COMITÉ PERMANENT DES MÉDECINS EUROPÉENS
STANDING COMMITTEE OF EUROPEAN DOCTORS

The CPME Statement on Medical Devices and In Vitro Medical Devices may be accessed here.

Amendments

Summary of amendments in the present document:	
In Vitro draft regulation	
Ethics committee: *CPME believes that compliance with ethics principles would also need to be ensured with regard to the IVD draft regulation, where and as appropriate within the legal text. Where possible, an ethics committee would be necessary to give its advice before interventions comparable to clinical trials for medicines.*	
	Sponsors
	Data protection, confidentiality
	Quality management
Medical devices draft regulation	
Definitions of:	**Medical device**
	Active device
	Health institution
	Clinical investigation
	Sponsor
	Reprocessing
	Inspection
Clinical investigations :	**Requirements for clinical investigations** **In general** **In relation to ethics committees**
Member state scrutiny (New article proposed to the draft regulation)	

IV VITRO MEDICAL DEVICES

Amendment 1

Recital 46

Proposal of the Commission	Amendment
(5930) Sponsors should report certain adverse events occurring during interventional clinical performance studies and other clinical performance studies involving risks for the subjects to the Member States concerned which should have the possibility to terminate or suspend these studies if considered necessary to ensure a high level of protection of the subjects enrolled in such studies. Such information should be communicated to the other Member States.	(5931) Sponsors should report ~~certain~~ **all** adverse events occurring during interventional clinical performance studies and other clinical performance studies involving risks for the subjects to the Member States concerned which should have the possibility to terminate or suspend these studies if considered necessary to ensure a high level of protection of the subjects enrolled in such studies. Such information should be communicated to the other Member States.

Justification:

This is in tune with article 15 of the World Medical Association's Declaration of Helsinki on Ethical principles for medical research involving human subjects.

Amendment 2

Recital 29

Proposal of the Commission	Amendment
(29) (…)The objectives of the database are to enhance overall transparency, to streamline and facilitate the flow of information between economic operators, notified bodies or sponsors and Member States as well as between Member States among themselves and with the Commission, to avoid multiple reporting requirements and to enhance the coordination between Member States. Within an internal market, this can be ensured effectively only at Union level and the Commission should therefore further develop and manage the European databank on medical devices (Eudamed) by further developing the databank set up by Commission Decision 2010/227/EU of 19 April 2010 on the European Databank for Medical Devices.	(29) (…)The objectives of the database are to enhance overall transparency, to streamline and facilitate the flow of information between economic operators, notified bodies or sponsors and Member States as well as between Member States among themselves and with the Commission, to avoid multiple reporting requirements and to enhance the coordination between Member States**, guaranteeing that confidentiality and data protection are insured, especially with regard to sensitive data (e.g. genetic data)**. Within an internal market, this can be ensured effectively only at Union level and the Commission should therefore further develop and manage the European databank on medical devices (Eudamed) by further developing the databank set up by Commission Decision 2010/227/EU of 19 April 2010 on the European Databank for Medical Devices.

Justification:

Whenever information is exchanged, data protection rules and principles need to be adequately upheld.

Amendment 3

Article 39 (new)

Title: Chapter IV Notified Bodies and Ethics Committees

Proposal of the Commission	Amendment
	(Subpar. 1) Approval may only be granted if an independent ethics committee has previously submitted a positive evaluation of the clinical investigation. The statement of the ethics committee shall cover in particular the medical justifiability, the consent of the test subject following the provision of full information about the investigation and the suitability of the investigators and investigative facilities. **(Subpar. 2) The ethics committee serves to protect the rights, safety and well-being of all test subjects, users and third parties. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards. The ethics committee should be made up of an appropriate number of members, who together are in possession of the relevant qualifications and experience in order to be able to assess the scientific, medical and ethical aspects of the clinical investigation under scrutiny.** **(Subpar. 3) Member States shall take the necessary measures to set up ethics committees and to facilitate their work, and guarantee their independence as in par 6a Supar. 2 .**

Justification

It is ethically imperative that human genetic data to be collected, processed, used and stored on the basis of transparent and ethically acceptable procedures. Thus, the role of Ethics Committees should not be underestimated. If the ethical standards do not comply with the decision of the Ethics Committee, the studies should not be authorised.

Amendment 4

Recital 59

Proposal of the Commission	Amendment
(59) This Regulation respects the fundamental rights and observes the principles recognized in particular by the Charter of Fundamental Rights of the European Union and notably human dignity, the integrity of the person, the protection of personal data, the freedom of art and science, the freedom to conduct business and the right to property. This Regulation should be applied by the Member States in accordance with those rights and principles.	(60) This Regulation respects the fundamental rights and observes the principles recognized in particular by the Charter of Fundamental Rights of the European Union and notably human dignity, the integrity of the person, the protection of personal data, **especially genetic data, confidentiality** the freedom of art and science, the freedom to conduct business and the right to property. This Regulation should be applied by the Member States in accordance with those rights and principles.

Justification

CPME believes that a balance between the information needs of society and the right to privacy requires medically driven criteria. The respect of human dignity and protection of human rights and fundamental freedoms in the collection, processing, use and storage of human genetic data should always be ensured.

Amendment 5

Article 60 – Electronic system on vigilance

Proposal of the Commission	Amendment
4. On the basis of arrangements between the Commission and competent authorities of third countries or international organizations, the Commission may grant those competent authorities or international organizations access to the database at the appropriate level. Those arrangements shall be based on reciprocity and make provision for confidentiality and data protection equivalent to those applicable in the Union.	4. On the basis of arrangements between the Commission and competent authorities of third countries or international organizations, the Commission may grant those competent authorities or international organizations access to the database at the appropriate level. Those arrangements shall be based on reciprocity and make provision for confidentiality and data protection equivalent to those applicable in the Union. **Such processes should seek to ensure that the receiving party provides adequate protection in accordance with data protection law.**

Justification

CPME believes that full transparency should be involved concerning the transfer of personal data, in particular genetic data, to authorized countries, organizations or authorities with adequate levels of protection.

Amendment 6

Quality management

Annex I, No. 16

The annex puts devices which are intended by the manufacturer for self-testing and devices which are used professionally in association with near-patient testing in the same category. This is not appropriate, because it results in members of the health professions being put on the same footing as non-medical persons.

Bibliography:

(1) CPME Statement on Medical Devices and In Vitro Medical Devices.

(2) CPME Statement on the proposal for a regulation on Data Protection

(3) CPME Statement on Clinical Trials

(4) Declaration of Helsinki

Medical devices draft regulation

Amendment 1

Article 2 .par 1, points (1), (5), (24), (28), (34), (38), (39)

Definitions

Proposal of the Commission	Amendment
(1) 'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific medical purposes of: – diagnosis, prevention, monitoring, treatment or alleviation of disease, – diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability, – investigation, replacement or modification of the anatomy or of a physiological process or state, – control or support of conception, – disinfection or sterilisation of any of the above-mentioned products, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.	(1)'medical device' means any instrument, apparatus, appliance, **hardware and software other than exclusively used for administrative purposes in healthcare**, implant, reagent, material or other article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific medical purposes of: – diagnosis, prevention, monitoring, treatment or alleviation of disease, – diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability, – investigation, replacement or modification of the anatomy or of a physiological process or state, – control or support of conception, – disinfection or sterilisation of any of the above-mentioned products, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.
(5) 'active device' means any device, the operation of which depends on a source of electrical energy or any source of power other than that directly generated by gravity and which acts by changing the density of or converting this energy. Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be considered to be active devices. Standalone software shall	(5) 'active device' means any device, the operation of which depends on a source of electrical energy or any source of power other than that directly generated by gravity and which acts by changing the density of or converting this energy. Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be considered to be active devices. Standalone software, **other**

be considered an active device;	**than software used for administrative purposes,** shall be considered an active device;
(24) 'health institution' means an organization whose primary purpose is the care of treatment of patients or the promotion of public health.	(24) 'health institution' means an organization whose primary purpose is the care of treatment of patients or the promotion of public health **and is recognized as such under national law: it does not mean an individual healthcare professional.**
(28) 'reprocessing' means the process carried out on a used device in order to allow its safe reuse including cleaning, disinfection, sterilization and related procedures, as well as testing and restoration of the technical and functional safety of the used device;	(28) 'reprocessing' means the process carried out on a used device in order to allow its safe reuse including cleaning, disinfection, sterilization and related procedures, as well as testing and restoration of the technical and functional safety of the used device; **Within the meaning of this article, single use devices are excluded from 'reprocessing'.**
(34) 'clinical investigation' means any systematic investigation in one or more human subjects, undertaken to assess the safety or performance of a device;	(34) 'clinical investigation' means any systematic investigation in one or more human subjects, undertaken to assess the safety**, ~~or~~** performance **or effectiveness** of a device;
(38) 'sponsor' means an individual, company, institution or organization which takes responsibility for the initiation and management of a clinical investigation;	(38) 'sponsor' means an individual, company, institution or organization which takes responsibility for the initiation**, ~~and~~ management, conduct and/or financing** management of a clinical investigation;
	(38a (new)) 'Inspection' refers to the act by a competent authority of conducting an official review of documents, facilities, records, quality assurance arrangements, and any other resources that are deemed by the competent authority to be related to the clinical investigation and that may be located at the site of the investigation, at the sponsor's and/or contract research organization's facilities, or at other establishments which the competent authority sees fit to inspect;

Justifications:

Paragraph 1 and Paragraph 5

With regard to definition no. (1) "Medical device" pertaining to devices and software, a differentiation should be made between these, as opposed to hardware and software which are used exclusively for administrative purposes in healthcare. In this area there are repeatedly attempts to escalate costs by designating hardware and software as medical devices as soon as they are used in healthcare contexts. In view of the prevailing pressure on costs, this cannot be justified. The same applies to paragraph (5) "active medical device", last sentence.

Paragraph 24

The definition of health institutions needs to have legal coherence and consider the impact of such a wide and inclusive definition of individual medical practices and small practices. Additionally, by linking health institutions to the existing national legal definitions of what is considered as health institution, the definition provides for better legal clarity.

Paragraph 28

In absence of a comprehensive risk assessment and complete impact assessment on reprocessing of single-use devices, the present definition should explicitly excludes single use devices.

Paragraph 34

The clinical investigation of a medical device in terms of its effectiveness goes further than the clinical investigation of its performance. It is not only functionality which is investigated, but also the superiority or inferiority in comparison to non-treatment with the medical device. In order to protect the rights and the well-being of participants in such studies, which are frequently conducted independently of the manufacturer, and also those of future patients, in a fundamentally identical way to the protection afforded participants in clinical investigations conducted in association with manufacturers, an extension of the application area of Articles 50-60 of the Regulation is necessary.

Paragraph 38

Including the conduct of the study under the listed responsibilities of the sponsor is necessary on account of the additional obligations of the sponsor contained in Annex XIV Section III of the EU MD Regulation. Otherwise, if the study is customarily deemed to have been concluded following the last visit of the last test subject it would lack reference to the responsibility of the sponsor with regards to associated follow-up tasks, for example the

archiving of documentation or the necessary compilation of the clinical investigation report and the publishing of results. Supplementing this paragraph with a reference to the responsibility of the sponsor for financing corresponds to the definition in accordance with Article 2e) of Directive 2001/20/EC.

Paragraph 38a (new)

In contrast to the proposal of the Commission for a Regulation on clinical trials on medicinal products for human use (COM 2012, 369 final), the proposed Regulation contains no provisions dealing with inspections. It must not be left to the discretion of the Member States to decide whether to monitor the conduct of clinical investigations. This could lead to decisions on whether to monitor an investigation being made dependent upon the availability of necessary budgetary funds. Furthermore, this could result in clinical investigations being carried out preferentially in states which dispense with monitoring.

A concrete proposal for a new wording in this respect is submitted as Article 59a.

Ammendment 2

Article 15 Single use devices and their reprocessing

Proposal of the Commission	Amendment
1. Any natural or legal person who reprocesses a single-use device to make it suitable for further use within the Union shall be considered to be the manufacturer of the reprocessed device and shall assume the obligations incumbent on manufacturers laid down in this Regulation. 2. Only single-use devices that have been placed on the Union market in accordance with this Regulation, or prior to [date of application of this Regulation] in accordance with Directive 90/385/EEC or Directive 93/42/EEC may be reprocessed. 3. In the case of reprocessing of single-use devices for critical use, only reprocessing that is considered safe according to the latest scientific evidence may be carried out. 4. The Commission, by means of implementing acts, shall establish and regularly update a list of categories or groups of single-use devices for critical use which may be reprocessed in accordance with paragraph 3. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 88(3). 5. The name and address of the legal or natural person referred to in paragraph 1 and the other relevant information in accordance with Section 19 of Annex I shall be indicated on the label and, where applicable, in the instructions for use of the reprocessed device.	**DELETE**

Justification:

In absence of a comprehensive risk assessment and complete impact assessment on reprocessing of single-use devices, we propose the deletion of article 15.

The attempt to integrate an Article in the Regulation which provides a solution to the discussion which has taken place in the past on many different levels, and not always free of vested interests, in respect to the possibilities and limitations of reprocessing disposable devices, appears to have failed. The fundamental problem associated with a proper differentiation between the reprocessing of formally approved devices and devices which according to the manufacturer are not suitable for reprocessing is not tackled at all.

As a result of the wording of Article 15, it cannot be ruled out that healthcare facilities which carry out reprocessing of disposable devices at their own risk would have to act in such a situation as manufacturers, with all of the associated consequences. Such over-regulation would represent a case of the proverbial "throwing out the baby with the bathwater". Instead of this new regulation, it would make more sense to persuade EU Member States to bring the reprocessing of medical devices as a whole – regardless of whether they are formally declared as suitable for reprocessing or as disposable – up to the most modern scientific and technological standards through training and qualified monitoring. Apart from this, the impression is created that this regulation opens a back door to the imposition of a ban on the reprocessing of devices which have been declared by their manufacturers as disposable. This is certainly of no benefit to the manufacturer, let alone the user or the patient.

Amendment 3

Article 50

General requirements regarding clinical investigations

Proposal of the Commission	Amendment
Clinical investigations shall be subject to Articles 50-60 and Annex XIV if they are conducted for one or more of the following purposes: (a) to verify that, under normal conditions of use, devices are designed, manufactured and packaged in such a way that they are suitable for one or more of the specific purposes of a medical device referred to in number (1) of Article 2(1), and achieve the performances intended as specified by the manufacturer; (b) to verify that devices achieve the intended benefits to the patient as specified by the manufacturer; (c) to determine any undesirable side-effects, under normal conditions of use, an assess whether they constitute acceptable risks when weighed against the benefits to be achieved by the device. ... 3. Clinical investigations shall be designed and conducted in a way that the rights, safety and well-being of the subjects participating in a clinical investigation are protected and that the clinical data generated in the clinical investigation are going to be reliable and robust.	Clinical investigations shall be subject to Articles 50-60 and Annex XIV if they are conducted for one or more of the following purposes: (a) to verify that, under normal conditions of use, devices are designed, manufactured and packaged in such a way that they are suitable for one or more of the specific purposes of a medical device referred to in number (1) of Article 2(1), and achieve the performances intended as specified by the manufacturer **or sponsor**; (b) to verify that devices achieve the intended benefits to the patient as specified by the manufacturer **or sponsor**; (c) to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute acceptable risks when weighed against the benefits to be achieved by the device. ... 3. Clinical investigations shall be designed and conducted in a way that the rights, safety and well-being of the subjects participating in a clinical investigation are protected and that the clinical data generated in the clinical investigation are going to be reliable and robust. **They shall not be conducted if the risks associated with the investigation are not medically justifiable in terms of the potential benefits of the medical device.** **Member States shall reserve the right to preclude the conduct of clinical investigations involving certain groups of test subjects, or to make such investigations dependent upon specific prerequisites.**

Justifications

Paragraph 1

From the perspective of patient safety, it is irrelevant whether a clinical investigation is carried out under the responsibility of a manufacturer and is intended to form the basis for future CE marking, or whether a study is to be conducted for non-commercial, particularly scientific purposes. CPME therefore demands that clinical investigations which are the responsibility of or are managed by a person or organization other than a potential manufacturer (cf. Article 2 Par. 37), also be subject to the provisions of the Regulation. The standard for the inclusion of clinical investigations in the draft Regulation must, in light of the general principles of Equality before the Law (Article 20 of the EU Charter of Fundamental Rights) and the Right to the Integrity of the Person (Article 3 of the EU Charter of Fundamental Rights), be whether test subjects are at risk as a result of participation in such an investigation. In contrast, it is not appropriate – as provided for at the present time – to differentiate according to who takes responsibility for the initiation and management of a clinical investigation.

In this connection, we draw attention to the fact that in its proposal for a Regulation governing clinical investigations on medicinal products for human use, the Commission has, with the intended introduction of a national indemnification mechanism set out in Article 73 Par. 3, recognised that even in the case of alleged non-commercial clinical investigations (also known as IITs), subsidies are paid behind the scenes by commercial sponsors. The draft Regulation concerning medicinal products for human use states that the use of the national indemnification mechanism shall be free of charge where, for objective reasons, the clinical trial was not intended, at the time of submission of the application for authorisation of that clinical trial, to be used for obtaining a marketing authorisation for a medicinal product. The exclusion of IITs from the scope of application of Articles 50 to 60 and Annex XIV therefore leads to the exclusion of studies with the same risk profile, which in many cases later form the basis for the bringing new medical devices to market after all, even in the context of a clinical evaluation. The differentiation contained within the EU MD Regulation is therefore not factually justified.

Paragraph 3

The proposed amendment takes into account the fact that medical innovation cannot be reduced to the supply of new technological developments. In addition to proof of therapeutic benefit, it must show an acceptable risk-benefit ratio. The draft Regulation is inconsistent insofar as a clinical investigation in accordance with Article 50 Par. 1 lit c of the MD Regulation, is carried out, inter alia, for the purpose of evaluating whether undesirable side-effects represent an acceptable risk when compared to the benefits expected from the device. In such cases it would be necessary to be able to refuse approval for the clinical investigation if the benefit-risk ratio does not justify the involvement of test subjects in the study.

The second amendment is necessary to clarify that national legislation can make the conduct of clinical investigations involving vulnerable groups dependent upon specific prerequisites, or exclude them altogether (e.g. in the case of convicts).

Amendment 4

Article 51

Application for clinical investigations and favorable opinion by an ethics committee

Proposal of the Commission	Amendment
(1) Before making the first application, the sponsor shall procure from the electronic system referred to in Article 53 a single identification number for a clinical investigation conducted in one site or multiple sites, in one or more than one Member State. The sponsor shall use this single identification number when registering the clinical investigation in accordance with Article 52.	Before making the first application, the sponsor shall procure from the electronic system referred to in Article 53 a single identification number for a clinical investigation conducted in one site or multiple sites, in one or more than one Member State. The sponsor shall use this single identification number when registering the clinical investigation in accordance with Article 52.
(2) The sponsor of a clinical investigation shall submit an application to the Member State(s) in which the investigation is to be conducted accompanied by the documentation referred to in Chapter II of Annex XIV. Within six days after receipt of the application, the Member State concerned shall notify the sponsor whether the clinical investigation falls within the scope of this Regulation and whether the application is complete.	(2) The sponsor of a clinical investigation shall submit an application to the Member State(s) in which the investigation is to be conducted accompanied by the documentation referred to in Chapter II of Annex XIV. Within **~~six~~ fourteen** days after receipt of the application, the Member State concerned shall notify the sponsor whether the clinical investigation falls within the scope of this Regulation and whether the application is complete.
(3) […] Where the Member State has not notified the sponsor according to paragraph 2 within three days following receipt of the comments or of the completed application, the clinical investigation shall be considered as falling within the scope of this Regulation and the application shall be considered complete.	(3) […] Where the Member State has not notified the sponsor according to paragraph 2 within **~~three~~ seven** days following receipt of the comments or of the completed application, the clinical investigation shall be considered as falling within the scope of this Regulation and the application shall be considered complete.
(5) The sponsor may start the clinical investigation in the following circumstances:	(5) The sponsor may start the clinical investigation in the following circumstances:
(a) in the case of investigational devices classified as class III and implantable or	(a) **~~in the case of investigational devices classified as class III and implantable or~~**

long-term invasive devices classified as class IIa or IIb, as soon as the Member State concerned has notified the sponsor of its approval;	~~**long-term invasive devices classified as class IIa or IIb**~~, as soon as the Member State concerned has notified the sponsor of its approval;
(b) in the case of investigational devices other than those referred to in point (a) immediately after the date of application provided that the Member State concerned has so decided and that evidence is provided that the rights, safety and well-being of the subjects to the clinical investigation are protected;	~~**(b) in the case of investigational devices other than those referred to in point (a) immediately after the date of application provided that the Member State concerned has so decided and that evidence is provided that the rights, safety and well-being of the subjects to the clinical investigation are protected;**~~
(c) after the expiry of 35 days after the validation date referred to in paragraph 4, unless the Member State concerned has notified the sponsor within that period of its refusal based on considerations of public health, patient safety or public policy.	~~**(c**~~**b**) after the expiry of ~~**35**~~ **60** days after the validation date referred to in paragraph 4, unless the Member State concerned has notified the sponsor within that period of its refusal based on considerations of public health, patient safety or public policy.
	Paragraph 5a (new)
	Member States shall ensure that a clinical investigation is suspended, cancelled or temporarily interrupted if in the light of new facts it would no longer be approved by the competent authority or if it would no longer receive a favorable opinion from the ethics committee.
	Paragraph 6a (new) **Ethics committee**
	(Subpar. 1) Approval may only be granted if an independent ethics committee has previously submitted a positive evaluation of the clinical investigation. The statement of the ethics committee shall cover in particular the medical justifiability, the consent of the test subject following the provision of full information about the investigation and the suitability of the investigators and investigative facilities.

	(Subpar. 2) The ethics committee serves to protect the rights, safety and well-being of all test subjects, users and third parties. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards. The ethics committee should be made up of an appropriate number of members, who together are in possession of the relevant qualifications and experience in order to be able to assess the scientific, medical and ethical aspects of the clinical investigation under scrutiny. **(Subpar. 3) Member States shall take the necessary measures to set up ethics committees and to facilitate their work, and guarantee their independence as in par 6a Supar. 2 .**

Justification

Paragraph 1
This article par.1 makes reference to article 53 while article 53 refers to article 51. Article 53 would need to encompass a clearer and more detailed description of the electronic system, otherwise the references are redundant as none of the articles describe the electronic system.

Paragraph 2
The draft Regulation provides for the sponsor being notified within six days as to whether the application is complete and whether the clinical investigation falls within the scope of application of the Regulation. The deadline provided for this does not take into consideration that weekends and public holidays could mean that no time remains for actual examination of the application by the competent authority, and that for this reason alone the participation of an ethics committee, which for its part may deem certain documentation as essential, is de facto excluded.

Paragraph 5 lit a) und b)
The draft Regulation grants Member States the authority to permit sponsors to commence with the clinical investigation immediately after submission of the application for approval of

that clinical investigation, whereby investigations involving investigational devices classified as class III and implantable or long-term invasive devices classified as class IIa or IIb, are exempt. In addition, evidence is required that that the rights, safety and well-being of the subjects to the clinical investigation are protected.

This opt-out provision leads to pressure on Member States to permit the commencement of clinical investigations – according to the current draft Regulation – 35 days earlier than in other countries, and therefore to relegate the protection of test subjects in favour of competitive advantages. At the same time, it must be taken into consideration that clinical investigations in this sector are only carried out if a clinical evaluation is not sufficient anyway, i.e. when there are uncertainties regarding the functional suitability, side-effects or risks associated with the use of a medical device. If only clinical investigations related to the suitability, performance, benefits, side-effects and an acceptable benefit-risk analysis are subject to the EU MD Regulation in accordance with Article 50, Paragraph 1, the protection of test subjects dictates that they be protected in every Member State by an approval process conducted by the competent authority and an evaluation process conducted by the ethics committee in order to safeguard them from useless, inappropriate and risky medical devices. In addition, this means that it is accepted that those test subjects who are the first to be subjected to the clinical investigation enjoy less protection than those who participate at a later date. While the first test subjects participate on the basis of the representations of the sponsor, the latter enjoy the benefit of the knowledge made available by the competent authority and / or ethics committee.

Paragraph 5 lit c)
The adjustment of the deadline is necessary in order to facilitate an effective assessment of the clinical investigation. Particularly, in the case of clinical investigations conducted in several Member States, sufficient time must remain for coordinated evaluation in accordance with Article 58. As the Regulation does not provide for any special evaluation deadline for multinational clinical investigations, the general evaluation deadline in this Regulation must be appropriately adjusted.

The Regulation does not prescribe any circumstances on the basis of which approval is to be denied. For the protection of test subjects, the prerequisites specified in the list, must under all circumstances, result in a denial of approval.

Paragraph 5a (new)
Article 56 provides for an exchange of information between Member States insofar as one Member State orders the suspension, cancellation or temporary interruption of a clinical investigation. However, the EU MD Regulation does not regulate the circumstances under which a Member State is entitled to make such a decision. This can only be the case if new information is available which would stand in the way of an approval.

Paragraph 6a (new) Subparagraphs 1 and 2

Clinical investigations are designed and carried out in accordance with Article 50 Par. 3 in such a manner that the protection of the rights, safety and well-being of the subjects participating in a clinical investigation are protected. To implement those objectives, it is necessary to make approval by Member States dependent upon the decision of the competent, independent, interdisciplinary ethics committee formed under their respective national laws. A negative decision handed down by an ethics committee must necessarily result in the denial of approval for a clinical investigation. At the same time, the ethics committee must be independent of the sponsor and the investigators, as well as of state agencies – in particular those state agencies responsible for the approval of a clinical investigation or the licensing of medicines. The proposed Paragraph 6a complies with that requirement and secures the level of protection for test subjects, and is in harmony with internationally recognized protection standards, as set out in the Declaration of Helsinki.

Paragraph 6a (new) Subparagraph 3

With the express regulation of ethics committees, an EU Regulation can make a substantial contribution towards setting up independent ethics committees in accordance with international ethical standards for the protection of the rights, safety and well-being of study participants, including in countries in which this has not been the case until now. Dispensing with the requirement of independent ethics committees will weaken this independent protection of study participants in third countries, and also in numerous Member States. This stands in contradiction to the objective declared in recital 47, that clinical investigations conducted outside the Union in accordance with international guidelines can be accepted under this Regulation.

Amendment 5

Article 59a (new)

Member State scrutiny

Proposal of the Commission	Amendment
	1. Member States shall appoint inspectors to supervise compliance with this Regulation. They shall ensure that those inspectors are adequately qualified and trained. **2. Inspections shall be conducted under the responsibility of the Member State where the inspection takes place.** **3. Where a Member State concerned intends to carry out an inspection with regard to one or several clinical trials which are conducted in more than one Member State concerned, it shall notify its intention to the other Member States concerned, the Commission and the Agency, through the EU portal, and shall inform them of its findings after the inspection.** **4. The Agency shall coordinate cooperation on inspections between Member States and on inspections conducted by Member States in third countries.** **5. Following an inspection, the Member State under whose responsibility the inspection has been conducted shall draw up an inspection report. That Member State shall make the inspection report available to the sponsor of the relevant clinical trial and shall submit the inspection report through the EU portal to the EU database. When making the inspection report available to the sponsor, the Member State referred to in the first subparagraph shall ensure that confidentiality is protected.** **6. The Commission shall specify the modalities for the inspection procedures**

	by the way of implementing acts. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 84(2).

Justification

In contrast to the proposal of the Commission for a Regulation on clinical trials on medicinal products for human use (COM 2012, 369 final), the proposed Regulation contains no provisions regarding inspections. It must not be left to the discretion of the Member States to decide whether to monitor the conduct of clinical investigations. This could lead to decisions on whether to monitor an investigation being made dependent upon the availability of appropriate budgetary means. This could result in clinical investigations being carried out preferentially in states which dispense with monitoring. The concrete wording of the proposal follows Articles 75 and 76 of the proposal of the Commission for a Regulation on clinical trials on medicinal products for human use (COM 2012, 369 final).

Amendment 6

Annex XIV

Clinical investigations

Proposal of the Commission	Amendment
1. Ethical considerations Every step in the clinical investigation, from first consideration of the need and justification of the study to the publication of the results, shall be carried out in accordance with recognized ethical principles, as for example those laid down in the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th World Medical Association General Assembly in Helsinki, Finland, in 1964, and last amended by the 59th World Medical Association General Assembly in Seoul, Korea, in 2008.	1. Ethical considerations Every step in the clinical investigation, from first consideration of the need and justification of the study to the publication of the results, shall be carried out in accordance with recognized ethical principles, as for example those laid down in the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th World Medical Association General Assembly in Helsinki, Finland, in 1964, and last amended by the 59th World Medical Association General Assembly in Seoul, Korea, in 2008. **The regulation of more detailed prerequisites regarding the involvement of test subjects in clinical investigations shall be the responsibility of the Member States.**
3.1.3. Information on the principal investigator, coordinating investigator, including their qualifications, and on the investigation site(s).	3.1.3. Information on the principal investigator, coordinating investigator, including their qualifications, and on the investigation site(s) **as well as details of the contracts concluded between the sponsor and the investigating agency / investigator, including details of remuneration and financing.**
3.1.4. Overall synopsis of the clinical investigation.	3.1.4. Overall synopsis of the clinical investigation **in the national language of each of the affected Member States.** **3.15.a (new) A plan for the further treatment and medical care of test subjects following conclusion of the clinical investigation.**

Justification

Regarding 1.
This amendment serves to clarify that the Member States must define the prerequisites for the participation of test subjects in clinical investigations. In this respect they are bound to the definitions of minimum standards set out in the Declaration of Helsinki of the World Medical Association in the version of 2008.

Regarding 3.1.3.
It is standard practice for ethics committee to be given access to the contracts concluded between the sponsor and the investigating agency/investigator and to take these into consideration in the evaluation of the study protocol.

Regarding 3.1.4.
In order to facilitate an objective evaluation of the application, a synopsis of the investigative plan in the respective national language is of central significance.

Regarding 3.15.a (new)
The Declaration of Helsinki provides that the protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.

Ammendment 7

Annex I
General Safety and Performance Requirements
19.2 Information on the label Point (o)

Proposal of the Commission	Amendment
(o) If the device is a single use device that has been reprocessed, an indication of that fact, the number of reprocessing cycles already performed, and any limitation as regards the number of reprocessing cycles.	~~**(o) If the device is a single use device that has been reprocessed, an indication of that fact, the number of reprocessing cycles already performed, and any limitation as regards the number of reprocessing cycles.**~~

Justification

CPME proposes the deletion of this point in line with the previous amendments on single use devices and their reprocessing (lack of risk assessment and impact assessment to properly address reprocessing of single use devices).

Bibliography:

(5) CPME Statement on Medical Devices and In Vitro Medical Devices.

(6) CPME Statement on the proposal for a regulation on Data Protection

(7) CPME Statement on Clinical Trials

(8) Declaration of Helsinki