**EPF draft position paper for consultation.**

**Please do not share externally.**

**Clinical Trials Regulation: Informed consent and information to patients**

 16/02/2016

Contents

[1. Introduction 3](#_Toc443379638)

[2. The EU Regulation 3](#_Toc443379639)

[General provisions for informed consent 4](#_Toc443379640)

[Provisions for specific populations 5](#_Toc443379641)

[Children 7](#_Toc443379642)

[Breastfeeding or pregnant women 8](#_Toc443379643)

[Trials in emergency situations 9](#_Toc443379644)

[Simplified informed consent in cluster trials 10](#_Toc443379645)

[3. Information to patients – an ongoing process 11](#_Toc443379646)

[4. Informed consent and technology 12](#_Toc443379647)

[Electronic / online consent and information tools 13](#_Toc443379648)

[Citizen science 14](#_Toc443379649)

[Consent to use of one’s data in future research 14](#_Toc443379650)

[5. Patient involvement 15](#_Toc443379651)

[Selected References 17](#_Toc443379652)

# Introduction

Informed consent is a core prerequisite for enrolling any person in a clinical trial. It is a patient’s right and a fundamental principle of medical ethics, enshrined in the Declaration of Helsinki and other international conventions and regulations, such as the European Convention on human rights in biomedicine (the Oviedo Convention) and its additional protocols and the CIOMS guidelines.[[1]](#footnote-1)

Informed consent is not simply a process of providing information to the patient. Neither is it about obtaining a signature on a form. From a patient’s perspective, informed consent should be seen as a process, a kind of “decision aid” that should enable a patient to make an *enlightened decision* – in the words of the Nuremberg Code, the 1947 precedent of the Declaration of Helsinki – about whether or not to participate in the study

Regrettably, this is largely not the case. There are still disparities across the EU, both in terms of the quality and quantity of the information provided to patients, and the effectiveness of the informed consent process.[[2]](#footnote-2) Consent is still often regarded as a ritual or a box-ticking exercise, rather than a crucial means by which patients are able to fully comprehend and evaluate the risks and potential benefits they will be taking in participating in a clinical trial.[[3]](#footnote-3) Patients, not surprisingly, often do not recognise written consent as serving their interest, but rather the interest of researchers and hospitals.[[4]](#footnote-4)

As EPF pointed out in its input into the legislative process, the patient community does not regard the ethical aspects of clinical trials as a national issue. On the contrary, in our view better European co-operation is essential to ensure benefits for patients and high-quality of clinical trials in Europe, therefore supporting Europe’s future competitiveness in research.

The new Regulation will be guiding clinical trials in the EU for many years. Meanwhile, the medical landscape is changing fast: innovation has potential to transform the lives of patients with serious, lifelong conditions; but resources are limited and need to be focused on innovation that provides real value. There is a pressing need for new kinds of partnerships – between researchers, regulators, academia, industry and patients – to move from doing research “on patients” to doing (better) research *with* patients.

# The EU Regulation

There are many positive aspects to the new EU Regulation; EPF welcomed the single submission through an electronic portal and the streamlined application process with tighter timelines that should lead to closer collaboration between competent authorities in ethics committees at national level. Overall, the hope is the new rules will make the clinical trials registration and evaluation process quicker and more efficient whilst maintaining quality.

We also warmly welcomed the stronger transparency provisions, and called for EU guidance on the development of the “lay summary” of clinical trials results – a process which is now ongoing.

We are also pleased that the Regulation is more specific regarding the quality of information given to patients and the process of informed consent (Articles 28 and 29).

However, we regretted the Council’s deletion of the European Parliament’s provision for a process to develop EU-level guidelines addressing the core elements and main principles of information and informed consent. This was critical, given the current unacceptable divergence in the quality and quantity of information referred to above.

Below, we will address the specific provisions of the Regulation.

## General provisions for informed consent

Information and consent are included under Chapter V, “Protection of subjects and informed consent”. Article 28 gives the general rules, such as the fact that informed consent must have taken place, no undue influence is exerted, the right to withdraw from the study at any time, and that the patient or their representatives are given contact details where they can obtain more information.

Article 29 outlines the specific conditions for informed consent. This shall be preferably written and must be documented, and the patient must be given a copy of the document or record. The patient must be given sufficient time to consider the decision. (The provision about time was inserted following EPF’s request.)

Paragraph 2 explains what information must be given and how (these provisions were made more specific based on EPF’s request).

* The information must enable the person to understand
	+ “the nature, objectives, benefits, implications, risks and inconveniences of the clinical trial”;
	+ their rights, including the right to refuse to participate and the right to withdraw;
	+ the conditions of the trial, such as its duration; and
	+ “the possible treatment alternatives, including the follow-up measures if the participation of the subject in the clinical trial is discontinued”.
* The information must be “comprehensive, concise, clear, relevant, and understandable to a layperson”.
* It must be provided in an interview with someone who is appropriately qualified. “Special attention shall be paid to the information needs of specific patient populations and of individual subjects, as well as to the methods used to give the information.” Also, “it shall be verified that the subject has understood the information.”
* The patient must be told about what damage compensation system applies.
* They must be given the EU trial registration number and told about the availability of the results on the EU database, if possible with an indication of when the result may be available.

The information must be available in writing.

**EPF comments:**

In our view, good information is a fundamental patients’ right, regardless of where in the EU a clinical trial takes place, and this is not a matter that can be left to individual Member States. EPF believes that there must be certain core elements of information and informed consent that should be the same across the EU, while other aspects can be adjusted according to local needs. Indeed, our proposal was that “core” consent should be part of the joint assessment. Unfortunately, this is not reflected in the final text.

However, we believe that even for the purpose of implementing Article 29 of the Regulation, and for evaluating the implementation and member states’ compliance with the provisions, there is a need for guidance at EU level.

This is a vital step towards ensuring that every person in the EU will have access to high-quality information and informed consent, regardless of in which Member State they happen to reside. Moreover, if there is no common benchmark, there is a risk that some countries may be less strict in their implementation of the requirements of consent in order to attract trials.

**EPF recommendations:**

1. **EU guidelines/core elements.**

Common guidance should be developed at EU level, for example through an expert group consisting of patients and other stakeholders, combined with a public consultation. The process should be facilitated by the European Commission.

1. **Evaluating the consent process.**

Often problems for patients lie in the process of consent. This is difficult to evaluate, but EPF believes that the process itself should be the subject of evaluation. There should be a reflection in the EU guidance on the criteria for evaluation and how this could be done in practice, for example by recording examples.

## Provisions for specific populations

The Regulation includes several Articles laying out the rules for informed consent in research involving persons for incapacitated, children, women who are pregnant or breastfeeding, and persons who are unable to give informed consent because they are in an emergency situation.

In all of these cases, the general principles of article 28 must be fulfilled and additional requirements are given. Article 10 also specifies that whenever the trial participants may be representing “vulnerable populations”, the ethics review must include specific expertise.

**Incapacitated persons**

Article 31 specifies that a trial can only be conducted involving incapacitated persons if the following specific conditions are met:

* the legally designated representative has provided informed consent
* the incapacitated person has received the information required under Article 29(2) “in a way that is adequate in view of their capacity to understand it”
* the explicit wishes of the incapacitated person are respected
* there are no incentives or financial inducements beyond compensation for expenses
* the trial is essential and “data of comparable validity” cannot be obtained in other ways
* the trial relates directly to a medical condition of the person
* there are scientific grounds for expecting the trial to produce either direct benefit to the person, which outweighs the risks/burdens, or benefit for the patient population that “relates directly to the life-threatening or debilitating medical condition from which the subject suffers”
* the trial will pose only “minimal risk” and “minimal burden” compared with standard treatment.
* The person “shall as far as possible take part in the informed consent procedure”.

The Article remarks that more stringent national rules in some member states must be respected (e.g., requirement that the study have potential direct benefit to the person, not only the patient group).

**EPF comments:**

EPF is broadly satisfied with these provisions. The following recommendations are based on feedback from our member organisation Alzheimer Europe.

We note that the wording “relates directly to the life-threatening or debilitating medical condition from which the subject suffers” implies that research subjects who lack capacity can participate in trials for conditions *other than that which causes their incapacity*. For example, research subjects with a rare life-threatening cancer, but also dementia, should be allowed the opportunity to participate in a trial on the rare cancer so that they are treated equally with those who have capacity. We wish to uphold the principle of equity: people with dementia and other causes of mental incapacity should not be disadvantaged just because of their incapacity.

There may be rare occasions when people with such conditions are unable to voice their views (e.g. people with profound learning disabilities) when opinions from relatives and other carers may be appropriate. However, in principle the people concerned are best placed to decide on the need for “protection” and weigh this up against the potential benefits of research. This is important because ethics committees and other regulatory bodies may err on the side of *over-protection* and impede scientific advances that would benefit these patients. To facilitate the participation of persons with diminished capacity in research trials and enable them to make an informed choice, it is important to have “easy read” versions of all the documents available.

We would also recommend that the views of people representing the target population should be sought whenever possible, as they can provide advice on personal ethical and practical questions regarding trials in such populations. Patient organisations can identify such individuals, or can be consulted as representatives of their members.

Alzheimer Europe’s publication *The Ethics of Dementia Research* [[5]](#footnote-5) gives recommendations on informed consent to dementia research. These recommendations cover the assessment of capacity to consent to research; the provision of information, willingness to and factors affecting consent to research; ongoing consent and withdrawal from the study; issues surrounding loss of capacity to consent; the involvement of third parties in the consent process; advance directives for research; proxy decision-makers; issues surrounding the further use of data; and the restrictions on the right to participate in research.

**EPF recommendations:**

* In designing and assessing trials involving minors or vulnerable groups, the views of representatives of the target population should be sought whenever possible.
* In trials involving persons with diminished capacity, information and informed consent documents should always be made available in “easy read” versions to facilitate informed decision.
* Persons with dementia or other form of incapacity should be supported as much as possible to take part in appropriate clinical trials. They should not be excluded from clinical trials purely based on the incapacity.
* Alzheimer Europe’s recommendations could be used as a basis for a European template for informed consent involving persons with diminished capacity.

## Children

Article 32 lays out the rules on clinical trials in children (called “minors” in the Regulation, due to the differences in the legal definition in member states). Trials can only be conducted in children if the additional conditions set out in this article (in addition to Article 28) are met. These are similar to the conditions for incapacitated persons:

* informed consent given by legally designated representatives
* the information under Article 29 has been given “in a way adapted to their age and mental maturity and from investigators or members of the investigating team who are trained or experienced in working with children”
* the explicit wishes of the child are respected
* no undue inducements are given
* the trial investigates a condition where research in children is essential, either because the condition only occurs in children or the trial is needed to validate data obtained in other ways
* the trial relates directly to the condition from which the child suffers, or it must be of such a nature that can only be carried out on children
* there are scientific reasons for expecting benefit either directly for the child concerned (outweighing the risks and burdens) or for the population represented by the child
* the trial must only post “minimal risk” and minimal burden” compared to standard treatment.

The child must be involved in the informed consent process in a way adapted to their age and maturity; and if they reach the age of legal competence during the trial they must re-consent. In addition, Recital 32 clarifies that in principle children should also give their assent to the participation.

**EPF comments:**

These provisions seem reasonable.

During the legislative process EPF did not comment on these provisions, as we did not have sufficient expertise in paediatric research. They appear satisfactory, but if you have specific points or recommendations you wish to make please do so.

## Breastfeeding or pregnant women

Under the Regulation, trials on pregnant or breastfeeding women can only take place if specific conditions are met (in addition to Article 28):

* the trial has the potential to produce a direct benefit for the pregnant or breastfeeding woman concerned, or her embryo/foetus/child after birth, outweighing the risks and burdens
* if the trial has no such direct benefit it can be done only if:
	+ a trial of comparable effectiveness cannot be carried out otherwise
	+ the trial contributes to potential benefits for “pregnant or breastfeeding women or other women in relation to reproduction or other embryos, foetuses or children”
	+ the trial poses a “minimal risk” and minimal burden on the woman concerned and her embryo/foetus/child after birth
* particular care must be taken to avoid any adverse impact on the health of the child
* no undue incentives or financial inducements are given.

**EPF comments:**

These provisions seem reasonable.

During the legislative process EPF did not comment on these provisions, as we did not have sufficient expertise. They appear satisfactory, but if you have specific points or recommendations you wish to make please do so.

## Trials in emergency situations

Previously, the EU Clinical Trials Directive did not provide clear rules on trials in emergency situations, and this was identified as a major gap. Article 35 provides essentially a derogation from the requirement of the patient having been informed and then having given informed consent to the trial. In certain emergency situations, it is not possible to go through the informed consent procedure and obtain the consent of the patient or even a legal representative prior to the intervention, as time can be of the essence. It is important to bear in mind that consent is not waived in such cases, but it is postponed.

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.” (Recital 36)

The following conditions apply:

* the situation must be urgent, caused by a sudden life-threatening or other sudden serious medical condition due to which the person is unable to receive information or provide prior informed consent
* there are scientific grounds to expect the trial to produce “direct clinically relevant benefit for the subject resulting in a measurable health-related improvement alleviating the suffering and/or improving the health of the subject, or in the diagnosis of its condition”
* there is no time to obtain prior informed consent (within the “therapeutic window”)
* there are no known previous objections from the person
* the trial relates directly to the person’s medical condition that caused the emergency, and the trial cannot be done in non-emergency situations
* the trial poses “minimal risk” and “minimal burden” compared with standard treatment.

Informed consent must be sought as soon as possible following the intervention. If the person does not consent, they must be given an opportunity to refuse to use of the data in the study.

**EPF comments**

In principle, EPF welcomes these new explicit rules, which will facilitate this type of vital research.

The question of who takes the decision on the case of emergency to go ahead with the clinical trial varies between Member States. In principle, this decision should be made by an independent third party, but researchers have argued that obtaining such third-party consent often loses valuable time when the urgency of the situation does not allow for any time to be lost.

**EPF recommendations :**

**Case-by-case assessment.**

It is crucial that emergency studies are carefully assessed by an ethics committee. Where possible, a panel consisting of representatives of the target patient population should be consulted to elicit their views in advance as to whether in a hypothetical case scenario they would themselves wish to be part of a trial.

We do not have any expertise in this type of research and do not intend to make further comments or recommendations on this provision, beyond the above. If you disagree please comment.

## Simplified informed consent in cluster trials

Article 30 discusses so-called “cluster trials”. These are trials conducted only in one member state, mainly in the field of public health. The member state may “allow the investigator to obtain informed consent by the simplified means … provided that all of the conditions set out in paragraph 3 of this Article are fulfilled.”

The simplified means required that the same information as required under Article 29(2) is given before anyone is enrolled in a trial, and the person after being informed does not object.

The conditions simplified consent are that:

* the trial methodology “requires that groups of subjects [“clusters”] rather than individual subjects are allocated to receive different investigational medicinal products in a clinical trial”
* the trial must be a low-intervention one[[6]](#footnote-6) and the products used must be in accordance with their marketing authorisation
* no interventions are used other than standard treatment, and
* the simplified consent is justified in the protocol, and the information as well as the process to give it is described in the protocol.

All refusals and withdrawals must be documented and no data for the trial must be collected from anyone who refuses to participate or has withdrawn.

**EPF comments**

The same information requirements apply in the case of cluster trials as another trials, i.e. the people involved must be given full information on the trial. The conditions seem reasonable.

We do not have any expertise in this type of research and do not intend to make further comments or recommendations on this provision. If you disagree please comment.

# Information to patients – an ongoing process

Meaningful informed consent hinges on the quality of information. Information and health literacy are critical tools for patient empowerment, enabling patients to get more involved in their own health /care. Therefore, the lack of information to patients or it inadequate quality are of paramount importance to patients. As a point of principle, all patients should have easy access to the same high quality of information about clinical trials, regardless of where in the EU they happen to live. However this is not the case.

Patients’ access to quality information is closely linked to their willingness to participate in clinical trials, as well as their commitment and adherence within trials.[[7]](#footnote-7) A lack of information is apparent throughout the clinical trial: patients often do not know how to find a clinical trial and ow to enrol in a trial; they often do not know what they are participating in;[[8]](#footnote-8) and they are not informed of the results or outcomes of the trial in which they participated.

Although the Regulation gives some indication of the type of information that must be given to patients as part of the informed consent process, we already noted that no guidance exists at EU level. Moreover, the question of ongoing information provision is left entirely in the hands of Member States.

What is perceived as high quality information does not differ for patients living in different countries: guidance on the quality of information exists in the form of “core quality principles” adopted in 2008 .[[9]](#footnote-9)

Member States may need to address specific aspects of information documents that are language or culture-bound, but the core elements of information good practices for providing information should be agreed at EU level and implemented across the EU.

**The role of patient organisations**

Many patient organisations have concrete experience of providing information to patients on clinical trials, often using *innovative, user-friendly formats*.[[10]](#footnote-10) EPF has described many examples in our previous statements on clinical trials.[[11]](#footnote-11)

EPF member organisations have concrete experience of providing information on clinical trials. As an example, Europa Donnahas contributed to the EU-funded MINDACT trial for several years and has been responsible for the development, review and dissemination of information and educational materials both for patients (e.g. DVDs, brochures, consent forms and information sheets) and the public (web content, presentations, brochures, training course and media material).

Patient organisations can also provide *peer support* throughout the trials, and also help manage the expectations of participants, by clearly stating what the aim of the study is, and whether patients can realistically expect an immediate personal health benefit from their participation (e.g. a cure, improved survival, or alleviated symptoms). Patients sometimes overestimate the benefits of the treatments being studied in clinical trials, expecting a cure.[[12]](#footnote-12)

The findings of the EU-funded RESPECT project on the needs of children and their families regarding participation in clinical trials suggested that while children and parents decide to participate in trials for reasons that range from expectation of personal benefit to altruism, the concrete reality of a trial is often different from what they had initially thought.[[13]](#footnote-13) There are clearly issues around autonomous and objective decision-making, and around consent and assent: the children rely on the parents, who in turn rely on the doctors. Participants in the RESPECT project suggested that it could be helpful to have a *neutral support figure*, who would provide the information patients and parents/carers need and support their empowerment. Patient organisations, for example, could fulfil such a role if adequately resourced and financed.

Many organisations have extensive experience in producing patient-centred, patient-friendly information on complex scientific and medical issues for the general public, including through online Patient University initiatives.[[14]](#footnote-14) This collective experience and expertise could be much better harnessed and used to improve the patient experience of participation in clinical trials as well as the awareness of the wider public.

**EPF recommendations:**

Patient organisations’ experience and expertise should be better used and more widely shared. Their input should be recognised as a kind of expertise in its own right, and adequately resourced including through grants from public funds.

Question to members: do you wish to include other recommendations?

# Informed consent and technology

The clinical trials regulation will be in place for a long time – even into 2020s or 30s. Meanwhile, the research landscape is changing very fast, eHealth/mHealth resources and tools are proliferating and ”connected health” is becoming reality. The 2014 Eurobarometer on digital health literacy showed that 6 out of 10 people used the Internet to search for health-related information. Most people who did so felt that it improved their knowledge. However, on the average 4 out of 10 people had doubts about the trustworthiness of the information sources (with a great deal of variation depending on the Member State).[[15]](#footnote-15)

“If Web 1.0 was basically pages and links and Web 2.0 added forums and social networking, Web 3.0 is another leap forward. While it is not clear exactly what shape Web 3.0 will take, it will rule around a number of key concepts. These include: universality, the need to be able to run on any platform; accessibility (of data); semantics – data with meaning; interaction with Web apps; BYOD – bring your own device – people want to use their own devices to connect to big systems; big data –“data warehouses”, potential goldmines for researchers; mobility – access on the move; and cloud computing.” [[16]](#footnote-16)

This poses a challenge to clinical trials, especially information and the consent process which has been traditionally focused on paper documents and physical meetings.

**How do we “future proof” informed consent? Please feel free to comment below!**

## Electronic / online consent and information tools

Online tools can be used effectively to provide information to patients in a way that is user-friendly, individually tailored, dynamic and accessible over time according to need. Such tools could be used in much the same way as patient decision aids are in clinical practice, to take a patient through the informed consent process and the decisions involved, with greater understanding and empowerment of the patient during the process.

Online tools can also be used for recruitment, reminders and remote monitoring as well as online adverse reaction reports for real-time collection of safety information. The first FDA-approved trial in the US to be run completely remotely was a study on overactive bladders by by Pfizer, which recruited patients online, consented them remotely and then sent them a mobile phone and the study drug. The informed consent was aided by a video, written material and test. These were well received but the challenge of this trial was that the system was designed to be too complicated and the study did not recruit enough patients.[[17]](#footnote-17)

At a recent conference of the EFGCP, the idea of “dynamic consent” was discussed to adapt to patients’ varying information requirements which can also change over time. This refers to as “a range of approaches and IT tools put together in one conceptual framework to enhance consent and put the patient at centre of decision-making … They can, for example choose how much information they need” - just the basics, a little more, or the fine detail of everything.

On the other hand, web-based tools present specific challenges. Capturing reliable, valid data may be difficult. Focusing on online tools only risks the exclusion of certain patient population groups. Data privacy (from the patient’s perspective) and data reliability (from the research perspective) may be difficult to control. Unblinding of randomised trials happens on the Internet as people connect with others in the study and try to find out which study arm they are in.

**Questions to members:**

* Do you have experience of using online consent?
* How about co-designing electronic information to patients or consent tools? Please provide links to examples, if possible.
* What do you feel are the pros and cons?
* How should the EU Regulatory Framework be adapted to ongoing technological change, assuming that the regulation is going to stay with us for the next 10 to 20 years?

## Citizen science

Citizen science is another emerging theme. In some areas, particularly in rare diseases, patients are increasingly using new kind of tools to conduct their own research. PatientsLikeMe has conducted its own trial into the use of lithium in patients with ALS, “one of the first examples of a really genuine citizen study in which patients decided on and designed the study” which later led to randomised clinical trials.[[18]](#footnote-18)

These developments raise the question of who can and should “do” science, and how. Can patients who are active in research, either by using a tools to monitor and upload their own data or even designing the research, still be called “research subjects”? Or are these genuine moves from protection and paternalism towards partnership: from research “on” patients to research “with” patients?

**Questions to members:**

* Are you aware of patients designing and/or conducting their own trials? Please tell us!
* Any other feedback is welcome

## Consent to use of one’s data in future research

Paragraph 2 of Article 28 states that the patient may be given an opportunity to consent to the use of their data in other research outside the specific study. (This was termed “broad consent” during the legislative process, and was a rather controversial provision.)

Broad consent is often seen as agreeing to future research of a particular type specified at the type of consent; this frees researchers to use the data as long as it is within the scope of the original broad consent. Another possibility is the dynamic model discussed above, where individuals can choose again with regard to each new research application, using an online platform. Thus if their preferences change over time, the dynamic model can accommodate that. Ultimately it remains an opt-in model. One recent proposal was termed “meta-consent”, combining to an extent both approaches.[[19]](#footnote-19)

**EPF comments:**

Whichever term one chooses to use, EPF is supportive of the principle of Article 28(2). Health and medical research contributes to our present level of understanding of the impact of therapies diagnosis and prevention strategies, and to evaluate health policies. The ability to conduct health research depends on data accessibility. Please see EPF’s position on the EU Data Protection Regulation for more information. [[20]](#footnote-20)

We believe that there is more reflection needed on how “broad consent” should be defined, and this needs the close involvement of patients as well as researchers. Patients may, for example, be happy to grant blanket permission for use of their data in specific types of research, or for a specific purpose, or by a specific type of organisation; or they may wish to opt out of specific types of research. The parameters of broad consent should therefore be flexible to take into account individual patients’ preferences and values.

In any case, informed consent in this context should involve a full and frank discussion on data protection and privacy ­– to what extent it is possible to make the patient’s data and identifiable, and what level of protection can be offered in future given the rapid increase in the capacity to store, link and analyse health data from different sources.

**Questions to members:**

* Do you have views this topic, other than what is expressed above?

# Patient involvement

Patients have an obvious and central role in clinical trials: they provide the information and ultimately manage the personal risks attached to participation in trials. Patients therefore have a moral right to be involved in the way clinical trials are developed, managed and evaluated. Fortunately, this is now increasingly acknowledged as a priority in all aspects of healthcare, including research.

Meaningful Patient involvement is vital for better informed consent and information to patients: they can review the documents and processes for informed consent to ensure that all information is relevant, comprehensive and clearly understandable for patients, and that it is presented in a patient friendly language.

**The Regulation recommends but does not mandate patient involvement**

The new Regulation recommends but does not make it mandatory for patients to be involved in reviewing trial applications. Article 9 merely states that “At least one layperson shall participate in the assessment.” The article also requires that all persons involved in the assessment “do not have conflicts of interest, are independent of the sponsor, of the clinical trial site and the investigators involved and of persons financing the clinical trial, as well as free of any other undue influence.”

The recommendation to involve patients comes under the definition of an ethics committee (Article 2): “an independent body established in a Member State in accordance with the law of that Member State and empowered to give opinions for the purposes of this Regulation, taking into account the views of laypersons, in particular patients or patients' organisations”. This recommendation is backed up by Recital 18 which clarifies that whilst it should be up to the member states to determine the appropriate bodies for the assessment of trial applications, “… When determining the appropriate body or bodies, Member States should ensure the involvement of laypersons, *in particular* patients or patients' organisations.” (Emphasis added.)

**The patient perspective is different from a “lay” perspective**

The need for more patients’ involvement in ethics committees has been highlighted many times. The final report of ICREL (2007) noted that there were patients involved in about half of the ethics committees surveyed with slight growth.[[21]](#footnote-21) No recent mapping exists, however.

The CIOMS guidance (currently under review) specifies that ethics committees should include “lay persons qualified to represent the cultural and moral values of the community”.[[22]](#footnote-22) however, the perspective of patients is not equivalent to the perspective of lay persons: these roles are both different and complementary. Lay representatives, being often ethics experts or lawyers (or even religious representatives), do not possess the knowledge of patients, which is derived from lived experience. The unique value of the patient perspective lies in this knowledge. Patients and their representative organisations also have a unique insight into the feasibility of certain practical aspects of trials, and a different perception of the appropriateness of some decisions, such as regarding endpoints or comparators. Meaningful patient involvement can also help improve participation rates and public perceptions about clinical research.

But patient involvement is needed at a much earlier point. By the time a trial application is discussed by an ethics committee, improvements can be made but it is too late to re-design documents and re-think processes, especially in view of the stricter timelines that will apply under the new EU Regulation. Patients really need to be involved from the start in co-designing the research, including the information strategy and informed consent documents and process.

Patients contribution to trial design goes beyond the information material. The EU-funded project PatientPartner (FP7) found the following impacts in its extensive literature survey:

* + - Changes in the design of the study such as: ways of collecting data, identification of endpoints that are relevant to patients but had not occurred to researchers; analysis of qualitative data; different research questions, tools, priorities and outcomes;
		- Increased recruitment and better recruitment strategy;
		- Increased response rates;
		- More patient-relevant research findings and methods;
		- Challenged the assumptions made by researchers;
		- Wider dissemination of findings.

**EPF recommendations:**

1. The European Commission should carefully monitor the implementation of these provisions to ensure that ethics committees really do ensure the participation of patients, alongside lay persons.
2. There should be a mapping study examining patient involvement in ethics committees across the EU, including the type of involvement, its extent and what kind of patient representatives are participating.

Question to members: do you wish to include further recommendations?

## Selected References

To be added in the final version

1. International Ethical Guidelines for Biomedical Research Involving Human Subjects. The CIOMS guidelines reiterate three fundamental ethical principles that all research should adhere to: respect for persons (including respect for autonomy and protection of dependent and vulnerable persons), beneficence/non-maleficence (obligation to maximise benefits and avoid or minimise harms), and justice (fair distribution of the burdens and benefits of research). [↑](#footnote-ref-1)
2. Project website: [www.patientneeds.eu](http://www.patientneeds.eu) [↑](#footnote-ref-2)
3. Edwards J, Lilford R, Hewison J (1998). The ethics of randomised controlled trials from the perspectives of patients, the public and health care professionals. *British Medical Journal*, 317, pp. 1209-1212. [↑](#footnote-ref-3)
4. Akkad A, et al. “Patients' perceptions of written consent: questionnaire study”. British Medical Journal. 2006 Sep; 333 (7567):528. [↑](#footnote-ref-4)
5. The Ethics of Dementia Research, Alzheimer Europe, 2011, 182p. [↑](#footnote-ref-5)
6. “Low-intervention clinical trials” are trials where the investigational product already has a marketing authorisation and is used in accordance with its terms; or its use is based on published scientific evidence on safety and efficacy. The trial must pose only minimal additional risk or burden compared to normal clinical practice. The initial assessment of the trial application includes a decision on whether the trial can be classified as low-intervention. [↑](#footnote-ref-6)
7. Sood et al., "Patients' attitudes and preferences about participation and recruitment strategies in clinical trials". *Mayo Clin Proc* 2009;84(3):243-247; Eldh AC, Ekman I, Ehnfors M (2008). "Considering patient non-participation in health care". Health Expectations, 11, pp.263-271. [↑](#footnote-ref-7)
8. For example Edwards SJL, Lilford RJ, Hewison J, “The ethics of randomised controlled trials from the perspectives of patients, the public, and healthcare professionals”. BMJ 1998;317:1209–12; [↑](#footnote-ref-8)
9. A set of “core quality principles” on information to patients was developed by the High-Level Pharmaceutical Forum and endorsed by all Member States in 2008. [↑](#footnote-ref-9)
10. Elberse et al., "Patient involvement in agenda setting for respiratory research in the Netherlands", European respiratory Journal, vol.40 no.2, pp. 508-510. [↑](#footnote-ref-10)
11. See EPF’s website: [www.eu-patient.eu](http://www.eu-patient.eu) [↑](#footnote-ref-11)
12. Cheng J et al. (2000). Impact of quality of life on patient expectations regarding phase I clinical trials, *Journal of Clinical Oncology*, Vol. 18(2), pp. 421-428. [↑](#footnote-ref-12)
13. [www.patientneeds.eu](http://www.patientneeds.eu) [↑](#footnote-ref-13)
14. The “Patient University Project” in Barcelona, run by the University of Barcelona in cooperation with the Spanish Patients’ Forum (EPF member) and the Josep Laporte Library, and includes courses and information toolkits for patients about specific chronic diseases and disease self-management. See website: <http://www.universidadpacientes.org/index.php> [↑](#footnote-ref-14)
15. Flash Eurobarometer 404, European Citizens’ Digital Health Literacy. Report, November 2014 [↑](#footnote-ref-15)
16. EORTC presentation by Pascal Ruyskart, Head of IT. Report of the EFGCP Annual Conference 2013, p.7. [↑](#footnote-ref-16)
17. Report of the EFGCP Annual Conference 2013, p.5 [↑](#footnote-ref-17)
18. Report of the EFGCP Annual Conference 2013, p.4. [↑](#footnote-ref-18)
19. Ploug T and Holm S, "Meta consent: a flexible and autonomous way of obtaining informed consent for secondary research." BMJ 2015; 350:h2146. [↑](#footnote-ref-19)
20. [www.eu-patient.eu](http://www.eu-patient.eu) [↑](#footnote-ref-20)
21. ICREL final report, p. 116. <http://www.efgcp.be/downloads/icrel_docs/Final_report_ICREL.pdf> [↑](#footnote-ref-21)
22. International Ethical Guidelines for Biomedical Research Involving Human Subjects, CIOMS/WHO (2002) [↑](#footnote-ref-22)