“State-of-the-art” in new EU medical device regulations: a review of its development in medical device law, the interpretations from stakeholders, impacts, and possible solutions for implementation

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LIST OF ABBREVIATIONS

Table 1 List of abbreviations

Abbreviation	Meaning
ABHS	Advisory Board for Healthcare Standards
AIMDD	Active Implantable Medical Device Directive
CEN	*Comité Européen de Normalisation,* European Committee for Standardisation
CENELEC	*Comité Européen de Normalisation en Électronique et en Électrotechnique,* European Committee for Electrotechnical Standardisation
CEP	Clinical Evaluation Plan
CER	Clinical Evaluation Report
CPSP	Clinical Performance Study Plan
CS	Common Specifications
EMA	European Medicines Agency
EC	European Communities
EN	*Europäische Norm*, European Standard
EU	European Union
ETSI	European Telecommunications Standards Institute
GHTF	Global Harmonization Task Force
GSPR	General Safety and Performance Requirements
IEC	International Electrotechnical Commission
IMDRF	International Medical Devices Regulators Forum
IVDD	In-vitro Diagnostics Directive
IVDR	In-vitro Diagnostics Regulation
ISO	International Organisation for Standardisation
ITU	International Telecommunication Union
MDCG	Medical Device Coordination Group

Abbreviation	Meaning
MDD	Medical Device Directive
MDR	Medical Device Regulation
MS	Member State
NB	Notified Body
NCA	National Competent Authority
NLF	New Legislative Framework
OSH	Occupational Safety and Health
OJ	Official Journal
OJEU	Official Journal of the European Union
PMCF	Post-Market Clinical Follow-up
PMPF	Post-Market Performance Follow-up
PSUR	Periodic Safety Update Report
Reg.	Regulation
RQ	Research Question
SReq	Standardisation Request[1]
SSCP	Summary of Safety and Clinical Performance
SSP	Summary of Safety and Performance
TÜV	*Technischer Überwachungsverein*, Technical Inspection Association[2]
ZLG	*Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten,* Central Authority of the Laender for Health Protection with regard to Medicinal Products and Medical Devices

[1] Mandate
[2] Wikipedia

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Table 2 List of terms

Term	Meaning
medical device	means "medical device" as defined in point (1) of Article 2 of Regulation (EU) 2017/745 and/or "in vitro diagnostic medical device" as defined in point (2) of Article 2 of Regulation (EU) 2017/746, unless specified
new regulations	same as "new regulations governing medical devices", means the Regulation (EU) 2017/745 and Regulation (EU) 2017/746, unless specified

CHAPTER 1 INTRODUCTION AND AIM

1.1 New European regulations governing medical devices

The European Union (EU) has introduced in 2017 two new regulations (MDR [1] and IVDR [2]) (the new regulations) as a fundamental revision of the three previous directives (MDD [3], AIMDD [4] and IVDD [5]) governing medical devices which include the general medical devices, the active implantable medical devices and the in vitro diagnostic medical devices over the last two decades. With this approach, the establishment of a "*robust, transparent, predictable and sustainable regulatory framework ensuring high level of safety and health"* and *"supporting innovation*" (Recital 1 of MDR; Recital 1 of IVDR) are aimed to achieve. Besides the enlargement of their content (see Table 3 below), the revision of these European harmonised legislations is regarded as fundamental as it has kept recent technical developments to place more emphasis on clinical evidence-based life-cycle approach to meet common safety concerns, introduced high level of safety and performance requirements on the medical devices, more stringent requirements for the designation of notified bodies and has increased supervision from national competent authorities and the European Commission [6] [7] [8]. Certain groups of products which are claimed by the manufacturer only an aesthetic or another non-medical purpose but have similar functioning and risk profile to medical device are regulated under the new legislation framework as medical devices as well. [9] Moreover, the IVDR has also made the involvement of the EU Reference Laboratory for the conformity assessment of certain products and the consultation procedure with competent authorities for medicinal products for companion diagnostics mandatory [8].

Table 3 Comparison of the EU new legislations and old directives for medical devices[3]

Items	**MDR**	**MDD**	**AIMDD**	**IVDR**	**IVDD**
Number of articles	123	23	17	120	24
Numbers of annexes	17	12	9	15	10

[3] (Own illustration)

Items	MDR	MDD	AIMDD	IVDR	IVDD
Number of classification rules	22	18	-/-[4]	7	-/-, list[5]
Number of sections in GSPR / Essential Requirements	23	14	16	20	8
Number of pages[6]	175	43	20	157	37

As required, in order to create legally binding obligations that can be enforced, essential requirements set under the European new legislative framework (NLF) [10] for the marketing of products must be "*worded precisely enough*". [11] Nevertheless, comparing to the directives they are repealing, the new regulations governing medical devices and in vitro diagnostics both refer more frequently the blanket clauses referring "state-of-the-art", without providing a clear definition, across various aspects as legislative requirements (see comparison tables Table 10 and Table 11 in Annex 1) including the general safety and performance requirements (GSPR). This leaves the stakeholders involved plenty of space for interpretations [12] [13].

Both new regulations have been fully applied [7] [8], and certificates issued in accordance with the old directives may only at latest be valid until, respectively, 26 May 2024 (MDD/AIMDD)[7] and 26 May 2025 (IVDD)[8]. In the recently (as of in June 2022) published Position Paper from the Medical Device Coordination Group (MDCG), Notified Bodies (NB) have provided data and indicated that, over 90% MDD/AIMDD certificate that are currently (as of in April 2022) valid will expire in between 2023 and 2024, whilst there are only 30 NB which are designated under the MDR available and can cover only about 80% of those currently valid MDD/AIMDD certificates [14]. Due to these reasons, a consensus understanding of these blanket clauses across all stakeholders has become of great importance and urgency.

[4] -/-: not applicable
[5] predetermined list
[6] as in the legal act that is published on the Official Journal
[7] Article 120 of MDR, except for certificates issued in accordance with Annex 4 to MDD or Annex IV to AIMDD which shall become void at the latest on 27 May 2022
[8] Article 110 of IVDR

1.2 Aim of the study

This study aims to investigate the use of the term “state-of-the-art” in the new European harmonised regulations for medical devices and summarise the interpretations from different stakeholders and analyse their impacts. Possible solutions for implementation are followed by mainly taking the point of view of manufacturers into consideration, while the opinions from certain notified bodies about this topic is also taken into account.

CHAPTER 2 MATERIAL AND METHODS

First of all, the term “state-of-the-art” and its variants are checked across the new European regulations governing medical devices and in vitro diagnostics, with a non-exhaustive list of certain language versions of the regulations, including their possible interactions with understandings at international level and across the EU/EFTA Member States, and the results are briefly listed. Together, the stakeholders who are either obligated to fulfil or set out such requirements are studied.

Then, the evolvement of the “state-of-the-art” across old and new regulation frameworks is reviewed. In this phase, the study tries to find out reasons why such blanket clauses have remained in the new regulations.

Additionally, public articles or announcements from the stakeholders including authorities, notified bodies, technical and standardisation organisations, and trade organisations are addressed based on different aspects relating to the “state-of-the-art” requirements in the new regulations. Here aims to answer what different stakeholders may concern.

In the same chapter, discussion is followed to complement the results from literature research and the point of view from the author of this study is presented to deepen the understanding of relevant topics. Interpretations about “state-of-the-art” from different stakeholders are grouped and analysed. A focus is given to manufacturers about how they may fulfil the “state-of-the-art” requirements.

Last but not least, an outlook for the smooth functioning of the new regulations governing medical devices is provided regarding the “state-of-the-art” requirements based on conclusions drawn at the end of the study.

Throughout the study, literature research is applied to EU provisions and regulations, guidelines, standards, and public articles, books, reports and websites related to the concerns raised in the introduction and aim.

Online tools as their free version are used for data illustration (e.g., Datawrapper provided by the Datawrapper GmbH, Visual Paradigm Online) and translation (e.g., DeepL provided by the DeepL SE).

CHAPTER 3 RESULTS AND DISCUSSION

3.1 State of the art

3.1.1 Variants in the new regulations

By reading the text from the new legislations governing medical devices, inconsistent use of the term "state-of-the-art" with various modifiers can be also found as from the summaries of Table 10 and Table 11 (see below, Annex 1). Examples are: "*state of the art*", "*generally acknowledged state of the art*", "*state of the art in medicine*", "*state of the art in clinical care*", "*state of the art of clinical practice*", "*clinical state of the art*", "*generally acknowledged state of the art in the field of medicine*", and "*state of the art in diagnosis and/or medicine*" [1] [2].

This term has been extended with more details, without knowing if it is intentional, which may generate even more different interpretations, when it is translated into the different official languages of Member States (MS) [15]. Table 12 (see below, Annex 2) reports how this term from the same clause is translated in the MDR in five different official EU languages. Similar phenomena can be observed in the text of IVDR. [16] This may have left the harmonisation of the regulations for medical devices across MS being challenged. For example, the difference between the *"generally acknowledged state of the art"* in EU English, the *"état de l'art généralement admis (generally accepted state of the art)"* in French and the *"stato dell'arte generalmente riconosciuto (generally recognised state of the art)"* in Italian might imply different levels of requirement on the accreditation for someone capable to make a judgement. The Spanish text of the regulation has also differentiated *"los conocimientos más recientes de la medicina (latest medical knowledge)"* and *"el estado actual de la técnica (state-of-the-art technology)"* whilst the same clauses are all *"state of the art"* in EU English (see Table 12).

3.1.2 "State-of-the-art" in general

Regardless the fact that not being defined as such in the MDR or IVDR, the term "state of the art" generally means "*the most recent stage in the development of a*

product, incorporating the newest technology, ideas, and features" [17] in EU English[9] [18].

Representatives from the EU are among the founders of the voluntary group of regulators – the International Medical Devices Regulators Forum (IMDRF) since October 2011 [19]. In order to promote convergence of regulations at international level aiming at high level of safety protection, during the development of MDR and IVDR, the guidance developed for medical devices and in vitro diagnostics by the IMDRF and its predecessor initiative, the Global Harmonization Task Force (GHTF), is to certain extent taken into account by the EU legislators (Recital 5 of MDR [1]; Recital 5 of IVDR [2]).

Following this hint, the definition given in the IMDRF/GHTF guidance should logically provide stakeholders a clue about the "state-of-the-art" in the new regulations, even though there is a lack of guideline indicating the use of the IMDRF/GHTF guidance to support the demonstration of compliance to the new regulations.

In the IMDRF Guidance, IMDRF/GRRP WG/N47 FINAL:2018, *Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices*, "state-of-the-art" means *"developed stage of* ***technical capability*** *at a* ***given time*** *as regards products, processes and services, based on the relevant* ***consolidated*** *findings of science, technology and experience." [emphasis added]* (Section 3.43, p11) [20]. This guidance further explains that the "state-of-the-art" "*embodies what is* ***currently and generally*** *accepted as* ***good practice in technology and medicine***" and *"****does not necessarily imply the most technologically advanced solution****" [emphasis added].* The definition and explanation of the "state-of-the-art" presented in this IMDRF guidance fully correspond to the Section 3.18 of the ISO/IEC Guide 63:2019 (the ISO/IEC Guide 63:2019), which is further analysed and discussed in chapter 3.1.3 below.

It is worth to mention that, since the use of any guidance is a choice by the stakeholder(s), unlike the mandatory regulations, it cannot be expected that the definition and explanation from this IMDRF guidance would apply in every corner.

[9] based on Irish/British English

3.1.3 "State-of-the-art" provided by standards

As defined in Section 1.4 in the ISO/IEC Guide 2:2004 (the ISO/IEC Guide 2:2004) - Standardisation and related activities – General vocabulary, "state-of-the-art" means "*developed stage of* ***technical capability*** *at a* ***given time*** *as regards products, processes and services, based on the relevant* ***consolidated*** *findings of science, technology and experience*" *[emphasis added]* [21]. The ISO/IEC Guide 2:2004 also explains in its section 1.5 that, if a normative document on certain technical subject is, through consultation and consensus procedures, acknowledged by the majority experts as reflecting the "state-of-the-art", this presumes so-called "acknowledged rule of technology" at the time of its approval.

More precisely for medical devices, as further explained in the Section 3.18 of the ISO/IEC Guide 63:2019 (the ISO/IEC Guide 63:2019) - Guide to the development and inclusion of aspects of safety in International Standards for medical devices - the "state-of-the-art *embodies what is* ***currently and generally*** *accepted as* ***good practice in technology and medicine****. The state of the art* ***does not necessarily imply the most technologically advanced solution****. The state of the art described here is* ***sometimes referred to as the 'generally acknowledged state of the art'"*** *[emphasis added]* [22].

Thus, the author of this thesis can outline certain key elements abstracted from the term "state-of-the-art" for medical devices and the normative documents which representing "state-of-the-art"[10]: (1) reflecting timeliness, (2) no mandatory to be the latest, (3) being subject-orientated, (4) being acknowledged by majority, (5) being on the basis of opinions from experts, (6) publication being approved through a due process (e.g., consensus procedure) and (7) technical capacity[11].

However, one should be aware that the interpretation from international standard organisations cannot directly and fully represent the actual requirements in EU regulations.

As of the opinion of the author of this thesis, the definition and interpretation of "state-of-the-art" from the ISO/IEC Guide 63:2019 has become the source for

[10] Supplemented by the discussion in chapter 3.1.4, where one more element is discovered and introduced

[11] Or "technical feasibility", see chapter 3.1.4

certain key standards for medical devices. For instance, the Section 3.28 of ISO 14971:2019 - Medical devices – Application of risk management to medical devices (ISO 14971:2019) has been introduced (Foreword) [23], whose text has been subsequently approved as EN ISO 14971:2019[12] without modifications by the European Committee for Standardisation (CEN) (Endorsement notice of SIST EN ISO 14971:2020) [24].

Together with the introduction of Annex ZA and ZB ("Annex Z") in its amendment EN ISO 14971:2019/A11:2021 (the Amendment 11) that CEN approved on 27 October 2021 [25], the harmonised standard EN ISO 14971:2019 has been adopted through the Commission Implementing Decision (EU) 2022/757 of 11 May 2022 [26] and Commission Implementing Decision (EU) 2022/729 of 11 May 2022 [27] for the application of risk management to medical devices to confer presumption of conformity to the parts of the new regulations that are covered by the standard and the amendment.

Nevertheless, one should be aware that, even the presumption of conformity is conferred, the harmonised standard EN ISO 14971:2019 and its Amendment 11 do not cover all requirements from the new regulations where "state-of-the-art" shall be taken into consideration, because simply utilising the "Annex Z" cannot fully cover the compliance to all the requirements in the new regulations.

As an example, an article published on 17 December 2021 by John Lafferty has indicated that the "Annex Z" of the harmonised standard EN ISO 14971:2019 and its Amendment 11 does not list section 1, 2, 7, or 10 to 23 of the general safety and performance requirements (GSPR) in the MDR. Because the standard was never intended for specific safety requirements on the design and manufacture of the device nor specific safety information supplied with the device. Similar gaps are also found in the requirements on usability-specific aspects such as the section 6 of the MDR GSPR [28]. Taking the analysis from the Table 10 (see below, Annex 1), the stakeholders may only

[12] This European Standard was approved by CEN on 5 August 2019, and then given relevant national standard status by publication or endorsement as EN ISO 14971:2020 through their members, as stated in the European foreword. Reference in this paper takes its approval date as EN ISO 14971:2019 and does not seek for any differentiation if the published or endorsed date is mentioned, because "*CEN and CENELEC members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration*" [22].

benefit from presumption of conformity to the "state-of-the-art" requirements in the first paragraph of the section 4 of the MDR GSPR, where evidence related to the clauses / subclauses 4.2 "Management responsibilities", 4.4 "Risk management plan", 6 "Risk evaluation", 7 "Risk control", and 8 "Evaluation of overall residual risk" in the harmonised standard EN ISO 14971:2019 [29] is provided (Table ZA.1 of the Amendment 11) [30]. To fulfil the "state-of-the-art" requirements stipulated in the section 1 of the MDR GSPR, the stakeholders may have to turn to other measures. Similar phenomenon can be observed in the Table ZB1 of the Amendment 11 depicting correspondence between the EN ISO 14971:2019 and the IVDR GSPR as well [30].

Due to the voluntary nature of using standards including European harmonised standards, only when the relevant stakeholders choose the way of utilising the reference of "Annex Z" to benefit from the presumption of conformity, the definition and the interpretation of the "state-of-the-art" sourced from the ISO/IEC Guide 63:2019 (or even the ISO/IEC Guide 2:2004) are further extended to the relevant parts of MDR and IVDR through compliance. This can be understood by considering a certain situation, in which a manufacturer has a well-established risk management system documenting "state-of-the-art" evidence (sourced from the ISO/IEC Guide 63:2019) in accordance with the clauses / subclauses 4.2, 4,4, 6, 7 and 8 of the ISO 14971:2019 for his medical devices. – But this is yet not enough for this manufacturer to make a conclusion of compliance to the first paragraph of the section 4 of the MDR/IVDR GSPR, where "state-of-the-art" is also required. Later, also later than 17 May 2022 (see Table 13 below in Annex 3), the manufacturer upgrades its risk management system to using the EN ISO 14971:2019 together with the application of the Amendment 11, without changing any of the documented evidence. After this procedure, the exact same "state-of-the-art" evidence (sourced from the ISO/IEC Guide 63:2019) can now be claimed as fulfilling the "state-of-the-art" requirements in the section 4 of the MDR/IVDR GSPR. – Still, one cannot say that the meaning of the "state-of-the-art", or more precisely, the "generally acknowledged state of the art", as required in the section 4 of the MDR/IVDR GSPR would be equal to the definition and the interpretation of the "state-of-the-art", where it is deemed to be synonym of the "generally acknowledged state of the art", sourced from the Section 3.18 of the ISO/IEC Guide 63:2019.

Therefore, the author of this thesis reserves the opinion that the actual meaning of "state-of-the-art", together with its variants like "generally acknowledged state of the art", etc. (see more details in chapter 3.1.1 above), in the new regulations may not be revealed unless an official explanation is published by the regulators.

3.1.4 "State-of-the-art" in legislations from EU/EFTA Member States

Even though the EU legislations supersede the national legislations in the Member States, taking a look at the "state-of-the-art" in legislations from EU Member States can provide a better insight of the background of this blanket clause for medical devices. Opinions from the experts of EFTA Member States like Norway and Switzerland are also taken into the analysis due to the adoption of EU regulations governing medical devices in their law system.

In the 2000 published book *Legal aspects of standardisation in the Member States of the EC and EFTA, Volume 1*, "*the 'Stand der Technik', the 'state of the art', is a requirement that lies on the frontier of science, imposing to do what is technically feasible"* (Section 10.4, p 204) [31].

The authors of this book, Harm Schepel and Josef Falke, have also mentioned that conformity to the "Stand der Wissenschaft und Technik (state of the art in science and technology [13])" in the German law system gives the highest requirement where "*those precautions against harm should be taken which are deemed necessary according to the latest developments in science. This is a yardstick that lies higher even than technical feasibility: the requirement sees to an objective, disregarding the means available to reach that objectiv*e" *[originally in English, text is quoted unchanged from the book]* (Section 10.4, p 203).

As it can be seen from the Table 12 (see below, Annex 2), the German translation variants of "state of the art" in the MDR, which though presents certain deviations from its English counterpart, do not present any use of the term "Stand der Wissenschaft und Technik (state of the art in science and technology). By the interpretation from the author of this thesis, during the translation the German experts have avoided taking these requirements which are higher even than technical

[13] Translated by DeepL (free version)

feasibility for the stakeholders. Logically speaking, the state-of-the-art in science should usually be way more advanced than their translational applications in industry.

Quoted by the authors in the same book, *"in an authoritative French definition, a règle de l'art (rule of art[14]) constitutes 'appropriate technical conduct which corresponds to the state of the art and is accessible to all professionals concerned'"* (Section 10.4, p 204) [31].

Compared to the French translations collected in Table 12 (see below, Annex 2), the term "règle de I 'art (rule of art)" is also not used in the French version MDR.

In the book *Legal aspects of standardisation in the Member States of the EC and EFTA, Volume 2*, where country reports are presented, "state-of-the-art" are discussed by different authors [32], where huge differences can be observed as listed and discussed below.

In Austria, Peter Draxler, Alexander Petsche et al. have pointed out that according to the Austrian Supreme Court, "*the state of the art is not a legal phenomenon... It merely informs a party if and how something should be done... the state of the art is not a legal obligation to behave in a certain manner but only mirrors how parties behave*" (Austria, Section 8.1). The authors have also suggested that *"**If a certain state of the art is not yet generally used, it does not have the status of an acknowledged state of the art**" [emphasis added]* (Austria, section 8.1, p 46).

This probably provides an interpretation of the synonyms used in the GSPR of MDR and IVDR on the device risk management and the risk control measures. If taking the Austrian experts' opinion into consideration, the device risk management system and the risk control measures taken cannot be established without putting into actual use. In other words, risk information collected from the post production activities, its review and actions that have been taken should play an indispensable role, which correspond to the Chapter 10 of the standard ISO 14971:2019 – "Production and post-production activities" (Table of contents) [23]. Moreover, comparing to the statement that *"the state of the art described here is sometimes referred to as the 'generally acknowledged state of the art'"* from the ISO/IEC Guide 63:2019 (see chapter 3.1.3

[14] Translated by DeepL (free version)

above), which seems to give the two different requirements same status, the author of this thesis believes that, the Austrian interpretation with proper differentiation provides a better understanding for the stakeholder. Furthermore, it has indicated the method to fulfil a requirement with the "acknowledged status" as well.

The author of this thesis is convinced that this interpretation from Austrian law experts is able to outline another key element for the concept of the "state-of-the-art" as supplementing the discussion in chapter 3.1.3 above: (8) acknowledged status based on record of use. A summary of the elements, taking the discussions in chapter 3.1.3 above, is depicted in Table 14, see Annex 4 below.

In Finland, the author Marja-Leena Mansala has indicated the concept like "state-of-the-art" has no specific content or meaning in Finnish law, nor in the Finnish language. The author further states, *"generally, the content of the state of the art could be described as a 'level of pertinent scientific and technical knowledge existing at certain time'"* (Finland, section 8.1, p 206).

In Irish law system, the author Robert Clark has quoted that the "state of the art" is *"... narrowly defined as including, in a failure to warn case, the scientific knowability at the time of manufacture of a* ***risk associated*** *with a product, and in a design defect case, the technological feasibility at the time of manufacture of producing a* ***safer product****" [emphasis added]* (Ireland, Section 7).

With this interpretation from the Irish author, one may compare the interpretation of "acknowledged state of the art" in Austria when mentioning the GSPR of MDR and IVDR on the device risk management and the risk control measures.

Another country example is Norway – as indicated by the author Sverre Sandvik, concepts like the "state-of-the-art" *"reflect that fact that, when establishing rules of law, it is often natural to take into consideration what is customary within a profession or a sector of society.* ***The use of such concepts is often due to a failure of the legislator to establish more precise rules****.* ***Sometimes*** *references to such concepts* ***are used deliberately in order to create a legal framework which is more flexible*** *than would have been possible with more 'sharp-edged' rules" [emphasis added]* (Norway, Section 8.1, p 654).

As can be perceived from the comparison tables Table 10 and Table 11 (see below, Annex 1), the use of the concept of "state-of-the-art" has been broadened in the

new regulations governing medical devices to the same or similar topics. This must have been done in a deliberate manner by the legislator, as presumed by the author of this thesis in a logical manner. So that this phenomenon can be interpreted as the need of providing more flexible rules in the MDR and IVDR.

Due to its similar legislative system with the EU, the "state-of-the-art" in Swiss law system can also reveal a possible interpretation of the topic concerned. The authors Dirk Trüten, Karin Bürgi and Leena Kriegers-Tejura has quoted that *"in the German literature, the opinion is widespread that the state of the art concerns the technical possibilities already applied in a certain branch or the practical application of scientifically researched and 'proven' laws of nature"* and *"State of the art... also comprises new technical developments which have not yet been tested in practice"* (Switzerland and Lichtenstein, Section 8.1.3, p 872).

3.2 Stakeholders

3.2.1 Manufacturers

It is one the obligations of manufacturers to ensure that their devices have been designed and manufactured in accordance with the requirements of the new regulations governing medical devices, when they place the devices on the market or put them into service (Article 10, MDR; Article 10, IVDR). This includes the GSPR set out in the Annex I of MDR and Annex I of IVDR, among which *"taking into account the state of the art"* has been referred to in a few aspects.

Section 1 of the Annex I to the MDR/IVDR states that *"**Devices**... shall be safe and effective and shall not compromise the clinical condition or the safety... provided that any risks... constitute acceptable risks when weighed against the benefits... **are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art**." [emphasis added]* Furthermore, section 4 of the Annex I to the MDR (same as in IVDR) requires that *"**Risk control measures adopted** by manufacturers for the design and manufacture of the devices shall **conform to safety principles, taking account of the generally acknowledged state of the art**." [emphasis added]* In other words, the risk management system adopted by manufacturers for medical devices shall be able to provide

state-of-the-art high level of protection of health and safety and conform to the state-of-the-art safety principles.

For manufacturers of devices that incorporate electronic programmable systems and of software, the state-of-the-art safety principles concerned are extended to the field of information security. Moreover, they must demonstrate their development life cycle is also state-of-the-art, as another reference is given to the requirement on devices that incorporate electronic programmable systems and software that are devices in themselves. Section 17.2 of the Annex I to the MDR (section 16.2 of the Annex I to the IVDR as counterpart) states that *"For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the* ***state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation****." [emphasis added]*

Without a counterpart in the MDR, the section 9.1 of Annex I to IVDR refers the performance characteristics of in vitro diagnostic medical devices that "*Devices shall be designed and manufactured in such a way that they are… suitable with regard to the* ***performance they are intended to achieve, taking account of the generally acknowledged state of the art***" *[emphasis added]*, which is logic due to the nature of an in vitro diagnostic medical device with purposes referred to in point (2) of Article 2 of IVDR.

3.2.2 Standardisation bodies and the Commission

Since it is a means for the manufacturer to demonstrate conformity with GSPR and other legal requirement laid down in the new regulations by complying with harmonised standards as defined in the Article 2 of the Regulation (EU) No 1025/2012 [33] (Recital 22 of MDR; Recital 20 of IVDR), the relevant European standardisation organisations, which are the European Committee for Standardisation (CEN), the European Committee for Electrotechnical Standardisation (CENELEC) and the European Telecommunications Standards Institute (ETSI) [34], together with their members at national level, may be regarded as stakeholders setting up "state-of-the-art" requirements recognised by the regulations. According to a study on ENs in EU and

EFTA, there are over 155'000 experts participating in the standardisation at national and European level, which presents 0.1% of the whole EU employee [35].

Besides, the international standardisation bodies, namely the International Organisation for Standardisation (ISO), the International Electrotechnical Commission (IEC) and the International Telecommunication Union (ITU), may also be involved, when the expert panels as mentioned in chapter 3.2.8 are conducting their tasks according to Article 106(10), Point (d) of MDR and providing their "state-of-the-art" expertise during the development of relevant standards in the international level.

Previously having been introduced in the IVDD and now applying to both new regulations (Recital 21 of IVDR), to address public health concerns in case harmonised standards do not exist or are insufficient, the Commission may, by means of implementing acts, adopt common specifications (CS) in respect of GSPR, technical documentation, clinical evaluation, PMCF or clinical investigation (Article 9 of MDR) or in respect of GSPR, performance requirements and performance evaluation for in vitro diagnostics (Article 9 of IVDR), providing a means of compliance with relevant applicable legal obligations (Article 2(71) of MDR; Article 2(74) of IVDR). Therefore, in the opinion of the author of this thesis, during the development of CS, any relevant stakeholders besides the Commission that are involved in the consultation (Recital 24 of MDR; Recital 22 of IVDR) are relevant to setting or applying the "state-of-the-art" requirements as well.

3.2.3 Notified Bodies

Table 4 below shows the involvement of the notified bodies (NB) to procedures for product conformity assessments and compliance certification. Therefore, the judgement of device compliance to "state-of-the-art" requirements shall be part of their proper performance of designated tasks relating to technical, scientific and administrative aspects entailed in the conformity assessment activities which are in concern as mentioned in chapter 3.2.1, based on the technical documentation provided by the manufacturer. (Annex VII, Section 3.1 of MDR)

Table 4 Involvement of notified bodies during procedures for the assessment of product compliance[15]

Reg.	Involvement of notified bodies
MDR	Conformity assessment procedure for class IIa, IIb and III medical devices (Recital 60 of MDR)
	Conformity assessment procedure to the aspects relating to establishing, securing and maintaining sterile conditions for class I medical device in sterile condition (Article 52(7) of MDR)
	Conformity assessment procedure to the aspects relating to the conformity of the devices with the metrological requirements for class I medical device having a measuring function (Article 52(7) of MDR)
	Conformity assessment procedure to the aspects relating to the reuse of the device, in particular cleaning, disinfection, sterilisation, maintenance and functional testing and the related instructions for use, in case of class I medical device which are reusable surgical instrument (Article 52(7) of MDR)
	Certifying the compliance with CS or relevant harmonised standards and national provisions for reprocessing and further use of single-use devices (Article 17(5) of MDR)
	Conformity assessment procedure relating to ensuring sterility for systems and procedure packs to be placed on the market (Article 22(3) of MDR)
	Validation of SSCP (Article 32 of MDR)[16]
	Clinical evaluation consultation procedure for class III implantable devices and class IIb active devices intended to administer and/or remove a medicinal product (Rule 12) (Article 54(1) of MDR)
	Check for the appropriateness of the PMCF Plan of manufacturer, including post market studies to demonstrate the safety and performance of class III devices and implantable devices, where clinical investigation to be exempt (Article 61(4) of MDR)
	Evaluation of PSUR for class III devices and implantable devices (Article 86(2) of MDR)
	Reconsideration of conformity assessment of drug-device combination product where the substance has an ancillary action, when the consulted medicinal products authority challenges the previously established risk or benefit (Annex IX, Section 5.2, Point (g) of MDR)

[15] Own illustration

[16] part of the technical documentation review for class III devices and implantable devices

Reg.	Involvement of notified bodies
	Conformity assessment for devices manufactured utilising, or incorporating, tissues or cells of human or animal origin, or their derivatives, that are non-viable or rendered non-viable, providing information including the risk or benefit of the incorporation of the tissues or cells of human origin or their derivatives into the device (Annex IX, Section 5.3, Point (a) of MDR)
	Applying relevant requirements laid down in the Regulation (EU) No 722/2012 [36] during conformity assessment procedure for devices manufactured utilising tissues or cells of animal origin or their derivatives.
IVDR	Conformity assessment procedure for class B, C and D in vitro diagnostics (Recital 56 of IVDR)
	Conformity assessment procedure to the aspects relating to establishing, securing and maintaining sterile conditions for class A devices that are placed on the market in sterile condition (Article 48(10) of IVDR)
	Validation of SSP for class C and class D devices (Article 29 of IVDR)
	Consultation with a medicinal products authority for companion diagnostics (Article 48(3), (4), (7), (8); Annex IX, Section 5.2, Point (c) and Annex X, Section 3, Point(k) of IVDR)
	Request for laboratory testing by EU reference laboratory to verify the claimed performance and the compliance of the device with the applicable CS, or with other solutions chosen by the manufacturer (Article 48(5); Annex IX, Section 4.9 and Annex X, Section 3, Point (j) of IVDR)
	Consultation with relevant expert panel, where no CS are available for class D devices and where it is also the first certification for that type of device (Article 48(6) of IVDR)

Moreover, the European Parliament and the Council of the European Union have indicated the obligations for the notified bodies to keep themselves apprised any changes to the "state-of-the-art" regarding their conformity assessment approvals in the Decision No. 768/2008/EC (the Decision), which lays out the template for product harmonisation legislations under the NLF after 2008, including the new regulations governing medical devices and in vitro diagnostics [10], as it can be read from that "*the notified body shall keep itself apprised of* ***any changes in the generally acknowledged state of the art*** *which indicate that the* ***approved type*** */* ***design*** *may no longer comply with the applicable requirements of the legislative instrument, and shall determine whether such changes require further investigation*" *[Emphasis added, text*

recombined] (Module B, Section 7; Module H1, Section 4.4 of the Decision). This may imply the decision-making role of the NB during their interactions with the manufacturers about what a "state-of-the-art" requirement actually means and how to fulfil it, since the conformity assessment procedures provided by the MDR and IVDR which the NB conduct will either based on EU Type-examination, which corresponds to the Module B "EC-type examination" of the Decision (Annex X of MDR and IVDR), or based on a quality management system and on assessment of technical documentation, which is derived from the Module H1 "full quality assurance plus design examination" of the Decision (Annex IX of MDR and IVDR).

3.2.4 Sponsors

Without prejudice to any of the obligations set out for manufacturer as mentioned in chapter 3.2.1 above, a sponsor "takes responsibility for the initiation, for the management and setting up of the financing of the clinical investigation/performance study", as defined in the Article 2(49) of the MDR and the Article 2(57) of the IVDR. For the investigational device in a clinical investigation, according to the Article 62(4), point (l) in the MDR, it must firstly conform to the applicable GSPR set out in the Annex I excepting those aspects to be covered by the clinical investigation, thus including the reference to the "stat-of-the-art" as mentioned in chapter 3.2.1 above, and "*every precaution has been taken to protect the health and safety of the subjects… (including)* ***provisions in the field of occupational safety and accident prevention, taking into consideration the state of the art***." *[emphasis added]*

Similar requirements referring to the "state-of-the-art" can be observed in the IVDR for the "additional performance studies" as specified in the Article 58(1) and performance studies involving companion diagnostics, except for those using left-over samples, as required in the Article 58(2). In these cases, the Article 58(5) states that *"… (m) in the case of clinical performance studies, the* ***analytical performance has been demonstrated, taking into consideration the state of the art****; (n) in the case of interventional clinical performance studies, the* ***analytical performance and scientific validity has been demonstrated, taking into consideration the state of the art****…; (o) the* ***technical safety*** *of the device with regard to its use* ***has been***

proven, taking into consideration the state of the art as well as provisions in the field of occupational safety and accident prevention*; …" [emphasis added]*

As emphasis is given on the provisions in the field of occupational safety and accident prevention in these new regulations, sponsors must consider the "state-of-the-art" in a larger extent than only product requirements such as the GSPR. For instance, the European directives on safety and health at work - OSH Framework Directive plus other subject-matter directives covering specific topics like "Workplaces, equipment, signs, personal protective equipment", "Exposure to chemical agents and chemical safety", "Exposure to physical hazards", etc. - are deemed to be state-of-the-art because they are subject-oriented and are kept constantly up-to-date [37].

3.2.5 Member States

Corresponding to the responsibilities set out for the sponsor as mentioned in chapter 3.2.4 above, the Member States (MS), or in other words - the national competent authorities (NCA) for in vitro diagnostics, are involved in the case of performance studies to particularly examine the evaluation of the analytical performance, or in the case of interventional clinical performance studies, the evaluation of the analytical performance, clinical performance and scientific validity, where ***"taking into consideration the state of the art"*** *[emphasis added]* is required (Article 67(3), point (a) of the IVDR).

As part of the ongoing monitoring of NB, the authorities responsible for notified bodies appointed by the MS shall sample and review certain technical documentation assessments done by the NB, where the clinical evaluation plan (CEP), the clinical evaluation report (CER), the post-market clinical follow-up (PMCF) plan and PMCF evaluation report are given emphasis (Article 45 of MDR). Same applies to the in vitro diagnostics, where the authorities responsible for notified bodies conduct the checks for the assessment of NB of technical documentation and performance evaluation documentation utilising CS (Article 41 of IVDR).

For instance, the German Central Authority of the Laender for Health Protection with regard to Medicinal Products and Medical Devices (ZLG) is the authority responsible for designation and monitoring of the NB in Germany in the field of medical devices and in vitro diagnostics [38] [39]. *"The ZLG is the office for the exchange*

of experience of the recognised and notified bodies. It participates in the exchange of experience on the level of the European Union and in consultations within the framework of the agreements of the EC with third countries (texts of agreements) and cooperates in confidence building measures and in working groups of the Joint Committees"[17] [40].

3.2.6 Medicinal products authority

"Medicinal products authority" means the European Medicines Agency (EMA)[18] or one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC [41], which the NB may seek a scientific opinion from during the conformity assessment procedure for medical devices incorporate substance which, if used separately, may be considered to be a medicinal product and has an action ancillary to that of the device. Such medicinal product shall be within the meaning of point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma. In the case where medical device incorporates ancillary substance that could have an impact on the previously established risk or benefit concerning such incorporation, the medicinal products authority will provide its advice to the related NB for possible reconsideration of the conformity assessment (Annex IX, Section 5.2, Point (g) of MDR). Therefore, the consulted medicinal products authority is logically – as the author of this thesis suggests - involved as well when the "state-of-the-art" requirement for risk and benefit of the device is in concern as mentioned in chapter 3.2.1.

This may apply to cases where devices are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body as well (Annex IX, Section 5.4, Point (a) of MDR), since the views expressed in the scientific opinion from the consulted medicinal products authority must be taken into the decision-making process from the NB (Annex IX, Section 5.4, Point (d) of MDR).

[17] Translation from the original text on website, provided by DeepL (free version)
[18] Where the medicinal product falls exclusively within the scope of the Annex to Regulation (EC) No 726/2004 of the European Parliament and of the Council [60], the notified body shall seek the opinion of the EMA.

Medicinal products authority is also involved in the consultation procedure for companion diagnostics of NB regarding the suitability of the device in relation to the medicinal product concerned (Article 48(3), (4), (7), (8) of IVDR). Such suitability assessment shall be based on performance studies documentation where "state-of-the-art" is taken into account (Article 58(1) of IVDR).

3.2.7 Other competent authorities

"Human tissues and cells competent authority" means one of the competent authorities designated by the Member States in accordance with Directive 2004/23/EC where the NB seeks a scientific opinion from on the aspects relating to the donation, procurement and testing of tissues or cells of human origin or their derivatives, when the medical device in conformity assessment procedure is manufactured utilising, or incorporating, tissues or cells of human or animal origin, or their derivatives, that are non-viable or rendered non-viable (Annex IX, Section 5.3, Point (a) of MDR). Such tissues or cells of human origin, or their derivatives, as an integrated part of the device, shall be covered by Directive 2004/23/EC [42]. As the NB submits to the authority a summary of the preliminary conformity assessment which includes the risk or benefit of the incorporation of the tissues or cells of human origin or their derivatives into the device, the consulted human tissues and cells competent authority should be logically involved in the scrutiny of fulfilment of "state-of-the-art" requirement for risk and benefit of the device as mentioned in chapter 3.2.1.

3.2.8 Designated experts

To provide advice and to assist the Commission and the Member States in ensuring a harmonised implementation of the new regulations governing medical devices, the Medical Device Coordination Group (MDCG), composed of experts in fields of medical devices and in vitro diagnostics designated by the Member States, is established (Recital 82 of MDR).

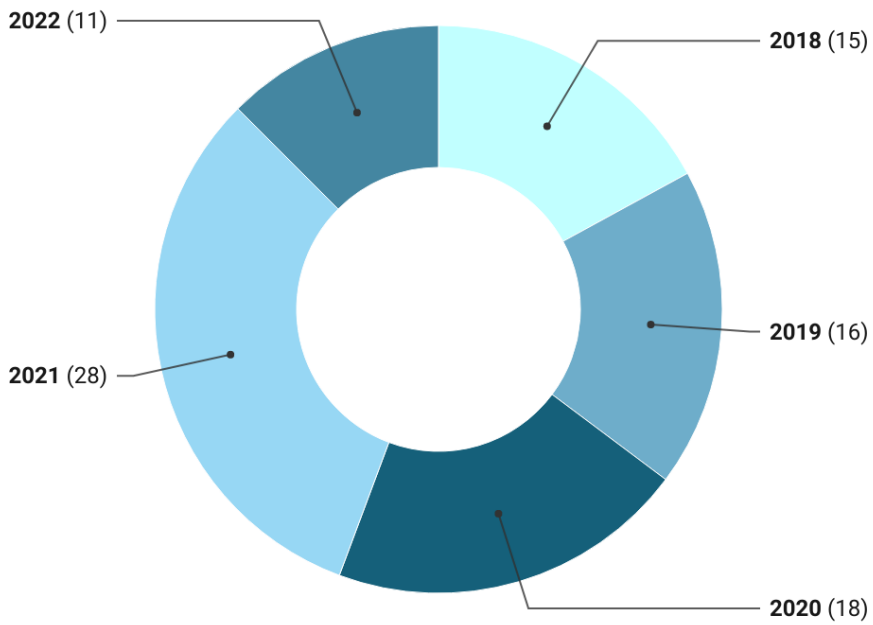
Figure 1 illustrates the current (as of the 11 June 2022) number of MDCG endorsed documents and their related topics, including the MDCG Guidance, for the stakeholders involved in the MDR and IVDR. Even though these documents are not legally binding, they "*present a **common understanding** of how the MDR and IVDR*

should be applied in practice aiming at an effective and harmonised implementation of the legislation" [emphasis added] [43].

In many of the MDCG endorsed documents, "state-of-the-art" requirements are mentioned. For instance, in the *MDCG 2020-6 - Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC*, the definition of the "state-of-the-art" given in the IMDRF/GRRP WG/N47 is referred to, and the "state-of-the-art" for treatment is further described, as it can be read that *"… it is necessary to describe the 'state of the art' for the treatment of the indicated clinical condition taking alternative treatments into account. The state of the art in this context can be taken to mean the* ***generally accepted most effective treatment option****, for the intended purpose relevant to the device under consideration. Occasionally, this may be subject to differences of opinion between clinical evaluators as to what is the state of the art, and where such differences exist, these should be described and taken into account insofar as is possible."* [emphasis added] (MDCG 2020-6, p 15) [44]. The author of this thesis believes that the MDCG endorsed documents are powerful tools to specify detailed requirements of the "state-of-the-art", as a supplement to the MDR and IVDR.

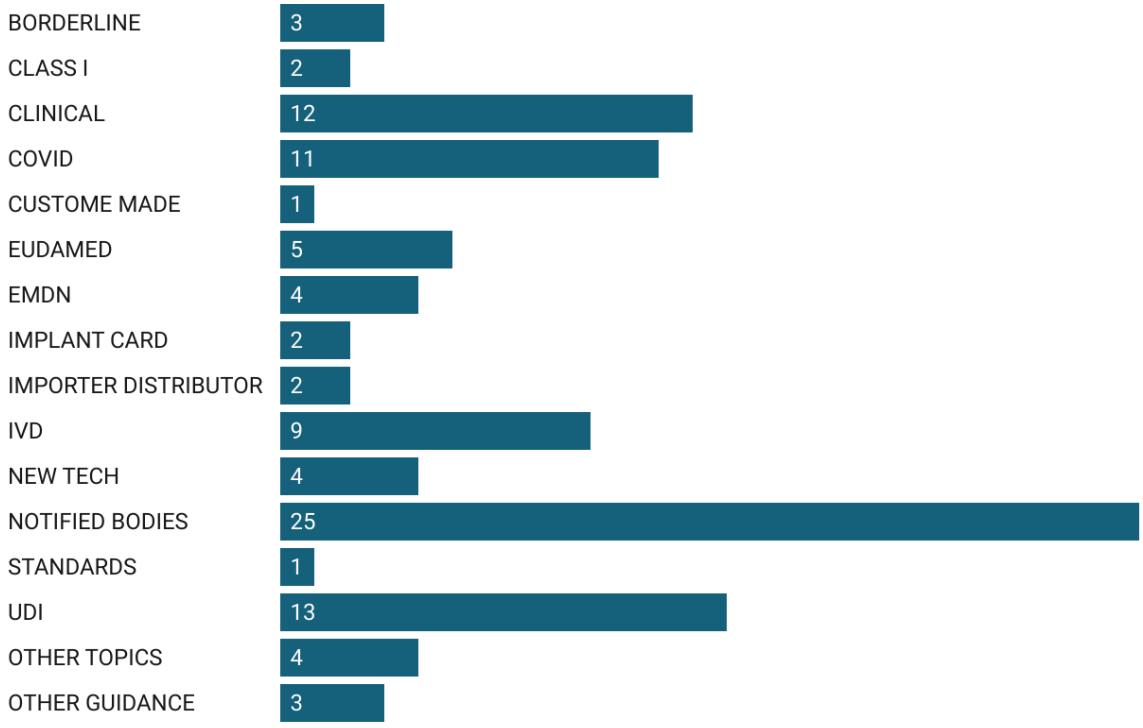
Moreover, based on their "***up-to-date clinical, scientific or technical expertise***" *[emphasis added]*, expert panels and expert laboratories are designated by the Commission, by means of implementing acts and in consultation with the MDCG, aiming at providing assistance to the Commission, the MDCG, manufacturers and NB (Recital 83; Article 106(1) of MDR). Expert panels *"shall consist of* ***advisors*** *appointed by the Commission on the basis of* ***up-to-date clinical, scientific or technical expertis****e in the field and with a* ***geographical distribution that reflects the diversity of scientific and clinical approaches in the Union****" [emphasis added]* (Article 106(3) of MDR).

MDCG Guidance (Status: 2022-06-11)



Source: Bodo Mestmacher, FL MDR, TÜV Nord, Essen, 2022-06-28 (own illustration by the author of this thesis)
Created with Datawrapper

MDCG endorsed documents (Status: 2022-06-11)



Source: Bodo Mestmacher, FL MDR, TÜV Nord, Essen, 2022-06-28 (own illustration by the author of this thesis)
Created with Datawrapper

Figure 1 Factsheet MDCG Guidance

As part of the possible tasks, expert panels and expert laboratories may be involved in developing and reviewing guidance for the performance of conformity assessment *"in line with the **state of the art** with regard to **clinical evaluation, performance evaluation, physico-chemical characterisation, and microbiological, biocompatibility, mechanical, electrical, electronic or non-clinical toxicological testing**" [emphasis added]* (Article 106(10), Point (c) of MDR) and contributing to the development of standards at international level, *"ensuring that **such standards reflect the state of the art**" [emphasis added]* (Article 106(10), Point (d) of MDR).

Expert panels are also involved in consultation for manufacturer prior to their clinical evaluation/investigation, or to scrutinise the clinical evaluation assessment report from NB for class III implantable devices and certain class IIb active devices (Recital 56; Article 61(2) of MDR), or the consultation for NB on the performance evaluation report provided by manufacturer (Article 48(6) of IVDR) or the performance evaluation assessment reports from NB for certain class D in vitro diagnostics (Recital 53 of IVDR), which should lead to a harmonised evaluation and development of CS.

The designation of expert panels and expert laboratories is based on their expertise and is realised through implementing acts from the Commission (Article 106(1) and (7) of MDR). The tasks of the expert panels and expert laboratories can be amended through delegated acts adopted by the Commission (Article 106(15) of MDR). For example, as supplement with further details to the MDR and IVDR, the Commission Implementing Decision (EU) 2019/1396 lays down the rules for the designation of expert panels, where in the each of the areas listed in the *Table* 5 below there is one expert panel (Article 1 of the Implementing Decision (EU) 2019/1396) [45]. Besides, to support the work of expert panels, a central list of currently available experts, *"who have been considered eligible and apt for the work of the panels, but who have not been appointed to an expert panel, are included in a central list of available experts"*, has been published on the website of the European Commission [46].

Table 5 List of areas that designated expert panels cover

No.	area
01	Orthopaedics, traumatology, rehabilitation, rheumatology

No.	area
02	Circulatory system
03	Neurology
04	Respiratory system, anaesthesiology, intensive care
05	Endocrinology and diabetes
06	General and plastic surgery and dentistry
07	Obstetrics and gynaecology, including reproductive medicine
08	Gastroenterology and hepatology
09	Nephrology and urology
10	Ophthalmology
11	In-vitro diagnostic medical devices (IVD)

Compared to the analysis provided by Table 14 in Annex 4, see below, the Implementing Decision (EU) 2019/1396 has set down rules which tackle certain core elements, as outlined by the author of this thesis, to build up the expert group regarding the "state-of-the-art". For instance, in this Implementing Decision, the Article 3 "Subgroups" has enabled the experts entrusted with specific tasks, so that the work from expert panels can correspond to the element "(3) being subject-orientated"; the Article 6 "Voting rules", which is in accordance with the Article 106(12) of the MDR, *"when adopting its scientific opinion … expert panels shall use their best endeavours to reach consensus. If consensus cannot be reached, the expert panels shall decide by a majority of their members, and the scientific opinion shall mention the divergent positions and the grounds on which they are based*", which should be logically correlated to the elements "(4) being acknowledged by majority, (5) being on the basis of opinions from experts, and (6) publication being approved through a due process (e.g., consensus procedure)", see discussion in chapter 3.1.3 above.

Therefore, the author of this thesis strongly agrees that referencing the consensus opinion from expert panels and expert laboratories (or EU Reference Laboratories for IVDR) would provide solid evidence in line with the requirements on the "state-of-the-art" in the MDR and IVDR.

3.3 Evolvement of the "state-of-the-art"

Relating to the legislation for medical devices, the concept of the "state-of-the-art" has also evolved. In the Section 1.1 "A Historical Perspective", p 5-6, of the *Commission Notice – The "Blue Guide" on the implementation of EU products rules 2016* (The "Blue Guide (2016)") [47], four major historical phases of progression of EU legislation for goods are concluded. Through a recently (as of July 2022) published revision, the *Commission Notice – The "Blue Guide" on the implementation of EU products rules 2022* (The "Blue Guide (2022)") has supplemented a fifth phase (Section 1.1. "A Historical Perspective", p5-6) [48], whose summarisation can be seen in Table 6 below.

Table 6 Historical phases of EU legislation for goods[19]

Phase	Name	Features
01	"Traditional Approach" or "Old Approach"	*"Detailed texts containing all the necessary technical and administrative requirements"*
02	"New Approach"	*"Developed in 1985, which restricted the content of legislation to 'essential requirements' leaving the technical details to European harmonised standards."*
03	"Conformity assessment instruments"	*"Development of the conformity assessment instruments made necessary by the implementation of the various Union harmonisation acts, both New Approach and Old Approach"*
04	"New Legislative Framework" (NLF)	*"Adopted in July 2008, which built on the New Approach and completed the overall legislative framework with all the necessary elements for effective conformity assessment, accreditation and market surveillance including the control of products from outside the Union"*
05	Market Surveillance and Mutual Recognition	*"Adoption of a new Regulation on Market Surveillance and a new Regulation on Mutual Recognition of goods lawfully marketed in another Member State in 2019"*

Based on their initial publication year, the MDD, AIMDD and IVDD are originally based on the "New Approach" provisions, while the MDR and IVDR are from the beginning NLF regulations.

[19] Own illustration based on Section 1.1 of the "Blue Guide (2022)"

3.3.1 "New Approach" directives for medical devices

During the creation process of a single market in the European Community[20], by 31 December 1992, a new regulatory technique was introduced to set down general essential requirements that are to be harmonised and made mandatory by the directives [49]. As the foundation, this technique was laid down by the *Council Resolution of 7 May 1985 on the "New Approach" to technical harmonisation and standardisation* [50] (the Resolution), where four fundamental principles are mentioned, on which the "New Approach" is based. *Table 7* below summarises the four fundamental principles for the "New Approach" directives as quoted from the Annex II – Guidelines for a new approach to technical harmonisation and standards – of the Resolution.

Table 7 Principles established by "New Approach"[21]

No.	Principles established by "New Approach"	OJ reference
01	*"— legislative harmonization is limited to the adoption, by means of Directives based on Article 100 of the EEC Treaty, of the essential safety requirements... with which products put on the market must conform, and which should therefore enjoy free movement throughout the Community"*	*Official Journal of the European Communities, p2-3, No C 136, Volume 28, – 1985-06-04*
02	*"— the task of drawing up the **technical specifications** needed for the production and placing on the market of products conforming to the essential requirements established by the Directives, while **taking into account the current stage of technology**, is entrusted to organizations competent in the standardization area." [Emphasis added]*	
03	*"— these technical specifications are not mandatory and maintain their status of voluntary standards"*	
04	*"—but at the same time national authorities are obliged to recognize that products manufactured in conformity with harmonized standards (or, provisionally, with national standards) are presumed to conform to the "essential requirement" established by the Directive. (This signifies that the producer has the choice of not manufacturing in conformity with the standards but that in this event he has an obligation to prove that his products conform to the essential requirements of the Directive.)"*	

[20] Nowadays the European Union

[21] Own illustration based on the Annex II of the Resolution

Since the MDD, AIMDD and IVDD were initially published between 1990 and 1998, they all belong to the "New Approach" directives (Recitals of MDD and IVDD), and the principles laid out above shall apply to them. So applies the No. 02 principle as summarised in the Table 7 above to the medical devices under MDD, AIMDD and IVDD. When entrusting the European standard organisations like CEN, CENELEC or ETSI any task to draw up technical specifications correlating to the conformity of essential requirements laid out in the "New Approach" directives, the so-called "current stage of technology" must be taken into account by the standard organisations.

Corresponding to the explanation from the IMDRF Guidance - IMDRF/GRRP WG/N47 FINAL:2018 (see the results in chapter 3.1 above) and the ISO/IEC Guide 63:2019 (see the results in chapter 3.1.3 above) for medical devices, where the "state of the art" shall embody what is currently and generally accepted as good practice in technology and medicine, the similarity between the "state-of-the-art" and the so-called "current stage of technology" can be found. The author of this thesis is thus convinced that, as early as drafting the resolution for "New Approach" directives, the European regulators have considered what nowadays recognised as the "state-of-the-art" requirements, although with wording that is deemed simpler. Logically speaking, since the IMDRF Guidance - IMDRF/GRRP WG/N47 FINAL:2018 and the ISO/IEC Guide 63:2019 are specific for medical devices, there is additional consideration of the "good practice in medicine".

In order to achieve what this principle requires, the entrusted standardisation organisations must regularly update, or check for the necessity to update, the relevant technical specifications to demonstrate that these documents are able to demonstrate the compliance to the essential requirements in the "New Approach" directives.

This can be verified by taking an example from the CEN/CENELEC: in their Internal Regulations Part 2 (the Internal Regulations), it can be read that the "*responsible technical body shall ensure that European Standards (ENs) are periodically reviewed*" and the "*periodical review shall occur at intervals not exceeding five years*", which would result in an "old" EN to be confirmed, revised or withdrawn (Section 11.2.6 of the Internal Regulations) [51]. With this internal approach, the second principle established in the "New Approach" directives is deemed to be ensured.

Similarly, the ETSI has also announced on their website that, the ETSI *"standards are updated as required to* ***take account of the latest developments*** *and revised versions are published" [emphasis added]* [52].

3.3.2 NLF regulations for medical devices

Later in 2008, the new legislative framework (NLF) was adopted [10] as common legal framework aiming to improve market surveillance rules, set clear and transparent rules for accreditation, boost the quality of and confidence in conformity assessment and consolidate the meaning of CE marking [53] [54] while update, harmonise and consolidate various technical instruments that have already been used in the existing Union harmonised legislations [11]. Based on the ISO/IEC documentation, *"the Council in its Decisions developed consolidated conformity assessment procedures and the rules for their selection and use in directives"*, which are called "the modules" (The "Blue Guide (2022)", p 9, [48]). Both MDR and IVDR are initially based on the NLF provisions.

As the "Blue Guide (2022)" states, the "*concept of essential requirements is based on the assumption that the harmonised standards reflect* ***generally acknowledgeable state of the art*** *and the CEN, CENELEC or ETSI review standards regularly in accordance with the relevant standardisation request" [emphasis added and rephrased]* (Section 4.1.2.4, p 53, of the "Blue Guide (2022)") [48]. In the opinion of the author of this thesis, it clearly corresponds to the No. 02 principle as summarised in the Table 7 in chapter 3.3.1 above, and confirms the presumption about the link between the so-called "current stage of technology" back in the 1985 Resolution and the "generally acknowledgeable state-of-the-art" mentioned in the "Blue Guide (2022)". In other words, the second principle from the "New Approach" has not been altered under the NFL.

Since the NLF "essential requirements" "*deal with the protection of health and safety of users (usually consumers and workers)"* and *"are designed to provide and ensure a high level of protection"*, in the MDR and IVDR, the GSPRs are regarded as the variant to the "essential requirements" (Section 4.1.1, p 47-48, "Blue Guide (2022)").

3.3.3 Reference to the "state-of-the-art"

In a 2002 report analysing standards referencing in European legislation prepared by G. Leibrock [55], reference to the "state-of-the-art" is a legislative method used in parallel to the "New Approach", where they are both made use of to provide "indirect references to standards" in order to allow or promote the voluntary use of those standards in the legislative framework. The author of this report has indicated that, compared to the method of direct references, as in the "Old Approach", the indirect references overcome disadvantages like barriers to trade, need for adjustment, confusion of dated and undated reference and constitutional problems.

Nevertheless, in this report, G. Leibrock has also criticised that "*the disadvantages prevail*" when making use of the reference to the "state-of-the-art", because in this case the non-legitimised organisations (e.g., CEN/CENELEC/ETSI) would be involved in the complementary work of the legislation in an uncontrolled manner. Moreover, there is no certainty for the manufacturer to decide which standard would exactly correspond to the "state-of-the-art" [55].

However, the author of this thesis does not totally agree with this opinion within the framework of the new regulations governing medical devices. During the last two decades, together with the evolvement of the "state-of-the-art", the functions of regulators have also been developed. Especially after the introduction of the NLF in 2008, the market surveillance rules are improved to better protect health from unsafe medical devices in the EU market [10]. This has assumed a pivotal role of regulators due to the big data collected during the market surveillance and thus called for a more flexible open clause, such as the "state-of-the-art", to set up and update requirements on the medical devices.

Furthermore, as analysed in chapter 3.2 above, the new regulations of medical devices do not make use of the reference to the "state-of-the-art" in an isolated way. Instead, there are many new tools besides making use of European harmonised standards where the regulators can participate in to provide more detailed requirements alongside. Since both new regulations governing medical devices are relatively "young", the effectiveness of these new tools making use of the reference to the "state-

of-the-art" is still under question. Further explanations by the author of this thesis can be seen in chapter 5.1 below.

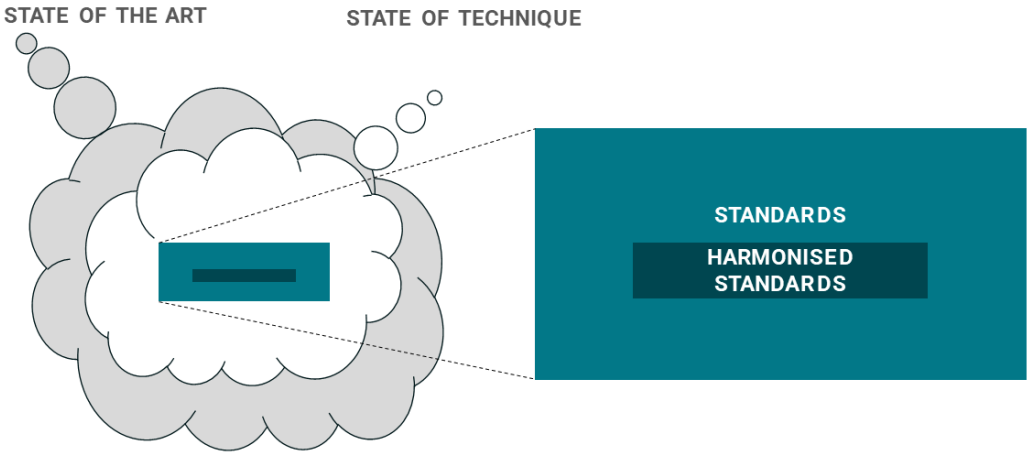
3.4 Use of standards to demonstrate the "state-of-the-art"

Following the analysis of the definition and explanation of the term "state-of-the-art" in chapter 3.1.3 above, which is based on the ISO/IEC Guide 2:2004, the ISO/IEC Guide 63:2019 and the European harmonised standards for medical devices, it has been discussed how the interpretation of the concept of the "state-of-the-art" originated from international standards is taken to understand the "state-of-the-art" in the MDR and IVDR. Going beyond the use of the European harmonised standards for the presumption of conformity in MDR and IVDR, it is also worth to analyse and discuss the use of standards to demonstrate the "state-of-the-art" in the regulations by the stakeholders.

Again to take the risk management standard EN ISO 14971:2019 and its Amendment 11 as example, by further comparing to the "state-of-the-art" requirements mentioned in the new regulations (see below, Table 10 and Table 11 in Annex 1), the EN ISO 14971:2019 and its Amendment 11 can hardly cover every aspect, since the new regulations governing medical devices have made use of requirement reference to the "state-of-the-art" beyond the GSPR. Even though stakeholders could apply other European harmonised standards, together with the definition and explanation of the "state-of-the-art" in these standards, to demonstrate the compliance to the "state-of-the-art" in other aspects within the MDR and IVDR, following the scope those standards can cover.

Table 13 in the Annex 3 below has depicted the current (until May 2022) harmonised standards which confer the presumption of conformity to the MDR and IVDR, where the stakeholders may pay attention to relevant definitions of or reference to the "state-of-the-art" in the standards, if there is any. There will be more and more European harmonised standards for medical devices published on the OJEU in the near future, as it can be read from the Mandate No. 575 of the European Commission (M/575 Commission Implementing Decision C(2021) 2406 of 14 April 2021) [56]. Along with this progress, it can be expected that utilising the presumption of

conformity will cover a larger extent of the "state-of-the-art" requirements in the new regulations governing medical devices.



Source: Bodo Mestmacher, FL MDR, TÜV Nord, Essen, 2022-06-28 (original illustration modified by the author of this thesis)

Figure 2 Relationship between the "state-of-the-art" and harmonised standards

Figure 2 illustrates the relationship between "state-of-the-art" requirements and the European harmonised standards from a Notified Body point of view [57]. "State-of-the-art" is apparently a much broader concept than the standards, let alone using harmonised standards.

Moreover, as perceived by the author of this thesis from the take-home messages in a recently (as of on 28 June 2022) held training organised by this Notified Body, it is suggested that in most cases, instead of presenting any best practice or the state of research., standards are actually from the minimum consensus of the relevant standards committees [57].

This perception asserts the contrary of the assumption where the second principle for the "New Approach" directives (see Table 7 in chapter 3.1 above) and the concept of essential requirements in the successor NLF regulations (see chapter 3.3.2 above) are based on. It also seems contradictory to the internal rules from the standardisation organisations like CEN/CENELEC (the Internal Regulations) or claims on the ETSI website as discussed in the chapter 3.3.1 above.

In the final report of a study over a period of 18 months on the functions and effects of European Standards (ENs) and Standardisation in the EU and EFTA Member States (the Study on ENs) that was published in November 2021, where different

categories of stakeholders across EU and EFTA were consulted, five research questions (RQs) were answered [35]. In the main conclusion of the answer to the third RQ (RQ3), feedbacks from the stakeholder have indicated that *"The content of European standards may be difficult to understand and may be the result of a compromise being the lowest common denominator which repeatedly leads to a dilution of the technical requirements or to a very limited area of application.* ***ENs are sometimes perceived to not timely keeping up with the state of the art*** *(e.g. reviewed international standards). This perception is* ***even stronger when European standards adopting the latest technology cannot be used in the context of legislation, because it is still recognising the previous version of the European standards (for instance, if the latest version of the standard is not considered to be aligned with European legislation)"*** *[emphasis added]* (the Study on ENs, p. 11) [35].

As data presented in the Section 4.2.2.2 "Dissemination of information" in the Study on ENs indicate, in the medical device sector, only 49% of the feedbacks believe ENs "*contain information about the current* ***state of the art****" [emphasis added]*, which is lower than the cross-sectoral average at 53% (the Study on ENs, p. 101).

However, in the Section 4.2.2.4 "Promoting consumer protection" in the Study on ENs, results from medical device sector are given as that 63% of the feedbacks think that ENs *"****allow companies to demonstrate to their consumers the incorporation of state of the art*** *and consensus-based safety requirements, and increase company's reputational value and trust for consumers" [emphasis added]*, which is slightly higher than the cross-sectoral average at 62% (the Study on ENs, p 104) [35].

What has been suggested by the comparison between ENs and the international standards in the Study on ENs is that results *"clearly show that EU/EFTA-based companies heavily rely on international standards across all sectors"*, which is *"particularly true with regards to* ***ENs lagging behind international standards when it comes to keeping up with the state of the art*** *and this is generally attributed to a too-lengthy standardisation process. Relevance was mentioned across all sectors and* ***especially by respondents in the medical devices*** *one" [emphasis added]* (the Study on ENs, p 112) [35].

Moreover, at medical device sectoral level, more precisely speaking, in the area of radiation protection in medicine, when considering one of the elements which the

author of this thesis has abstracted from the interpretation of the "state-of-the-art" – the "(3) being subject-orientated" (see Table 14, below in Annex 4), national standards which *"often contain more concrete specifications, are generally more detailed and are often faster and easier (fewer stakeholders involved) to develop compared to ENs"*, have a higher frequency of implementation by the EU and EFTA companies (Section 4.3, the Study on ENs, p 113) [35].

Therefore, the author of this thesis holds the opinion that it would become inaccurate due to the simplicity and absoluteness to conclude that "most standards present no best practice or the state of research". Although it may happen that some stakeholders, like manufacturers, may sacrifice catching up with the latest development of technology, in order to fully benefit from the presumption of conformity to the MDR and IVDR, like choosing to use harmonised ENs only, this is deemed as very extreme case and does not reflect the majority of decisions made in reality, as indicated by the report of Study on ENs. In many cases, manufacturers would not easily trade off the timeliness of technology they choose for the design and development of their medical devices due to logical reasons like fulfilling the expectations of the rapid-changing global market and less frequent need for new technical testing, as experienced by the author of this thesis in the medical device industry. Furthermore, if the "best practice" and "state of research" mentioned here imply going beyond technical feasibility, they would fall outside of the interpretation of "state-of-the-art" as discussed in 3.1.4 above, and would be required as the "state of the art in science and technology" [31].

To adjust such statement, it can be rephrased as, when considering using standards to demonstrate the "state-of-the-art" in the medical device sector, one must look at several factors like his purpose (e.g., dissemination of information or promoting consumer / patient protection), the timeliness represented by the technology chosen (e.g., latest published international standards or ENs which may lag behind) and the subject matter or level of specification (e.g., national standards with more detailed specifications or ENs which may be less precise, as in the area of radiology). From the author's point of view of this thesis, one may also consider raising more questions based on the elements listed in Table 14 (see Annex 4 below), so that she/he can better construct the process of judgement-making related to this topic.

Further supports on the standards could be found in the Commission Staff Working Document SWD(2015) 205 Part1/3 - *Vademecum on European Standardisation in support of Union Legislation and policies, Part I: Role of the Commission's Standardisation requests to the European standardisation organisations*, where it can be read: *"as standardisation brings together experts from all domains, it is an* ***appropriate and powerful tool*** *for* ***consolidating consensually a body of knowl****edge which is then reflected in technical specifications* ***based on the 'state of the art'****. Standards should be reviewed regularly in line with technological developments." [emphasis added]* (Annex I – Background, p28) [58].

In the position paper provided by the MedTech Europe, *Use of international generally acknowledged state-of-the-art standards in the absence of harmonised standards under the IVDR and MDR*, a hierarchy of standards to be used to support GSPR in MDR and IVDR is shown (Annex I, the MedTech Europe Position Paper) [59]. However, in the opinion of the author of this thesis, this position paper did not differentiate the requirements of "state-of-the-art" and the GSPRs. Thus, based on the hierarchy initiated by the MedTech Europe and the own analysis from the author of this thesis, a modified hierarchy of documents to be used for demonstration of "state-of-the-art" in MDR and IVDR is generated and presented in the CHAPTER 5 below.

3.5 Some "missing" state-of-the-art requirements in MDR and IVDR

As it can be seen from the comparison (see below, Table 10 and Table 11 in Annex 1), there are some state-of-the-art requirements from the amended MDD (M5), AIMDD (M4) and IVDD which disappear in the new regulations. What also to be noticed is that the MDD and AIMDD have only introduced these requirements after their amendments in 2007.

Taking the MDD as the example, in the amended MDD (M5) Annex IV, Section 6.3, it can be read that "*statistical control of products will be based on attributes and/or variables, entailing sampling schemes with operational characteristics which* ***ensure a high level of safety and performance according to the state of the art*** *…" [emphasis added]* [60]. On the other hand, in MDD before M5 it was written as "*statistical*

control of products will be based on attributes, entailing a sampling system ***ensuring a limit quality corresponding to a probability of acceptance of 5 %, with a non-conformity percentage of between 3 and 7 %*** *…" [emphasis added]* [3] This amendment was introduced by the Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007 [61]. Comparing to the fixed number in the requirement before the amendment, MDD (M5) This provides evidence that utilising reference to the "state-of-the-art" as a legislative tool could ensure stakeholders to benefit from more flexibility.

However, no similar requirement of the "state-of-the-art" in the corresponding part of the MDR can be found. As originated from the conformity assessment "Module F - Conformity to EU-type based on product verification" under the NLF, where the *"manufacturer ensures compliance of the manufactured products to approved EU-type. The notified body carries out product examinations (testing of every product or statistical checks) in order to control product conformity to EU-type."* (The "Blue Guide (2022)", p 77, [48]), the previous Annex IV in MDD is replaced by the Annex XI Part B in the MDR. By comparing these two corresponding parts (see in *Table* 8 below) in the directive and regulation, the text correlated with the Annex IX, Section 6.3 could not be found in the MDR.

Table 8 Comparison of MDD and MDR in accordance with Module F[22]

Module F	**MDD**	**MDR**	**Comments**
Testing of every product	Annex IV, Section 6.1, 6.2	Annex XI, Section 15.1, 15.2	More stringent
Statistical checks	Annex IV, Section 6.3	-/-	Less stringent
-/-: the counterpart not found in comparison			

Although the exact reason remains unknown by the time the author of this thesis conducted this study, the difference shown in the comparison *Table* 8 above does logically indicate that the MDR sets more stringent requirements on the verification of products. Therefore, the author of this thesis holds the opinion that this

22 Own illustration

"disappearance" of "state-of-the-art" requirement does not contradict the trend where the reference to the "state-of-the-art" is increasing.

Similarly, the "missing" "state-of-the-art" requirement in IVDR can also be explained by the change of requirements on batch testing process (e.g., involvement of the EU Reference Laboratory for IVDs) (Section 4.12 of Annex IX of IVDR; Annex IV, Section 3.2, Point (e) of IVDD), and the change of conformity assessment module, as compared to the IVDD - in the IVDR there is *"no equivalent to the IVDD's Annex VI 'EC Verification'"* (Annex VI, Section 2.1; Annex VI, Section 6.3 of IVDD) [62]. The IVDR sets also more stringent requirements. This is also indirect evidence that the opinions or reports from designated experts (e.g., EU Reference Laboratory) may be deemed as "state-of-the-art".

CHAPTER 4 CONCLUSION

4.1 What are the key elements of "state-of-the-art"

As it can be seen from the analysis given in Table 14 in Annex 4 below, taking into account both what is internationally agreed and what law experts from EU/EFTA Member States have written, a ranking is introduced, about the key element in the definition, explanation or interpretation of the "state-of-the-art" outlined by the author of this thesis, as:

No. 1	"(3) being subject-orientated"
No. 2	"(1) reflecting timeliness"
No. 3	"(7) technical capacity / technical feasibility"
No. 4	"(2) no mandatory to be the latest"
	"(5) being on the basis of opinions from experts"
No. 6	"(4) being acknowledged by majority"
	"(8) acknowledged status based on record of use"
No. 8	"(6) publication being approved through a due process (e.g., consensus procedure)".

The ranking itself is only for reference and is not intended to indicate which element is overwhelming. This list should also be understood as a non-exhaustive list where possible extensions can be made by new findings from other sources or the evolvement of the concept of the "state-of-the-art" itself.

In fact, the author of this thesis considers, if any document used by the stakeholders can present one of these elements, it should be regarded as representing the "state-of-the-art". This is because references to "state-of-the-art" in legislation are primarily used to provide flexibility (see chapter 3.3.3 above). This is further presented in the chapter 4.4 below.

Nevertheless, the "(3) being subject-orientated", "(1) reflecting timeliness", and "(7) technical capacity / technical feasibility" are found to be very much in favour by stakeholders who provide such definition, clarification, or interpretations.

In Austria, law experts have differentiated the terms "generally acknowledged state of the art" from the "state-of-the-art" in their law systems, that the status of

“being generally acknowledged” should be based on the record of use, which is not seen in the other countries or at the international level. The author of this thesis stands up by this point, because such differentiation can enable a finer way to regulate medical devices and in vitro diagnostics based on data from market surveillance and manufacturer’s post-market surveillance.

4.2 Why certain statement may be inaccurate

From the study, several opinions frequently heard or seen in open discussions in industry may be deemed as “inaccurate” or “too extreme” through misunderstanding of the “state-of-the-art”.

Statements such as "using only available harmonised ENs to demonstrate the state of the art" would be too extreme because they misunderstand the use of the terms "presumption of conformity" and "state-of-the-art."

Similarly, saying “using only the latest standards” is also deemed too narrow-minded. Although always considering the most recent published standards is a good business strategy for manufacturers, the author of this thesis recommends taking the element of “no mandatory to be the latest” as a proper interpretation of the “state-of-the-art”.

4.3 What else to be included besides the standards

Mandatory requirements in other EU legislations are to be considered as representing the “state-of-the-art” as well, especially when they are “subject-oriented”, even though they may not present the best timeliness compared to the voluntary standards.

Newly introduced to the MDR, mandatory requirements on CS are deemed as to present the “state-of-the-art” due to their basis of opinions from designated experts. For this reason, referencing to published reports from the expert laboratories or EU Reference Laboratories should be given the same status.

As MDCG documents are endorsed by the designated experts from Member States, an emphasis should be given on them when considering the “state-of-the-art” requirements in line with MDR and IVDR.

4.4 What factors be considered by manufacturers when implementing the "state-of-the-art"

Languages used in the text of the MDR and IVDR may result in different interpretations across the EU. However, this may not be the major issue compared to other factors concluded below.

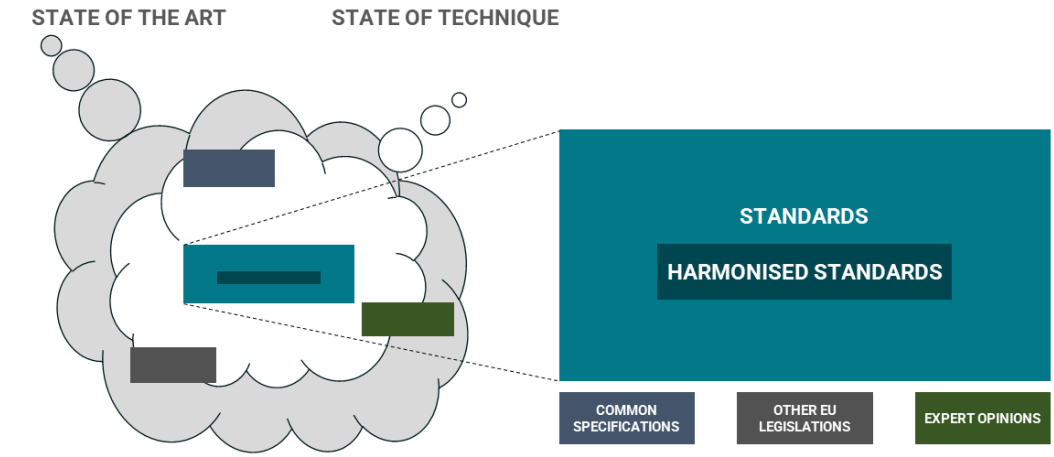
Figure 3 illustrates the factors for manufacturers to consider when they demonstrate medical devices fulfilling the requirements of the "state-of-the-art" from the MDR and IVDR using different publications (standards, CS, EU legislations, MDCG Guidance, reports from expert laboratories, etc.).

As concluded in the chapter4.3 above, unlike to conventional way of using the standards, which is voluntary, under the MDR and IVDR, attention must also be paid to the mandatory CS, to other relevant EU legislations, and to the MDCG endorsed documents as they are deemed to represent the "state-of-the-art", too.

Manufacturers should also consider the additional requirements on them if they play the role of clinical investigation sponsor. In such cases, the European directives on safety and health at work must be taken into consideration.

Moreover, interactions between manufacturers and other stakeholders are also influencing factors, as discussed in chapter 3.2 above. NB is regarded as playing a pivotal role to approve the manufacturer's claim of fulfilling the "state-of-the-art" and to decide whether the previously approved "state-of-the-art" demonstrated by manufacturers would still remain its status. The authorities responsible for NS are subsequently involved, e.g., ZLG, even though they are not the primary contact to the manufacturers.

Furthermore, involvement of other authorities like medicinal products authorities, human tissues and cells competent authorities may as well affect the decision on the "state-of-the-art" as presented in chapter 3.2.6 and chapter 3.2.7 above.



Own illustration based on TÜV Nord training materials

Figure 3 Concluded relationship between "state-of-the-art" and publications

4.5 Why certain "state-of-the-art" requirements are "missing"

As discussed in chapter 3.5 above, when compared to the MDD, AIMDD and IVDD, the MDR and IVDR set more stringent requirements in many areas, including conformity assessment and expert involvement. The missing "state-of-the-art" requirements are due to either the cancellation of the conformity assessment according to the NLF Module F, partially or completely, or the introduction of the involvement of the EU Reference Laboratories for IVDs.

Such differences reveal two facts: the expert's opinion could represent the "state-of-the-art"; the reduction of conformity assessment options in the MDR and IVDR does not deny the increase of "state-of-the-art" requirements in the new regulations governing medical devices and in vitro diagnostics.

CHAPTER 5 OUTLOOK

5.1 Participation of regulators

Conventional "New Approach" directives which make use of European harmonised standards have met its bottleneck in terms of the participation of regulators in the development of standard. In the strategy to 2020 of the CEN-CENELEC Advisory Board for Healthcare Standards (ABHS) (the ABHS Strategy to 2020), complaints have been made to the situation where there is a lack of participation of regulators (e.g., authority members) during standard drafting in the EU (Section 4.1 of the ABHS Strategy to 2020). The ABHS Strategy to 2020 has pointed out that *"regulators possess an extensive and invaluable amount of information contained in adverse event reporting",* which is very valuable in the drafting, maintaining and periodically updating the standards [63].

With the increase of reference to the "state-of-the-art" in the new regulations, the regulators have now more interfaces to be involved in the on-going establishment of regulatory requirements in greater details for medical devices. For instance, the development of CS and MDCG Guidelines, designating expert panels and expert laboratories (or EU Reference Laboratories for IVDs), or reference to the other EU legislations (as illustrated in the Figure 3 in CHAPTER 4 above), may theoretically presume a better involvement of regulators under the new legislative framework.

On the other hand, since it is still the beginning stage of the implementation of MDR and IVDR, very little experience has been gained by the stakeholders involved, and especially for the regulators as well. For instance, in the *Report from the Commission to the European Parliament and the Council on the exercise of the power to adopt delegated acts conferred on the Commission pursuant to Regulation (EU) 2017/745 on medical devices and Regulation (EU) 2017/746 on in vitro diagnostic medical devices*, it has been clarified that *"the Commission has not yet exercised the delegated powers conferred to it under the respective provisions of Regulations (EU) 2017/745 and (EU) 2017/746"* and "*there is at present only limited experience on their application in practice*" (see also *Table* 9 below) [64].

Table 9 Delegation of power to the Commission to adopt delegated acts[23]

No.	Empowerment	Based on
01	Products without an intended medical purpose	Article 1(5) of MDR
02	Amendment of the definition of 'nanomaterial' and related definitions	Article 3 of MDR
03	Elements to be included in the technical documentation and technical documentation on post-market surveillance	Article 10(4) of MDR Article 10(4) of IVDR
04	Exemption from the requirement of an implant card	Article 18(3) of MDR
05	Minimum content of the EU declaration of conformity	Article 19(4) of MDR Article 17(4) of IVDR
06	Information to be submitted as part of the Unique Device Identification (UDI) system	Article 27(10) of MDR Article 24(10) of IVDR
07	Frequency of complete re-assessment of notified bodies	Article 44(11) of MDR Article 40(11) of IVDR
08	Exemption of certain well-established technologies from assessment of technical documentation for every single device	Article 52(5) of MDR
09	Minimum content of certificates issued by a notified body	Article 56(6) of MDR Article 51(6) of IVDR
10	Exemption of certain well-established technologies from assessment of technical documentation for every single device and from the requirement to perform clinical investigations	Article 61(8) of MDR
11	Documentation regarding the application for clinical investigation and interventional clinical performance studies	Article 70(8) of MDR Article 66(8) of IVDR
12	Tasks of expert panels and expert laboratories	Article 106(15) of MDR

And as concluded in the report, the Commission asserts that *"it is important to maintain the necessary flexibility in the legal framework, to supplement or adjust it to* ***technical and scientific developments*** *with a view to protect health and safety of patients, users and public health in general based also on more experience gained with*

[23] Own illustration

the application of the Regulations." [emphasis added] (Chapter 4 "Conclusion" in the report) [64]. As concluded in the previous chapter, the author of this thesis believes that the involvement of the regulators in the further development of the MDR and IVDR will not be limited only to the standardisation. The legislative tool as reference to the "state-of-the-art" has proved the flexibility to the regulators to supplement or adjust according to technical, clinical and scientific development status.

Nonetheless, while the involvement of regulators is critical to the work on promoting the application of state-of-the-art technical and clinical knowledge in medical devices and the in vitro diagnostic sector, it should not be forgotten that the industry should retain the lead position in deciding what technology to use in medical devices and in vitro diagnostics on patients to achieve paramount safety and effectiveness due to the availability of much more abundant resources. The manufacturers are also in more frequent communications with medical care professionals, who are usually costumers of them. Therefore, experience from the industry and medical care shall also be taken into account to tell if the new regulations governing medical device tend to become over demanding by "potentially unlimitedly" requiring the "state-of-the-art", and, if so, what remedy or adjustment can be taken in the near future.

5.2 Up-coming MDCG Guidance

About the upcoming guidance planned by the MDCG, as of in the beginning of July 2022, there will be a "Cookbook" for harmonised standards by the Q2 of 2022 and an updates of the guidance document MDCG 2021-5 on the standardisation for medical devices by the Q3 of 2022 being published, among many other planned documents in a non-exhaustive list from the MDCG [65]. Although having not seen by the time of publishing this thesis, the author of this thesis believes that these two documents will further tackle the topic relating to the "state-of-the-art" requirements in the MDR and IVDR.

As stated in the *Minutes of the meeting held on 19 June 2020* from the MDCG Subgroup on Standards (WG2), *"problem of possible inconsistent approach for implementation of standards with respect to the concept of 'state of the art' was raised by Notified Bodies, as harmonised European standards cited in the OJEU may not be the latest version available" [reiterated with slight modifications; emphasis added]* [66].

According to the minutes, the Commission has also "*confirmed that the EU legislation on medical devices refers to the need to 'take into account the generally acknowledged state of the art'; however,* ***it is not a legally defined concept****" [emphasis added]*. It has further suggested measures to be taken from the MDCG as clarifying the use of standards through guidance documents (e.g., MDCG 2021-5), and has also clarified what NB and manufacturers may resolve this problem. It can be read from the minutes that NB *"cannot require the use of a certain version of a standard, but they must check whether a standard (as any other technical solution) is properly implemented by the manufacturer to comply with the legal requirements. Manufacturers may choose between the use of a harmonised standard conferring presumption of conformity, even being an old version, or of a more recent standard that would represent the 'state of the art'"* [62].

5.3 Hierarchy of documents for implementing the "state-of-the-art"

As concluded in the CHAPTER 4 above, based on the schematics provided by the MedTech Europe Position Paper [59], the author of this thesis has come up with a flowchart (see Figure 4, below) to consider how to implement the "state-of-the-art" in a manufacturer's point of view. This hierarchy is proposed in general based on the ranking and number of elements that the relevant documents may represent, as abstracted by the author of this thesis (see Table 14 and the conclusion in CHAPTER 4 above). Moreover, priority is given to CS, publications from the designated experts and other EU legislations (e.g., OSH Framework Directive and associated directives as discussed in chapter 3.2.4 above), etc., because of their mandatory nature. So, it is more practical for manufacturers to make decisions. Other stakeholders may also refer to this flowchart when considering the "state-of-the-art" under MDR and IVDR.

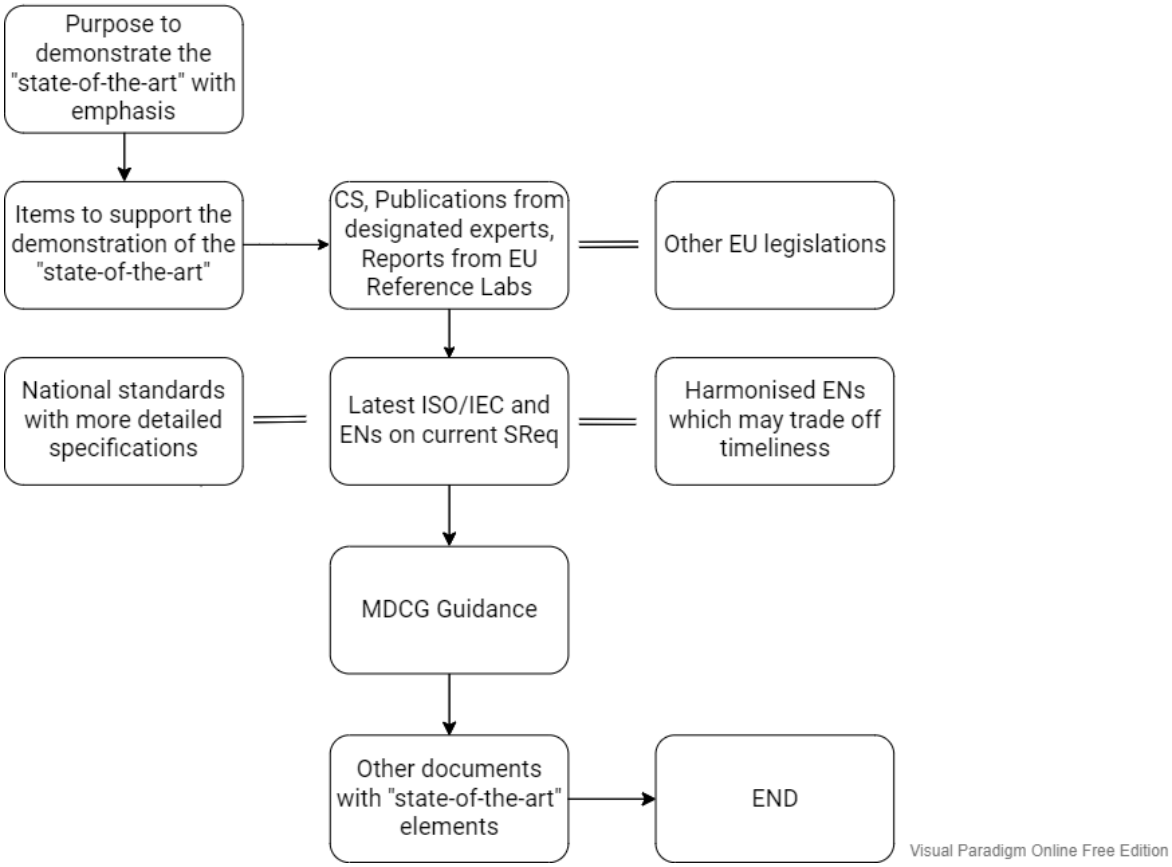


Figure 4 Hierarchy of documents for implementing the "state-of-the-art"[24]

[24] Own illustration based on the MedTech Europe Position Paper on the use of state-of-the-art standards

CHAPTER 6 SUMMARY

To begin with, this study highlights the absence of a clear definition of "state-of-the-art" in MDR and IVDR, and the need to conduct a study to address it.

Besides unclarity, inconsistency of reference to the term “state-of-the-art” is found in different language versions of MDR and IVDR. Then the definitions, explanations, and interpretations of the “state-of-the-art” have to be taken from other sources. Across guidance from international organisations to law experts in the EU/EFTA countries, the definitions, explanations, and interpretations of the “state-of-the-art” are summarised and presented.

Subsequently, key elements in the “state-of-the-art” as perceived by the author of this thesis are abstracted and analysed. This serves as a tool, presenting a non-exhaustive list of the key elements, to conduct further research on the opinions of stakeholders in terms of defining and understanding the “state-of-the-art”.

In the research on stakeholders, the involvement, responsibilities, abilities, designated status, and roles in either giving or fulfilling the requirements of the “state-of-the-art” are presented.

At application level, the decision-making about “state-of-the-art” among the stakeholders is also mentioned, as the NB plays a central role. Together, publications from the designated experts by Member State and the rules of their designation are further analysed to illustrate why their opinions matter in light of the “state-of-the-art”.

As followed, the study goes on into the topic of the evolvement of the “state-of-the-art” requirements in the medical device law, from the introduction of the “New Approach” directives back in 1985 to the development of “NLF” after 2008, aiming to deepen the understanding of the logic behind using the reference to the “state-of-the-art” as a legislative tool, and what potential pros and cons may be associated with it. “State-of-the-art” requirements turned out to be inbuilt very early as one of the principles of the “New Approach”, and was rooted in the use of standards for compliance with the essential requirements set out in the directives, which has not become the GSPRs in the MDR and IVDR. Moreover, the “state-of-the-art” requirements in the MDR and IVDR already go beyond the GSPR.

Together with deepening the knowledge, the discussion goes a step further by introducing a specific topic about the use of standards to demonstrate the “state-of-the-art” for medical devices. Relevant opinions from a Notified Body are presented, and the discovery from previous analysis is used to discuss this topic.

There is a difference between the “state-of-the-art” requirements in MDD, AIMDD, IVDD and the MDR and IVDR, where a phenomenon of “missing” the “state-of-the-art” requirements has been discovered and further explained.

It also provides some insight into the future about what to focus on regarding the topic "state-of-the-art" in the MDR and IVDR in accordance with the discussion in previous chapters. For relevant stakeholders, a hierarchy of documents is also suggested for implementing the "state-of-the-art."

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Annex 1 Comparison of new regulations and repealed directives

Table 10 Comparison of MDR and MDD/AIMDD: the "state-of-the-art" requirements[25]

No.	State of the art requirements on	MDR (2020-04-24) amended M1 [67]	MDD (2007-10-11) amended M5 [60]	AIMDD (2007-10-11) amended M4 [68]	MDD before M5 [69]	AIMDD before M4 [70]
01	Products without an intended medical purpose	Article 1(2)	-/-	-/-	-/-	-/-
02	GSPR of investigational devices	Article 62(4), Point (l)	-/-	-/-	-/-	-/-
03	Task of expert panels and expert laboratories - develop and review guidance of conformity assessment	Article 106(10), Point (c)	-/-	-/-	-/-	-/-
04	Task of expert panels and expert laboratories - contribute to the development of standards at international level	Article 106(10), Point (d)	-/-	-/-	-/-	-/-
05	Device risk management	Annex I, Section 1	Annex I, Section 2	Annex 1, Section 6	Annex I, Section 2	Annex 1, Section 6
06	Risk control measures	Annex I, Section 4	Annex I, Section 2	Annex 1, Section 6	Annex I, Section 2	Annex 1, Section 6
07	Software	Annex I, Section 17.2	Annex I, Section 12.1a	Annex 1, Section 9	-/-	-/-

25 Own illustration

No.	State of the art requirements on	MDR (2020-04-24) amended M1 [67]	MDD (2007-10-11) amended M5 [60]	AIMDD (2007-10-11) amended M4 [68]	MDD before M5 [69]	AIMDD before M4 [70]
08	Clinical evaluation plan	Annex IX, Section 2.1	-/-	-/-	-/-	-/-
09	Clinical evaluation plan (documentation requirement – indicative list and parameters to determine the acceptability of the benefit-risk ratio)	Annex XIV, Section 1	-/-	-/-	-/-	-/-
10	Clinical Investigational Plan (documentation requirement - clinical care in the relevant field of application)	Annex XV, Chapter II, Section 3.2	-/-	Annex 7, Section 2.3	-/-	Annex 7, Section 2.3
11	Clinical Investigational Plan (documentation requirement – relevance of the clinical investigation in clinical practice)	Annex XV, Chapter II, Section 3.4	-/-	Annex 7, Section 2.3	-/-	Annex 7, Section 2.3
12	Clinical Investigational Report (documentation requirement - clinical relevance)	Annex XV, Chapter III, Section 7	-/-	-/-	-/-	-/-
13*	(Under MDD/AIMDD, instead of MDR) Statistical control	-/-	Annex IV, Section 6.3	Annex 4, Section 6.3	-/-	-/-

-/-: not applicable; *: clause that is disappeared in the new regulation

Table 11 Comparison of IVDR and IVDD: the "state-of-the-art" requirements[26]

No.	State of the art requirements on	IVDR (2022-01-28) amended M1 [71]	IVDD (2012-01-11) amended M3 [72]	IVDD Legal Act [5]
01	Performance evaluation and clinical evidence	Article 56	-/-	-/-
02	Analytical performance in clinical performance studies	Article 58(5), Point (m)	-/-	-/-
03	Analytical performance and scientific validity in interventional clinical performance studies	Article 58(5), Point (n)	-/-	-/-
04	Proof of device technical safety (for performance study)	Article 58(5), Point (o)	-/-	-/-
05	GSPR of the device(s) for performance study (assessment by MS)	Article 67(3), Point (a)	-/-	-/-
06	Task of EU reference laboratories - scientific advice	Article 100(2), Point (d)	-/-	-/-
07	Task of EU reference laboratories – network of coordination and harmonisation (reassessment)	Article 100(5), Point (j)	-/-	-/-
08	Device risk management	Annex I, Section 1	Annex I, Section 2	Annex I, Section 2
09	Risk control measures	Annex I, Section 4	Annex I, Section 2	Annex I, Section 2
10	Performance characteristics	Annex I, Section 9.1	Annex I, Section 3	Annex I, Section 3
11	Software	Annex I, Section 16.2	-/-	-/-
12	Performance evaluation plan	Annex IX, Section 2.1	-/-	-/-

[26] Own illustration

No.	State of the art requirements on	IVDR (2022-01-28) amended M1 [71]	IVDD (2012-01-11) amended M3 [72]	IVDD Legal Act [5]
13	Performance evaluation plan (documentation requirement - description)	Annex XIII, Section 1.1	-/-	-/-
14	Performance evaluation plan (documentation requirement – indication and parameters to determine the acceptability of the benefit-risk ratio)	Annex XIII, Section 1.1	-/-	-/-
15	Clinical evidence quality	Annex XIII, Section 1.3.1	-/-	-/-
16	Performance Evaluation Report (documentation requirement)	Annex XIII, Section 1.3.2	-/-	-/-
17	Clinical Performance Study Plan (documentation requirement - overall synopsis of the clinical performance study)	Annex XIII, Section 2.3.2, Point (g)	-/-	-/-
18	Clinical Performance Study Plan (documentation requirement – clinical practice)	Annex XIII, Section 2.3.2, Point (h)	-/-	-/-
19	PMPF Plan (documentation requirement – equivalent or similar device)	Annex XIII, Section 5.2, Point (f)	-/-	-/-
20*	(Under IVDD, instead of IVDR) – (quality) controls and tests carried out by manufacturer	-/-	Annex IV, Section 3.2, Point (e)	Annex IV, Section 3.2, Point (e)
21*	(Under IVDD, instead of IVDR) – EC Verification (testing procedures)	-/-	Annex VI, Section 2.1	Annex VI, Section 2.1
22*	(Under IVDD, instead of IVDR) – EC Verification (statistical verification)	-/-	Annex VI, Section 6.3	Annex VI, Section 6.3

-/-: not applicable; *: clause that is disappeared in the new regulation

Annex 2 Comparison of the translation of "state-of-the-art" from the same clauses of MDR in different EU languages

Table 12 Translation of "state-of-the-art" from the same clauses of MDR[27]

Language	**01, 03, 07, 08[28]**	**02**	**04**	**05, 06**	**09**	**10**	**11**	**12**
EU English	state of the art	state of the art	state of the art	generally acknowledged state of the art	state of the art in medicine	current state of the art in clinical care	state of the art of clinical practice	clinical state of the art
German	Stand der Technik	neuester Erkenntnis-stand	neuester Stand der Technik	allgemein anerkannter Stand der Technik	neuester medizinischer Kenntnisstand	gegenwärtiger Stand der Technik bei der klinischen Versorgung	Stand der Technik bei der klinischen Praxis	Stand des klinischen Wissens
Meaning in German[29]	state of the art[30]	latest state of knowledge	latest state of the art	generally recognised state of the art	latest state of medical knowledge	current state of the art in clinical care	state of the art in clinical practice	state of clinical knowledge

[27] Own illustration
[28] clause No. as listed in Table 10, Annex 1
[29] provided by DeepL translator (free version), and adjusted by native speaker
[30] It literally means "status of the technique" in German.

Language	01, 03, 07, 08[28]	02	04	05, 06	09	10	11	12
French	état de l'art	état de l'art	état de l'art	état de l'art généralement admis	état de l'art dans le domaine médical	état de l'art concernant les soins cliniques	état de l'art dans le domaine de la pratique clinique	pertinence clinique selon l'état de l'art
Meaning in French	state of the art	state of the art	state of the art	generally accepted state of the art	state of the art in medicine	state of the art in clinical care	state of the art in clinical practice	state of the art clinical relevance
Italian	stato dell'arte	stato dell'arte	stato dell'arte	stato dell'arte generalmente riconosciuto	stato dell'arte in campo medico	l'attuale stato dell'arte dell'assistenza clinica	stato dell'arte della pratica clinica	stato dell'arte in campo clinico
Meaning in Italian	state of the art	state of the art	state of the art	generally recognised state of the art	state of the art in the medical field	the current state of the art of clinical care	state of the art in clinical practice	state of the art in the clinical field
Spanish	los conocimientos más recientes de la medicina / el estado actual de la técnica[31]	los conocimientos más recientes	los últimos avances técnicos[32]	el estado de la técnica generalmente reconocido	los avances más recientes de la medicina	la situación actual de los conocimientos en atención clínica	los últimos adelantos de la práctica clínica	la pertinencia clínica de acuerdo con los conocimientos más actuales

[31] For Spanish version: Anexo I, 17.2

[32] For Spanish version: Artículo 106(10), c) and Artículo 106(10), d)

Language	**01, 03, 07, 08**[28]	**02**	**04**	**05, 06**	**09**	**10**	**11**	**12**
Meaning in Spanish	latest medical knowledge / state-of-the-art technology	the latest knowledge	the latest technical developments	the generally recognised state of the art	the latest advances in medicine	the current state of knowledge in clinical care	the latest developments in clinical practice	the clinical relevance in accordance with the latest knowledge

Annex 3 List of harmonised standards published in the OJEU for medical devices

Table 13 Harmonised standards for MDR and IVDR, published in the OJEU[33]

Legislation Reference	European standardisation body	Reference number of the standard	Title of the standard	Presumption of conformity on	OJEU reference
MDR	CEN	EN 285:2015+A1:2021	Sterilization - Steam sterilizers - Large sterilizers	2022-05-17	OJ L 138 – 2022-05-17
MDR	CEN	EN ISO 10993-9-2021	Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products (ISO 10993-9-2019)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 10993-12-2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 10993-23-2021	Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)	2021-07-19	OJ L 256 - 2021-07-19
MDR	CEN	EN ISO 11135:2014 EN ISO 11135:2014/A1:2019	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014)	2021-07-19	OJ L 256 - 2021-07-19

[33] Source: Summary of references of harmonised standards published in the Official Journal – Regulation (EU) 2017/745, 17 May 2022; Summary of references of harmonised standards published in the Official Journal – Regulation (EU) 2017/746, 12 May 2022, correction is made, own illustration

Legislation Reference	European standardisation body	Reference number of the standard	Title of the standard	Presumption of conformity on	OJEU reference
MDR	CEN	EN ISO 11137-1:2015 EN ISO 11137-1:2015/A1:2019	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137- 1:2006, including Amd 1:2013)	2021-07-19	OJ L 256 - 2021-07-19
MDR	CEN	EN ISO 11737-1:2018 EN ISO 11737-1:2018/A1:2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 11737-2:2020	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)	2021-07-19	OJ L 256 - 2021-07-19
MDR	CEN	EN ISO 13408-6:2021	Aseptic processing of health care products - Part 6: Isolator systems (ISO 13408-6:2021)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 13485:2016 EN ISO 13485:2016/A11:2021	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 13485:2016 EN ISO 13485:2016/A11:2021, EN ISO 13485:2016/AC:2018	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)	2022-05-17	OJ L 138 – 2022-05-17

Legislation Reference	European standardisation body	Reference number of the standard	Title of the standard	Presumption of conformity on	OJEU reference
MDR	CEN	EN ISO 14160:2021	Sterilization of health care products - Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives - Requirements for characterization, development, validation and routine control of a sterilization process for medical devices (ISO 14160:2020)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 14971:2019, EN ISO 14971:2019/A11:2021	Medical devices - Application of risk management to medical devices (ISO 14971:2019)	2022-05-17	OJ L 138 – 2022-05-17
MDR	CEN	EN ISO 15223-1:2021	Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements (ISO 15223- 1:2021)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 17664-1:2021	Processing of health care products - Information to be provided by the medical device manufacturer for the processing of medical devices - Part 1: Critical and semi-critical medical devices (ISO 17664-1:2021)	2022-01-05	OJ L 1 – 2022-01-05
MDR	CEN	EN ISO 25424:2019	Sterilization of health care products - Low temperature steam and formaldehyde - Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 25424:2018)	2021-07-19	OJ L 256 - 2021-07-19

Legislation Reference	European standardisation body	Reference number of the standard	Title of the standard	Presumption of conformity on	OJEU reference
MDR	CENELEC	EN IEC 60601-2-83:2020, EN IEC 60601-2-83:2020/A11:2021	Medical electrical equipment - Part 2-83: Particular requirements for the basic safety and essential performance of home light therapy equipment	2022-01-05	OJ L 1 – 2022-01-05
IVDR	CEN	EN ISO 11135:2014, EN ISO 11135:2014/A1:2019	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014)	2021-07-20	OJ L 258 - 2021-07-20
IVDR	CEN	EN ISO 11137-1:2015, EN ISO 11137- 1:2015/A2:2019	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137-1:2006, including Amd 1:2013)	2021-07-20	OJ L 258 - 2021-07-20
IVDR	CEN	EN ISO 11737-1:2018, EN ISO 11737- 1:2018/A1:2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018)	2022-01-07	OJ L 4- 2022-01-07
IVDR	CEN	EN ISO 11737-2:2020	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)	2021-07-20	OJ L 258 - 2021-07-20
IVDR	CEN	EN ISO 13408-6:2021	Aseptic processing of health care products - Part 6: Isolator systems (ISO 13408-6:2021)	2022-01-07	OJ L 4- 2022-01-07

Legislation Reference	European standardisation body	Reference number of the standard	Title of the standard	Presumption of conformity on	OJEU reference
IVDR	CEN	EN ISO 13485:2016, EN ISO 13485:2016/A11:2021	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)	2022-01-07	OJ L 4-2022-01-07
IVDR	CEN	EN ISO 13485:2016 EN ISO 13485:2016/A11:2021, EN ISO 13485:2016/AC:2018	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)	2022-05-12	OJ L 135 – 2022-05-12
IVDR	CEN	EN ISO 14971:2019, EN ISO 14971:2019/A11:2021	Medical devices - Application of risk management to medical devices (ISO 14971:2019)	2022-05-12	OJ L 135 – 2022-05-12
IVDR	CEN	EN ISO 15223-1:2021	Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements (ISO 15223-1:2021)	2022-01-07	OJ L 4-2022-01-07
IVDR	CEN	EN ISO 17511:2021	In vitro diagnostic medical devices - Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples (ISO 17511:2020)	2022-01-07	OJ L 4-2022-01-07
IVDR	CEN	EN ISO 25424:2019	Sterilization of health care products - Low temperature steam and formaldehyde - Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 25424:2018)	2021-07-20	OJ L 258 - 2021-07-20

Annex 4 Comparison of interpretations of "state-of-the-art"

There are certain key elements relating to the definition, explanation or interpretation of the "state-of-the-art" outlined by the author of this thesis based on chapter 3.1 above:

(1) reflecting timeliness

(2) no mandatory to be the latest

(3) being subject-orientated

(4) being acknowledged by majority

(5) being on the basis of opinions from experts

(6) publication being approved through a due process (e.g., consensus procedure)

(7) technical capacity / technical feasibility

(8) acknowledged status based on record of use

Table 14 Comparison of the interpretations of "state-of-the-art" listed in this study[34]

Source of or author(s) for the definition, explanation or interpretation of the "state-of-the-art"	**Key elements outlined**							
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**
IMDRF/GRRP WG/N47 FINAL:2018 (chapter 3.1 above)	X	X	X	X	X	-/-	X	-/-
ISO/IEC Guide 63:2019 (chapter 3.1.3 above)	X	X	X	X	X	X	X	-/-

[34] Own illustration

Source of or author(s) for the definition, explanation or interpretation of the "state-of-the-art"	**Key elements outlined**							
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**
Harm Schepel and Josef Falke, Germany (chapter 3.1.4 above)	X	-/-	X	-/-	-/-	-/-	X	-/-
Harm Schepel and Josef Falke, France (chapter 3.1.4 above)	X	-/-	X	-/-	X	-/-	-/-	-/-
Peter Draxler, Alexander Petsche et al., Austria (chapter 3.1.4 oben)	-/-	X	-/-	-/-	-/-	-/-	-/-	X
Marja-Leena Mansala, Finland (chapter 3.1.4 above)	X	X	X	-/-	-/-	-/-	-/-	-/-
Robert Clark, Ireland (chapter 3.1.4 above)	X	-/-	X	-/-	-/-	-/-	X	-/-
Sverre Sandvik, Norway (chapter 3.1.4 above)	-/-	-/-	-/-	-/-	X	-/-	-/-	-/-
Dirk Trüten, Karin Bürgi and Leena Kriegers-Tejura, Switzerland and Lichtenstein (chapter 3.1.4 oben)	-/-	-/-	X	-/-	-/-	-/-	X	X
Sum of the counts of "X"	6	4	7	2	4	1	5	2
Ranking by the counts of "X"	No. 2	No. 4	No. 1	No. 6	No. 4	No. 8	No. 3	No.6
X: applicable; -/-: not applicable								

EIDESSTATTLICHE ERKLÄRUNG

Hiermit erkläre ich an Eides statt, die Arbeit selbständig verfasst und keine anderen als angegebenen Hilfsmittel verwendet zu haben.

Karlsruhe, 2022-07-09

Unterschrift des Studierenden

ELEKTRONISCHE ZUSAMMENFASSUNG

Yuan Shi (2022)

Titel/Title

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Zusammenfassung/Summary

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