

# Clinical Trials Regulation: Informed Consent and Information to Patients

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## 1. 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, and the UN Convention on the Rights of Persons with Disabilities.<sup>1</sup>

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.<sup>2</sup> 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.<sup>3</sup> Patients, not surprisingly, often do not recognise written consent as serving their interest, but rather the interest of researchers and hospitals.<sup>4</sup>

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.

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<sup>1</sup> 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). The UN CRPD, Article 25 on health, states persons with disabilities have a right to care of the same quality as others, including free and informed consent.

<sup>2</sup> Project website: [www.patientneeds.eu](http://www.patientneeds.eu)

<sup>3</sup> 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.

<sup>4</sup> Akkad A, et al. "Patients' perceptions of written consent: questionnaire study". *British Medical Journal*. 2006 Sep; 333 (7567):528.

## 2. Patients' Perspective on 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 Principles of 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 without the need for any justification or reason for their decision; 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.

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.

There are common patient concerns which should be taken into account and incorporated into recognised “good practice” that is applied across the EU. For example, a common problem for patients is that they are often given *too much information at once*, and cannot necessarily take it in, so it does not contribute to their understanding of what the trial is all about, or help in balancing the risks and benefits involved. Thus a more flexible and tailored approach should be applied that allows individual needs to be met – which is actually a requirement of the Regulation!

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 evaluating member states’ implementation of Article 29 – for example, to ensure that the informed consent was based on real understanding by the participants – there is a need for methodological guidance and benchmarking.

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. Common guidance on core elements and methodologies/good practice 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.**
- 2. Often problems for patients lie in the process of consent. 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 the process could be documented in practice.**

## Special Considerations

The Regulation includes several Articles laying out the rules for informed consent in research involving persons with incapacity, 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.

## Persons with Incapacity

Article 31 specifies that a trial can only be conducted involving persons with incapacity (referred to in the Regulation as “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 wish of an incapacitated person “who is capable of forming an opinion and assessing the information referred to in Article 29(2) to refuse participation in, or to withdraw from, the clinical trial at any time, is 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).

Article 31 is phrased in such a way that there is an assumption that a person who lacks the capacity to consent (presumably to participate in a trial) will have a legally designated representative. However, as consent is task-specific, a person might lack the capacity to consent to a specific clinical trial but might have sufficient capacity to manage everyday life without a legally designated representative. This situation does not seem to be addressed.

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*<sup>5</sup> 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.

This issue is sensitive for persons with mental health problems, as the right to informed consent of persons with psychosocial disabilities are often abused through legislation which denies them the right to make decisions for themselves and leads to forcible treatment. The UN CRPD calls for a move away from substituted decision-making and has a specific provision on free and informed consent.<sup>6</sup> We therefore stress that the individual person’s wishes are always to be considered and respected.

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<sup>5</sup> The Ethics of Dementia Research, Alzheimer Europe, 2011, 182p.

<sup>6</sup> UN CRPD, Article 25.

### EPF Recommendations:

3. In designing and assessing trials involving minors or vulnerable groups, the views of representatives of the target population should be sought whenever possible.
4. 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.
5. 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.
6. Alzheimer Europe’s recommendations could be used as a basis for a European template for informed consent involving persons with diminished capacity.
7. For persons with psychosocial disabilities, the provisions of Article 31 should be interpreted in line with the UN CRPD.

### Other Provisions

EPF does not have sufficient expertise to make recommendations regarding specific concerns around informed consent for children, pregnant or breastfeeding women, trials in emergency situations, or cluster trials (Articles 32, 33, 35 and 30, respectively).

We would merely stress that the same fundamental principles of meaningful informed consent should be applied in these situations. EPF supports the provisions of Article 10 that in trials involving any potentially vulnerable populations, specific consideration must be given to the assessment of the trial application on the basis of specific expertise in such populations or expert advice on the clinical, ethical and other specific problems in that field.

## 3. 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 its 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.<sup>7</sup> A lack of information is apparent throughout the clinical trial: patients often do not know how to find a clinical trial

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<sup>7</sup> 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.

and how to enrol in a trial; they often do not know what they are participating in;<sup>8</sup> 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.<sup>9</sup>

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*.<sup>10</sup> EPF has described many examples in our previous statements on clinical trials.<sup>11</sup>

EPF member organisations have concrete experience of providing information on clinical trials. As an example, Europa Donna has 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. Many lay people do not understand the fundamental difference between research such as clinical trials (designed to produce generalizable knowledge) and care or treatment intended to be of benefit to the individual.<sup>12</sup>

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<sup>8</sup> 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;

<sup>9</sup> 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.

<sup>10</sup> Elberse et al., “Patient involvement in agenda setting for respiratory research in the Netherlands”, *European respiratory Journal*, vol.40 no.2, pp. 508-510.

<sup>11</sup> See EPF’s website: [www.eu-patient.eu](http://www.eu-patient.eu)

<sup>12</sup> 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.

The findings of the EU-funded RESPECT project 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.<sup>13</sup> 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.<sup>14</sup> 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:

8. **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.**
9. **Patient organisations should be adequately resourced, including through grants from public funds at national and EU level as appropriate, to ensure they are able to perform their essential public service.**

## 4. Informed Consent and Future Developments

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).<sup>15</sup>

“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

<sup>13</sup> Relating Expectations and Needs to the Participation and Empowerment of Children in Clinical Trials (RESPECT), co-funded under FP7. Website: [www.patientneeds.eu](http://www.patientneeds.eu)

<sup>14</sup> 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>

<sup>15</sup> Flash Eurobarometer 404, European Citizens’ Digital Health Literacy. Report, November 2014

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.”<sup>16</sup>

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

**Online /ICT-based 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 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.<sup>17</sup>

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.

A risk of “online informed consent” is that the researcher may not know how much information the person has understood, unless the test at the end is very comprehensive and hence time-consuming. People may just click their way through the different sections without actually reading or understanding properly. Another possible risk is online tests to ensure comprehension may be detrimental to people’s wellbeing, affecting their self-esteem e.g. if

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<sup>16</sup> EORTC presentation by Pascal Ruyskart, Head of IT. Report of the EFGCP Annual Conference 2013, p.7.

<sup>17</sup> Report of the EFGCP Annual Conference 2013, p.5

they “fail”. In a face-to-face meeting, the researcher can be sensitive to the person’s needs and help them to understand, in ways that online tools cannot.

**Citizen science** is an 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.<sup>18</sup>

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, as co-researchers and partners?

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.<sup>19</sup>

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.<sup>20</sup>

### **EPF Recommendations:**

- 10. Informed consent should involve a full and frank discussion on data protection and privacy – including to what extent it is possible to make the patient’s data “unidentifiable”, 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.**
- 11. More reflection is needed on how the “broad consent” should be *defined and implemented*. This needs the close involvement of patients as well as researchers.**

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<sup>18</sup> Ibid, page 4.

<sup>19</sup> Ploug T and Holm S, "Meta consent: a flexible and autonomous way of obtaining informed consent for secondary research." BMJ 2015; 350:h2146.

<sup>20</sup> [www.eu-patient.eu](http://www.eu-patient.eu)

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.

12. The possibilities of advance directives for research should be explored.

## 5. Patient Involvement Matters for Better Trials

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: the documents and processes for informed consent should be co-produced with patients 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 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.”

However, ethics committees should take into account “the views of laypersons, *in particular* patients or patients' organisations” (Article 2, emphasis added). This 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 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.<sup>21</sup> No recent mapping exists, however.

<sup>21</sup> ICREL final report, p. 116. [http://www.efgcp.be/downloads/icrel\\_docs/Final\\_report\\_ICREL.pdf](http://www.efgcp.be/downloads/icrel_docs/Final_report_ICREL.pdf)

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”.<sup>22</sup> But **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 added 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.

The EU-funded project PatientPartner (FP7) found the involvement of patients often resulted in changes to the design of the study, including ways of collecting data; identification of endpoints that were relevant to patients but had not occurred to researchers; analysis of qualitative data; different research questions, tools, priorities and outcomes; more patient-relevant research findings and methods; challenges to researchers’ assumptions; increased recruitment and better recruitment strategy; better response rates; and wider dissemination of findings.

Patients really need to be involved from the start in co-designing the research, to ensure that the trial design is ethical and will produce results that will really benefit patients.<sup>23</sup>

### **EPF Recommendations:**

- 13. The European Commission should carefully monitor the implementation of the Regulation’s provisions for ethics review to ensure that ethics committees really do ensure the participation of patients alongside lay persons.**
- 14. There should be an EU-funded mapping study on patient involvement in ethics committees across the EU, including the current state of the art, types of involvement, its extent, and types of patient representatives involved. The study should include case examples and recommendations on good practices.**
- 15. Good practices in patient involvement in trial prioritisation and design (co-production/co-research) should be further explored and made available for sharing.**

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<sup>22</sup> International Ethical Guidelines for Biomedical Research Involving Human Subjects, CIOMS/WHO (2002)

<sup>23</sup> See e.g. The Lancet series “Research: increasing value, reducing waste” [www.thelancet.com/series/research](http://www.thelancet.com/series/research)