medical purpose. Here we evaluate why the risks that have been stated in the justification text for reclassification do not correctly reflect the adverse events that have been reported in the five most cited papers on TMS or tES safety [5,6,9–11].

1. Atypical brain development has not been reported after NIBS.
2. Increased metabolic consumption is not even an adverse effect but simply the physiological consequence of increased neuronal activity (also observable e.g. following natural sensory stimulation and cognitive processes).
3. Abnormal patterns of brain activity (epileptic seizures) - TMS/rTMS [10]**:** The best current evidence suggests that the risk of seizures (abnormal brain activity) induced by (r)TMS is less than 0.03 %. Importantly, even in the rare event of a seizure occurring during rTMS, no permanent damage has been reported in current clinical practice. Seizures, if induced by rTMS, typically occur mainly during the stimulation session, and a significant portion of reported seizures may have been misdiagnosed as being in fact convulsive syncopes. Even studies conducted specifically in patients with epilepsy have not reported an increased incidence of rTMS-associated seizures occurring within hours or days after the end of stimulation. In fact, low-frequency rTMS is known to have anticonvulsant effects and can be used in the treatment of epilepsy. For tES, only isolated cases of serious AEs have been reported (one epileptic seizure after stimulation in a child with epilepsy, cannot be causally linked to the stimulation [6].
4. Concerning *tES:* " *….fatigue, anxiety, irritability, headaches, muscle twitches, tics, …., vertigo, skin irritation at the electrode site" …* [5,6,12]*:* Studies examining the safety profile of tES generally report mild tingling sensations (about 70 %) and mild itching under the stimulus electrode (about 40 %) as the most common side effects. The most common adverse events were moderate fatigue (about 40 %), headache (between 10 and 20 %), nausea (less than 3 %), and very rarely insomnia (less than 2 %). A prospective study compared active and sham (i.e., placebo) tDCS in 131 participants (277 tDCS sessions with a stimulation intensity of 1–2 mA) [9](Kessler et al., 2012). In this study the active stimulation group reported a higher incidence of tingling (89 % versus 53 %), itching (81 % versus 42 %), burning sensation (65 % versus 33 %), pain (31 % versus 11 %), and headache (15 % versus 9 %) than the sham group [9]. Persistent skin lesions under the electrodes in some subjects, typically on the forehead were rarely observed, mainly after repeated daily tDCS, most often with sponge electrodes, with a current density of about 0.06 mA/cm2 (i.e., electrodes 25–35 cm2, currents 1.5–2.1 mA) [5,6,11]. Contributing factors were pre-existing conditions such as allergies to skin creams, high impedance (electrode dry or defect, solution salinity of electrode sponges and deterioration of the sponges, unsuitable contact solution, incorrect electrode fixation, non-uniform contact pressure of electrodes to skin), prolonged duration or repeated sessions, high current density (high current, small electrode). One study using a home-stimulation design was terminated prematurely, because of inappropriate electrode design [13].

In summary, only isolated cases of serious adverse events have been reported in several thousand sessions, including healthy participants and patients (referred to in the papers cited above). Occasionally, after tES, people experienced moderate AEs such as skin burns, often attributed to poor contact between the electrodes and the skin and mostly due to an inadequate preparation of the electrodes. For rTMS, depending on the type of protocols (e.g., theta burst versus 10 Hz), the disorder, the

[6] https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/Archive/CTCAE_4.02_2009-09-15_QuickReference_5x7_Locked.pdf.

[7] https://lne-gmed.com/news/implementing-regulation-eu-2022-2347-laying-down-rules-for-the-application-of-regulation-eu-2017-745-as-regards-reclassification-of-groups-of-certain-active- products-without-an-intended-medical-purpose.

frequency of the stimulation, etc., 102 publications between 2020 and 2024 reported fatigue (about 40–60 %), headache (between 10 and 40 %), vertigo (10–40 %), muscle twitching (10–90 %) and rarely insomnia (less than 10 %).

4. Recent regulatory state

In April 2024, the European Ombudsman stated that the Commission had not adequately verified whether the scientific sources provided by the Member States represented the most recent published scientific evidence on the risks associated with the use of brain stimulation devices.[8] Consequently, the Ombudsman concluded that the Commission's assessment of these sources was insufficient to enable it to determine whether there was 'new scientific evidence' justifying the reclassification of these products.

The Ombudsman recommended that the Commission thoroughly examine the sources provided originally by six Member States to ensure that they are comprehensive and representative of the latest scientific evidence regarding the risks associated with brain stimulation devices. If the Commission concludes that the current scientific evidence does not support the reclassification, it should take corrective actions. The Commission accepted the Ombudsman's proposed solution and asked the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) to issue a scientific opinion on the risk that is posed by using brain stimulation devices for non-medical purposes. Based on this scientific opinion, the Commission intends to assess the need for further action in the near future. Having flagged significant concerns regarding the scientific basis for the commission's previous re-classification in this article, we highly welcome this decision for a reevaluation of the scientific evidence the original reclassification was based on. The letter justifying the reclassification of NIBS devices without medical purpose as Class III makes false and alarming claims about non-existent risks and creates serious problems and uncertainties for industry, researchers, and patients [1,2] even though it does not directly pertain to the use of NIBS devices in basic or clinical research studies that do not fall under the MDR [3].

We acknowledge that this is a critical issue requiring regulation. This can be addressed by ensuring that all NIBS devices are classified under the MDR as medical devices, with a risk classification that accurately reflects their actual risks. It is evident that NIBS devices belong in Class IIa, not Class III, irrespective of their intended use. In fact, the MDR Article 2(1) already provides a sufficiently broad definition, stating that "*'medical device' means any instrument [etc.] intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes [1]: diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease [2], diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability [3], investigation, replacement or modification of the anatomy or of a physiological or pathological process or state, […] and which does not achieve its principal intended action by pharmacological, immunological or metabolic means […]*", thus explicitly including beside the therapeutic and diagnostic purposes also the investigation and modification of a physiological process or state and thus the very purpose of NIBS neuromodulation, whether for fundamental and clinical research or neuroenhancement. A brain stimulators thus keeps being a medical device also when not used in patients for diagnostic or therapeutic purposes, based on a specific clinical "*indication*" (i.e., certain clinical symptoms; evaluated by the clinician), which is notably not to be confused with the more general cross-indicational "i*ntended medical use"* or "*medical purpose*" of the device (i.e., neuromodulation; defined by the manufacturer). Consequently, these devices should be regulated as medical products, not consumer goods, and when used on patients, should always be under medical supervision, whether direct or remote. However, none of this justifies a difference in risk classification between NIBS devices with and without a medical purpose; none of this requires justifying the reclassification to Class III on the basis of alleged safety concerns that are false, misleading, and create confusions for patients, researchers, ethics committees, and industry [1–4]. Class III should be restricted to invasive devices that require a surgical procedure to be placed into the brain.

Document C/2022/8638 (Implementing Regulation (EU) 2022/2347) is the source of most conflict. If, based on the latest scientific evidence, NIBS devices do not present risks warranting a Class III classification, the logical step would be to adjust the reclassification to Class IIa. In safety assessments—whether under the General Product Regulation or other frameworks—the "state of the art" must play a central role in the consideration. This includes recognizing international practices, standards, and the positions of global communities, which should significantly inform safety requirements. We acknowledge that while these practices, standards, and positions are not legally binding under EU law, they are still highly relevant and should be considered in regulatory decisions.

CRediT authorship contribution statement

Andrea Antal: Writing – original draft, Methodology, Conceptualization. **Alexander T. Sack:** Writing – original draft, Data curation, Conceptualization. **Til Ole Bergmann:** Writing – original draft, Data curation, Conceptualization. **Jovana Bjekic:** Writing – original draft, Data curation, Conceptualization. **Saša R. Filipovic:** Writing – original draft, Conceptualization. **Ana Ganho-Ávila:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Vera Moliadze:** Writing – original draft, Conceptualization. **Michael A. Nitsche:** Writing – original draft, Conceptualization. **Simone Rossi:** Writing – original draft, Conceptualization. **Teresa Schuhmann:** Writing – original draft, Conceptualization. **Hartwig Siebner:** Writing – original draft, Conceptualization. **Walter Paulus:** Writing – original draft, Methodology, Data curation, Conceptualization. **Chris Baeken:** Writing – original draft, Methodology, Data curation, Conceptualization.

Declaration of competing interest

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[8] https://www.ombudsman.europa.eu/en/news-document/en/186486.

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Andrea Antal[a,1,*], Alexander T. Sack[b,1], Til Ole Bergmann[c,d], Jovana Bjekic[e], Saša R. Filipovic[e], Ana Ganho-Ávila[f], Vera Moliadze[g], Michael A. Nitsche[h,r,s], Simone Rossi[i], Teresa Schuhmann[b], Hartwig Siebner[j,k,l], Walter Paulus[m,2], Chris Baeken[n,o,p,q,1]

[a] *Department of Neurology, University Medical Center Göttingen, Germany*
[b] *Department of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, the Netherlands*
[c] *Neuroimaging Center, Focus Program Translational Neuroscience, Johannes Gutenberg University Medical Center, Mainz, Germany*
[d] *Leibniz Institute for Resilience Research (LIR), Mainz, Germany*
[e] *Human Neuroscience Group, Centre for Neuroscience and Neuromodulation, Institute for Medical Research, University of Belgrade, Serbia*
[f] *Center for Research in Neuropsychology and Cognitive Behavioral Intervention, Faculty of Psychology and Educational Sciences, University of Coimbra, Coimbra, Portugal*
[g] *Institute of Medical Psychology and Medical Sociology, University Medical Centre Schleswig-Holstein, Kiel University, Kiel, Germany*
[h] *Dept. Psychology and Neurosciences, Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany*
[i] *Department of Medicine, Surgery and Neuroscience, Siena Brain Investigation & Neuromodulation Lab (Si-BIN Lab), University of Siena, Italy*
[j] *Danish Research Centre for Magnetic Resonance, Department of Radiology and Nuclear Medicine, Copenhagen University Hospital Amager and Hvidovre, Copenhagen, Denmark*
[k] *Department of Neurology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark*
[l] *Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*
[m] *Department of Neurology, Ludwig-Maximilians University, Munich, Germany*
[n] *Faculty of Medicine and Health Sciences, Department of Head and Skin, Ghent Experimental Psychiatry (GHEP) lab, Ghent University, Ghent, Belgium*
[o] *Neuroprotection and Neuromodulation Research Group (NEUR), Center for Neurosciences (C4N), Vrije Universiteit Brussel (VUB), Brussels, Belgium*
[p] *Department of Psychiatry, Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium*
[q] *Center for Care and Cure Technology (C3Te), Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands*
[r] *University Clinic of Psychiatry and Psychotherapy, Protestant Hospital of Bethel Foundation, University Hospital OWL, Bielefeld University, Bielefeld, Germany*
[s] *German Center for Mental Health (DZPG), Bochum, Germany*

[*] Corresponding author. Department of Neurology, University Medical Center Göttingen, Robert Koch Str. 40, 37075, Göttingen, Germany.
E-mail address: andrea.antal@med.uni-goettingen.de (A. Antal).

[1] AA and ATS: shared first authorship.
[2] WP and CB: shared last authorship.