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A BSI white paper

Article 61.10

Clinical Evaluation based on non-clinical data

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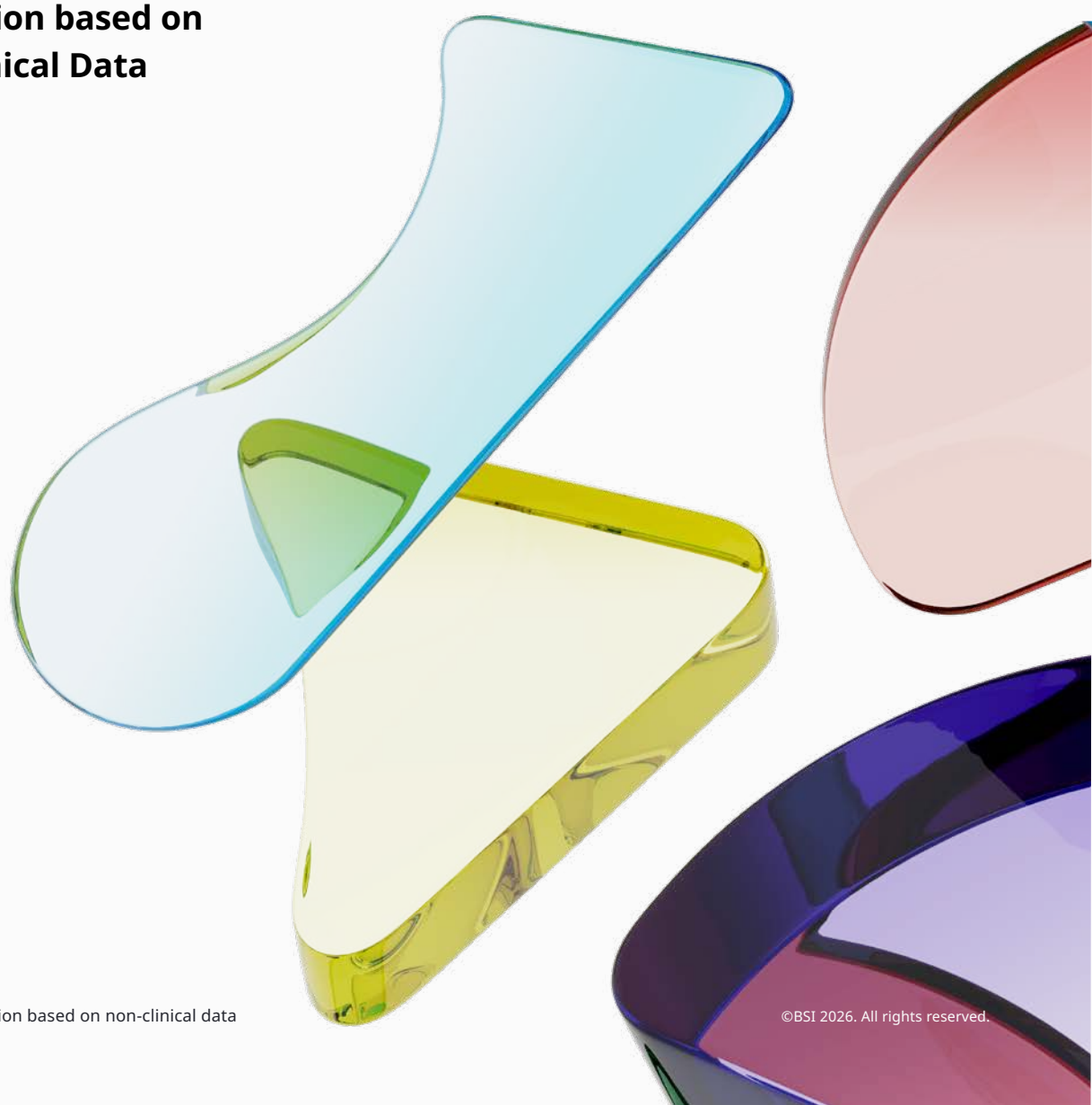
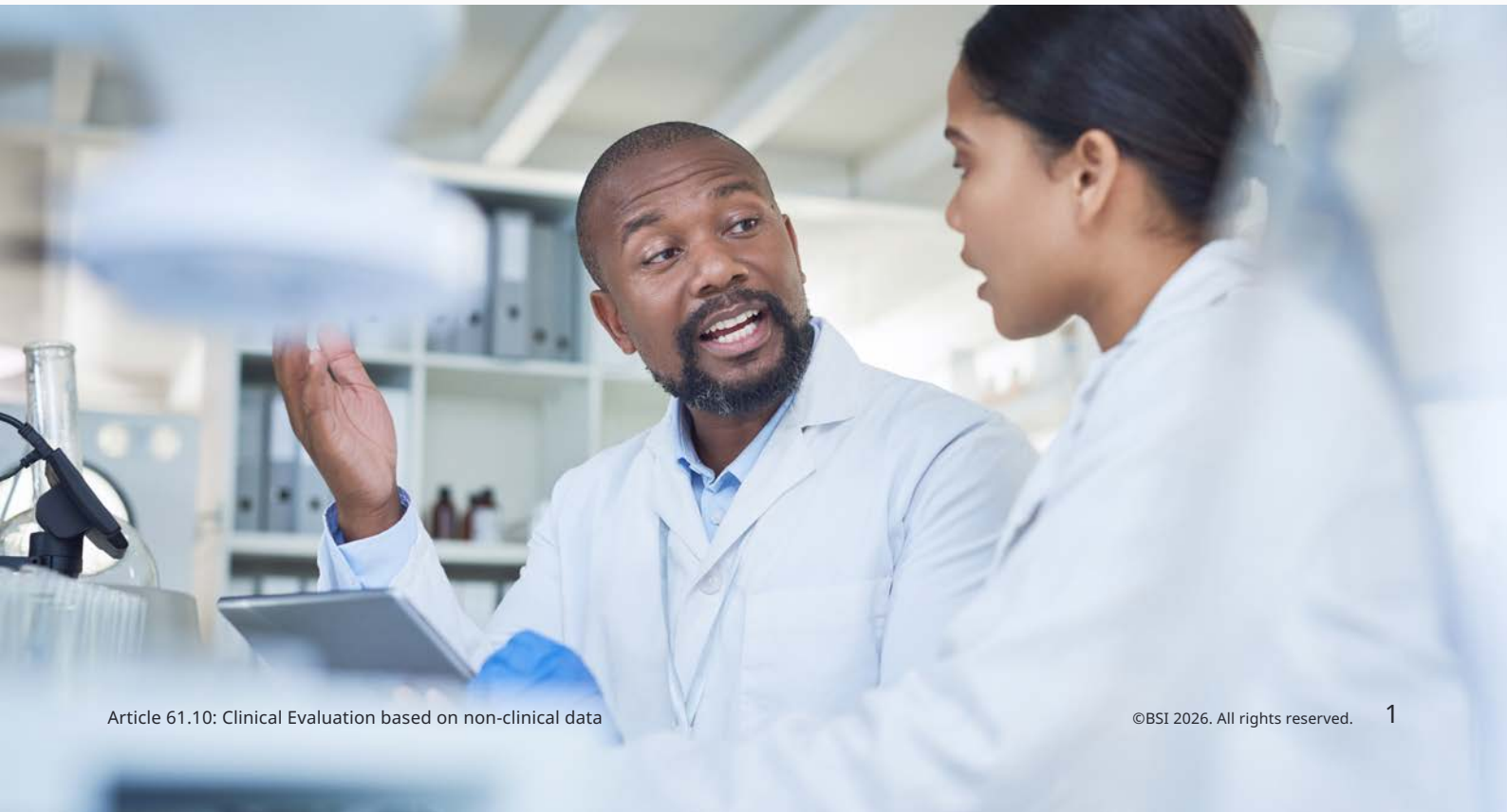


Introduction

Within the healthcare sector, there are thousands of different types of medical devices, ranging from low-medium risk devices such as wheelchairs, contact lenses, surgical instruments to more complex higher-risk devices such as cardiac pacemakers, heart valves and orthopaedic implants. With rapid advances in technology, the healthcare sector has also seen an explosion in digital medical devices (Software as a medical device) some of which incorporate artificial intelligence and machine learning.

Dependent on the manufacturers intended use, these medical devices can be found in a diverse range of settings such as a person's home, health care centres, local sports facilities, emergency response units/vehicles, hospitals, warzones and can be used by lay-users and/or by experienced health care professionals. Irrespective of the medical device type or its intended clinical application, the overall goal of all stakeholders involved in the medical device ecosystem is to ensure that medical devices provide a clinical benefit by improving patient health/quality of life, patient management or public health, whilst also reducing the risk of causing additional and unexpected patient harm. However, despite best efforts to ensure patient safety, history demonstrates that medical devices can cause unanticipated harm. Therefore, it's not surprising that in Europe, the medical devices sector is highly regulated in accordance with (EU) 2017/745 (MDR).

It is widely acknowledged that the MDR requirements governing clinical data can be challenging to interpret and to address. Whilst the regulation provides stringent requirements for providing high quality clinical data for higher-risk devices (Class III and implantable), there is uncertainty regarding clinical data requirements for certain lower risk devices (Class IIa and Class IIb non-implantable). MDR Article 61.1 requires that conformity with the relevant general safety and performance requirements be based on clinical data providing sufficient clinical evidence. However, Article 61.10 introduces a clause for exceptional cases, where certain lower risk devices are exempt from the requirement to use clinical



data to demonstrate safety and performance and instead can rely on non-clinical data (e.g., bench testing, performance evaluation, compliance to standards etc). Reliance on non-clinical data alone to demonstrate conformity, assumes that if well designed and constructed, these devices will perform as intended in the diseased state and will not cause additional or unexpected harm to the patient. However, this assumption does not always hold true when the device is used in the clinical setting, underpinning the importance of clinical data and the application of Article 61.10 in exceptional cases only.

To apply Article 61.10, manufacturers must be able to adequately justify why clinical data is not appropriate for demonstrating device safety and performance. It is accepted that demonstration of conformity based on non-clinical data is justifiable for devices such as disinfectants, sterilisers, and medical fridges, as well as basic tools, such as forceps, surgical gloves and drapes, which are used in a wide range of procedures and clinical settings. Based on the characteristics of these devices and the intended purpose, the performance and safety parameters can be fully addressed by non-clinical testing including in most cases, compliance to technical and/or product standards.

But what about devices which are intended for use in more limited or specific clinical situations, such as biopsy needles, surgical instruments for use with a specific implant and/or specific procedures, software as a medical device (SaMD) or devices that are intended to be used as part of a system? The decision on whether clinical data is appropriate for these types of devices, and therefore the applicability of Article 61.10, has been the subject of much debate, and in the absence of specific guidance, there is a lack of clarity among medical device manufacturers, notified bodies and other regulatory experts on how to apply Article 61.10.

The purpose of this white paper is to clarify BSI's interpretation of and position regarding the applicability of MDR Article 61.10 and to manage expectations for generating a clinical evaluation based solely on non-clinical data.

Non-Clinical (Pre-Clinical) and Clinical Data

Non-clinical data refers to data which is relevant to safety and performance but not generated from actual use of the medical device in humans.

Typically, this data is derived from technical/ laboratory testing, animal testing, cadaveric testing, biocompatibility testing, usability testing and/or simulated use studies or modelling. This data typically confirms that the device was designed correctly and is compliant to product specific standards or common specifications, as applicable. The value of non-clinical data lies in the fact that it provides a strong indication/prediction that once used in humans or in the case of software, once used as part of the intended clinical workflow, the device will perform as intended and will not cause unexpected harm to the patient.

In the case of software, retrospective human datasets/images are often used for algorithm training and testing. Although the data is derived from humans, the output of this testing is categorized as non-clinical. Clinical data is typically only generated when the software is evaluated within the intended clinical environment and workflow by the intended user and for example, compared to the output of the same workflow in the absence of the software.

Clinical data refers to any data that is derived from actual use of the medical device or an equivalent device in humans (MDR Article 2 (48)). It can be generated in a controlled environment via a clinical investigation and from use of the medical device once on the market. Compared to pre-market clinical investigations, clinical data generated in the post market phase, provides real world experience obtained in larger, heterogeneous and more complex populations, with a broader range of end-users. This real-world data is particularly useful for identifying less common but serious device related adverse events, providing long term information about safety and performance and determining the end-user “learning curve”. It is also a particularly useful source of clinical data for low-medium risk devices that are based on long standing, well

characterised technology and, therefore, unlikely to be the subject of either reporting in the scientific literature or clinical investigation. Irrespective of whether it is obtained pre and/or post market, the value of clinical data is that it provides objective and verifiable evidence that, in the clinical setting, the device does indeed perform as intended and does not cause unexpected harm to the patient.

While non-clinical performance objectives may be appropriate measures of specific functional characteristics of the device, the value of clinical data to verify the safety and performance during actual use should not be underestimated. This is well understood for higher risk devices, such as total joint replacement, where extensive pre-clinical testing is performed but with known limitations to the transferability of data to the clinical setting, for example in relation to movement patterns or biotribology. For lower risk devices, there is often a greater reliance on non-clinical data to demonstrate that the device performs according to its intended purpose, but even for these types of devices, clinical data plays an

important role. Cadaver testing of drills or screws can be used to verify device usability and technical function but does not fully replicate the potential for bone necrosis or adequately simulate the bone density of young healthy patients, which can lead to intraoperative complications or unexpected clinical failures. Similarly, high-frequency surgical equipment for cutting, coagulation and ablation of tissue has been shown to perform as intended on porcine tissue or saline soaked sponge, but poor seals, poor cutting or incomplete ablations have been observed in the clinical environment.

Clinical data is required to support devices with a direct clinical benefit and therefore, in these cases, Article 61.10 cannot be applied. By contrast, the safety and performance of devices with an indirect clinical benefit can be supported using one of the following options:

- Non-clinical data (Article 61.10 – accompanied by an acceptable justification to explain why clinical data is not appropriate).
- Clinical data.
- A combination of both non-clinical and clinical data.

Indirect clinical data is derived from the system/procedure or another device that the device under evaluation is intended to be used with. Although this data is generated from the complete system or procedure, in some cases, it can also be used in combination with non-clinical data and other sources of clinical data, to support conformity of the individual system devices or the accessory devices used during the surgical procedure.

When determining the relevance of indirect clinical data, manufacturers should consider the role of the device in the overall procedure (clinical performance) and whether it could potentially influence the success of the procedure or therapy and therefore the patient's clinical outcome.

The greater the potential impact of the device, the more relevant indirect clinical data becomes.

For example, a surgical instrument with the intended purpose to facilitate implantation of an associated device. Procedural success can demonstrate that the device achieved its intended purpose when used in a clinical environment in combination with other devices. Additionally, intraoperative complications can provide useful clinical information about the safety of the device during clinical use.

Where limitations in indirect clinical data are identified, for example limited relevance of clinical outcome measures, it is expected that other sources of data are evaluated, such as non-clinical or PMS to bridge these gaps, but it is not expected that Article 61.10 would necessarily apply.

Recently, it has been observed within the regulatory community that for certain lower risk legacy devices that lack sufficient clinical evidence, manufacturers are increasingly applying Article 61.10 as the basis of their clinical evaluation. However, it's important to clarify that if a manufacturer makes a justification for applying Article 61.10 based on a lack/absence of, difficulty collecting, or insufficient clinical data on the device, it is very unlikely to be accepted by notified bodies. Particularly if clinical data is currently available for equivalent and/or similar devices. For these cases, manufacturers should consider the guidance for providing sufficient clinical evidence per **MDCG 2020-6 Appendix III** which allows for demonstration of conformity via an evaluation of cumulative evidence including non-clinical and lower levels of clinical data (PMS, user surveys etc).

MDR Article 61.10 requirements

To determine if it is possible to provide an acceptable justification for demonstrating device safety and performance without the need for clinical data, the elements addressed by Article 61.10 need to be carefully considered by the manufacturer.

Device Classification

Article 61.10 cannot be applied to Class III and/or implantable medical devices (i.e., only Class IIa and IIb non-implantable medical devices can consider Article 61.10).

Recently, there has been discussion regarding the applicability of Article 61.10 to certain Class IIb implantable WET devices (Listed by MDR Article 52.4 and MDR Article 61.6b – sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips, connectors).

Article 61.6b exempts these medical devices from clinical investigations but goes on to say that the clinical evaluation must be based on sufficient clinical data and compliance to product specific common specifications (if available). For these medical devices, it may be more appropriate to consider cumulative evidence as outlined by MDCG 2020-6 Appendix III to support conformity.

Clinical Performance: MDR Article 2(52)

The clinical performance of the medical device is based on the intended purpose and indications for use, if applicable, and essentially describes the clinical function/role of the medical device in the procedure/therapy/treatment.

It should be clear whether the medical device achieves its intended purpose as part of a system (MDR, Annex I, GSPR 14.1) or if it's a standalone device, and whether through achievement of its intended purpose, it could potentially influence the health outcomes for the patient - if something goes wrong with the medical device, it needs to be clear what the impact will be on patient.

Clinical Benefit: MDR Article 2(53)

Article 61.10 does not explicitly refer to clinical benefits however, per MDR Article 2(52), it is intrinsically related to clinical performance.

A common pitfall when it comes to Article 61.10 is that many manufacturers claim that their device does not provide any clinical benefit and therefore is exempt from clinical data. However, per MDR Annex I, GSPR 1 and 8, the manufacturer must demonstrate that the risks associated with using the device are acceptable when weighed against the clinical benefits. Thus, all medical devices must be able to demonstrate that they can provide a clinical benefit, otherwise it is not possible to demonstrate conformity to the GSPRs.

Clinical benefit refers to the positive impact of the device on patient health expressed in terms of meaningful, patient related clinical outcomes or a positive impact on patient management or public health. Certain medical devices do not directly achieve a positive impact on the patient but may influence the clinical outcome. These medical devices provide an indirect clinical benefit by enabling a procedure to be undertaken, a therapy to be delivered or another device to achieve its intended purpose. Only those medical devices which provide an indirect clinical benefit may be eligible to demonstrate conformity based solely on non-clinical data (Article 61.10). Therefore, it's important that the manufacturer clearly define if their medical device is providing a direct or indirect clinical benefit.

Manufacturers' Claims

Claims can be clinical or non-clinical (technical). Non-clinical claims are not related to health outcomes or to performance in a clinical setting. Examples may include claims related to ease of use, design, durability, sterility etc. Whereas clinical claims relate to a positive impact on patient health, patient management or public health and can be measured. Examples may include claims related to operation times, healing rates, reduced risk of complications, etc. Medical devices which make clinical claims require support from clinical data and Article 61.10 cannot be applied.

Claims can be implicit as well as explicit. For example, there is always an implicit claim that the medical device performs as well as other state of the art alternatives.

It's also important to consider if the claims made by the manufacturer align with the current state of art. For example, if similar or benchmark medical devices make specific clinical claims, and the manufacturer has decided to limit their claims to non-clinical claims only, it brings into question whether the medical device under evaluation aligns with state of the art.

Risk Management

From the state of the art discussion, the key clinical risks associated with use of the medical device per its intended purpose will be identified and these are expected to be clearly traceable to the risk management file. If the manufacturer determines that non-clinical testing methods alone are sufficient to verify and validate the effectiveness of the measures taken to control these risks, a rationale must be provided giving due consideration to state of the art and acceptance of the benefit to risk ratio.

Device-Human Body Interaction

Article 61.10 talks about the specifics of the interaction between the medical device and human body. To address this requirement, it is expected that the following parameters are considered:

- Type and Duration of Contact: how does the medical device interact with the body, what is the degree of invasiveness, and duration of contact (transient, short-term, long term).
- Body Tissues/Anatomical Location: clearly identify the types of body tissue and anatomical locations that the medical device will or could potentially interact with during use. Is the medical device in contact with injured or intact skin or mucous membranes or is it near high-risk areas such as central nervous system or central circulatory system.

- Novelty of Interaction: is the interaction type/ duration/mode of action with the human body novel? If yes, clinical data is likely to be required.

Appropriateness of Clinical Data

The appropriateness of clinical data is a key consideration in the successful application of Article 61.10. The term “appropriate” is not defined in the MDR, but the current understanding is that use of Article 61.10 is limited to exceptional cases where it can be justified. The appropriateness of clinical data should not be confused with concepts such as “adequacy” or “sufficiency”, as these terms relate to the level or quantity of data. Exceptional cases implies that this is not considered to be the typical or normal approach, and this is supported by Article 61.1, which is the starting point for all clinical evaluations, and makes clear that clinical data is expected for demonstration of conformity.

Clinical data may be deemed as “not appropriate” for a variety of reasons. However, an absence of clinical evidence or challenges faced when trying to collect clinical data are not valid reasons for claiming that clinical data is not appropriate. More acceptable reasons could include:

- Clinical investigations that would expose patients to unnecessary burden or harm may be considered unethical, for example, devices intened for use in emergency situations.
- Where meaningful, measurable and significant clinical endpoints cannot be determined, the appropriateness of conducting a clinical investigation to generate new clinical data can be questioned. For example, very simple surgical devices used in a range of procedures and where the generic device group has a long history of use and an established safety profile.
- Medical devices that do not have a direct medical effect and cannot be evaluated in a clinical setting with patients. Consider a refrigeration device that is intended to store tissue samples. There are no clinically relevant endpoints associated with the medical device, rather its clinical performance is reliant on its technical capabilities (e.g., ability to maintain a consistent and accurate temperature profile) or in the case of an autoclave, its clinical performance is reliant on its ability to achieve a certain microbial load log reduction.

For legacy medical devices or medical devices sold outside of the EU, clinical data may be available through standard of care use, and, where available, this data should be incorporated into the clinical evaluation. However, clinical data may not be available for certain medical devices that are new to the market, as in the first scenario described above. In these very rare circumstances, the expectation is that Article 61.10 may be applied at initial conformity with clinical data collected in the post market phase and presented at recertification. However, this can only be applied where all other aspects of Article 61.10, including clinical performance, risk management and device-body interaction are duly justified, and other clinical routes to conformity have been considered including equivalence and/or leveraging similar device data.

Documentation to support a Clinical Evaluation based on non-clinical Data

All medical devices, including Article 61.10 devices, require a clinical evaluation plan, clinical evaluation report and PMS/PMCF plan.

In addition, a clear and robust justification to support the determination that, for this exceptional case, clinical data is not appropriate for demonstrating conformity, must be provided. This justification must address each of the factors detailed in Article 61.10, specifically results of risk management, clinical performance, claims and specifics of the interaction between the device and the human body and is subject to scrutiny by the notified body. Failure to adequately justify the use of Article 61.10, may lead to rejection of this approach.

The clinical evaluation plan (CEP) should be generated in accordance with Annex XIV Part A, including reference to the relevant GSPRs which require support from non-clinical data.

The clinical evaluation report (CER), should include a discussion of state of the art for the purposes of understanding the clinical landscape within which the medical device operates, identify clinically relevant risks and to determine if previously unknown clinical data is available for the device under evaluation and/or similar and equivalent devices. Based on the state of the art, clinically relevant safety and performance outcome measures which require support from non-clinical testing must be identified along with the associated acceptance criteria.

The CER should present a summary of the non-clinical data including identification of the applicable common specifications, harmonised standards and product standards that the manufacturer is demonstrating compliance against. Pre-clinical testing involving animals, phantoms, or cadavers, should also be presented and ideally these studies should involve the intended user (usability testing). It’s important to compare the non-clinical data against the pre-defined safety and performance acceptance criteria and demonstrate acceptability or otherwise of the benefit-risk ratio.

The application of Article 61.10 does not provide an exemption from the requirement to perform PMS including PMCF activities – typically this is limited to general PMCF such as screening of scientific literature and gathering user feedback. The purpose of these activities is to confirm that the device continues to align with current state of the art, identify new risks and/or confirm risk estimation scores and to confirm that clinical data is not available for the device under evaluation, similar device or equivalent devices and therefore Article 61.10 continues to be applicable. If new clinical data becomes available as part of PMS activities, the manufacturer may need to revisit the suitability of their justification regarding applicability of Article 61.10.

Typically, specific PMCF activities such as registry studies, clinical studies, patient level surveys are not expected for Article 61.10 devices. These activities are designed to gather clinical data to address specific clinical questions and directly contradict the determination that clinical data is not appropriate.

Conclusion

Article 61.10 can be considered for certain Class IIa/IIb non-implantable medical devices, where demonstration of conformity based on clinical data is deemed to be not appropriate. Application of this approach must be robustly justified, considering the results of risk management, clinical performance, claims and specifics of the interaction between the device and the human body.

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Article 61.10 scenarios

These scenarios are provided for illustrative purposes only and are not intended to provide pre-determined decisions regarding acceptance of Article 61.10. Due to the diverse nature of medical devices, each medical device is assessed on a case-by-case basis, considering the information provided by the manufacturer regarding clinical performance and benefit, claims, device and human body interaction, output of risk management and justification for determining that clinical data is not appropriate.

Scenario 1: Software

Device	Summary justification
Software application	**Device Classification:** Class IIa, non-implantable **Clinical Performance:** the medical device is a software application that is used to support the monitoring of patients undergoing treatment for an autoimmune disorder. The main role of the medical device is to act as an electronic diary whereby patients can record health events related to the disorder, such as incidences of bleeds, bruises, fatigue and platelet counts. By recording this data, the medical device helps the patient to better understand their condition and will support the quality of the treatment plan as determined by the health care professional based on a review of the patients' electronic data. The medical device itself does not provide specific treatment recommendations to the user or their healthcare professional. **Clinical Benefit:** the benefit of the medical device is that it assists patients and healthcare professionals in the management of the disorder, by contributing to the monitoring of disease treatment and its outcomes. These benefits are considered as indirect. **Claims:** there are no clinically relevant performance or safety claims. **Device-Human Body Interaction:** the medical device is non-invasive and non-patient contacting. The patient downloads a software application on their mobile device. **Risk Management:** the medical device is not associated with any clinical risks or undesirable side effects. All identified risks are technical in nature and relate to incorrect use of the medical device (e.g., incorrect data recorded, account deleted) or software issues (e.g., incorrect data shown, cybersecurity). These risks were reduced to an acceptable level with risk control measures verified and validated through usability and other pre-clinical testing (IEC 62304 and IEC 62366). PMS activities will be used to continuously monitor changes to state of the art and the emergence of new and/or changing risks. **Clinical Data Collection Appropriate:** demonstration of conformity to GSPRs based on clinical data is not appropriate as the device's performance is limited to its ability to adequately record, store and present the data from a patient. The device does not provide treatment recommendations and therefore does not have a direct clinical outcome. A review of the state of the art, confirms that expected performance outcomes are technical in nature, and there is no clinical data for similar and/or equivalent devices. Therefore, design verification and validation tests and compliance to the to the applicable standards, including IEC 62304 and IEC 62366, confirm the device performs as intended.
Is Article 61.10 acceptable for this scenario? Yes	

Scenario 2: Software

Device	Summary justification
Image Management Software	**Device Classification:** Class IIa, non-implantable **Clinical Performance:** the image management software is used by dentists to centralize all the patient's information in a single place and streamline the treatment process. The software is cloud based and runs in a web browser containing a user interface. Through the user interface, the dentist can access display, annotate, store, and make measurements and visualization adjustments of digital dental images of the oral cavity that have been generated via X-ray radiography, oral scan and/or computed tomography scans. The software is not intended to take any clinical decisions, provide any diagnosis or propose any treatment regarding the patient. **Clinical Benefit:** the software provides an indirect clinical benefit by facilitating patient management. **Claims:** the software is a visualization enhancement tool to allow for better visualization of a given dental structure and contains a distance measuring function. These claims are technical in nature and can be supported by non-clinical testing. There are no clinical claims. **Device-Human Body Interaction:** the software is non-invasive and non-patient contacting. **Risk Management:** the product has well-known clinical performance characteristics, a well-known safety profile and is a well-documented technology with dedicated software system, cybersecurity and risk management standards (IEC/EN 62304, EN 82304-1, IEC 62336-1 and ISO 14971). Based on the state of the art and the manufacturers risk management, the main clinical risks associated with use of the device include: exposure to unnecessary irradiation due to need to reshoot the image, incorrect diagnosis information and undue security problems for both the patient and the end-user. The clinical risks have been reduced as far as possible and the effectiveness of the risk control measures verified through usability and technical performance testing. Residual risks are communicated to the user via warning messages displayed directly in the software interface and in the IFU. PMS activities, including the use of user surveys, will be used to continuously monitor changes to state of the art and the emergence of new and/or changing risks. **Clinical Data Collection Appropriate:** the software does not detect dental problems and is not considered to be a diagnostic tool, rather it provides additional information to a qualified professional who already has experience of reading dental images. Use of the software is optional. Without the software, the images can be read and diagnosis made by the dentist using routine alternative methods. The benefit lies in the fact that it facilities patient management and provides additional information to the dentist to support diagnosis. The performance and safety outcome parameters are technical in nature and can be validated by non-clinical testing methods: software testing, cybersecurity, usability and performance validation studies. A review of state of the art did not identify any clinically relevant outcomes, and clinical data is not reported for similar and/or equivalent devices.

Is Article 61.10 acceptable for this scenario? Yes

Scenario 3: Disinfectant

Device	Summary justification
Peracetic acid based high-level disinfectant	**Device Classification:** Class IIb, non-implantable **Clinical Performance:** the medical device is a rapid action disinfectant for invasive and non-invasive medical devices in all settings where such medical devices are typically used, for example hospitals. It is routinely used for rigid and flexible endoscopes, catheters, transducers and other thermolabile instruments and equipment. The medical device has broad-spectrum efficacy against pathogens of interest to human health. It is provided as a powder and dissolved in water. **Clinical Benefit:** the medical device provides an indirect clinical benefit through disinfection of a range of heat sensitive medical equipment for reuse. **Claims:** claims of the medical device are that it offers broad spectrum decontamination against viruses, mycobacteria, bacteria, yeasts and bacterial spores. These claims are related to the performance of the device and are evidenced through bench testing, in-vitro tests for antimicrobial efficacy and compliance to specifications and standards, including relevant standards for demonstrating disinfectant performance. There are no clinical claims. **Device-Human Body Interaction:** the disinfectant is non-patient contact even though it is used on medical devices which make direct contact with the skin, intact mucosal membranes and breached or compromised surfaces. The medical devices are rinsed post disinfection to remove any residual disinfectant. **Risk Management:** the key safety risks associated with the disinfectant are related to user or patient exposure to the disinfectant and include toxicity, sensitivity, irritation etc. The controls in place to mitigate these risks are supported by non-clinical data such as validation of the procedure for post disinfection rinsing, residual analysis, biocompatibility including biological safety evaluations. **Clinical Data Collection Appropriate:** the medical device has no novel features, is not intended for use for any specific medical indication nor is it intended for use on human beings. The role of the medical device is to decontaminate invasive and non-invasive medical devices, for the purposes of preventing patient infection. Considering that infections can be acquired from a wide range of sources during the medical intervention and is influenced by a wide range of variables (e.g., entry points to the body, types of equipment, variety of pathogens), it is not possible to define clinically relevant endpoints which would require support from clinical data. The performance of the medical device as a disinfectant can be readily demonstrated using non-clinical data (microbiology efficacity, toxicological safety, in-use simulation, material and device compatibility, usability, stability, packaging integrity and in vitro studies conducted via harmonised standards and/or reported in the literature). Data and information from PMS and general PMCF will be used to monitor safety concerns and to identify systematic misuse or off-label use of the device.

Is Article 61.10 acceptable for this scenario? Yes

Scenario 4: Surgical instrument

Device	Summary justification
Spinal Cement Delivery Instrument	**Device Classification:** Class IIa, non-implantable **Clinical Performance:** the medical device is a surgical instrument for use during vertebral body augmentation procedures and are intended to create access to a vertebral body to inject bone cement during cementoplasty procedure. The medical device is intended for a single patient and applicable to a single vertebra and are used in conjunction with "Company X" spinal cement in skeletally mature patients in accordance with approved intended purpose. The cement is indicated for the augmentation of pathological fractures of the vertebral body in skeletally mature patients. **Clinical Benefit:** the surgical instrument does not provide a direct clinical benefit. When dealing with spinal cementoplasty procedures, the clinical benefits are associated with the implant (the injected spinal cement), whereas the medical device is only the instrument for injection of the cement. **Claims:** there are no clinical claims for the instruments (the clinical claims are related to performance of the cement and the procedural outcomes). Non-clinical claims include - The instrument can penetrate the skin, soft tissues and bone without breaking or bending during insertion and is capable of cement delivery. These claims can be supported by performance testing. **Device-Human Body Interaction:** the instrument is surgically invasive, intended for transient use (<60 mins), and encounters tissue, spongy bone and cortical bone. The contact duration is <24 hours. **Risk Management:** the instrument does not contain any novel features and has a long safe history of market use. There are no residual risks or side effects associated with the instrument. The main residual clinical risks are solely related to the cement and associated procedure, rather than the instrument (i.e., cement leakage, bone fracture, pulmonary embolism, neurological injuries, post operative infection etc). PMS activities will be used to continuously monitor changes to state of the art and the emergence of new and/or changing risk.

Device	Summary justification
Spinal Cement Delivery Instrument *- continued*	**Clinical Data Collection Appropriate:** • The manufacturer has determined that clinical data is not appropriate for the instrument. This is based on consideration of the fact that the instruments provide indirect clinical benefits and are not extensively covered in clinical research publications. Indeed, the scientific literature does not explicitly focus on clinical data regarding spinal cement needles for cementoplasty, instead focusing on procedure related clinical outcomes. • Performance of the instrument can be readily demonstrated by non-clinical testing specifically: Assembly and pulling tests, handle resistance, cement injection testing, sterilisation, usability testing and biocompatibility • Post CE marking, the manufacturer plans to conduct specific PMCF activities (Survey and Study). The specific PMCF activities will gather data for the cement and the instrumentation that is used with the cement.

Is Article 61.10 acceptable for this scenario? No

Rationale: the instrument is intended for use with a specific implant and as part of a specific surgical procedure. A review of the state of the art identified that the instrument can potentially influence/impact the overall outcome of the procedure, specifically the degree of cement leakage and post-operative fracture rate. The state of the art also identified that manufacturers of similar devices leveraged indirect clinical evidence from the associated procedure, in addition to data obtained via non-clinical testing methods, to support safety and performance of the needles. Additionally, in this case, the manufacturer has planned to conduct specific PMCF activities, addressing both the instrument and the cement, which directly contradicts their position that clinical data is not appropriate.

For this legacy device, a more appropriate approach would be to consider adopting the guidance for providing sufficient clinical evidence provided by MDCG 2020-6, Appendix III, which allows for demonstrating of conformity via an evaluation of cumulative evidence from both clinical and non-clinical data sources, in addition to leveraging relevant indirect clinical evidence from associated procedure.

Scenario 5: Biopsy needle

Device	Summary justification
Biopsy Needle	**Device Classification:** Class IIa, non-implantable **Clinical Performance:** the biopsy needle is used to obtain specimens from soft tissues including breast, kidney, liver, lung, thyroid, lymph nodes and various soft tissue masses. **Clinical Benefit**: there is no direct clinical benefit stated for the biopsy needle. There is an indirect benefit realised through subsequent diagnosis/ exclusion of a medical condition following biopsy. **Claims:** there are no clinical claims. Claims relate to the functional performance of the needle, specifically in relation to technical characteristics allowing the operator to reach further, collect a bigger sample, ergonomic features and spring release mechanism. **Device-Human Body Interaction:** this is a surgically invasive medical device intended for transient use (< 60 mins) and penetrates soft tissues including various organs (kidney, liver, etc.). **Risk Management:** risks were reduced through IFU, labelling and pre-clinical testing. Residual risks deemed acceptable, reduced as far as possible and support an acceptable risk benefit. Clinical risks: • Bleeding in patients on anticoagulation therapy • Hematoma • Infection • Cardiac tamponade • Hemothorax • Inadvertent perforation resulting in bleeding including large artery • Haemorrhage • Pain • Pneumothorax The biopsy needle was not considered novel, but there were some novel aspects in the technical function of the spring release mechanism. **Clinical Data Collection Appropriate:** the manufacturer has determined that clinical data is not appropriate for the biopsy needle. This was based on there being no safety issues or clinical claims that needed to be addressed through clinical data. Clinical data collection was planned in the post market phase through PMS, internal registries, and user feedback.

Is Article 61.10 acceptable for this scenario? No

Rationale: this is a surgically invasive medical device and, while uncommon, there are some serious clinical risks associated with the use of the needle. It is a lower-class medical device, but it forms part of a higher risk procedure, and this should be considered. Furthermore, while biopsy needles in general are not considered novel devices, functional claims around the spring release mechanism had some novel aspects.

It was accepted that some endpoints may be more appropriately addressed through non-clinical methods, the purpose of the needle is to retrieve a specimen from different anatomies and pre-clinical is a very specific environment that does not translate to all clinical environments. There is a difference between living and dead tissue, and it was determined that this may have an impact on device performance.

Although new to the EU market, clinical data from other regions was available to support initial conformity. The manufacturer was proposing to retrieve clinical data on similar medical devices and had planned to collect some EU specific user feedback and registry data in the post market phase. This suggests that clinical data is appropriate, and collection is possible. A high level of evidence was not expected, but clinical data was deemed to be appropriate ruling out article 61(10).

Scenario 6: Injector systems

Device	Summary justification
Microprocessor-controlled powered injector systems	**Device Classification:** Class IIb, non-implantable **Clinical Performance:** the medical device under evaluation is an injector. Syringes are loaded into the injector and can be filled either manually or automatically (preset volume). After loading the syringes, the user interacts with the injector via a touch screen interface and intravenously administers the contrast agent or flushing solution as required, into adult patients during Computed Tomography (CT) imaging diagnostic procedures. There are no specific indications for use. **Clinical Benefit:** the benefit of the medical device is that it provides a consistent flow rate of contrast media into the patient's body prior to and / or simultaneous with a scan for even image density. Additionally, X-ray exposure can be reduced as the user does not need to be near the patient / scanner during a CT scan for administration of contrast media. The benefits are categorised as indirect - the direct benefit to the patient is derived from the subsequent diagnosis. **Claims:** all claims are related to technical performance of the injector system and are non-clinical. **Device-Human Body Interaction:** the medical device is externally communicating, indirect contact with the blood pathway, ≤ 24-hour contact duration. Compared to similar medical devices on the market, there are no novel features associated with the interaction. **Risk Management:** the medical device does not contain any novel features and has a long safe history of market use. Generally, injection systems have relatively consistent technical capabilities and clinical risks associated with the device are common to all injection systems and include air embolism, extravasation, contamination (environmental or particulate), incorrect test injection. Effectiveness of the Risk control measures are adequately verified and validated by non-clinical test methods. PMS activities will be used to continuously monitor changes to state of the art and the emergence of new and/or changing risks.

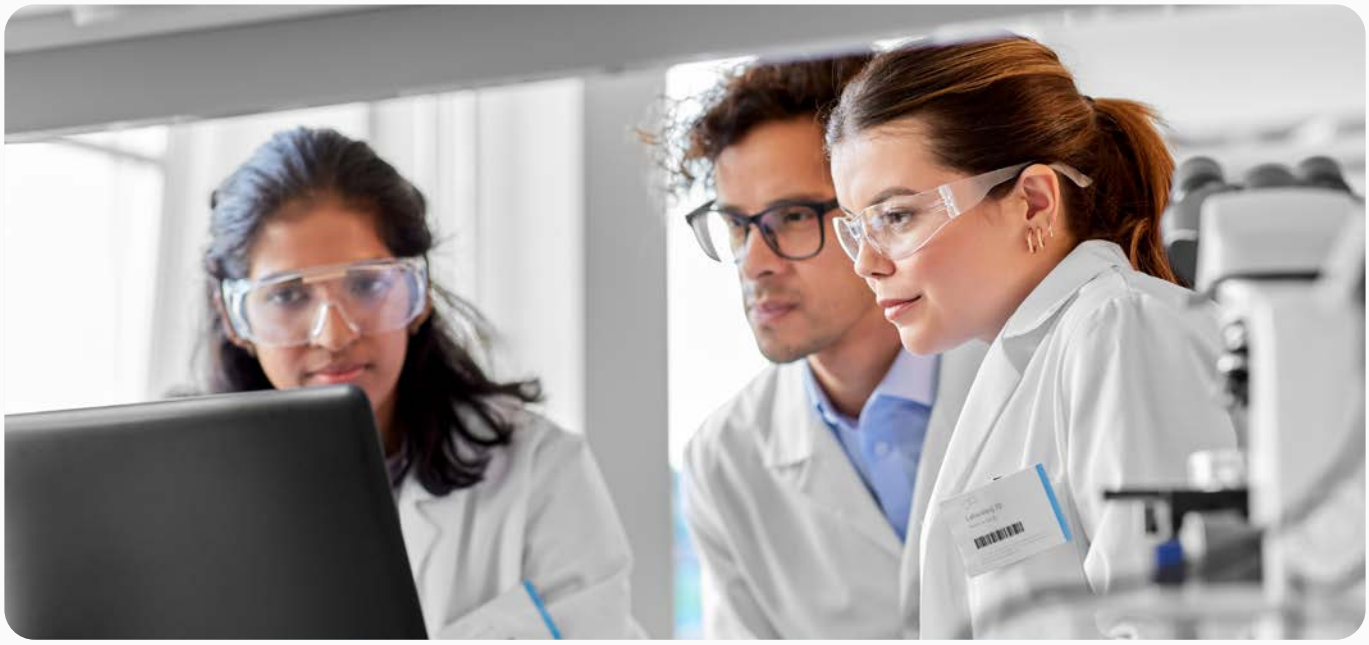
Device	Summary justification
Microprocessor-controlled powered injector systems *- continued*	**Clinical Data Collection Appropriate:** to achieve its performance, the injection system must deliver the contrast media safely and accurately according to a pre-programmed protocol. The main clinically relevant outcome parameter is therefore diagnostic image quality and whether it can be obtained with the injector. These parameters are readily demonstrated by non-clinical data such as image measurements, ability of the radiologist to make a diagnosis, bench testing with regards to fluid delivery performance (e.g., flow rate, volume, pressure settings, compatibility with IC access devices etc.) and usability studies. Additionally, there are no direct clinical benefits or clinical claims; therefore, clinical data was deemed to be not appropriate.

Is Article 61.10 acceptable for this scenario? No

Rationale: a review of the state of art demonstrates that clinical claims, supported by clinical data, are routinely reported for similar medical devices. These claims related to the specificity and sensitivity of the injection system which enables the location and identification of a variety of disease states during Computed Tomography (CT) imaging diagnostic procedures and is considered state of the art in terms of performance. For the medical device under evaluation, the manufacturer has decided not to make these clinical claims and as a result, cannot demonstrate that their device is as good as or better than the current state of the art. Therefore, the application could not be accepted.

Scenario 7: Wound care device

Device	Summary justification
Device for wound and skin care	**Device Classification:** Class IIb, non-implantable **Clinical Performance:** the medical device is a saline solution (0.9% w/v sodium chloride) and is intended for use in topical irrigation, wound cleansing, irrigation of mucous membranes and rinsing of eyes. **Clinical Benefit:** the benefit of the solution is that it facilitates wound cleansing in preparation for subsequent wound treatment and clears congestion thereby relieving symptoms of rhinitis. **Claims:** claims are technical in nature – medical device is for single use, and is non-sensitising, non-toxic, sterile. These claims can be supported by pre-clinical testing. **Device-Human Body Interaction:** the medical device is non-invasive, comes into direct contact with injured skin and is intended to be used principally with wounds which have breached the dermis and can only heal by secondary intent. **Risk Management:** the medical device is a well-established product, with a long history on the market (over 30 years). State of the art assessment confirms that it is recommended to be used as an irrigation solution for cleansing of wounds, irrigation of mucous membranes and rinsing of eyes, with no or few documented side effects. Key risks are related to opening sachet, spillage of solution, inadequate irrigation due to uncontrolled delivery of solution, product re-use, use after expiry date, non-sterile solution, concentration of sodium chloride too high, use with incompatible materials, Contamination of outside of sachet, weak seal – solution leakage, injected into patient. All risks have been reduced as far as possible with supporting evidence based on pre-clinical and biological safety testing and the device is compliant with the British Pharmacopoeia standards. There are no residual clinical risks which require support from clinical data. PMS activities will be used to continuously monitor changes to state of the art and the emergence of new and/or changing risks.



Device	Summary justification
Device for wound and skin care *- continued*	**Clinical Data Collection Appropriate:** • Clinical data from clinical investigations are not deemed appropriate for demonstration of performance and safety. Normal saline is well-established technology and a standard solution that has been used in medicine for close to 200 years and still is widely used both for cleansing and irrigation as well as for injection (hydration, dilution of pharmaceuticals etc.). Being one of the gold standard irrigation solutions in medicine today, few studies are carried out to evaluate performance and safety of the device. • Whereas there are no ethical considerations regarding patient safety in the collection of clinical data on the device by clinical investigation, performing studies on such a well-established device as normal saline that is used routinely in clinical settings is not considered defendable in terms of health care resources or the time of the patients. State of the Art strongly supports the use of normal saline for its intended use. In addition, clinical data from post market surveillance is continuously collected.

Is Article 61.10 acceptable for this scenario? No

Rationale: The state-of-the-art review discusses clinically relevant endpoints for which it is appropriate to gather clinical data. These endpoints include infection rate, wound healing, mucociliary clearance time, nasal resistance, decreased symptoms of rhinoconjunctivitis and improved quality of life.

Considering the nature of the medical device, it is accepted that collection of clinical data by clinical investigation may not be practical. However, the manufacturer did not consider other sources of clinical data. A more appropriate approach would be to consider adopting the guidance for providing sufficient clinical evidence provided by MDCG 2020-6, Appendix III, which allows for demonstrating of conformity via an evaluation of cumulative evidence from both clinical and non-clinical data sources.

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