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Committee on Industry, Research and Energy

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DRAFT OPINION

of the Committee on Industry, Research and Energy

for the Committee on the Environment, Public Health and Food Safety

on the proposal for a regulation of the European Parliament and of the Council
on clinical trials on medicinal products for human use, and repealing Directive
2001/20/EC
(COM(2012)0369 – C7-0194/2012 – 2012/0192(COD))

Rapporteur: Michèle Rivasi

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SHORT JUSTIFICATION

The adoption of the Directive 2001/20/EC marked an important milestone in the development of the standards for the conduct of clinical trials, both within the Union and on the international level.

It is understood however that this Directive created difficulties for the facilitating of clinical trials in several Member States and there is a need for harmonisation, as well as a thorough assessment of the existing legal framework. It is of the utmost importance that the high standards set out in the previous Directive are adhered to and not lost in efforts to simplify procedures across Member States.

Your rapporteur introduces a number of amendments in her opinion to ensure that high standards of care and treatment of patients is upheld in the Union; while stimulating scientific research and innovation through public access to data in the form of a full clinical trial report. Given the current economic crisis, money must not be wasted on medicines that are not effective, and the public must be able to make informed decisions about their health.

Your rapporteur is of the view that the new definitions, including the new definitions of a clinical trial, a clinical study, and 'low intervention trials' as set out in Article 2 are unnecessarily complicated and open to misinterpretation. Instead they should follow a simple principle: 'observations' fall into the 'study' category and 'interventions' fall into the 'trial' category. Without such an amendment the existing text, taken together with the definition by default of a 'non-interventional study', would allow for 'clinical studies' (which do not fall under the definition of a clinical trial) to be conducted without asking patients for prior consent. Further reintroductions of definitions from the present Directive are also proposed following the same reasoning.

Your rapporteur fears that the current proposal weakens the present role of Ethics Committees without providing a proper legal base for an equivalent independent assessment body. The Union should show due respect for human rights, patient safety, and high standards of ethical scrutiny, by reintroducing independent ethics committees in the Regulation.

Article 28(2) stipulates that “the rights, safety and well-being of the subjects shall prevail over the interests of science and society”. To achieve these objectives, it is necessary to make authorisation by the Member States contingent on the decision of the interdisciplinary and independent Ethics Committee which is responsible according to their national law.

Clinical trials data are scientific data, which are gained from the inclusion of the public and which have significant impacts on the public. They therefore belong first and foremost to the public. It needs to also be reminded that swift and well-monitored access to the results of clinical trials has its ethical aspect, since it enables patients to gain direct and rapid access to the latest pharmacological accomplishments.

Science is hampered and the social value of research is diminished if the data are never made public. That is why your rapporteur calls for a clear statement in the Regulation that enables Union citizens to have access to clinical information about medicinal products, in order to enable them to make informed decisions about their health.

Your rapporteur calls for the clinical information stored in the EU database to be in clinical study report form. Experience gained so far show that submission of a summary is not sufficient to protect patient's rights and interests. The non-disclosure of the detailed results of clinical trials impairs scientific knowledge and leads to publication bias (where negative findings are not published), which in turns paints an inaccurate picture of a medicine's effectiveness. For example, publication bias led to the wide use of the antidepressant paroxetine in children and teenagers despite a lack of effectiveness and more worrying despite an increased risk of suicide in this population.

For further transparency, your rapporteur calls for the clinical trial master file to be archived indefinitely, as opposed to the suggested five years. Some long-term adverse drug reactions such as cancer or teratogenicity only appear after decades of use, sometimes even going beyond one generation of patients, i.e. Diethylstilbestrol (DES) disaster between the 1950s and 1970s, therefore it is important to guarantee the conservation of the master file for an indefinite time.

AMENDMENTS

The Committee on Industry, Research and Energy calls on the Committee on the Environment, Public Health and Food Safety, as the committee responsible, to incorporate the following amendments in its report:

Amendment 1 **Proposal for a regulation** **Recital 3**

Text proposed by the Commission

(3) The existing definition of a clinical trial as contained in Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use ***should be clarified. For that purpose, the concept of clinical trial should be more precisely defined by introducing the broader concept of 'clinical study' of which the clinical trial is a category. That category should be defined on the basis of specific criteria. This approach takes due account of international guidelines, and is in line***

Amendment

(3) The existing definition of a clinical trial as contained in Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use ***does not need to be changed, and many other definitions in the previous Directive should be upheld.***

with the EU legislation governing medicinal products, which builds on the dichotomy of ‘clinical trial’ and ‘non-interventional study’.

Or. en

Amendment 2
Proposal for a regulation
Recital 6

Text proposed by the Commission

(6) The Member States concerned should cooperate in assessing a request for authorisation of a clinical trial. ***This cooperation should not include aspects of an intrinsically national nature, nor ethical aspects of a clinical trial, such as informed consent.***

Amendment

(6) The Member States concerned should cooperate in assessing a request for authorisation of a clinical trial.

Or. en

Amendment 3
Proposal for a regulation
Recital 7

Text proposed by the Commission

(7) The procedure should be flexible and efficient, in order to avoid administrative delays for starting a clinical trial.

Amendment

(7) The procedure should be flexible and efficient, in order to avoid administrative delays for starting a clinical trial, ***without compromising patient safety or public health.***

Or. en

Amendment 4
Proposal for a regulation
Recital 8

Text proposed by the Commission

(8) The timelines for assessing an application dossier for clinical trials should be sufficiently long to assess the file, while ensuring quick access to new, innovative treatments and ensuring that the Union remains an attractive place for conducting clinical trials. Against this background, Directive 2001/20/EC introduced the concept of *tacit* authorisation. This concept should be maintained in order to ensure that timelines are adhered to. In the event of a public health crisis, Member States should have the possibility to assess and authorise a clinical trial application swiftly. No minimal timelines for approval should therefore be established.

Amendment

(8) The timelines for assessing an application dossier for clinical trials should be sufficiently long to assess the file, while ensuring quick access to new, innovative treatments and ensuring that the Union remains an attractive place for conducting clinical trials. Against this background, Directive 2001/20/EC introduced the concept of *implicit* authorisation ***if there has been a vote in favour by the Ethics Committee and the competent authority has not objected within the deadline***. This concept should be maintained in order to ensure that timelines are adhered to. In the event of a public health crisis, Member States should have the possibility to assess and authorise a clinical trial application swiftly. ***In the event of a public health crisis***, no minimal timelines for approval should therefore be established.

Or. en

Justification

The reference to Directive 2001/20/EC should be more accurate. According to the Directive, authorisation should be implicit, i.e. if there has been a vote in favour by the Ethics Committee and the competent authority has not objected within a given period. In exceptional cases raising especially complex problems, explicit written authorisation should, however, be required. It should be made clearer that the last sentence of the paragraph refers only to the event of a public health crisis.

Amendment 5
Proposal for a regulation
Recital 9

Text proposed by the Commission

(9) The risk to subject safety in a clinical trial mainly stems from two sources: the investigational medicinal product and the intervention. Many clinical trials, however, pose only a minimal additional

Amendment

deleted

risk to subject safety compared to normal clinical practice. This is in particular the case where the investigational medicinal product is covered by a marketing authorisation (i.e. the quality, safety and efficacy has already been assessed in the course of the marketing authorisation procedure) and where the intervention poses only very limited additional risk to the subject compared to normal clinical practice. Those 'low-intervention clinical trials' are often of crucial importance to assess standard treatments and diagnoses, thereby optimising the use of medicinal products and thus contributing to a high level of public health. They should be subject to less stringent rules, such as shorter deadlines for approval.

Or. en

Amendment 6
Proposal for a regulation
Recital 52

Text proposed by the Commission

(52) The database should contain all relevant information as regards the clinical trial. *No personal data of data subjects participating in a clinical trial should be recorded in the database. The information in the database should be public, unless specific reasons require that a piece of information should not be published, in order to protect the right of the individual to private life and the right to the protection of personal data,* recognised by Articles 7 and 8 of the Charter of Fundamental Rights of the European Union.

Amendment

(52) The database should contain all relevant information as regards the clinical trial, *including the clinical trial report which contains a statistical analysis plan and details of the protocol as well as raw data, and should be in easily searchable form. All personal data of data subjects participating in a clinical trial should be anonymised in the database and the information should be public in line with the specific requirements of Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents¹ and bearing in mind the right of access to documents,* recognised by Article 42 of the Charter of Fundamental

Or. en

Justification

The non- disclosure of the detailed results of clinical trials, in the form of clinical study reports, impairs scientific knowledge, leads to publication bias (negative findings are not published), which in turns paints an inaccurate picture of a medicine's effectiveness. For example, publication bias led to the wide use of the antidepressant paroxetine (Seroxat^o) in children and teenagers despite a lack of effectiveness and more worrying despite an increased risk of suicide in this population.

Amendment 7
Proposal for a regulation
Recital 63

Text proposed by the Commission

(63) This Regulation is in line with the major international guidance documents on clinical trials, such as the most recent (2008) version of the World Medical Association's Declaration of Helsinki and good clinical practice, which has its origins in the Declaration of Helsinki.

Amendment

(63) This Regulation is in line with the major international guidance documents on clinical trials, such as the most recent (2008) version of the World Medical Association's Declaration of Helsinki, ***in particular ethical principles for medical research involving human subjects, including research on identifiable human material and data***, and good clinical practice, which has its origins in the Declaration of Helsinki.

Or. en

Amendment 8
Proposal for a regulation
Article 2 – paragraph 2 – point 1 – introductory part

Text proposed by the Commission

(1) 'Clinical ***study***': any investigation in relation to humans intended

Amendment

(1) 'Clinical ***trial***': any investigation in relation to humans intended

(This amendment applies throughout the

text. Adopting it will necessitate corresponding changes throughout.)

Or. en

Justification

These new definitions are too complicated and difficult to implement, in practice, which will lead to additional bureaucracy. A simple principle should be that “observations” fall into the “study” category and “interventions” fall into the “trial” category. It is therefore necessary to re-introduce the more accurate wording from the previous Directive 2001/20/EC.

Amendment 9

Proposal for a regulation

Article 2 – paragraph 2 – point 2

Text proposed by the Commission

Amendment

(2) ‘Clinical trial’: a clinical study which fulfils any of the following conditions: ***deleted***

(a) the investigational medicinal products are not authorised;

(b) according to the protocol of the clinical study, the investigational medicinal products are not used in accordance with the terms of the marketing authorisation of the Member State concerned;

(c) the assignment of the subject to a particular therapeutic strategy is decided in advance and does not fall within normal clinical practice of the Member State concerned;

(d) the decision to prescribe the investigational medicinal products is taken together with the decision to include the subject in the clinical study;

(e) diagnostic or monitoring procedures in addition to normal clinical practice are applied to the subjects.

Or. en

Justification

See previous justification

Amendment 10

Proposal for a regulation

Article 2 – paragraph 2 – point 3

Text proposed by the Commission

Amendment

(3) ‘Low-intervention clinical trial’: a clinical trial which fulfils all of the following conditions: **deleted**

(a) the investigational medicinal products are authorised;

(b) according to the protocol of the clinical trial, the investigational medicinal products are used in accordance with the terms of the marketing authorisation or their use is a standard treatment in any of the Member States concerned;

(c) the additional diagnostic or monitoring procedures do not pose more than minimal additional risk or burden to the safety of the subjects compared to normal clinical practice in any Member State concerned.

Or. en

Justification

Where the authorised investigational medicinal product is subject to a post-authorisation study, it takes place just because of a suspicion of insufficient efficacy or of an additional risk to patients’ safety compared to normal clinical practice even if it used in accordance with the terms of the marketing authorisation. It was the case of the Regulate study using benfluorex (Mediator^o), of the Vigor study using rofecoxib (Vioxx^o).

Amendment 11

Proposal for a regulation

Article 2 – paragraph 2 – point 12

Text proposed by the Commission

(12) ‘Substantial modification’: any change to any aspect of the clinical trial which is made after notification of the decision referred to in Articles 8, 14, 19, 20 and 23 and which **is likely to** have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial;

Amendment

(12) ‘Substantial modification’: any change to any aspect of the clinical trial, **including early termination of the trial and change in number of subjects participating in the trial**, which is made after notification of the decision referred to in Articles 8, 14, 19, 20 and 23 and which **could** have a substantial impact on the safety or rights of the subjects, or on the reliability and robustness of the data generated in the clinical trial, **i.e. change the interpretation of the scientific documents used to support the conduct of the trial, or if the modifications are otherwise significant.**

Or. en

Justification

Early termination allows the sponsor to avoid the risk that such difference could lose statistical significance during the end of the trial if it was due to the hazard. Any modifications in the conduct, design, methodology, investigational or auxiliary medicinal product of clinical trials after they have been authorized can impair the data reliability and robustness. Therefore the more accurate wording from Directive 2001/20/EC Article 10(a) has been reintroduced.

Amendment 12

Proposal for a regulation

Article 2 – paragraph 2 – point 14 a (new)

Text proposed by the Commission

Amendment

(14a) ‘Ethics Committee’: an independent body in a Member State, consisting of healthcare professionals and non-medical members, whose responsibility it is to protect the rights, safety and wellbeing of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of

facilities, and on the methods and documents to be used to inform trial subjects and obtain their informed consent;

Or. en

Justification

Re-introduction of the definition from Directive 2001/20/EC.

Amendment 13
Proposal for a regulation
Article 2 – paragraph 2 – point 28

Text proposed by the Commission

(28) ‘Adverse ***event***’: any untoward medical occurrence in a subject administered a medicinal product ***and which does not necessarily have a causal relationship with this treatment;***

Amendment

(28) ‘Adverse ***reaction***’: any untoward medical occurrence in a subject administered a medicinal product ***related to any dose administered;***

(This amendment applies throughout the text. Adopting it will necessitate corresponding changes throughout.)

Or. en

Justification

Re-introducing the good wording from the previous Directive 2001/20/EC.

Amendment 14
Proposal for a regulation
Article 2 – paragraph 2 – point 30 a (new)

Text proposed by the Commission

Amendment

(30a) ‘Clinical study report’: a report containing the full protocol and its eventual subsequent modifications, a statistical analysis plan, summarised efficacy and safety data on all outcomes, and individual anonymised patient data in

the format of tabulations or listings.

Or. en

Justification

The non-inclusion of clinical study reports in systematic reviews results in an incomplete evidence base and potentially biased conclusions about the effects of an intervention; e.g. published data alone on reboxetine actually overestimated the benefits of reboxetine by up to 115% versus placebo and also underestimated harms. E.g.2: the neuraminidase inhibitor oseltamivir (Tamiflu^o) was stockpiled by millions by Member States without evidence of efficacy on important complications of influenza.

Amendment 15
Proposal for a regulation
Article 3 – indent 2

Text proposed by the Commission

– the data generated in the clinical trial are going to be reliable **and robust**.

Amendment

– the data generated in the clinical trial are going to be **relevant**, reliable, **robust and fully-recorded; and**

Or. en

Justification

When data is not fully-recorded the research becomes redundant. The non- disclosure of the detailed results of clinical trials, in the form of clinical study reports, impairs scientific knowledge, leads to publication bias (negative findings are not published), which in turns paints an inaccurate picture of a medicine's effectiveness.

Amendment 16
Proposal for a regulation
Article 3 – indent 2 a (new)

Text proposed by the Commission

Amendment

- the data generated in the clinical trial address a documented gap in scientific knowledge that could not be acquired through other means.

Or. en

Justification

Good quality and ethical clinical trials should be designed to generate relevant data for scientific knowledge on human beings and on the means to improve its condition and this knowledge should be recorded for future reference. New research should not be done unless, at the time it is initiated, the questions it proposes to address cannot be answered satisfactorily with existing evidence, e.g. in Cochrane reviews.

Amendment 17
Proposal for a regulation
Article 4 a (new)

Text proposed by the Commission

Amendment

Article 4a

Role of and guidelines for Ethics Committees

- 1. An authorisation for the conduct of a clinical trial by a competent authority of a Member States concerned may be given after and only if the concerned Ethics Committee has given its approval.***
- 2. The Commission shall, within one year, come forward with guidelines for Member States on Ethics Committees in order to streamline procedures and make it easier to conduct trials in several Member States, without compromising the safety of subjects.***

Or. en

Justification

The Helsinki Declaration and Oviedo Convention state that "research on a person may only be undertaken if...the research project has been approved by the competent body after...multidisciplinary review of its ethical acceptability". Article 28.2 of this Regulation states "The rights, safety and well-being of the subjects shall prevail over...interests of science and society". To be consistent authorisation by the Member States must be contingent on the decision of their responsible Ethics Committee.

Amendment 18
Proposal for a regulation
Article 6 – paragraph 1 – point a – point i – indent 2 a (new)

Text proposed by the Commission

Amendment

- the similarity of the subjects to the intended recipients of the medicinal products in terms of age, gender, and whether the subjects are healthy volunteers or patients;

Or. en

Justification

In order for medicinal products to be most effective they should be tested on similar populations to those that they will be used on, for example certain drugs are metabolised differently by women and men.

Amendment 19

Proposal for a regulation

Article 6 – paragraph 5 a (new)

Text proposed by the Commission

Amendment

5a. The assessment report shall be submitted through the EU portal, stored in the EU database, and made publicly available.

Or. en

Justification

The assessment report shall be made publicly available for allow for public confidence in the authorisation process.

Amendment 20

Proposal for a regulation

Article 8 – paragraph 2 – subparagraph 2 – point b a (new)

Text proposed by the Commission

Amendment

(ba) refusal of the Ethics Committee to approve the conduct of the clinical trial in the Member State concerned.

Amendment 21
Proposal for a regulation
Article 12 – paragraph 1

Text proposed by the Commission

The sponsor may withdraw the application at any time until the assessment date. In such a case, the application may only be withdrawn with respect to all Member States concerned.

Amendment

The sponsor may withdraw the application at any time until the assessment date. In such a case, the application may only be withdrawn with respect to all Member States concerned. ***A record of withdrawn applications shall remain in the EU database and reasons for each withdrawal shall be given.***

Justification

This amendment is an effort to gain some insight into why clinical trials applications are withdrawn. There are a number of genuine reasons to withdraw an application or stop a clinical trial, related to safety of patients and efficacy of the product. Commercial reasons are also commonly cited as motivators to halt trials. Withdrawing an application for a clinical trial for commercial reasons only is unethical as it deprives patients and society of a potentially effective medical innovation.

Amendment 22
Proposal for a regulation
Article 15 – paragraph 1

Text proposed by the Commission

A substantial modification may only be implemented if it has been approved in accordance with the procedure set out in this Chapter.

Amendment

A substantial modification may only be implemented if it has been approved in accordance with the procedure set out in this Chapter ***and if it has previously been approved by an Ethics Committee.***

Justification

Since a substantial modification is defined as a “change (...) which (...) is likely to have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial”, the same procedure as for the authorisation of a clinical trial should apply.

Amendment 23 **Proposal for a regulation** **Article 20 – paragraph 7**

Text proposed by the Commission

Amendment

7. Where the Member State concerned has not notified the sponsor of its decision within the time periods set out in paragraphs 5 and 6, the substantial modification shall be considered as authorised. **deleted**

Or. en

Justification

This is not consistent with Directive 2001/20/EC: recital 11 of Directive 2001/20/EC does not allow for tacit authorisation by competent authorities if there has not be a vote in favour of the clinical trial by Ethics Committee. Such a tacit authorisation procedure would impair the safety and rights of subjects.

Amendment 24 **Proposal for a regulation** **Article 23 – paragraph 4**

Text proposed by the Commission

Amendment

4. Where the Member State concerned has not notified the sponsor of its decision within the time periods referred to in paragraph 1, the conclusion on the substantial modification of aspects covered by Part I of the assessment report shall be considered as the decision of the Member State concerned on the application for authorisation of the substantial modification. **deleted**

Justification

To retain recital 11 of Directive 2001/20/EC which does not allow for tacit authorisation by competent authorities if there has not been a vote in favour of the clinical trial by an Ethics Committee.

Amendment 25
Proposal for a regulation
Article 25 – paragraph 5

Text proposed by the Commission

5. Where the clinical trial has been conducted outside the Union, it shall comply with principles ***equivalent to those*** of this Regulation as regards subject rights and ***safety and*** reliability and robustness of data generated in the clinical trial.

Amendment

5. Where the clinical trial has been conducted outside the Union, it shall ***fully*** comply with ***the*** principles of this Regulation as regards subject rights and ***wellbeing, and the*** reliability and robustness of data generated in the clinical trial.

Or. en

Justification

The requirements for the clinical trials conducted outside the Union should be identical to those of the proposed Regulation. Equivalence to these principles would enable variations in their interpretations by third party sponsors.

Amendment 26
Proposal for a regulation
Article 29 – paragraph 1 and 1a

Text proposed by the Commission

1. Informed consent shall be written, dated and signed and given freely by the subject or his or her legal representative after having been ***duly*** informed of the nature, significance, implications and risks of the clinical trial. ***It*** shall be appropriately documented. Where the subject is unable to write, oral consent in the presence of at least one impartial witness may be given in

Amendment

1. Informed consent shall be written, dated and signed and given freely by the subject or his or her legal representative after having been ***comprehensively*** informed of the nature, ***duration***, significance, implications and risks of the clinical trial ***including if the clinical trial has to be discontinued, the eventual treatment alternatives, and any other information***,

exceptional cases. The subject or his or her legal representative shall be provided with a copy of the document by which informed consent has been given.

as provided for in national legislation. The information provided and the informed consent shall be appropriately documented. Where the subject is unable to write, oral consent in the presence of at least one impartial witness, *trustful for the subject*, may be given in exceptional cases. The subject or his or her legal representative shall be provided with a copy of the document by which informed consent has been given.

1a. Two mentions shall systematically be on the document by which informed consent is given:

- the trial registration number in the EU portal and

- a statement that the results will be made available in the EU portal within one year after completion of the trial together with an approximate date.

Or. en

Justification

Reintroduction of a minimum set of information in the informed consent that was provided in Directive 2001/20/EC, in order to provide for equal rights among European citizens. The “impartial witness” should be identified and sign the informed consent form for the subject.

Amendment 27

Proposal for a regulation

Article 34 – paragraph 3 a (new) and 3 b (new)

Text proposed by the Commission

Amendment

3a. In case of sponsor non-compliance with the obligation referred to in paragraph 3, harmonised penalties shall be enforced by the concerned Member States. The amount shall be up to 7 000 EUR for the 30 first day of non-compliance and up to 7 000 EUR per each additional delay day until compliance.

3b. A Certificate of Compliance Form in

accordance with the obligation referred to in paragraph 3 is to be submitted and provided as part of the Common technical document.

Or. en

Justification

In order to encourage the sponsor to report the information to the competent authorities within one year of the end of the clinical trial, dissuasive and harmonized penalties among Member States should be applied. In the US, such penalties exist (up to \$10,000 civil monetary penalty during the first 30 days + up to \$10,000 for each day until the violation is corrected after the first 30 days). This will ensure the trust of patients in the process.

Amendment 28

Proposal for a regulation

Article 34 – paragraph 3 – subparagraph 1

Text proposed by the Commission

Within one year from the end of a clinical trial, the sponsor shall submit to the EU database a summary of the results of the clinical trial.

Amendment

Within one year from the end of a clinical trial, the sponsor shall submit to the EU database a summary of the results of the clinical trial *and a clinical study report*. *All new clinical trial applications from a given sponsor shall not be evaluated until the clinical study reports related to its previously registered and approved trials have been submitted to the EU database. Sponsors shall provide a justification why they have not submitted the summary of the results and the clinical study reports. The justification shall be made publicly accessible.*

Or. en

Justification

The non- disclosure of the detailed results of clinical trials, in the form of clinical study reports, impairs scientific knowledge, leads to publication bias (negative findings are not published), which in turns paints an inaccurate picture of a medicine's effectiveness. For example, publication bias led to the wide use of the antidepressant paroxetine (Seroxat^o) in children and teenagers despite a lack of effectiveness and more worrying despite an increased

risk of suicide in this population

Amendment 29

Proposal for a regulation

Article 34 – paragraph 3 – subparagraph 2

Text proposed by the Commission

However, where, for scientific reasons, it is not possible to submit a summary of the results within one year, ***the summary of results shall be submitted as soon as it is available***. In this case, the protocol shall specify when the results ***are going to be submitted***, together with an explanation.

Amendment

However, where, for scientific reasons, ***which are duly justified and approved as valid by an Ethics Committee***, it is not possible to submit a summary of the results ***and the clinical study report*** within one year, ***they shall be submitted as soon as they are available***. In this case, the protocol shall specify when the results ***and the clinical study report are to become available***, together with an explanation.

Or. en

Amendment 30

Proposal for a regulation

Article 34 – paragraph 4

Text proposed by the Commission

4. For the purpose of this Regulation, if a suspended or temporarily halted clinical trial is not restarted, the date of the decision of the sponsor not to restart the clinical trial shall be considered as the end of the clinical trial. In the case of early termination, the date of the early termination shall be considered as the date of the end of the clinical trial.

Amendment

4. For the purpose of this Regulation, if a suspended or temporarily halted clinical trial is not restarted, the date of the decision of the sponsor not to restart the clinical trial shall be considered as the end of the clinical trial. In the case of early termination, the date of the early termination shall be considered as the date of the end of the clinical trial. ***After 12 months of temporary halt, the clinical trial's data, even if incomplete, shall be made publicly accessible.***

Or. en

Justification

The use of indefinite temporary halts, to prevent, de facto, results from being made publicly available, should be avoided.

Amendment 31 **Proposal for a regulation** **Article 37 – paragraph 2**

Text proposed by the Commission

2. The investigator shall immediately report serious adverse events to the sponsor ***unless the protocol provides, for certain adverse events, that no reporting is required. The investigator shall record all serious adverse events.*** Where necessary, the investigator shall send a follow-up report to the sponsor.

Amendment

2. The investigator shall immediately report serious adverse events to the sponsor. ***The investigator shall record all serious adverse events, and send copies to the Ethics Committee and shall submit copies to the EU database through the EU portal.*** Where necessary, the investigator shall send a follow-up report to the sponsor. ***The immediate report shall be followed by detailed, written reports, and sent to the Ethics Committees and Member States and stored in the EU database.***

Or. en

Justification

It is only through the collection of accurate and complete adverse event reports that safety concerns about medicines can be identified and addressed in a timely manner, thereby limiting otherwise preventable risks to public health and avoidable healthcare costs.

Amendment 32 **Proposal for a regulation** **Article 38 – paragraph 3**

Text proposed by the Commission

3. Where a sponsor, due to a lack of resources, does not have the possibility to report to the electronic database referred to in Article 36, it may report to the Member State where the suspected unexpected serious adverse reaction occurred. That Member State shall report

Amendment

deleted

the suspected unexpected serious adverse reaction in accordance with paragraph 1.

Or. en

Amendment 33
Proposal for a regulation
Article 53 – paragraph 1

Text proposed by the Commission

1. All clinical trial information shall be recorded, processed, handled, and stored 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 legislation on personal data protection.

Amendment

1. All clinical trial information shall be recorded, processed, handled, and stored in ***easily searchable clinical study reports format so*** 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 legislation on personal data protection.

Or. en

Justification

Evidence from research studies has shown that the exclusion of clinical study reports from systematic reviews results in an incomplete evidence base and leads to potential bias in the conclusions about the effects of an intervention.

Amendment 34
Proposal for a regulation
Article 55 – paragraph 1

Text proposed by the Commission

Unless other Union legislation requires archiving for a longer period, the sponsor and the investigator shall archive the content of the clinical trial master file for at least five years after the end of the clinical trial. However, the medical files of subjects shall be archived in accordance with national legislation.

Amendment

The clinical trial master file shall be archived ***indefinitely***.

Justification

Some long-term adverse drug reactions such as cancer or teratogenicity only appear after decades of use, sometimes even going beyond one generation of patients, i.e. Diethylstilbestrol (DES) disaster between the 1950s and 1970s.

Amendment 35**Proposal for a regulation****Article 75 – paragraph 5 – subparagraph 2***Text proposed by the Commission*

When making the inspection report available to the sponsor, the Member State referred to in the first subparagraph shall ensure that confidentiality is protected.

Amendment

A summary of the inspection report shall be made publicly available.

Justification

Member States' inspectors are often paid by public money and both their mission and mandate are of public interest. In addition, subjects who take part to a clinical trial have the right to know whether the trial has been/is conducted in accordance with the regulation(s) in order to be able to withdraw their consent should they wish to do so.

Amendment 36**Proposal for a regulation****Article 76 – paragraph 2***Text proposed by the Commission*

2. The Commission may conduct inspections where it considers necessary.

Amendment

2. The Commission may conduct inspections where it considers necessary. *A summary of the Commission's inspection report shall be made publicly available.*

Justification

See justification for amendment to article 75

Amendment 37

Proposal for a regulation

Article 78 – paragraph 2

Text proposed by the Commission

2. The EU database shall be established to enable the co-operation between the competent authorities of the Member States to the extent that it is necessary for the application of this Regulation and to search for specific clinical trials. It shall also enable sponsors to refer to previous submissions of an application for authorisation of a clinical trial or a substantial modification.

Amendment

2. The EU database shall be established to enable the co-operation between the competent authorities of the Member States to the extent that it is necessary for the application of this Regulation and to search for specific clinical trials. It shall also enable sponsors to refer to previous submissions of an application for authorisation of a clinical trial or a substantial modification. ***It shall also be established to enable citizens of the Union to have access to clinical information, in easily searchable form, about medicinal products in order to enable them to make informed decisions about their health.***

Or. en

Justification

Clinical trials data are scientific data and therefore belong to the public. Patients accept to participate in clinical trials because their participation will benefit the public through the advancement of science. Science is hampered when the data are never made public. Moreover, industry-funded research benefits from publicly funded research bodies -access to investigators and research teams at publicly research sites; public funding for basic research.

Amendment 38

Proposal for a regulation

Article 78 – paragraph 3 – introductory part

Text proposed by the Commission

3. The EU database shall be publicly accessible ***unless, for all or parts of the data and*** information ***contained therein,*** confidentiality is ***justified on any of the***

Amendment

3. The EU database shall be publicly ***accessible in line with Regulation (EC) No 1049/2001. When the protection for commercially confidential information is***

following grounds:

to be applied, unreasonable degree of prejudice to the commercial interests if the information is disclosed should be duly justified and documented, the period of time for which commercial confidentiality is required should be duly specified and notified to the requesting person, and there should be no overriding public interest that justifies immediate disclosure.

Or. en

Amendment 39
Proposal for a regulation
Article 78 – paragraph 3 – indent 1

Text proposed by the Commission

Amendment

– protecting personal data in accordance with Regulation (EC) No 45/2001;

deleted

Or. en

Amendment 40
Proposal for a regulation
Article 78 – paragraph 3 – indent 2

Text proposed by the Commission

Amendment

– protecting commercially confidential information;

deleted

Or. en

Amendment 41
Proposal for a regulation
Article 78 – paragraph 3 – indent 3

Text proposed by the Commission

Amendment

– ensuring effective supervision of the

deleted

conduct of a clinical trial by Member States.

Or. en