EUROPEAN PARLIAMENT 2009 - 2014

Committee on the Environment, Public Health and Food Safety

2012/0192(COD)

1.3.2013

AMENDMENTS
75 - 180

Draft report
Glenis Willmott
(PE504.236v01-00)

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

Proposal for a regulation
(COM(2012)0369 – C7-0194/2012 – 2012/0192(COD))

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Amendment 75
Richard Seeber

Proposal for a regulation
Recital 1

Text proposed by the Commission	*Amendment*
(1) In a clinical trial the safety ***and*** rights of subjects should be protected and the data generated should be reliable and robust.	(1) In a clinical trial the safety**,** rights ***and well-being*** of subjects should be protected and the data generated should be reliable and robust.

Or. en

Justification

According to Article 3 of the proposed Regulation and to Article 6 of the World Medical Association of Helsinki on Ethical principles for medical research involving human subjects (Seoul 2008), priority should be given to the safety, rights and well-being of individuals.

Amendment **76**
Anna Rosbach

Proposal for a regulation
Recital 1

Text proposed by the Commission	*Amendment*
(1) In a clinical trial the safety ***and*** rights of subjects should be protected and the data generated should be reliable and robust.	(1) In a clinical trial the safety**,** rights ***and health*** of subjects should be protected and the data generated should be reliable and robust.

Or. en

Amendment 77
Christel Schaldemose

Proposal for a regulation
Recital 1

Text proposed by the Commission	*Amendment*
(1) In a clinical trial the safety and rights of subjects should be protected and the data generated should be reliable ***and*** robust.	(1) In a clinical trial the safety and rights of subjects should be protected and the data generated should be reliable***,*** robust ***and reflect the diversity of the population in terms of age and gender balance***.

Or. en

Amendment 78
Zofija Mazej Kukovič

Proposal for a regulation
Recital 1

Text proposed by the Commission	*Amendment*
(1) In a clinical trial the safety and rights of subjects should be protected and the data generated should be reliable and robust.	(1) In a clinical trial the safety and rights of subjects should be protected and the data generated should be reliable and robust. ***The interests of the participants should always take priority over other interests.***

Or. sl

Amendment 79
Anna Rosbach

Proposal for a regulation
Recital 2

Text proposed by the Commission	*Amendment*
(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation.	(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation ***and it should be ensured that those granting the authorisation do not have conflicts of interest and are independent of the sponsor, the institution of the trial site and the investigators involved***.

Or. en

Amendment 80
Peter Liese, Anne Delvaux, Anna Rosbach, Jolanta Emilia Hibner, Margrete Auken, Thomas Ulmer, Alojz Peterle, Miroslav Mikolášik, Paolo Bartolozzi, Zofija Mazej Kukovič, Horst Schnellhardt, Elena Oana Antonescu, Philippe Juvin, Filip Kaczmarek, Richard Seeber, Georgios Koumoutsakos

Proposal for a regulation
Recital 2

Text proposed by the Commission	*Amendment*
(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation.	(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation***, and approval by an ethics committee prior to commencement.***

Or. en

Justification

This addition conforms to Article 9 (1) of Directive 2001/20/EC and enshrines the principle of prior authorisation of a study protocol pursuant to Article 15 of the WMA Declaration of Helsinki (Seoul, 2008) and Section 2.6 of the ICH-GCP Guideline in the recitals of the proposed Regulation.

Amendment 81
Petru Constantin Luhan

Proposal for a regulation
Recital 2

Text proposed by the Commission	*Amendment*
(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation.	(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation ***which should include review by an Ethics Committee***.

Or. en

Justification

Although we agree that approval of an Ethics Committee is necessary, we strongly adhere to the current proposal of one decision per member state. The current wording gives the impression that there are two steps, which should clearly not be the case. Wording should be worked out in a way that make sure Ethics approval is included within the authorization and specified by the regulation and in respect of timelines.

Amendment 82
Roberta Angelilli

Proposal for a regulation
Recital 2

Text proposed by the Commission	*Amendment*
(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation.	(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation. ***This authorisation should include scientific, ethical and administrative aspects.***

Or. en

Justification

The scientific evaluation and the ethical one could not be separated.

Amendment 83
Margrete Auken
on behalf of the Verts/ALE Group

Proposal for a regulation
Recital 3

Text proposed by the Commission	*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	(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 with the EU legislation governing medicinal products, which builds on the dichotomy of 'clinical trial' and 'non-interventional study'.***	States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use should be clarified.

Or. en

Justification

The old definition from Directive 2001/20/EC of a "clinical trial" should be maintained along with the new introduction of low-intervention trials with one clarification; it should be clear that post authorisation safety and efficacy trials are covered by the definition of a clinical trial and thereby by the regulation. These changes are introduced in our amendments 3,4 and 5.

Amendment 84
Philippe Juvin

Proposal for a regulation
Recital 3 a (new)

Text proposed by the Commission	*Amendment*
	(3a) The scope of this Regulation is essentially identical to that of Directive 2001/20/EC. Although it is limited to clinical research on medicinal products for human use, it is very wide in that it only excludes clinical studies that do not involve an 'intervention' i.e. surveys by medical practitioners without additional intervention. 'Non-interventional studies' are post-authorisation safety studies

initiated, managed or financed by the marketing authorisation holder. These enable data to be 'mined', and are covered by Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

Or. fr

Amendment 85
Riikka Manner, Eija-Riitta Korhola

Proposal for a regulation
Recital 4

Text proposed by the Commission	*Amendment*
(4) Directive 2001/20/EC aimed to simplify and harmonise the administrative provisions governing clinical trials in the European Union. However, experience shows that a harmonised approach to the regulation of clinical trials has only been partly achieved. This makes it in particular difficult to perform a clinical trial in several Member States. Scientific development however, suggests that future clinical trials will target more specific patient populations, such as subgroups identified through genomic information. In order to include a sufficient number of patients for such trials it may be necessary to involve many, or all, Member States. The new procedures for the authorisation of clinical trials should stimulate the inclusion of as many member states as possible. Therefore, in order to simplify submission procedures, the multiple submission of largely identical information should be avoided and replaced by the submission of one application dossier through a single submission portal to all the Member States concerned.	(4) Directive 2001/20/EC aimed to simplify and harmonise the administrative provisions governing clinical trials in the European Union. However, experience shows that a harmonised approach to the regulation of clinical trials has only been partly achieved. This makes it in particular difficult to perform a clinical trial in several Member States. Scientific development however, suggests that future clinical trials will target more specific patient populations, such as subgroups identified through genomic information. In order to include a sufficient number of patients for such trials it may be necessary to involve many, or all, Member States. The new procedures for the authorisation of clinical trials should stimulate the inclusion of as many member states as possible. Therefore, in order to simplify submission procedures, the multiple submission of largely identical information should be avoided and replaced by the submission of one application dossier through a single submission portal to all the Member States concerned. ***The portal should reduce unnecessary red tape so***

that not only sponsors and academic researchers carrying out multinational research but also public authorities may benefit from its use.

Or. fi

Amendment 86
Philippe Juvin, Antonyia Parvanova, Nora Berra

Proposal for a regulation
Recital 4

Text proposed by the Commission	*Amendment*
(4) Directive 2001/20/EC aimed to simplify and harmonise the administrative provisions governing clinical trials in the European Union. However, experience shows that a harmonised approach to the regulation of clinical trials has only been partly achieved. This makes it in particular difficult to perform a clinical trial in several Member States. Scientific development however, suggests that future clinical trials will target more specific patient populations, such as subgroups identified through genomic information. In order to include a sufficient number of patients for such trials it may be necessary to involve many, or all, Member States. The new procedures for the authorisation of clinical trials should stimulate the inclusion of as many member states as possible. Therefore, in order to simplify submission procedures, the multiple submission of largely identical information should be avoided and replaced by the submission of one application dossier through a single submission portal to all the Member States concerned.	(4) Directive 2001/20/EC aimed to simplify and harmonise the administrative provisions governing clinical trials in the European Union. However, experience shows that a harmonised approach to the regulation of clinical trials has only been partly achieved. This makes it in particular difficult to perform a clinical trial in several Member States. Scientific development however, suggests that future clinical trials will target more specific patient populations, such as subgroups identified through genomic information. In order to include a sufficient number of patients for such trials it may be necessary to involve many, or all, Member States. The new procedures for the authorisation of clinical trials should stimulate the inclusion of as many member states as possible. Therefore, in order to simplify submission procedures, the multiple submission of largely identical information should be avoided and replaced by the submission of one application dossier through a single submission portal to all the Member States concerned. ***Given that clinical trials carried out in a single Member State are equally indispensable to European clinical research, the procedure under this regulation should also cover such trials. The application dossier for***

such clinical trials should also be sent via the single European portal.

Or. fr

Amendment 87
Roberta Angelilli

Proposal for a regulation
Recital 5

Text proposed by the Commission	*Amendment*
(5) Experience with Directive 2001/20/EC has also shown that the aim of simplifying and harmonising the ***administrative*** provisions governing clinical trials in the Union cannot be achieved in the legal form of a Directive but can only be achieved with the legal form of a Regulation. Only the legal form of a Regulation ensures that the Member States base their assessment of an application for authorisation of a clinical trial on identical criteria, rather than on diverging national transposition measures. This holds not only for the entire authorisation process, but also for all other issues addressed in this Regulation, such as safety reporting during clinical trials, and the requirements for labelling of the medicinal products used in the context of a clinical trial.	(5) Experience with Directive 2001/20/EC has also shown that the aim of simplifying and harmonising the provisions governing clinical trials in the Union cannot be achieved in the legal form of a Directive but can only be achieved with the legal form of a Regulation. Only the legal form of a Regulation ensures that the Member States base their assessment of an application for authorisation of a clinical trial on identical criteria, rather than on diverging national transposition measures. This holds not only for the entire authorisation process, but also for all other issues addressed in this Regulation, such as safety reporting during clinical trials, and the requirements for labelling of the medicinal products used in the context of a clinical trial.

Or. en

Justification

The adjective administrative should be deleted, as there is the need for harmonising not only the administrative aspects, but also the ethical ones.

Amendment 88
Anna Záborská

Proposal for a regulation
Recital 6

Text proposed by the Commission	*Amendment*
(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.***	(6) The Member States concerned should cooperate in assessing a request for authorisation of a clinical trial.

Or. fr

Amendment 89
Roberta Angelilli

Proposal for a regulation
Recital 6

Text proposed by the Commission	*Amendment*
(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***.	(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.

Or. en

Amendment 90
Philippe Juvin

Proposal for a regulation
Recital 8

Text proposed by the Commission	*Amendment*
(8) The timelines for assessing an application dossier for clinical trials should be sufficiently long to assess the file, while	(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.

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. ***If a Member State concerned and a reporting Member State do not produce the assessment report, the assessment or the decision within the set deadlines, the concept of tacit authorisation should apply automatically.*** 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.

Or. fr

Amendment 91
Elena Oana Antonescu

Proposal for a regulation
Recital 8

Text proposed by the Commission	*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 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	(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***, unless Member States indicate that exceptional circumstances apply which justify minimal delays***. In the event of a public health crisis, Member States should have the possibility to assess and authorise a

therefore be established.	clinical trial application swiftly. No minimal timelines for approval should therefore be established.

Or. en

Justification

While timelines should be adhered to, the ability of Member States to meet them depends both on routine and unforeseeable elements related to application content and operational capacity, which might prevent a swift assessment. Where exceptional circumstances apply, Member States should be able to flag these in order to prevent tacit authorisation, while still striving to complete the assessment in due time.

Amendment 92
Margrete Auken, Michèle Rivasi
on behalf of the Verts/ALE Group

Proposal for a regulation
Recital 8

Text proposed by the Commission	*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 ***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.	(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 93
Georgios Koumoutsakos

Proposal for a regulation
Recital 8

Text proposed by the Commission	*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 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.	(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***, ensuring first and foremost the safety and wellbeing of all participants.*** 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.

Or. el

Amendment 94
Antonyia Parvanova

Proposal for a regulation
Recital 8

Text proposed by the Commission	*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 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.	(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 ***as well as, existing (e.g. generic medicinal products)*** 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.

Or. en

Justification

It is important that an effective Clinical Trial authorisation system (particularly vis-à-vis timelines) is guaranteed for such trials related to generic medicinal products authorisation, so that existing treatments coming off patent can be registered rapidly as generic medicines to benefit a greater number of patients while providing savings to healthcare systems

Amendment 95
Cristina Gutiérrez-Cortines

Proposal for a regulation
Recital 8 a (new)

Text proposed by the Commission	*Amendment*
	(8a) The Member States must guarantee that clinical trials can be conducted in both public and private centres under equal conditions, subject to any statutory requirements.

Or. es

Justification

In Member States such as Spain, where there are substantial differences between the public and private health system, this clarification is necessary to ensure that there is nothing to prevent clinical trials being carried out in a private centre.

Amendment 96
Tadeusz Cymański

Proposal for a regulation
Recital 8 a (new)

Text proposed by the Commission	*Amendment*
	(8a) The modernisation of IT infrastructure, facilitating the Member States' adaptation to the authorisation timelines, could be cofinanced by the structural funds.

Or. pl

Amendment 97
Christel Schaldemose

Proposal for a regulation
Recital 9

Text proposed by the Commission	*Amendment*
(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 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	(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 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.

procedure) and where the intervention poses only very limited additional risk to the subject compared to ***the best current proven intervention***. 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 98
Roberta Angelilli

Proposal for a regulation
Recital 9

Text proposed by the Commission	*Amendment*
(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 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	(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 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 ***administrative*** rules, such as shorter deadlines for

shorter deadlines for approval. | approval.

Or. en

Justification

The concept of 'low-interventional clinical trial' is endorsed and a shorter deadline is welcomed. However it shouldn't imply a reduced protection of subjects in the trials. In addition the proposed EC-test seems to be in contrast with the recently approved Pharmcovigilance legislation where is underlined that the level of attention to the drug safety should be maintained high at any time in pre-approval and post-approval phase.

Amendment 99
Cristina Gutiérrez-Cortines

Proposal for a regulation
Recital 9

Text proposed by the Commission	*Amendment*
(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 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	(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 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, ***without compromising scientific standards and guaranteeing the safety of patients at all***

times.

Or. es

Amendment 100
Philippe Juvin

Proposal for a regulation
Recital 9

Text proposed by the Commission	*Amendment*
(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 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.	(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 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-***risk*** 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. fr

Amendment 101
Françoise Grossetête, Marina Yannakoudakis, Thomas Ulmer, Frédérique Ries, Philippe Juvin

Proposal for a regulation
Recital 9 a (new)

Text proposed by the Commission	*Amendment*
	(9a) In case of an urgent situation as well as for rare and ultra-rare diseases which are life-threatening and for which therapeutic options and expertise are limited and geographically spread across the world, Member-States should have the possibility to assess and authorise clinical trial applications in priority.

Or. en

Amendment 102
Rebecca Taylor

Proposal for a regulation
Recital 9 b

Text proposed by the Commission	*Amendment*
	(9b) The concept of 'Normal Clinical Practice' is of vital importance in determining whether an application is authorised as a 'low intervention clinical trial'. The definition of 'Normal Clinical Practice' should be clarified by the Commission in guidelines.

Or. en

Justification

The definition of 'Normal Clinical Practice' is vital in the first stage of the authorisation procedure when the reporting Member State makes the first assessment of a clinical trial application in Article 5. This definition should be flexible, though the Commission should provide non-legislative guidelines on this matter to assist the process.

Amendment 103
Antonyia Parvanova

Proposal for a regulation
Recital 9 c

Text proposed by the Commission	*Amendment*
	(9 c) Clinical studies supporting the registration of generic medicinal products (e.g. bioequivalence or therapeutic equivalence studies) pose minimal risks and inconveniences for the study subjects compared to the normal clinical practice, as defined in this Regulation, since the reference medicinal product, used as comparator, is a well-characterised authorised product for which the quality safety and efficacy have already been assessed.

Or. en

Amendment 104
Philippe Juvin

Proposal for a regulation
Recital 9 d

Text proposed by the Commission	*Amendment*
	(9d) 'Experimental medicinal product' means any active ingredient in a pharmaceutical or placebo form tested or used as a reference in a clinical trial, including a medicinal product which is covered by a marketing authorisation but which is used off-label or in accordance with current clinical practice.

Or. fr

Amendment 105
Philippe Juvin

Proposal for a regulation
Recital 9 e

Text proposed by the Commission	*Amendment*
	(9e) 'Auxiliary medicinal product' means any medicinal product used in the context of a clinical trial but not as an experimental medicinal product. Auxiliary medicinal products include, in particular, medicinal products used for background treatment, pharmacological agents, rescue medication or medicinal products used to assess end-points in a clinical trial. Auxiliary medicinal products do not include medicaments which are unconnected with the clinical trial and are not pertinent to the trial design.

Or. fr

Amendment 106
Philippe Juvin

Proposal for a regulation
Recital 9 f

Text proposed by the Commission	*Amendment*
	(9f) All the deadlines set out in this regulation should be based on calendar days. Since the Member States of the European Union have different calendars of public holidays, a procedure based on working days could result in different deadlines for validation, assessment and decisions in one of the Member States concerned.

Or. fr

Justification

The proposal for a regulation should refer to calendar days rather than working days.

Compliance with time-limits, which helps ensure the competitiveness of European clinical research, requires efficient cooperation between the Member States concerned. Public holidays differ from one Member State to another. A procedure based on working days could result in different deadlines for validation, assessment and decisions in each of the Member States concerned.

Amendment 107
Cristian Silviu Buşoi, Antonyia Parvanova

Proposal for a regulation
Recital 10

Text proposed by the Commission	*Amendment*
(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public health benefits (‘relevance’) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account, ***including*** whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.	(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public health benefits (′relevance′) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account, ***such as the subpopulations to be studied and the potential differences in efficacy and/or safety for specific subpopulations notably gender and age differences, or*** whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.

Or. en

Amendment 108
Esther de Lange

Proposal for a regulation
Recital 10

Text proposed by the Commission	*Amendment*
(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public	(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public

health benefits (‘relevance’) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account, including whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.	health benefits (‘relevance’) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account, ***which includes ensuring that the group of subjects participating in the trial represents the population,*** including ***women and the elderly, to be treated, and*** whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.

Or. en

Amendment 109
Riikka Manner

Proposal for a regulation
Recital 10

Text proposed by the Commission	*Amendment*
(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public health benefits (‘relevance’) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account, including whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.	(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public health benefits (‘relevance’) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account, ***which includes that the group of subjects is relevant to the aimed population to be treated and*** including whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.

Or. en

Amendment 110
Rebecca Taylor

Proposal for a regulation
Recital 10

Text proposed by the Commission	*Amendment*
(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public health benefits (‘relevance’) and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account***, including*** whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.	(10) The assessment of the application for a clinical trial should address in particular the anticipated therapeutic and public health benefits (′relevance′)**,** and the risk and inconveniences for the subject. Regarding the relevance, numerous aspects should be taken into account***; in later trial phases this should include whether the trial subjects are representative of the population for whom the medicinal product is targeted, and*** whether the clinical trial has been recommended or imposed by regulatory authorities in charge of the assessment and authorisation of the placing on the market of medicinal products.

Or. en

Justification

Trial participants should as closely as possible reflect the target audience for the medicinal product tested. This is particularly important for phase III and phase IV trials, wherein the safety and efficacy of the medicinal product should be assessed via trials on those who are likely to be using the product when it is on the market. Earlier phases test for more basic safety concerns where it is not as crucial to assemble a representative pool of trial participants.

Amendment 111
Antonyia Parvanova

Proposal for a regulation
Recital 10 a (new)

Text proposed by the Commission	*Amendment*
	(10a) In order to improve treatments available for vulnerable groups such as frail or older people, people suffering from multiple chronic conditions, and

people affected by mental health disorders, medicinal products which are likely to be of significant clinical value should be fully and appropriately studied for their effects in these specific groups, including requirements related to their specific characteristics and the protection of their health and well being.

Or. en

Amendment 112
Petru Constantin Luhan

Proposal for a regulation
Recital 10 a (new)

Text proposed by the Commission	*Amendment*
	(10a) Experience with Directive 2001/20/EC has also shown that 60% of clinical trials are sponsored by the pharmaceutical industry and 40% by other stakeholders, such as academics. The value of academic contribution should be duly recognized by member states. Academic sponsors frequently rely on funding which partly or entirely comes from the public funds or charities. In order to maximize the use of this valuable contribution and to further stimulate academic research but without any discrimination towards the quality of trials, measures should be put in place by member states to make appropriate exemptions from fees (application fees, inspection fees etc...) for trials conducted by academic sponsors.

Or. en

Justification

A waiver from fees does not have any impact on the trial quality. Public funds and support from charities should not be used to pay fees and other taxes, but to conduct research

otherwise not feasible.

Amendment 113
Philippe Juvin

Proposal for a regulation
Recital 11

Text proposed by the Commission	*Amendment*
(11) The authorisation procedure should provide for the possibility to suspend the assessment in order to allow the sponsor to address questions or comments raised during the assessment of the application dossier. The maximum duration of the suspension should reflect whether the clinical trial ***is a low-intervention*** clinical trial or not. Moreover, it should be ensured that, following the end of the suspension, there is always sufficient time for assessing the additional information submitted.	(11) The authorisation procedure should provide for the possibility to suspend the assessment in order to allow the sponsor to address questions or comments raised during the assessment of the application dossier. The maximum duration of the suspension should reflect whether the clinical trial is a ***low- or medium-risk*** clinical trial or not. Moreover, it should be ensured that, following the end of the suspension, there is always sufficient time for assessing the additional information submitted.

Or. fr

Amendment 114
Corinne Lepage

Proposal for a regulation
Recital 11 a (new)

Text proposed by the Commission	*Amendment*
	(11a) In order to follow a given trial from initial ethical approval to final publication, a Universal Trial Registration Number (UTRN) should be assigned to each trial to be conducted in the European Union or whose results are used as part of the Common technical document for a marketing authorisation of a medicinal product.

Or. en

Amendment 115
Cristian Silviu Buşoi

Proposal for a regulation
Recital 12 a (new)

Text proposed by the Commission	*Amendment*
	(12a) In the case of rare diseases as defined by EU legislation, the necessary data and expertise to perform a well-informed assessment of the application for authorisation of a clinical trial may be scarce at national level. Therefore, such expertise should be sought at European level. To this end, the reporting Member State should cooperate in the assessment process with the Scientific Advice Working Party of the European Medicines Agency which should provide an opinion on the disease or disease group concerned. Where relevant, this opinion may cover aspects related to Part II of the assessment, in which case the reporting Member State should notify it to the Member States concerned. This cooperation should be organised within the same deadlines foreseen in this Regulation for clinical trials conducted in the field of diseases other than rare diseases.

Or. en

Amendment 116
Françoise Grossetête, Marina Yannakoudakis, Thomas Ulmer, Frédérique Ries, Philippe Juvin

Proposal for a regulation
Recital 12 a (new)

Text proposed by the Commission	*Amendment*
	(12a) Whereas most clinical trials are conducted for the assessment of therapies, targeted at large patient populations, and involving a large sample of patient populations, the present regulation should not discriminate against patients suffering from rare and ultra-rare diseases, and should integrate the specificities of low-prevalence conditions into the assessment of a trial.

Or. en

Justification

The Commission's proposal does not reflect the specificities of rare and ultra-rare diseases. The future regulation must take into account therapeutic innovations and must be in compliance with policies on rare and ultra-rare diseases which have been developed since adoption of Directive 2001/20/EC.

Amendment 117
Roberta Angelilli

Proposal for a regulation
Recital 13

Text proposed by the Commission	*Amendment*
(13) The authorisation of a clinical trial should address all aspects in relation to subject protection and data reliability and robustness. The permission to conduct a clinical trial should therefore be contained in one single ***administrative*** decision by the Member State concerned.	(13) The authorisation of a clinical trial should address all aspects in relation to subject protection and data reliability and robustness. The permission to conduct a clinical trial should therefore be contained in one single decision by the Member State concerned.

Or. en

Justification

As for Recital 5, the adjective 'administrative' should be deleted. There is the need to simplify and to shorten the Ethical Approval process without reducing the patients' protection. To

initiate a trial a single approval including EC and administrative aspects should be obtain.

Amendment 118
Roberta Angelilli

Proposal for a regulation
Recital 14

Text proposed by the Commission	*Amendment*
(14) It should be left to the Member State concerned to determine the appropriate body or bodies to be involved in this assessment. This decision is a matter of internal organisation of each Member State. Member States, when determining the appropriate body or bodies, should ensure the involvement of lay persons and patients. They should also ensure that the necessary expertise is available. In any case, however, and in accordance with international guidelines, the assessment should be done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience. The persons assessing the application should be independent from the sponsor, the institution of the trial site, and the investigators involved, as well as free of any other undue influence.	(14) It should be left to the Member State concerned to determine the appropriate body or bodies to be involved in this assessment. ***These bodies should be established according to the ICH Topic E 6 (R1) Guideline for Good Clinical Practice, which details the responsibilities, composition, functions, operations and procedures.*** This decision is a matter of internal organisation of each Member State. Member States, when determining the appropriate body or bodies, should ensure the involvement of lay persons and patients. They should also ensure that the necessary expertise is available. In any case, however, and in accordance with international guidelines, the assessment should be done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience. The persons assessing the application should be independent from the sponsor, the institution of the trial site, and the investigators involved, as well as free of any other undue influence.

Or. en

Justification

The regulation could not ignore in its premise the internationally agreed methodological and ethical standard provided by the Good Clinical Practice.

Amendment 119
Antonyia Parvanova, Corinne Lepage

Proposal for a regulation
Recital 14

Text proposed by the Commission	*Amendment*
(14) It should be left to the Member State concerned to determine the appropriate body or bodies to be involved in this assessment. This decision is a matter of internal organisation of each Member State. Member States, when determining the appropriate body or bodies, should ensure the involvement of lay persons and patients. They should also ensure that the necessary expertise is available. In any case, however, and in accordance with international guidelines, the assessment should be done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience. The persons assessing the application should be independent from the sponsor, the institution of the trial site, and the investigators involved, as well as free of any other undue influence.	(14) It should be left to the Member State concerned to determine the appropriate body or bodies to be involved in this assessment. This decision is a matter of internal organisation of each Member State. Member States, when determining the appropriate body or bodies, should ensure the involvement of lay persons and patients. They should also ensure that the necessary expertise is available. In any case, however, and in accordance with international guidelines, the assessment should be done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience. The persons assessing the application should be independent from the sponsor, the institution of the trial site, and the investigators involved, as well as free of any other undue influence. ***Names, qualifications and declarations of interest of the persons assessing the application should be made publicly available.***

Or. en

Amendment 120
Christofer Fjellner

Proposal for a regulation
Recital 20 a (new)

Text proposed by the Commission	*Amendment*
	(20a) Before a marketing authorisation has been obtained, clinical trial data should be considered commercially confidential. Once a marketing

authorisation is obtained, it should be presumed that data contained in the marketing authorisation dossier may contain some confidential and commercially sensitive information.

Or. en

Justification

There should be a distinction between clinical trial data use pre- and post marketing authorisation. The presumption of confidentiality once market authorisation is obtained is in line with EMA/HMA guidance.

Amendment 121
Anna Rosbach

Proposal for a regulation
Recital 21

Text proposed by the Commission	*Amendment*
(21) It should be left to Member States to establish the language requirements for the application dossier. To ensure that the assessment of the application for authorisation of a clinical trial functions smoothly, Member States should ***consider*** accepting a commonly understood language in the medical field as the language for the documentation not destined to the subject.	(21) It should be left to Member States to establish the language requirements for the application dossier. To ensure that the assessment of the application for authorisation of a clinical trial functions smoothly, Member States should ***work towards*** accepting a commonly understood language in the medical field as the language for the documentation not destined to the subject***, such as the Patient Information and the Informed Consent Sheet.***

Or. en

Amendment 122
Roberta Angelilli

Proposal for a regulation
Recital 22

Text proposed by the Commission	*Amendment*
(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld**.** Regarding the rules concerning the determination of the legal representative of incapacitated persons and minors, those rules diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated ***persons*** and minors.	(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the person concerned. ***Subjects from vulnerable population groups such as incapacitated subjects, minors or other vulnerable people, require additional protection measures.*** Directive 2001/20/EC contained an extensive set of rules for the protection of subjects ***including children and incapacitated subjects. In addition, specific rules to be applied to the paediatric population have been stated in the Ethical Recommendation (EC, 2008)***. These rules should be upheld ***and further integrated in order to cover all the vulnerable groups (pregnancy females, old people, emergency, etc).*** Regarding the rules concerning the determination of the legal representative of incapacitated persons and minors, those rules diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated ***subjects*** and minors.

Or. en

Justification

This Regulation shouldn't result less protective than Dir. 2001/20/EC and related legislation such as the Paediatric Ethical Recommendations. On the contrary the Regulation should represent the occasion for implementing the existing rules and to cover the gap in specific sectors.

Amendment 123
Esther de Lange

Proposal for a regulation
Recital 22

Text proposed by the Commission	*Amendment*
(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld. Regarding the rules concerning the determination of the legal representative of incapacitated persons and minors, those rules diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated ***persons*** and minors.	(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld. ***Subjects from vulnerable population groups such as incapacitated subjects, minors, the elderly or other vulnerable people, require additional protection measures.*** Regarding the rules concerning the determination of the legal representative of incapacitated persons and minors, those rules diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated ***subjects, the elderly*** and minors.

Or. en

Amendment 124
Philippe Juvin, Nora Berra

Proposal for a regulation
Recital 22

Text proposed by the Commission	*Amendment*
(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the	(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the

person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld. ***Regarding the*** rules concerning the determination of the legal representative of incapacitated persons and minors, ***those rules*** diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated persons and minors.	person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld. ***The*** rules concerning the determination of the legal representative of incapacitated persons and minors, ***the definition of incapacitated and vulnerable persons and the provisions resulting from that definition,*** diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated persons and minors ***and where necessary to enact rules affording greater protection at national level***.

Or. fr

Justification

In providing for the protection of vulnerable persons the regulation must respect the restrictive provisions put in place by some Member States for other categories of vulnerable persons, including pregnant and breast-feeding women, women in labour, and persons deprived of their liberty.

Amendment 125
Anna Záborská

Proposal for a regulation
Recital 22

Text proposed by the Commission	*Amendment*
(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld. Regarding the rules concerning the determination of the legal representative of incapacitated persons and	(22) The human dignity and right to the integrity of the person are recognized in the Charter of Fundamental rights of the European Union ***and by the judgment in Case C-34/10 (Brüstle v. Greenpeace)***. In particular, the Charter requires that any intervention in the field of biology and medicine cannot be performed without free and informed consent of the person concerned. Directive 2001/20/EC contained an extensive set of rules for the protection of subjects. These rules should be upheld. Regarding the rules concerning

minors, those rules diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated persons and minors.	the determination of the legal representative of incapacitated persons and minors, those rules diverge in Member States. It should therefore be left to Member States to determine the legal representative of incapacitated persons and minors.
	Or. fr

Amendment 126
Philippe Juvin, Cristian Silviu Buşoi

Proposal for a regulation
Recital 23

Text proposed by the Commission	*Amendment*
(23) This Regulation should provide for clear rules concerning informed consent in emergency situations. Such situations relate to cases where for example a patient has suffered a sudden life-threatening medical condition due to multiple traumas, strokes or heart attacks, necessitating immediate medical intervention. For such cases, intervention within an ongoing clinical trial, which has already been approved, may be pertinent. However, in certain circumstances, due to the unconsciousness of the patient and the absence of an immediately available legal representative, it is not possible to obtain informed consent prior to the intervention. The Regulation should therefore set clear rules whereby such patients may be enrolled in the clinical trial under very strict conditions. In addition, the said clinical trial should relate directly to the medical condition which causes the impossibility of the patient to give informed consent. Any previously expressed objection by the patient must be respected, and informed consent from the subject or the legal representative should	(23) This Regulation should provide for clear rules concerning informed consent in emergency situations. Such situations relate to cases where for example a patient has suffered a sudden life-threatening medical condition due to multiple traumas, strokes or heart attacks, necessitating immediate medical intervention. For such cases, intervention within an ongoing clinical trial, which has already been approved, may be pertinent. However, in certain circumstances, due to the unconsciousness of the patient and the absence of an immediately available legal representative, it is not possible to obtain informed consent prior to the intervention. The Regulation should therefore set clear rules whereby such patients may be enrolled in the clinical trial under very strict conditions. ***For example, in cases where the research needs to start without delay and there is reason to expect that the potential benefit to the subject of taking part in the clinical trial outweighs the risks of the subject's participation or entails only a minimal risk, it should be possible for the clinical trial to begin without his or her prior consent.*** In

be sought as soon as possible.	addition, the said clinical trial should relate directly to the medical condition which causes the impossibility of the patient to give informed consent. Any previously expressed objection by the patient must be respected, and informed consent from the subject or the legal representative should be sought as soon as possible.

Or. fr

Justification

Philippe Juvin welcomes the fact that the proposal for a regulation provides for possible exemption from the requirement for prior consent in the event of emergencies. However, he does not wish this option to be restricted to minimum-risk clinical trials. In practice, this provision would be too restrictive. It would rule out a great deal of research in the field of intensive care and emergency medicine relating to innovative products.

Amendment 127
Alda Sousa

Proposal for a regulation
Recital 23

Text proposed by the Commission	*Amendment*
(23) This Regulation should provide for clear rules concerning informed consent in emergency situations. Such situations relate to cases where for example a patient has suffered a sudden life-threatening medical condition due to multiple traumas, strokes or heart attacks, necessitating immediate medical intervention. For such cases, intervention within an ongoing clinical trial, which has already been approved, may be pertinent. However, in certain circumstances, due to the unconsciousness of the patient and the absence of an immediately available legal representative, it is not possible to obtain informed consent prior to the intervention. The Regulation should therefore set clear rules whereby such patients may be	(23) This Regulation should provide for clear rules concerning informed consent in emergency situations. Such situations relate to cases where for example a patient has suffered a sudden life-threatening medical condition due to multiple traumas, strokes or heart attacks, necessitating immediate medical intervention. For such cases, intervention within an ongoing clinical trial, which has already been approved, may be pertinent. However, in certain circumstances, due to the unconsciousness of the patient and the absence of an immediately available legal representative, it is not possible to obtain informed consent prior to the intervention. The Regulation should therefore set clear rules whereby such patients may be

enrolled in the clinical trial under very strict conditions. In addition, the said clinical trial should relate directly to the medical condition which causes the impossibility of the patient to give informed consent. Any previously expressed objection by the patient must be respected, and informed consent from the subject or the legal representative should be sought as soon as possible.	enrolled in the clinical trial under very strict conditions. In addition, the said clinical trial should relate directly to the medical condition which causes the impossibility of the patient to give informed consent. Any previously expressed objection by the patient must be respected, and informed consent from the subject or the legal representative should be sought as soon as possible. ***An ethics committee should positively assess the direct benefit of the clinical trial to the patient, as well as the fact that the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject;***

Or. en

Justification

The responsible Ethics Committee should assess the direct benefit of the clinical trial to the patient. Emergency clinical trials should not be conducted for other means than the benefit of the concerned subject.

Amendment 128
Roberta Angelilli

Proposal for a regulation
Recital 24

Text proposed by the Commission	*Amendment*
(24) In accordance with international guidelines, the free and informed consent of the subject should be in writing, save in exceptional situations. It should be based on information which is clear, relevant and understandable to the subject.	(24) In accordance with international guidelines, the free and informed consent of the subject should be ***given*** in writing, save in exceptional situations. It should be based on information which is clear, relevant and understandable to the subject. ***Where possible, such information should be given orally, with the opportunity for the subject to ask questions, and the subject should be provided with comprehensive written information which he or she is allowed to keep. Adequate time should be provided for the subject to***

consider his or her decision.

Or. en

Justification

The possibility of providing oral information to trial subjects should be mentioned here.

Amendment 129
Anna Rosbach

Proposal for a regulation
Recital 24

Text proposed by the Commission	*Amendment*
(24) In accordance with international guidelines, the free and informed consent of the subject should be in writing, save in exceptional situations. It should be based on information which is clear, relevant and understandable to the subject.	(24) In accordance with international guidelines, the free and informed consent of the subject should be in writing, save in exceptional situations. It should be based on information which is clear, relevant and understandable to the subject***, and should be in the subject's own language.***

Or. en

Amendment 130
Roberta Angelilli

Proposal for a regulation
Recital 24 a (new)

Text proposed by the Commission	*Amendment*
	(24a) In accordance to the Ethical Recommendations (EC, 2008) and in addition to what is stated before, in paediatric clinical trials appropriate procedures on the informed assent should be applied. These procedures should take into account the age and maturity of children.

Or. en

Justification

The Paediatric Recommendations issued by the European Commission in 2008 have been drafted in order to increase the children protection in light of an experimental trial. These rules should be implemented in the Regulation to avoid that fundamental children rights are cancelled

Amendment 131
Philippe Juvin

Proposal for a regulation
Recital 25

Text proposed by the Commission	*Amendment*
(25) In order to allow patients to assess possibilities to participate in a clinical trial, and to allow for effective supervision of a clinical trial by the Member State concerned, the start of the clinical trial, the end of recruitment for the clinical trial and the end of the clinical trial should be notified. In accordance with international standards, the results of the clinical trial should be reported to the competent authorities within ***one year*** of the end of the clinical trial.	(25) In order to allow patients to assess possibilities to participate in a clinical trial, and to allow for effective supervision of a clinical trial by the Member State concerned, the start of the clinical trial, the end of recruitment for the clinical trial and the end of the clinical trial should be notified. In accordance with international standards, the results of the clinical trial should be reported to the competent authorities within ***two years*** of the end of the clinical trial.

Or. fr

Amendment 132
Anna Rosbach

Proposal for a regulation
Recital 26

Text proposed by the Commission	*Amendment*
(26) In order for the sponsor to assess all potentially relevant safety information, the investigator should report to him all serious adverse events.	(26) In order for the sponsor to assess all potentially relevant safety information, the investigator should report to him all serious adverse events ***and all suspected serious***

adverse events.

Or. en

Amendment 133
Antonyia Parvanova, Cristian Silviu Buşoi, Corinne Lepage

Proposal for a regulation
Recital 27

Text proposed by the Commission	*Amendment*
(27) The sponsor should assess the information received from the investigator, and report safety information on serious adverse events which are suspected unexpected serious adverse reactions to the Agency.	(27) The sponsor should assess the information received from the investigator, and ***immediately*** report safety information on serious adverse events which are suspected unexpected serious adverse reactions to the Agency ***via the electronic database referred to in Article 36***.

Or. en

Amendment 134
Anna Rosbach

Proposal for a regulation
Recital 28

Text proposed by the Commission	*Amendment*
(28) The Agency should forward this information to the Member States for them to assess this information.	(28) The Agency should ***as soon as possible*** forward this information to the Member States for them to assess this information.

Or. en

Amendment 135
Roberta Angelilli

Proposal for a regulation
Recital 29

Text proposed by the Commission	*Amendment*
(29) The members of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) have agreed on a detailed set of guidelines for good clinical practice which are now an internationally accepted standard for designing, conducting, recording and reporting clinical trials, consistent with principles that have their origin in the World Medical Association's Declaration of Helsinki. When designing, conducting, recording and reporting clinical trials, ***detailed questions may arise as to the appropriate quality standard. In such a case, the ICH*** guidelines ***on good clinical practice*** should be used as guidance for the application of the rules set out in this Regulation***, provided that there is no other specific guidance issued by the Commission and that those guidelines are without prejudice to this Regulation***.	(29) The members of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) have agreed on a detailed set of guidelines for good clinical practice which are now an internationally accepted standard for designing, conducting, recording and reporting clinical trials, consistent with principles that have their origin in the World Medical Association's Declaration of Helsinki. When designing, conducting, recording and reporting clinical trials, ***the ICH guidelines on good clinical practice (GCP) and other applicable*** guidelines ***published by the EC*** should be used as guidance for the application of the rules set out in this Regulation***. To this aim GCP should be made part of this Regulation and included in Annex [xxx].***

Or. en

Justification

For effect of Dir. 2001/20/EC, the compliance with 'GCP' became a legal obligation in Europe for all trials involving the investigation of medicinal products. GCP is complemented by the set of scientific guidelines prepared by the CHMP in consultation with MSs and released by the European Commission. These set of guidelines should continue to represent the basis for the MA application.

Amendment 136
Roberta Angelilli

Proposal for a regulation
Recital 30

Text proposed by the Commission	*Amendment*
(30) The conduct of a clinical trial should	***deleted***

be adequately monitored by the sponsor in order to ensure the reliability and robustness of the results. Monitoring may also contribute to subject safety, taking into account the characteristics of the clinical trial and respect for fundamental rights of subjects. When establishing the extent of monitoring, the characteristics of the clinical trial should be taken into account.

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 137
Philippe Juvin

Proposal for a regulation
Recital 30

Text proposed by the Commission	*Amendment*
(30) The conduct of a clinical trial should be adequately monitored by the sponsor in order to ensure the reliability and robustness of the results. Monitoring may also contribute to subject safety, taking into account the characteristics of the clinical trial and respect for fundamental rights of subjects. ***When establishing the extent of monitoring, the characteristics*** of the ***clinical*** trial ***should be taken into account***.	(30) The conduct of a clinical trial should be adequately monitored by the sponsor in order to ensure the reliability and robustness of the results. Monitoring may also contribute to subject safety, taking into account the characteristics of the clinical trial and respect for fundamental rights of subjects. ***Monitoring should be adapted to the nature*** of the trial ***and focus on mitigating the key risks***.

Or. en

Justification

Each trial application dossier should contain a risk assessment covering the whole spectrum of risk determinants, and defining its consequences on the trial management, including (but not limited to) the trial monitoring.

Amendment 138
Roberta Angelilli

Proposal for a regulation
Recital 31

Text proposed by the Commission	*Amendment*
(31) The individuals involved in conducting the clinical trial, in particular investigators and other healthcare staff, should be sufficiently qualified to perform their tasks in a clinical trial and the facilities where the clinical trial is to be conducted should be suitable for the clinical trial.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 139
Antonyia Parvanova

Proposal for a regulation
Recital 31

Text proposed by the Commission	*Amendment*
(31) The individuals involved in conducting the clinical trial, in particular investigators and other healthcare ***staff***, should be sufficiently qualified to perform their tasks in a clinical trial and the facilities where the clinical trial is to be conducted should be suitable for the clinical trial.	(31) The individuals involved in conducting the clinical trial, in particular investigators and other healthcare ***professionals***, should be sufficiently qualified to perform their tasks in a clinical trial and the facilities where the clinical trial is to be conducted should be suitable for the clinical trial.

Or. en

Amendment 140
Roberta Angelilli

Proposal for a regulation
Recital 32

Text proposed by the Commission	*Amendment*
(32) Depending on the circumstances of the clinical trial, it should be possible to trace the investigational and certain auxiliary medicinal products in order to ensure subject safety and data robustness and reliability. For the same reasons, those products should be destroyed where necessary and, depending on the circumstances of the clinical trial, subject to specific storage conditions.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 141
Roberta Angelilli

Proposal for a regulation
Recital 33

Text proposed by the Commission	*Amendment*
(33) During a clinical trial, a sponsor may become aware of serious breaches of the rules for the conduct of the clinical trial. This should be reported to the Member States concerned in order for action to be taken by those Member States, where necessary.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 142
Anna Rosbach

Proposal for a regulation
Recital 33

Text proposed by the Commission	*Amendment*
(33) During a clinical trial, a sponsor may become aware of serious breaches of the rules for the conduct of the clinical trial. This should be reported to the Member States concerned in order for action to be taken by those Member States, where necessary.	(33) During a clinical trial, a sponsor may become aware of serious breaches of the rules for the conduct of the clinical trial. This should be reported to the Member States concerned***, as well as to the Agency,*** in order for action to be taken by those Member States, where necessary.

Or. en

Amendment 143
Roberta Angelilli

Proposal for a regulation
Recital 34

Text proposed by the Commission	*Amendment*
(34) Apart from the reporting of suspected unexpected serious adverse reactions, there may be other events which are relevant in terms of benefit-risk balance and which should be reported in a timely manner to the Member States concerned.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 144
Roberta Angelilli

Proposal for a regulation
Recital 35

Text proposed by the Commission	*Amendment*
(35) Where unexpected events require an urgent modification of a clinical trial, it should be possible for the sponsor and the investigator to take urgent safety measures without awaiting prior authorisation.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 145
Roberta Angelilli

Proposal for a regulation
Recital 36

Text proposed by the Commission	*Amendment*
(36) In order to ensure compliance of the conduct of the clinical trial with the protocol, and in order for investigators to be informed about the investigational medicinal products they administer, the sponsor should supply the investigators with an investigator's brochure.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 146
Cristian Silviu Buşoi

Proposal for a regulation
Recital 36

Text proposed by the Commission	*Amendment*
(36) In order to ensure compliance of the conduct of the clinical trial with the protocol, and in order for investigators to be informed about the investigational medicinal products they administer, the sponsor should supply the investigators with an investigator's brochure.	(36) In order to ensure compliance of the conduct of the clinical trial with the protocol, and in order for investigators to be informed about the investigational medicinal products they administer, the sponsor should supply the investigators with an investigator's brochure. ***This brochure should be updated whenever new safety information becomes available, including information about events other than suspected unexpected serious adverse reactions.***

Or. en

Amendment 147
Roberta Angelilli

Proposal for a regulation
Recital 37

Text proposed by the Commission	*Amendment*
(37) The information generated in the clinical trial should be recorded, handled and stored adequately for the purpose of ensuring subject rights and safety, the robustness and reliability of the data generated in the clinical trial, accurate reporting and interpretation, effective monitoring by the sponsor and effective inspection by Member States or the Commission.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 148
Richard Seeber

Proposal for a regulation
Recital 37

Text proposed by the Commission	*Amendment*
(37) The information generated in the clinical trial should be recorded, handled and stored adequately for the purpose of ensuring subject rights ***and safety***, the robustness and reliability of the data generated in the clinical trial, accurate reporting and interpretation, effective monitoring by the sponsor and effective inspection by Member States or the Commission.	(37) The information generated in the clinical trial should be recorded, handled and stored adequately for the purpose of ensuring subject rights***,*** safety ***and well-being***, the robustness and reliability of the data generated in the clinical trial, accurate reporting and interpretation, effective monitoring by the sponsor and effective inspection by Member States or the Commission.

Or. en

Justification

According to Article 3 of the proposed Regulation and to Article 6 of the World Medical Association of Helsinki on Ethical principles for medical research involving human subjects (Seoul 2008), priority should be given to the safety, rights and well-being of individuals.

Amendment 149
Alda Sousa

Proposal for a regulation
Recital 37

Text proposed by the Commission	*Amendment*
(37) The information generated in the clinical trial should be recorded, handled and stored adequately for the purpose of ensuring subject rights ***and*** safety, the robustness and reliability of the data	(37) The information generated in the clinical trial should be recorded, handled and stored adequately for the purpose of ensuring subject rights***,*** safety ***and well-being, and*** the robustness and reliability of

generated in the clinical trial, accurate reporting and interpretation, effective monitoring by the sponsor and effective inspection by Member States or the Commission.	the data generated in the clinical trial, accurate reporting and interpretation, effective monitoring by the sponsor and effective inspection by Member States or the Commission.

Or. en

Justification

To be consistent with Article 3 of the proposed Regulation

Amendment 150
Christel Schaldemose

Proposal for a regulation
Recital 37 a (new)

Text proposed by the Commission	*Amendment*
	(37a) Within two years after the adoption of this Regulation, the Commission should submit the European Parliament an evaluation of the management of raw data, and the feasibility of introducing an open access for independent scientists to raw data from all clinical trials.

Or. en

Amendment 151
Roberta Angelilli

Proposal for a regulation
Recital 38

Text proposed by the Commission	*Amendment*
(38) In order to be able to demonstrate compliance with the protocol and with this Regulation, a clinical trial master file, containing relevant documentation to allow effective supervision (monitoring by	***deleted***

the sponsor and inspection by Member States and the Commission), should be kept by the sponsor and by the investigator. The clinical trial master file should be archived appropriately to allow for supervision after the clinical trial has ended.

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 152
Roberta Angelilli

Proposal for a regulation
Recital 39

Text proposed by the Commission	*Amendment*
(39) Medicinal products intended for research and development trials fall outside the scope of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Such medicinal products include medicinal products used in the context of a clinical trial. They should be covered by specific rules taking account of their peculiarities. In establishing these rules, a distinction should be made between investigational medicinal products (the tested product and its reference products, including placebos) and auxiliary medicinal products (medicinal products used in the context of a clinical trial but not as investigational medicinal products), such as medicinal products used for background treatment, challenge agents, rescue medication, or used to assess end-points in a clinical trial. Auxiliary	***deleted***

medicinal products should not include concomitant medications, i.e. medications unrelated to the clinical trial and not relevant for the design of the clinical trial.

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 153
Roberta Angelilli

Proposal for a regulation
Recital 40

Text proposed by the Commission	*Amendment*
(40) In order to ensure subject safety and the reliability and robustness of data generated in a clinical trial, and in order to allow for the distribution of investigational and auxiliary medicinal products to clinical trial sites throughout the Union, rules on the manufacturing and importation of both investigational and auxiliary medicinal products should be established. As is already the case for Directive 2001/20/EC, those rules should reflect the existing rules of good manufacturing practices for products covered by Directive 2001/83/EC. In some specific cases, it should be possible to allow deviations from those rules in order to facilitate the conduct of a clinical trial. Therefore, the applicable rules should allow for some flexibility, provided that subject safety, as well as reliability and robustness of the data generated in the clinical trial are not compromised.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 154
Roberta Angelilli

Proposal for a regulation
Recital 41

Text proposed by the Commission	*Amendment*
(41) Investigational and auxiliary medicinal products should be appropriately labelled in order to ensure subject safety and the reliability and robustness of data generated in a clinical trial, and in order to allow for the distribution of those products to clinical trial sites throughout the Union. The rules for labelling should be adapted to the risks to subject safety and the reliability and robustness of data generated in a clinical trial. Where the investigational or auxiliary medicinal product have already been placed on the market as an authorised medicinal product in accordance with Directive 2001/83/EC, as a general rule no additional labelling should be required for open-label trials. Moreover, there are specific products, such as radiopharmaceuticals used as diagnostic investigational medicinal product, where the general rules on labelling are inappropriate in view of the very controlled setting of the use of radiopharmaceuticals in clinical trials.	***deleted***

Or. en

Justification

The GCP ICH guideline should be part of the Regulation and therefore become an annex.

Amendment 155
Philippe Juvin

Proposal for a regulation
Recital 41

Text proposed by the Commission	*Amendment*
(41) Investigational and auxiliary medicinal products should be appropriately labelled in order to ensure subject safety and the reliability and robustness of data generated in a clinical trial, and in order to allow for the distribution of those products to clinical trial sites throughout the Union. The rules for labelling should be adapted to the risks to subject safety and the reliability and robustness of data generated in a clinical trial. Where the investigational or auxiliary medicinal product have already been placed on the market as an authorised medicinal product in accordance with Directive 2001/83/EC, as a general rule no additional labelling should be required for open-label trials. Moreover, there are specific products, such as radiopharmaceuticals used as diagnostic investigational medicinal product, where the general rules on labelling are inappropriate in view of the very controlled setting of the use of radiopharmaceuticals in clinical trials.	(41) Investigational and auxiliary medicinal products should be appropriately labelled in order to ensure subject safety and the reliability and robustness of data generated in a clinical trial, and in order to allow for the distribution of those products to clinical trial sites throughout the Union. The rules for labelling should be adapted to the risks to subject safety and the reliability and robustness of data generated in a clinical trial. ***In medium- or low-risk trials,*** where the investigational or auxiliary medicinal product have already been placed on the market as an authorised medicinal product in accordance with Directive 2001/83/EC, as a general rule no additional labelling should be required for open-label trials***. Instead of a useless and inappropriate product labelling, and in line with GMP 2009 (Annex 13, Article 27), the participants to such researches could be given a leaflet or card which provides useful information on the trial and be instructed to keep this in their possession at all times***. Moreover, there are specific products, such as radiopharmaceuticals used as diagnostic investigational medicinal product, where the general rules on labelling are inappropriate in view of the very controlled setting of the use of radiopharmaceuticals in clinical trials.

Or. en

Justification

Stratification based on the marketing authorisation status clarifies this provision.

Amendment 156
Roberta Angelilli

Proposal for a regulation
Recital 44

Text proposed by the Commission	*Amendment*
(44) The sponsor of a clinical trial may be located in a third country. In order to facilitate supervision and control, a sponsor located in a third country should establish a ***contact person*** in the Union to allow for the competent authority of the Member State concerned to communicate with the sponsor. ***That contact person may be a legal or a natural person.***	(44) The sponsor of a clinical trial may be located in a third country. In order to facilitate supervision and control, a sponsor located in a third country should establish a ***legal representative*** in the Union to allow for the competent authority of the Member State concerned to communicate with the sponsor.

Or. en

Justification

The presence of a legal representative and not only a contact person is necessary to facilitate supervision, control most of all in case of liability of sponsor even if it is established in third countries

Amendment 157
Riikka Manner

Proposal for a regulation
Recital 46

Text proposed by the Commission	*Amendment*
(46) In clinical trials with non-authorised investigational medicinal products, or where the intervention poses more than an insignificant risk to subject safety, compensation should be ensured for damages successfully claimed in accordance with the applicable laws.	(46) In clinical trials with non-authorised investigational medicinal products, or where the intervention poses more than an insignificant risk to subject safety, compensation should be ensured for damages successfully claimed in accordance with the applicable laws. ***The legal certainty of the subject should, however, always be guaranteed and the change under the regulation in the***

requirement to provide damage compensation must not lead to a reduction in legal certainty.

Or. fi

Amendment 158
Philippe Juvin, Antonyia Parvanova

Proposal for a regulation
Recital 46

Text proposed by the Commission	*Amendment*
(46) In clinical trials with non-authorised investigational medicinal products, or where the ***intervention*** poses more than an insignificant risk to subject safety, compensation should be ensured for damages successfully claimed in accordance with the applicable laws.	(46) In clinical trials with non-authorised investigational medicinal products, or ***with authorised investigational medicinal products used outside the terms of the marketing authorisation in a treatment regimen distinct from the standard of care, or*** where the ***diagnostic procedure*** poses more than an insignificant risk to subject safety, compensation should be ensured for damages successfully claimed in accordance with the applicable laws.

Or. en

Justification

Compensation should also be secured when an authorised investigational medicinal product is used outside the standard of care, or when the diagnostic procedure (a better wording than intervention) poses more than an insignificant risk.

Amendment 159
Theodoros Skylakakis

Proposal for a regulation
Recital 47

Text proposed by the Commission	*Amendment*
(47) At present, such damage	(47) At present, such damage

compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. ***Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance in accordance with those national laws. Therefore, each Member State should establish a national indemnification mechanism which compensates subjects in accordance with the laws of that Member State.***	compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator.

Or. el

Justification

Clinical trials generate both benefits and, under certain circumstances, risks. If these are compensated by national indemnification mechanisms, the final costs will be passed on to the nationals of the Member State concerned.

Amendment 160
Cristian Silviu Buşoi

Proposal for a regulation
Recital 47

Text proposed by the Commission	*Amendment*
(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without	(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without

prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are ***disproportionately*** high***. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance*** in accordance with ***those national laws. Therefore, each*** Member State ***should establish a*** national indemnification mechanism which ***compensates subjects in accordance with the laws of that Member State***.

prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are high***, especially for non-commercial sponsors. In order to facilitate the provision of damage compensation by non-commercial sponsors, each Member State should establish a national indemnification mechanism which compensates subjects*** in accordance with ***the laws of that*** Member State***. The use of the*** national indemnification mechanism ***should be free of charge or at a moderate cost and should be limited to clinical trials*** which ***are not intended to be used for obtaining a marketing authorisation for a medicinal product***.

Or. en

Amendment 161
Roberta Angelilli

Proposal for a regulation
Recital 47

Text proposed by the Commission	*Amendment*
(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance in accordance with those national laws.	(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. ***Compensation may also cover medical care for long or medium term physical injuries, pain and suffering.*** Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of

Therefore, each Member State should establish a national indemnification mechanism which compensates subjects in accordance with the laws of that Member State.	a multinational trial to obtain insurance in accordance with those national laws. Therefore, each Member State should establish a national indemnification mechanism which compensates subjects in accordance with the laws of that Member State***, and provide patients with clear and accessible information to facilitate the access to the compensation systems***.

Or. en

Justification

It *is established in current legal framework at national and international level that that compensation may consist of a sum of money to compensate psychological and social harms and economical losses, and it may cover medical care for the long or medium term physical injuries. Furthermore, doctrine demonstrate that it is quite difficult for research participants to access to compensation under current national laws including a set of limits and conditions that are unknown before the starting of the trial.*

Amendment 162
Riikka Manner

Proposal for a regulation
Recital 47

Text proposed by the Commission	*Amendment*
(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance in	(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance in

accordance with those national laws. Therefore, each Member State should establish a national indemnification mechanism which compensates subjects in accordance with the laws of that Member State.	accordance with those national laws. Therefore, each Member State should establish a national indemnification mechanism which compensates subjects in accordance with the laws of that Member State. ***However, traditional insurance-based solutions are regarded as acceptable national compensation mechanisms or as an independent solution.***

Or. fi

Amendment 163
Georgios Koumoutsakos

Proposal for a regulation
Recital 47

Text proposed by the Commission	*Amendment*
(47) At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance in accordance with those national laws. ***Therefore, each Member State should establish a national indemnification mechanism which compensates subjects in accordance with the laws of that Member State.***	(47)At present, such damage compensation is provided by way of insurance. This insurance may cover damages to be paid to the subject by the sponsor and investigator in the case of established liability. It may also compensate the subject directly without prior establishment of the liability of the sponsor or investigator. Experience shows that the insurance market is small and costs for insurance coverage are disproportionately high. Moreover, as liability regimes differ widely between Member States, it is difficult and burdensome for the sponsor of a multinational trial to obtain insurance in accordance with those national laws. ***The Member States shall take measures to encourage academic research. To this end, it would be appropriate to examine the possibility of introducing special indemnification mechanisms at European level. Use of these mechanisms could involve the payment of fees on a non-profit-making basis, taking account of the risks of clinical trials, possible damage***

and anticipated benefits for participants.

Or. el

Justification

While the initial proposal goes in the right direction, it will not be of equal benefit to all patients. Not all Member States have the experience or expertise for national mechanisms, resulting in two-tier patient services. Hence patients taking part in the same cross-border research programme will receive different treatment in different countries. One solution might be the introduction of special indemnification mechanisms based on experience and scope for cooperation at European level.

Amendment 164
Christel Schaldemose

Proposal for a regulation
Recital 51

Text proposed by the Commission	*Amendment*
(51) In order to streamline and facilitate the flow of information between sponsors and Member States as well as between Member States, the Commission should set up and maintain a database, accessed through a portal.	(51) In order to streamline and facilitate the flow of information between sponsors and Member States as well as between Member States, the Commission should set up and maintain a database, accessed through a portal. ***The Commission and the Member States should raise awareness among the general public about the existence of this portal.***

Or. en

Amendment 165
Dagmar Roth-Behrendt

Proposal for a regulation
Recital 51

Text proposed by the Commission	*Amendment*
(51) In order to streamline and facilitate the flow of information between sponsors and Member States as well as between Member States, the Commission should set up and maintain a database, accessed through a portal.	(51) In order to streamline and facilitate the flow of information between sponsors and Member States, the ***European Medicines Agency, on behalf of the*** Commission***,*** should set up and maintain a database, accessed through a portal.

Or. en

Amendment 166
Françoise Grossetête, Marina Yannakoudakis, Thomas Ulmer, Philippe Juvin

Proposal for a regulation
Recital 52

Text proposed by the Commission	*Amendment*
(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.	(52) The database should contain all relevant information as regards the clinical trial ***and allow public dissemination of objective information in order to support European research and to increase knowledge in the field of public health. It should not undermine innovation or competitiveness of European industries***. No personal data of data subjects participating in a clinical trial should be recorded in the database***, and it should not hamper the protection of commercial interests, including intellectual property, as provided for by Article 4 of Regulation 1049/2001***. 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***, or commercially confidential information, as foreseen by Article 4 of Regulation 1049/2001.***

Or. en

Justification

The database should allow public dissemination of reliable information on the latest advances of medical research, all the while respecting the competitiveness imperatives of the pharmaceutical industry, which finances in itself approximately 60 % of European clinical trials. Public disclosure should protect personal data and commercially confidential information, in order to avoid any stigmatisation of patients taking part in a clinical trial and in order to avoid stimulating unfair competition which would threaten the competitiveness of European medical research.

Amendment 167
Petru Constantin Luhan

Proposal for a regulation
Recital 52

Text proposed by the Commission	*Amendment*
(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.	(52) The database should contain all relevant information as regards the clinical trial. ***All clinical trials should be registered in the database prior to being started. The start and end dates of the recruitment of subjects should also be published in the database. It should be possible for sponsors to enter this information directly into the database without the need to further notify Member States.*** 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.

Or. en

Justification

currently several countries require notification of the first patient entered, and the paperwork associated with this is far too cumbersome for the kind of information which can just be directly inserted into the EU database. We would also suggest, that for international trials only the first and last patient for the study should be reported (not by country). At the end of recruitment, the sponsor should also be able to tick those countries which eventually did not recruit patients.

Amendment 168
Corinne Lepage

Proposal for a regulation
Recital 52

Text proposed by the Commission	*Amendment*
(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.	(52) The database should contain all relevant information as regards the clinical trial ***and should be publicly accessible***. 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.

Or. en

Amendment 169
Françoise Grossetête, Marina Yannakoudakis, Thomas Ulmer, Frédérique Ries, Philippe Juvin

Proposal for a regulation
Recital 52 a (new)

Text proposed by the Commission	*Amendment*
	(52a) Commercially confidential

information should be identified and protected in order to avoid harming the interests of patients and/or the competitive position of the sponsors.

Or. en

Justification

Public disclosure of information should guard protected personal data and commercially confidential information, in order to avoid any stigmatisation of patients taking part in a clinical trial and to avoid stimulating unfair competition which would threaten the competitiveness of European medical research.

Amendment 170
Antonyia Parvanova

Proposal for a regulation
Recital 52 b (new)

Text proposed by the Commission	*Amendment*
	(52b) Results of clinical trials, as well as clinical trial data, represent a relevant and valuable source of information for the continuation of biomedical or public health research on a medicinal product or active principle, and should be made available in order to support and foster the development of independent research related to a medicinal product and its clinical, pharmacological or other pharmacodynamic effects, or to its relative efficacy and effectiveness. The authorisation status of a medicinal product should however be duly considered before releasing data from clinical trial, in order not to disrupt the marketing authorisation process or the competition dynamics operating on the EU market while fostering attractiveness and long term viability of the EU based clinical research.

Or. en

Amendment 171
Antonyia Parvanova

Proposal for a regulation
Recital 52 c (new)

Text proposed by the Commission	*Amendment*
	(52c) Access to, release and processing of clinical trial data for medicines once the decision-making process on an application for a marketing authorisation is complete should be without prejudice to the protection of personal data, and should respond to specific guidelines in order to define and guarantee good analysis practice, clinical trial data formats, rules of engagement as well as other legal aspects. Such guidelines should promote an optimal level of transparency and public information, while ensuring the development of reliable scientific research and avoiding bias or misuse of information.

Or. en

Amendment 172
Georgios Koumoutsakos

Proposal for a regulation
Recital 55

Text proposed by the Commission	*Amendment*
(55) In order to carry out the activities provided for in this Regulation, Member States should be allowed to levy fees. ***However, Member States should not require multiple payments to different bodies assessing, in a given Member State, an application for authorisation of a clinical trial.***	(55) In order to carry out the activities provided for in this Regulation, Member States should be allowed to levy fees ***in accordance with the practices followed by each.***

Or. el

Amendment 173
Corinne Lepage

Proposal for a regulation
Recital 59 a (new)

Text proposed by the Commission	*Amendment*
	(59a) The right of access to documents is recognised by the Charter of Fundamental Rights of the European Union. In particular, Article 42 states the right of access to documents of the institutions, bodies, offices and agencies of the Union, regardless of the medium of the document. Those rules should be upheld.

Or. en

Amendment 174
Philippe Juvin

Proposal for a regulation
Recital 60

Text proposed by the Commission	*Amendment*
(60) Without prejudice to the national systems for the cost and reimbursement of medical treatments, subjects should not have to pay for investigational medicinal products.	(60) Without prejudice to the national systems for the cost and reimbursement of medical treatments, subjects should not have to pay for investigational medicinal products. ***For the low-risk trial, and the medium-risk trials (when the treatment regimen represents the standard of care), and when registration is not the initial objective of the investigator-initiated trial, the cost of the investigational medicinal product should be borne by the national healthcare system.***

Or. en

Justification

Trials comparing authorised products within their licenced indication or in regimens corresponding to the standard of care should be facilitated. As the treatment would be prescribed anyway, this does not impact the budget of the healthcare systems.

Amendment 175
Rebecca Taylor, Antonyia Parvanova

Proposal for a regulation
Recital 62 a (new)

Text proposed by the Commission	*Amendment*
	(62a) According to the Commission Communication on "An Integrated Industrial Policy for the Globalisation Era-Putting Competitiveness and Sustainability at Centre Stage", systematic evaluation of legislation should become an integral part of smart regulation. To ensure that this Regulation keeps pace with scientific, technological and medical progress with regard to the organization and conduct of clinical trials and that it interfaces with other legal provisions, the Commission should periodically report on the experience with and functioning of the Regulation, and present its conclusions to the Parliament and Council.

Or. en

Justification

Advances in technology and medical knowledge mean that Clinical Trials are rapidly evolving. A review clause will ensure that the Regulation reacts quickly to any necessary changes.

Amendment 176
Anna Rosbach

Proposal for a regulation
Recital 64 a (new)

Text proposed by the Commission	*Amendment*
	(64a) As stated in the Commission Communication on "An Integrated Industrial Policy for the Globalisation Era-Putting Competitiveness and Sustainability at Centre Stage", systematic evaluations of legislation should become an integral part of smart regulation. To ensure that this Regulation keeps pace with scientific and technological progress with regard to the organization and conduct of clinical trials and that it interfaces with other legal provisions, the Commission should periodically report on the experience with and functioning of the Regulation, and present its conclusions thereof.

Or. en

Justification

A regular review of the Regulation has to be established in order to ensure that the Regulation remains "fit for purpose" and is able to support advances in science and technology.

Amendment 177
Roberta Angelilli

Proposal for a regulation
Recital 63

Text proposed by the Commission	*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 and good clinical practice, which has its origins in the Declaration of Helsinki.	(63) This Regulation is in ***accordance with the Convention on Human Rights and Biomedecine (1997) and its Additional Protocol on biomedical research (2005) of the Council of Europe and the International Convention on the rights of the Child (UN-1989). It is*** 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 ***ICH-GCP*** good clinical practice, which has its origins in the Declaration of Helsinki. ***The WHO-CIOMS guidelines are also taken into account.***

Or. en

Justification

The EU Regulation has to be consistent with international treaties such as the Convention on Human Rights and Biomedecine (1997) and its Additional Protocol on biomedical research (2005) of the Council of Europe and the International Convention on the rights of the child, that have been ratified by many EU member States.

Amendment 178
Richard Seeber

Proposal for a regulation
Recital 66

Text proposed by the Commission	*Amendment*
(66) Since the objective of this Regulation, namely to ensure that, throughout the Union, clinical trial data are reliable and robust while ensuring the safety and rights of subjects, cannot sufficiently be achieved by the Member States and can, by reason of the scale of the measure, be better achieved at Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,	(66) Since the objective of this Regulation, namely to ensure that, throughout the Union, clinical trial data are reliable and robust while ensuring the safety and rights ***and well-being*** of subjects, cannot sufficiently be achieved by the Member States and can, by reason of the scale of the measure, be better achieved at Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,

Or. en

Justification

According to Article 3 of the proposed Regulation and to Article 6 of the World Medical Association of Helsinki on Ethical principles for medical research involving human subjects (Seoul 2008), priority should be given to the safety, rights and well-being of individuals.

Amendment 179
Alda Sousa

Proposal for a regulation
Recital 66

Text proposed by the Commission	*Amendment*
(66) Since the objective of this Regulation, namely to ensure that, throughout the Union, clinical trial data are reliable and robust while ensuring the safety and rights of subjects, cannot sufficiently be achieved by the Member States and can, by reason of the scale of the measure, be better achieved at Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,	(66) Since the objective of this Regulation, namely to ensure that, throughout the Union, clinical trial data are reliable and robust while ensuring the safety***, well-being*** and rights of subjects, cannot sufficiently be achieved by the Member States and can, by reason of the scale of the measure, be better achieved at Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,

Or. en

Justification

To be consistent with Article 3 of the proposed Regulation.

Amendment 180
Riikka Manner, Eija-Riitta Korhola

Proposal for a regulation
Recital 66 a (new)

Text proposed by the Commission	*Amendment*
	(66 a) The regulation should be assessed and where necessary revised at five-year intervals in order to ensure its flexibility. A continuing assessment process is essential so that innovations can continue to be made in future in the context of constantly developing medical science. The administrative burden of the current directive is regarded as a constraint on science and on the right of patients to obtain the best possible care. The regulation's impact in terms of red tape should therefore be monitored regularly and the assessment process should guarantee its effectiveness as legislation supporting clinical research. Particular attention should be paid to the position of academic research, and to ensuring that red tape does not divert resources from innovation in academic research and that the new tasks required by the regulation do not have a negative impact on the attractiveness of a research career. The importance of public access to information in making Europe attractive as a research environment and its effect on the balance between individual data protection, intellectual property, and contract, patent and intangible rights, should also be assessed. The assessment process should also look at the impact of the regulation on whether, in place of clinical trials, more experimental treatment is being carried out which has unpredictable effects on patient safety and the reliability of experimental results.

Or. fi