

Neural interface technologies: regulatory and policy considerations

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Now

The Medical Devices Regulation (MDR) () provides a formal definition of the two dichotomies (medical or non-medical; inside or outside the body) used in this perspective. A neural interface technology (NIT) is considered to have a medical purpose if its intended use falls within the definition of a medical device (MDR, Article 1, clause 1). The definitions for implantable devices (MDR, Article 1, clause 5) and invasive devices (MDR, Article 1, clause 6) formalise what is meant by use inside the body. Medical devices are classified by risk alone.

Medical devices placed on the market in the EU must meet 23 general safety and performance requirements (MDR, Annex I). Manufacturers normally demonstrate this by preparing a technical file that contains evidence of conformance with standards which are harmonised with the MDR and present it for scrutiny to one of the notified body, which are companies accredited by national designating and competent authorities, before being allowed to affix a CE mark. In the UK the national designating and competent authority is the MHRA.

Novel and emergent NITs, with insufficient evidence for efficacy to meet the general safety and performance requirements, would normally require a clinical investigation - or trial - involving human subjects. In the UK the clinical trial sponsor such as an NHS Hospital Trust, university or company would submit an investigator brochure (a technical file complete apart from the evidence to be generated by the trial) as part of the trial paperwork. In addition to review by a Research Ethics Committee (REC), the investigator brochure would be scrutinised by the MHRA, who have the right to object to the trial proceeding if they consider the device under investigation to be unsafe.

The MDR lists several products (MDR, Annex XVI) which do not have a medical purpose, including equipment intended for electrical or magnetic brain stimulation, such as trans cranial direct current stimulation for neuro-enhancement, but which must meet certain safety and performance requirements.

Non-medical NITs whose purpose falls outside the scope of MDR, and which are placed on the market, must conform with legislation applicable to their product category, and otherwise with the EU General Product Safety Directive (GPSD). The situation is less clear for non-medical NITs under development or intended for research, although any research involving human participants would require appropriate institutional approval.

It is not always straightforward to ascertain whether a technology has an intended medical purpose. Some aids to daily living are not classified as medical devices if they do not have a direct link to a compensation for an injury or a handicap.

Post-approval, the National Institute of Health and Care Excellence (NICE) publishes guidance on novel technologies for the NHS and social care in England and Wales (although other countries may adopt NICE guidance). Current programmes applicable to NITs include the Interventional Procedures Programme which considers safety and efficacy, the Medical Technologies Evaluation Programme (MTEP) which considers clinical and cost consequences, the Diagnostics Assessment Programme which considers diagnostic accuracy, clinical utility and cost utility, and the Technology Appraisals Programme which considers full cost effectiveness.

What's developing

The MDR has placed greater emphasis on manufacturers to provide robust evidence, at the regulatory approval stage, for safety and efficacy of their products compared with its predecessors (the Medical Devices Directive and the Active Implantable Medical Devices Directive). This includes, for example, an expectation that the design and conduct of clinical investigations are expected to conform to international standard BS EN ISO 14155 (14155) for good clinical practice in device trials. Hence pivotal device trials will be expected to be conducted to the same standards as pivotal drug trials.

Beyond the field of neural technologies, some categories of implanted devices have turned out to have poorer long-term safety outcomes than expected when the products were first placed on the market, leading to adverse effects for many patients. Recent examples include some metal-on-metal hip joints (MoM) and some mesh tapes for treating stress urinary incontinence (SUI). In the light of these experiences, it seems likely that there will be calls for further tightening of the regulations to require manufacturers to either provide more long-term safety data, or to collect long-term outcomes routinely as part of post-market surveillance, as a condition of approval.

In health technology assessment, the evidence base for novel devices, on which NICE and others are required to make decisions, is often less extensive than for new medicines. The use of real-world evidence (RWE), and the techniques for appraising it, is seen as one solution to the problem of lack of evidence, the limited generalisability of the results of formal trials to an NHS setting, and the lack of long-term safety evidence. Examples include NHS England's Commissioning through Evaluation (CtE) Programme (CTE) in which specialist technologies are commissioned on a limited basis with mandatory data collection.

Where it might go

There has been media interest (DM) in the possibility of "brain-jacking", through unauthorised remote access to implanted neural devices, with the intent of controlling behaviour. To date the risk is more theoretical than real but it does require further consideration as NITs become more common. In the EU, the Radio Equipment Directive (RED) 2014 (RED), which applies to manufacturers of devices which use wireless communication, including NITs, requires consideration of privacy and data security, although does not specify particular security standards. Encrypted communication is widely used in other fields, and it seems likely that the MDR and

associated standards will evolve to embrace such technologies, leading to greater security in NITs.

Regulations for medical devices have been in force in the EU for more than 20 years and have been based on the same principles, with the MDR being the latest evolutionary development. It seems likely that emergent medical NITs will not require a radical change in the regulatory framework, provided the UK continues to embrace the routine revisions to standards, for example for encrypted communications, and directives that keep the regulatory framework current. But there is a lack of clarity over how non-medical NITs, for example for neuro-enhancement, could or should be regulated. To some extent, by including Annex XVI in the MDR, EU lawmakers have anticipated the emergence of technologies which pose the kind of safety risks associated with medical devices, but which are not intended to diagnose or treat illness or injury. Additions to the Annex would require a change to the law, and there is a risk of confusion over what regulations apply to new categories of non-medical NITs, and which agencies would be responsible.

Few potential patients or consumers would argue against a stronger regulatory framework for NITs to ensure their safety. But a higher regulatory barrier may prove too high for some developers of medical NITs to cross and there is a risk that potentially beneficial technologies will not be made available to patients. Conversely, if non-medical NITs fall outside the scope of the MDR, there may be a safety risk to consumers. There is a clear need for developers of NITs, including industry and academia, to engage with the MHRA at an early stage, and for regulatory (eg MHRA) and HTA bodies (eg NICE) to have sufficient resources to work with UK based researchers and industry to ensure that consumers, patients and industry in the UK are able to benefit from the opportunities of novel NITs.

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