

8. ~~The Commission, by means of implementing acts, may adopt the modalities and the procedural aspects concerning the submission and analysis of the summary of the preliminary conformity assessment in accordance with paragraphs 2 and 3. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 88(3).~~

Article 45

Certificates

1. The certificates issued by the notified bodies in accordance with Annexes VIII, IX and X shall be in an official Union language determined by the Member State in which the notified body is established or otherwise in an official Union language acceptable to the notified body. The minimum content of the certificates is set out in Annex XII.
2. The certificates shall be valid for the period they indicate, which shall not exceed five years. On application by the manufacturer, the validity of the certificate may be extended for further periods, each not exceeding five years, based on a re-assessment in accordance with the applicable conformity assessment procedures. Any supplement to a certificate shall remain valid as long as the certificate which it supplements is valid.
- 2a. ***Notified bodies may impose restrictions to the intended purpose of a device to certain numbers or groups of patients or require manufacturers to undertake specific post-market clinical follow-up studies pursuant to Part B of Annex XIII.***
3. Where a notified body finds that requirements of this Regulation are no longer met by the manufacturer, it shall, taking account of the principle of proportionality, suspend or withdraw the certificate issued or impose any restrictions on it unless compliance with such requirements is ensured by appropriate corrective action taken by the manufacturer within an appropriate deadline set by the notified body. The notified body shall give the reasons for its decision.

4. The Commission, in collaboration with the Member States, shall set up and manage an electronic system to collate and process information on certificates issued by notified bodies. The notified body shall enter into this electronic system information regarding certificates issued, including amendments and supplements, and regarding suspended, reinstated, withdrawn or refused certificates and restrictions imposed on certificates. This information shall be accessible to the public.
5. In the light of technical progress, the Commission shall be empowered to adopt delegated acts in accordance with Article 89 amending or supplementing the minimum content of the certificates set out in Annex XII.

Article 46

Voluntary change of notified body

1. In cases where a manufacturer terminates his contract with a notified body and enters into a contract with another notified body in respect of the conformity assessment of the same device, the modalities of the change of notified body shall be clearly defined in an agreement between the manufacturer, *where practicable* the outgoing notified body and the incoming notified body. This agreement shall address at least the following aspects:
 - (a) the date of invalidity of certificates issued by the outgoing notified body;
 - (b) the date until which the identification number of the outgoing notified body may be indicated in the information supplied by the manufacturer, including any promotional material;
 - (c) the transfer of documents, including confidentiality aspects and property rights;
 - (d) ~~the date as of which the incoming notified body assumes full responsibility for the conformity assessment tasks.~~
 - (e) ***the date after which the conformity assessment tasks and the full responsibility for the manufacturer's products including products assessed by the outgoing Notified Body is assigned to the incoming notified body;***
 - (f) ***the last serial number or batch number for which the outgoing Notified Body is responsible.***

2. On their date of invalidity, the outgoing notified body shall withdraw the certificates it has issued for the device concerned.

Article 47

Derogation from the conformity assessment procedures

1. By way of derogation from Article 42, any competent authority may authorise, on duly justified request, the placing on the market or putting into service within the territory of the Member State concerned, of a specific device for which the procedures referred to in Article 42 have not been carried out and use of which is in the interest of public health or patient safety *or health*.
2. The Member State shall inform the Commission and the other Member States of any decision to authorise the placing on the market or putting into service of a device in accordance with paragraph 1 where such authorisation is granted for use other than for a single patient.
3. ~~Upon request by a Member State and where this is in the interest of~~ ***Following an notification pursuant to paragraph 2, the Commission, in exceptional cases relating to a*** public health or patient safety *or health*, ~~in more than one Member State, the Commission~~ may, by means of implementing acts, extend for a determined period of time the validity of an authorisation granted by a Member State in accordance with paragraph 1 to the territory of the Union and set the conditions under which the device may be placed on the market or put into service. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 88(3).

On duly justified imperative grounds of urgency relating to the health and safety of humans, the Commission shall adopt immediately applicable implementing acts in accordance with the procedure referred to in Article 88(4).

Article 48

Certificate of free sale

1. For the purpose of export and upon request by a manufacturer **or an authorised representative**, the Member State in which the manufacturer **or the authorised representative** has its registered place of business shall issue a certificate of free sale declaring that the manufacturer **or the authorised representative, as applicable**, is established and that the device in question bearing the CE-marking in accordance with this Regulation may be legally marketed in the Union. The certificate of free sale shall ~~be valid for the period indicated on it which shall not exceed five years and shall not exceed the validity of the~~ **set out the identification of the device in the electronic system set up under Article 25a. Where a notified body has issued a certificate referred to in Article 45, the certificate of free sale shall set out the number of the certificate** ~~issued for the device in question.~~
2. The Commission may, by means of implementing acts, establish a model for certificates of free sale taking into account international practice as regards the use of certificates of free sale. Those implementing acts shall be adopted in accordance with the advisory procedure referred to in Article 88(2).

Chapter VI

Clinical evaluation and clinical investigations

Article 49

Clinical evaluation

1. ***Confirmation of conformity with the requirements concerning the characteristics of safety and performances referred to in Annex I and where applicable relevant requirements of Annex IIa under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit/risk ratio referred to in Sections 1 and 5 of Annex I, shall be based on clinical data providing sufficient clinical evidence.***

The manufacturer shall specify and justify the level of clinical evidence necessary to demonstrate compliance with the relevant essential requirements on safety and performance which shall be appropriate to the characteristics of the device and its intended purpose.

~~Manufacturers~~ ***To that end, manufacturers shall plan, conduct and document a clinical evaluation in accordance with the principles set out in this Article and Part A of Annex XIII.***

- 1a. ***For devices classified as class III and following the exemptions for the procedure laid down in article 42(2a), the manufacturer may, prior to its clinical evaluation and/or investigation, consult an expert panel according to the procedure mentioned in article 81a, with the aim to review the manufacturer's intended clinical evaluation development strategy and proposals for clinical investigation(s). The manufacturer shall give due consideration to the views expressed by the expert panel. These considerations shall be documented in the clinical evaluation report referred to in paragraph 5.***

The manufacturer ~~cannot~~ may not evoke any rights to the views expressed by the expert panel with regard to any future conformity assessment procedure.

2. A clinical evaluation shall follow a defined and methodologically sound procedure based on the following:
- (a) a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device, where the following conditions are satisfied:
 - it is demonstrated that the device ***and its use*** subject to clinical evaluation and the device to which the data relate are equivalent ***in accordance with section A of Annex XIII***,
 - the data adequately demonstrate compliance with the relevant general safety and performance requirements;
 - (b) a critical evaluation of the results of all clinical investigations, ***having due regard to whether the investigations were*** performed in accordance with Articles 50 to 60 and Annex XIV;

- ~~(c) a critical evaluation of the combined clinical data referred to in points (a) and (b).~~
- (d) a consideration of currently available alternative treatment options for that purpose, if any.**

2a. In the case of implantable devices and devices falling within class III, clinical investigations shall be performed except if the device has been designed by modifications of a device already marketed by the same manufacturer if the modifications have been scientifically demonstrated by the manufacturer and accepted by the Notified Body as being equivalent in accordance to section A Annex XIII, to the marketed device and the clinical evaluation is sufficient to demonstrate conformity with the relevant safety and performance requirements. In this case the Notified Body shall check that the PMCF plan is appropriate and includes post market studies to demonstrate the safety and performance of the device.

With regard to the first subparagraph a manufacturer can seek to justify use of data from a demonstrated equivalent device from another manufacturer only if they have a clear contract in place with that manufacturer allowing full access to the technical documentation on an ongoing basis. The manufacturer must be able to provide clear evidence of this to the notified body, of the nature of any modification and also evidence that the original clinical investigations have been performed in compliance with the requirements of this Regulation.

3. ~~Where~~ Except for class III and implantable devices, where demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception shall be given based on the results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performances intended and the claims of the manufacturer. The adequacy of demonstration of conformity with the general safety and performance requirements based on the results of non-clinical testing methods alone, including performance evaluation, bench testing and pre-clinical evaluation, has to be duly substantiated in the technical documentation referred to in Annex II.

4. The clinical evaluation and its documentation shall be updated throughout the life cycle of the device concerned with *clinical* data obtained from the implementation of the manufacturer's *PMCF according to Annex XIII Part B and the* post-market surveillance plan referred to in Article 8(6 7).

For devices classified as class III and implantable devices, the PMCF report, and if indicated, the summary of safety and clinical performance referred to in Article 26(1) shall be updated at least annually with these data.

5. The clinical evaluation, *its results* and ~~its outcome~~ *the clinical evidence derived from it* shall be documented in a clinical evaluation report referred to in Section 6 of Part A of Annex XIII which shall be ~~included or fully referenced in~~ *part of* the technical documentation referred to in Annex II relating to the device concerned.
6. *Where necessary to ensure the uniform application of Annex XIII, the Commission may, having due regard to technical and scientific progress, adopt implementing acts. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 88(3).*

Article 50

General requirements regarding clinical investigations

1. Clinical investigations shall be ~~subject to~~ *designed, authorized, conducted, recorded and reported in accordance with the provisions of* 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 *sponsor manufacturer*;
 - (b) to verify ~~that devices achieve the intended benefits of the device for~~ the patient as specified by the *sponsor manufacturer*;

(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.

2. Where the sponsor *of a clinical investigation* is not established in the Union, ~~he~~ *that sponsor* shall ensure that a ~~contact~~ *natural or legal* person is established in the Union *as its legal representative*. ~~That contact person~~ *Such legal representative shall be responsible for ensuring compliance with the sponsor's obligations pursuant to this Regulation, and* shall be the addressee for all communications with the sponsor provided for in this Regulation. Any communication to that ~~contact person~~ *legal representative* shall be *deemed to be a* ~~considered~~ as communication to the sponsor.

Member States may choose not to apply the subparagraph above as regards clinical investigation to be conducted solely on their territory, or on their territory and the territory of a third country, provided that they ensure that the sponsor establishes at least a contact person on their territory in respect of that clinical investigation who shall be the addressee for all communications with the sponsor provided for in this Regulation.

3. Clinical investigations shall be designed and conducted in a way that the rights, safety, *dignity* and well-being of the subjects participating in a clinical investigation are protected and *prevail over all other interests and* ~~that the clinical data generated in the clinical investigation~~ are going to be *scientifically valid*, reliable and robust.

Clinical investigations shall be subject to scientific and ethical review. The ethical review shall be performed by an ethics committee in accordance with the law of the Member State concerned. Member States shall ensure that the timelines and procedures for the review by the ethics committees are compatible with the timelines and procedures set out in this Regulation for the assessment of the application for authorisation of a clinical investigation.

4. ~~Clinical investigations shall be designed, conducted, recorded and reported in accordance with the provisions of Articles 50 to 60 and of Annex XIV.~~

5. *A clinical investigation according to paragraph 1 may be conducted only where all of the following conditions are met:*
- (a) the clinical investigation was subject to an authorisation by a Member State(s) concerned, in accordance with this Regulation, unless otherwise stated,*
 - (b) an independent Ethics Committee, set up according to national law, has issued an opinion on the planned clinical investigation which is not negative and which, in accordance with the law of the Member State Concerned, is valid for that entire Member State;*
 - (c) the sponsor, or its legally designated representative or a contact person pursuant to paragraph 2, is established in the Union;*
 - (cb) vulnerable populations and subjects are appropriately protected according to relevant national provisions;*
 - (d) the foreseeable risks and inconveniences to the subject are medically justifiable when weighed against the device's potential relevance for the subjects and/or medicine;*
 - (e) the subject or, where the subject is not able to give informed consent, his or her legally designated representative has given informed consent in accordance with Article 29 of Regulation (EU) No 536/2014;*
 - (h) the rights of the subject to physical and mental integrity, to privacy and to the protection of the data concerning him or her in accordance with Directive 95/46/EC are safeguarded;*
 - (l) the investigational device(s) in question conform(s) to the applicable general safety and performance requirements apart from the aspects covered by the clinical investigation and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the subjects. This includes, where appropriate, technical and biological safety testing and pre-clinical evaluation, as well as provisions in the field of occupational safety and accident prevention, taking into consideration the state of the art.*
 - (m) requirements of Annex XIV are fulfilled.*

Any subject may, without any resulting detriment, withdraw from the clinical investigation at any time by revoking his or her informed consent. Without prejudice to Directive 95/46/EC, the withdrawal of the informed consent shall not affect the activities already carried out and the use of data obtained based on informed consent before its withdrawal.

- 8. The investigator shall be a person, as defined in national law, following a profession which is recognised in the Member State concerned, as qualifying for an investigator because of the necessary scientific knowledge and experience in patient care. Other individuals involved in conducting a clinical investigation shall be suitably qualified by education, training or experience in the relevant medical field and in clinical research methodology, to perform their tasks.*
- 9. The facilities where the clinical investigation is to be conducted shall be similar to the facilities of the intended use and suitable for the clinical investigation.*

Article 50a

General requirements regarding clinical investigations not covered by Article 50(1)

- 1. Clinical investigations, not covered by Article 50(1), shall be subject to the provisions of Article 50 paragraphs 2, 3, 5 point (b), 5 point (c), 5 point (cb), 5 point (e), 5 point (h), 5 point (l) and 8 of this Regulation.*
- 2. In order to protect the rights, safety, dignity and well-being of subjects and the scientific and ethical integrity of the clinical investigations not covered by Article 50(1), each Member State shall define any additional requirements for such investigations, as appropriate for each Member State concerned.*

Article 50c

Protection of vulnerable subjects; emergency situations

In order to specifically protect the rights, safety, dignity and well-being of vulnerable subjects in clinical investigations, Member States shall take appropriate measures, concerning clinical investigations

- (a) on minors,***
- (b) on incapacitated subjects,***
- (c) on pregnant and breastfeeding women,***
- (d) in emergency situations, and/or***
- (e) on persons in residential care institutions, persons performing mandatory military service, persons deprived of liberty, persons who, due to a judicial decision, cannot take part in clinical investigations.***

Article 50d

Damage compensation

- 1. Member States shall ensure that systems for compensation for any damage suffered by a subject resulting from participation in a clinical investigation conducted on their territory are in place in the form of insurance, a guarantee, or a similar arrangement that is equivalent as regards its purpose and which is appropriate to the nature and the extent of the risk.***

- 2. The sponsor and the investigator shall make use of the system referred to in paragraph 1 in the form appropriate for the Member State concerned where the clinical investigation is conducted.***

Article 51

Application for clinical investigation

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.~~

2. The sponsor of a clinical investigation shall *enter and submit by means of the electronic system referred to in Article 53* 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. *The electronic system referred to in Article 53 shall generate a union wide unique single identification number for this clinical investigation which shall be used for all relevant communication in relation to the clinical investigation concerned.* Within ~~six~~ *ten* 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.

~~Where the Member State has not notified the sponsor within the time period referred to in the first subparagraph, 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 finds that the clinical investigation applied for does not fall within the scope of this Regulation or that the application is not complete, it shall inform the sponsor thereof and shall set a maximum of ~~six~~ **thirty** days for the sponsor to comment or to complete the application.

Where the sponsor has not provided comments nor completed the application within the time-period referred to in the first subparagraph, the application shall be *deemed to have lapsed* ~~considered as withdrawn~~. *Where the sponsor considers the application does fall under the scope of the regulation and/or is complete but the competent authority does not, the application shall be considered as rejected. That Member State shall provide for an appeal procedure in respect of such refusal.*

~~Where~~ ~~†~~ The Member State has ~~not~~ **to notify** notified the sponsor according to paragraph 2 within ~~three~~ **five** days following receipt of the comments or of the **requested additional information** ~~completed application~~, **whether** the clinical investigation shall be ~~is~~ considered as falling within the scope of this Regulation and the application shall be ~~considered is~~ completed.

4. For the purposes of this Chapter, the date on which the sponsor is notified in accordance with paragraph 2 *or* 3 shall be the validation date of the application. ~~Where the sponsor is not notified, the validation date shall be the last day of the time periods referred to in paragraphs 2 and 3.~~ *The concerned Member State may also extend the period referred to in paragraph 2 and 3 each by a further 5 days.*

- 4a. In the period during which the application is being assessed the Member State may request, additional information from the sponsor. The expiry of the deadline pursuant paragraph 5(b) (second indent) shall be suspended from the date of the first request until such time as the additional information has been received.**
5. The sponsor may start the clinical investigation in the following circumstances:
- (a) in the case of investigational devices classified as class I ~~III and implantable or long-term~~ **or in the case of non-invasive devices classified as class IIa or IIb, as soon as the Member State concerned has notified the sponsor of its approval, unless otherwise stated by national provisions, immediately after the validation date of the application described in paragraph 4, and provided that the competent Ethics committee in the Member State concerned has issued an opinion which is not negative and which, in accordance with the law of the Member State concerned, is valid for that entire Member State;**
- (b) in the case of investigational devices other than those referred to in point (a):
- **as soon as the Member State concerned has notified the sponsor of its authorisation and provided that the competent Ethics committee in the Member State concerned has issued an opinion which is not negative and which, in accordance with the law of the Member State concerned, is valid for that entire Member State or**

- *after the expiry of 45 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 and provided that the Ethics committee in the Member State concerned has issued an opinion which is not negative and which, in accordance with the law of the Member State concerned, is valid for that entire Member State.*

The Member State concerned may also extend the period referred to in the previous sub-paragraph by a further 20 days for the purpose of consulting with experts. 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;

- (e) ~~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.~~

6. ~~Member States shall ensure that the persons assessing the application do not have conflicts of interest and that they are independent of the sponsor, the institution of the investigation site(s) and the investigators involved, as well as free of any other undue influence.~~

~~Member States shall ensure that the assessment is done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience. In the assessment, the view of at least one person whose primary area of interest is non-scientific shall be taken into account. The view of at least one patient shall be taken into account.~~

7. ~~The Commission shall be empowered to *may* adopt delegated *implementing* acts in accordance with Article 89 88(3) amending or supplementing, in the light of technical progress and global regulatory developments, *in order to assure the uniform application of* the requirements for the documentation to be submitted with the application for the clinical investigation that is laid down in Chapter II of Annex XIV.~~

Article 51a

Assessment by Member States

- 1. Member States shall ensure that the persons validating and assessing the application, or deciding on it, do not have conflicts of interest, are independent of the sponsor, the investigators involved and of persons or legal persons financing the clinical investigation, as well as free of any other undue influence.**
- 2. Member States shall ensure that the assessment is done jointly by an appropriate number of persons who collectively have the necessary qualifications and experience.**
- 3. Member States shall assess whether the clinical investigation is designed in such a way that potential remaining risks to subjects or third person, after risk minimization, are justified, when weighed against the clinical benefits to be expected. They shall examine, under consideration of applicable Common Specifications or harmonized standards, in particular:**
 - (a) the demonstration of compliance of the investigational device(s) with the applicable general safety and performance requirements, apart from the aspects covered by the clinical investigation and whether, with regard to these aspects, every precaution has been taken to protect the health and safety of the subjects. This includes, where appropriate, assurance of technical and biological safety testing and pre-clinical evaluation;**
 - (b) whether the risk-minimisation solutions employed by the sponsor are described in harmonised standards and, in those cases where the sponsor does not use harmonised standards, the equivalence of the level of protection to harmonised standards;**
 - (c) the plausibility of the measures planned for the safe installation, putting into service and maintenance of the investigational device;**
 - (d) the reliability and robustness of the data generated in the clinical investigation, taking account of statistical approaches, design of the investigation and methodological aspects (including sample size, comparator and endpoints);**
 - (da) requirements of Annex XIV are met.**

- (e) in the case of devices for sterile use, evidence of the validation of the manufacturer's sterilisation procedures or information on the reconditioning and sterilisation procedures which must be conducted by the investigation site;*
- (f) demonstration of safety, quality and usefulness of any components of animal or human origin or of substances, which may be considered medicinal products according to Directive 2001/83/EC.*

4. Member States may refuse the authorisation of the clinical investigation if:

- (a) the clinical investigation does not fall within the scope of this Regulation ;*
- (b) the application submitted according to Article 51 paragraph 2 remains incomplete;*
- (c) an ethics committee has issued a negative opinion which, in accordance with the law of the Member State concerned, is valid for that entire Member State;*
- (ca) the device or the submitted documents, especially the investigation plan and the investigator's brochure, do not correspond to the state of scientific knowledge, and the clinical investigation, in particular, is not suitable to provide evidence for the safety, performance characteristics or benefit of the device on patients, or*
- (d) the requirements of Article 50 are not met, or*
- (e) any assessment according to paragraph 3 is negative.*

Article 51e

Conduct of a clinical investigation

- 1. The sponsor and the investigator shall ensure that the clinical investigation is conducted in accordance with the approved clinical investigation plan.**

2. ***In order to verify that the rights, safety and well-being of subjects are protected, that the reported data are reliable and robust, and that the conduct of the clinical investigation is in compliance with the requirements of this Regulation, the sponsor shall adequately monitor the conduct of a clinical investigation. The extent and nature of the monitoring shall be determined by the sponsor on the basis of an assessment that takes into consideration all characteristics of the clinical investigation including the following characteristics:***
 - (a) ***the objective and methodology of the clinical investigation and***
 - (b) ***the degree of deviation of the intervention from normal clinical practice.***

3. ***All clinical investigation information shall be recorded, processed, handled, and stored by the sponsor or investigator, as applicable, in such a way that it can be accurately reported, interpreted and verified while the confidentiality of records and the personal data of the subjects remain protected in accordance with the applicable law on personal data protection.***

4. ***Appropriate technical and organisational measures shall be implemented to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss, in particular where the processing involves the transmission over a network.***

5. ***Member States shall inspect on an appropriate level investigation site(s) to check that clinical investigations are conducted according to the requirements of this Regulation and to the approved investigation plan.***

6. ***The sponsor shall establish a procedure for emergency situations which enables the immediate identification and, where necessary, an immediate recall of the devices used in the investigation.***

Article 52

Registration of clinical investigations

1. ~~Before commencing the clinical investigation, the sponsor shall enter in the electronic system referred to in Article 53 the following information regarding the clinical investigation:~~
 - ~~(a) the single identification number of the clinical investigation;~~
 - ~~(b) the name and contact details of the sponsor and, if applicable, his contact person established in the Union;~~
 - ~~(c) the name and contact details of the natural or legal person responsible for the manufacture of the investigational device, if different from the sponsor;~~
 - ~~(d) the description of the investigational device;~~
 - ~~(e) the description of the comparator(s), if applicable;~~
 - ~~(f) the purpose of the clinical investigation;~~
 - ~~(g) the status of the clinical investigation.~~

2. ~~Within one week of any change occurring in relation to the information referred to in paragraph 1, the sponsor shall update the relevant data in the electronic system referred to in Article 53.~~

3. ~~The information shall be accessible to the public, through the electronic system referred to in Article 53, unless, for all or parts of that information, confidentiality of the information is justified on any of the following grounds:~~
 - ~~(a) protection of personal data in accordance with Regulation (EC) No 45/2001;~~
 - ~~(b) protection of commercially sensitive information;~~
 - ~~(c) effective supervision of the conduct of the clinical investigation by the Member State(s) concerned.~~

4. ~~No personal data of subjects participating in clinical investigations shall be publicly available.~~