

GUIDELINES FOR TAILORING THE INFORMED CONSENT PROCESS IN CLINICAL STUDIES



Improving the
guidelines for
informed consent,
including vulnerable
populations under a
gender perspective



DRAFT



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[a] <https://i-consentproject.eu/workshop-a-step-closer-to-improving-informed-consent/>

[b] <https://i-consentproject.eu/project-recommendations-undergo-a-final-round-of-revision-with-experts/>



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GENERAL INFORMATION

These guidelines have been designed to provide information and evidence to assist with the development, or review of the consent process for use in clinical studies with human participants. These guidelines do not deal with issues related to informed consent in clinical practice.

The guidelines were developed by the i-CONSENT consortium. i-CONSENT (H2020, Grant Agreement number 741856) is a European Union H2020 funded program that aims to improve the information that individuals receive when deciding whether or not to take part in clinical studies. The guidelines were developed based on a review of the scientific and ethical literature; policy documents and legal instruments, enlarging the perspective also on international normative documents; comparative analysis of the legislations of selected countries; declarations of international organisms/institutions; reports and guidance documents; stakeholder

consultation. The deliverables and articles produced during the project, which have been used for the elaboration of these guidelines, are available in [CORDIS](#) on [the project's website](#) and a list is provided at the end of this document (section 4).

The multi-stakeholder i-CONSENT Consortium includes representatives from academia: Ateneo Pontificio Regina Apostolorum (UNESCOBIOCHAIR) and Libera Università Maria SS. Assunta di Roma (LUMSA); an investigation and public health center: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO); the pharmaceutical industry: Glaxosmithkline S.A. (GSK); a small and medium enterprise: AND Consulting Group; a patient association: Meningitis Research Foundation (MRF); and a tertiary care academic hospital: Ospedale Pediatrico Bambino Gesù (OPBG).

Introduction

The consent process is an essential procedure that ensures the fundamental rights and freedoms of the participant, allowing them to voluntarily decide whether or not to take part in a study, with the option to withdraw at any time, without consequences.

The format of the consent process for clinical studies has remained relatively unchanged for decades. In its current format, typically a long and complex text document, there are still areas for improvement in order to promote clear communication between participants and investigators. Effective communication is essential to uphold the

fundamental ethical principle of respect for the participant's autonomy.

Several guidelines, legal documents and legal instruments about the consent process have already been implemented. These cover what informed consent is and should be; why it is important in clinical studies; the main procedures to follow during the informed consent process and the minimum content to be covered. The i-CONSENT guidelines have been written in accordance with these documents and they should be read in conjunction with them.



What do i-CONSENT guidelines add?

These guidelines provide ethical recommendations and practical tools that aim to make the consent process more comprehensive, tailored and inclusive.

They include a new and broader concept of the informed consent process, more focused on the participants, and incorporating their point of view in every step, starting from the design.

These guidelines represent a change in mentality that gives greater prominence to informed consent, turning it

into a process that provides added value and prevents it from becoming a bureaucratic act focused solely on the participant's signature on the informed consent form.

These guidelines provide a step-by-step description of the informed consent process, and a checklist to implement comprehensive and inclusive informed consent, as well as 12 fact sheets and 6 tools with recommendations and examples to put ethical considerations into practice.

Scope and purpose

Who are these guidelines for?

These guidelines are relevant for all stakeholders involved in the design and implementation of the consent process. They can support the work of investigators and sponsors, but are also relevant for ethics committees involved in the evaluation and approval of consent materials.

What is the purpose of the guidelines?

Their purpose is to enhance the consent process in clinical studies, to make it more understandable, and where possible, tailored to the participants' needs, preferences and circumstances to ensure that individuals can make autonomous decisions about their participation in clinical research.

How to use these guidelines

The guidelines are divided into four parts. The first part describes the i-CONSENT perspective on the consent process and highlights the need to improve the traditional approach to obtaining informed consent. This includes specific recommendations in order to tailor the informed consent process to the target population. Parts two and three provide practical TOOLS and recommendations to implement a tailored and more understandable consent process. Part four lists the scientific deliverables and publications produced as part of the i-CONSENT project.



The contents of the four parts are:

1. CONSENT AS A PROCESS (Pp. 10-24)

This part of the guidelines explains four key aspects of designing a consent process that meets participants' needs: (a) clear and concise information; (b) interdisciplinary mixed-methods (quantitative and qualitative research methodologies) to gain informed consent design insights; (c) co-design as a central concept; (d) the importance of providing inclusive information and of personalizing the consent process to the needs of individuals. In addition to providing recommendations for each of these aspects, this part aims to change the way consent is conceptualized.

This part also describes the consent process step-by-step. It highlights the importance of understanding the process as a whole, rather than only focusing on the participants' signature on the form. It also provides specific recommendations for the informed consent (a) to apply a gender perspective; (b) when the studies involve minors; fertile, pregnant or breast-feeding women; participants coming from different cultural and religious backgrounds; or/and low-income populations.

2. CHECKLIST: STEP BY STEP GUIDE FOR INVESTIGATORS DESIGNING A CONSENT PROCESS (Pp. 25-28)

This checklist is a practical tool that aims to help investigators and organizations in fulfilling the requirements of regulatory, funding and other bodies. It also helps with identifying and reviewing all the key aspects that should be covered in the consent process.

3. FACT SHEETS AND TOOLS (Pp. 29-58)

The third part of the guidelines provides a series of easy-to-read fact sheets and tools which complement the core document, highlight the importance of several aspects of the informed consent process, and provide recommendations on how to implement best practice. The fact sheets and tools also emphasize the different factors involved in the informed consent process. The fact sheets deal with aspects directly related to the informed consent process, while the tools include aspects that do not strictly belong to the informed consent process but are useful for its improved development.

4. LIST OF i-CONSENT'S SCIENTIFIC DELIVERABLES & PUBLICATIONS (Pp. 59-61)

This section contains a list of public deliverables and publications prepared in the framework of the i-CONSENT project, with links to each publication.

These publications have been used to produce the guidelines.



The core elements of the i-CONSENT acronym

The acronym i-CONSENT contains the core elements of a comprehensive consent process (Table 1):

Table 1. The i-CONSENT acronym and core elements of the consent process

I	Information	Complete and clear information is essential for the potential participant to be able to make an autonomous decision.
C	Co-creation	The inclusion of potential participants during the design and review of study information materials is key to ensuring that they are understandable and address the target population's needs and preferences.
O	Ongoing process	Consent should be a two-way continuous communication process that begins at first contact with the potential participant, and continues until the end of the study.
N	New technologies, methods, and (innovative) processes	The consent process should include technical and methodological innovations to facilitate the participant's experience. Their appropriateness from a social, methodological, legal and ethical point of view should always be taken into consideration.
S	Self-determination (autonomy)	Autonomy is a fundamental principle. The purpose of the informed consent is to ensure that the potential participant is able to make an autonomous and free decision.
E	Empowerment	Participants should be empowered to make their own decisions.
N	Nonstandard (inclusive and tailored)	Research should be inclusive to meet the needs of the potential participants and respect the basic bioethics principle of justice. There is no single best way to conduct the consent process. The 'ideal' solution will differ in every setting and therefore needs careful design. Where possible, the consent process should be tailored to the needs of the target population.
T	Trusted	Good practices are essential to build trust between investigators and potential participants, and to increase society's trust in research.

Source: Own elaboration



1. CONSENT AS A PROCESS

In recent decades, informed consent has become a long and complex paper document which provides information about the study and documents, via the participants' signature, their acceptance to take part in the study. In practice, it is regularly perceived primarily as a "bureaucratic" and legal requirement. Often, it is prepared by only one interested stakeholder without taking into account other points of view and frequently using technical language. This can result in a "legal" document rather than a process to inform the potential participant and to ensure their autonomy.

The i-CONSENT consortium acknowledges that the current process of informed consent may not ensure participants' understanding and, may therefore, hinder their autonomy.

The i-CONSENT consortium recommends that the informed consent process should be a continuous, bidirectional

communication process that begins at the first contact with the potential participant and continues until the end of the study. It should incorporate key interventions designed to improve autonomy and inclusivity. This has the potential to generate research that is of higher quality, lower cost, and ethically justified.

It is crucial that informed consent enables a person to:

- Make an informed and autonomous decision about their participation in a study.
- Re-evaluate their participation throughout the study and understand their freedom to withdraw at any time.

The potential impact of better information and communication is high for clinical research, especially at an ethical level (safeguarding people's autonomy).

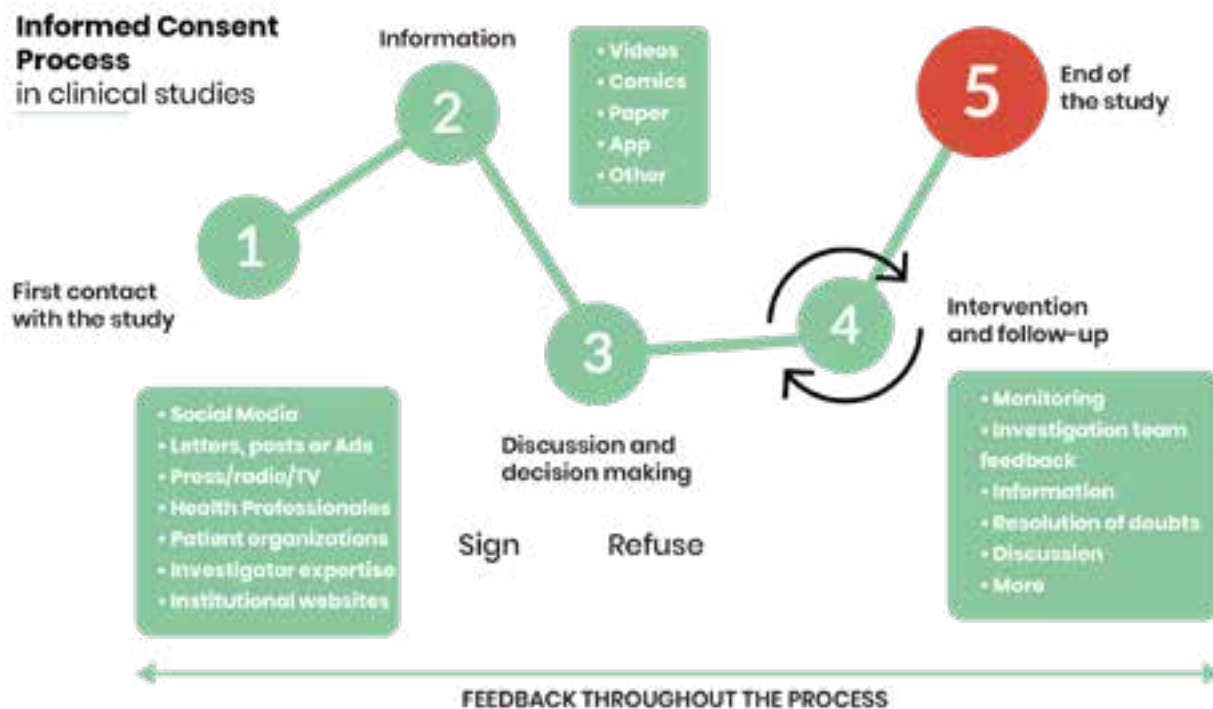
1.1 THE INFORMED CONSENT AS A PROCESS

i-CONSENT proposes a consent process for clinical studies that is designed to meet participants' needs. This process entails five different phases (Figure 1).

During the consent process, continuous feedback and communication between the potential or current participant and the research team is essential. Most phases can be done either face-to-face or virtually, depending on what is considered most appropriate for the study and target population. The consent process is also an opportunity to improve the health literacy of participants (FACT SHEET I).



Figure 1. The five steps of the Informed Consent Process in clinical studies



1- The potential participant’s first contact with the study

The “First Contact” stage aims to raise awareness of the study and provide essential study information before the recruitment process begins. i-CONSENT recommends:

1. Considering different channels for recruitment

The first contact can be established through different channels, such as health professionals, patient networks, institutional websites or social media; always taking into consideration the appropriateness from a social, methodological, legal and ethical point of view. It is vitally important that research is inclusive to ensure that health care interventions are fit for everyone. To abide by the principle of justice, and following the Declaration of Helsinki and the Clinical Trials Regulation, underrepresented groups should have opportunities to participate in studies, and this should be taken into account when designing the recruitment strategy. In clinical trials with drugs, it is important to ensure that the study sample is reasonably

representative of the potential users of the drug.

Access to different communication channels varies across different groups in society, so recruitment channels need to be carefully selected.

2. Using transparent, balanced and neutral recruitment messages

These messages should include objective information in neutral language. They should be clear and precise.

The information provided during this first contact should allow the potential participants to know if they are interested in the study and if they can participate (eligibility criteria).

3. Reviewing the recruitment strategy to ensure it is ethical

The relevant independent Ethics Committees should review and approve all the materials and methods for recruitment, including advertising.

RELATED FACT SHEETS:

FACT SHEET II. PRESENTING STUDY INFORMATION

FACT SHEET III. ADVERTISING THE STUDY



2- Provision of information

After the initial expression of interest, potential participants should be provided with additional information about the research. This may be provided in formats tailored to potential participants' characteristics or preferences. The provision of excessive information ('information overload') can amount to misinformation and thus hinder the quality of the informed consent process.

i-CONSENT recommends:

1. Provide the participant with all relevant information about the study before the discussion with the investigator, ensuring that they have sufficient time to consider it and to prepare any questions that they may have

This information should be delivered in a clear and concise way.

When providing information about alternative procedures or treatments, include information on effective treatments or tests available in other regions/countries. In some cases, particularly in translational research, participating in a clinical trial may be the only possibility of accessing a procedure or treatment (with uncertain results) because no

other treatment/procedure is available or reimbursed in the region of the study. The investigator has the duty to inform the potential participants about the treatments/procedures available in other regions/countries as well.

2. Consider new technologies and formats to deliver information to complement face-to-face discussion

Different instruments and media are used to deliver information to best meet the needs of the population. One way that technology could be used to convey relevant information is through audio-visuials. This format can be conducted remotely and, as it is delivered in the same way every time, the quality of delivery is consistent. Some factors that can enhance the impact of multimedia tools are to include interactive components or, in case of Randomised Clinical Trials, their use in presence of the investigator.

It is recommended to give more than one option of format (such as video, gamification or comic) that ensures that the information is delivered consistently and may improve the study understanding

RELATED FACT SHEETS:

FACT SHEET II. PRESENTING STUDY INFORMATION

FACT SHEET IV. INFORMATION TO GIVE TO POTENTIAL PARTICIPANTS DURING THE INFORMATION PHASE

3. Discussion and Decision Making

3.1 - Discussion

After the information has been provided to the potential participant and they have had time to reflect on the content, the investigators should resolve the concerns about the study and the participation.

Face-to-face discussion between the potential participant and the investigator should ensure that the participant fully understands all relevant aspects related to their participation.

i-CONSENT recommends:

1. Selecting an appropriate environment for the discussion

It should be conducive to facilitating the dialogue (e.g. a quiet, calm, and friendly environment) and it is essential to ensure privacy.

2. Strengthening the communication skills of the investigator

The investigator providing information to the participant should have good communication skills. It matters not only



“what” is said but also “how” and “by whom”. Investigators may speak to people of varying educational, cultural and social backgrounds and they should do so in an effective, caring and professional manner to convey a message and contribute to a participant’s understanding of the study.

3. Checking potential participants’ comprehension

Comprehension is a key element of the Consent Process,

and depends on the individual (maturity, educational level, etc.) and the investigator’s ability and willingness to communicate. The investigator must ensure that potential participants have understood the relevant information about the study in order to make an informed and autonomous decision.

Related FACT SHEETS:

FACT SHEET V. INVESTIGATOR–PARTICIPANT RELATIONSHIP DURING THE CONSENT PROCESS

FACT SHEET VI. HOW TO ASSESS PARTICIPANT’S COMPREHENSION

TOOL I. HOW TO BECOME A GOOD COMMUNICATOR

3.2 – Decision making

If the participant decides to take part in the study, a consent form should be signed and dated by both the participant and the investigator who conducted the discussion. A copy of the document should be provided to the participant.

In the case of minors, parental/legal representative consent is required, with the assent of the older minor, as well. When minors reach the legal age to consent during the research must have the opportunity to give their consent.

i-CONSENT recommends:

1. Ensuring that potential participants are able to make an autonomous decision about whether or not to take part

The decision must be made without any kind of coercion, undue inducement or deception not only from the research team, but also from family members or other persons.

2. Using decision aids to facilitate the decision-making process

A decision aid (for example animations, interactive information materials or infographics) is a useful tool designed to make specific and deliberative choices among various options and possible outcomes presented. It describes the decision to be taken, the options available,

and the outcomes of these options (including benefits, harms, and uncertainties) based on a careful review of the evidence.

3. Providing support and give adequate time for participants to make a decision

Participants should be given adequate time to consider their options, and they should be allowed to consult with others before making a final decision, if they wish to do so.

4. Ensuring participants are aware of all the information of the study and the possibility to withdraw at any stage

It is important to highlight this information and ensure its understanding before the signature.

5. Obtaining feedback from participants

Gathering experience and opinions of potential and current participants throughout the study can enable the informed consent process to be adapted to unforeseen situations and the different informational needs of participants. It helps to define and improve the process for both ongoing and future studies, making informed consent a dynamic process which can be adapted.



RELATED FACT SHEETS:

FACT SHEET VI. HOW TO ASSESS PARTICIPANT'S COMPREHENSION

FACT SHEET VII. THE USE OF DECISION AID TOOLS

TOOL II. HOW TO GAIN PARTICIPANT'S FEEDBACK

4- Intervention and Follow up

Throughout the duration of the study, participants must have access to the information used during the recruitment process and be informed on how to access it.

If at any point in the study there are changes in the protocol or new, relevant knowledge becomes available, participants should be informed and they will have to re-consent. The new consent should be approved by the ethics committee.

In addition to these i-CONSENT recommends:

1. Ensuring that members of the research team are available to respond to questions or concerns participants may have throughout the study

2. Providing updated study information to participants throughout the study

It is recommended that research teams provide regularly updated information about the development and the status of the study, to give the participant an understanding of how the study is progressing overall. This information may be provided online to facilitate its access.

3. Obtaining continuous feedback from participants.

Feedback should be obtained at all stages, including during the intervention and follow up.

RELATED FACT SHEETS:

FACT SHEET V. INVESTIGATOR-PARTICIPANT RELATIONSHIP DURING THE CONSENT PROCESS

FACT SHEET VIII. WHEN IS RE-CONSENT NEEDED?

TOOL II. HOW TO GAIN PARTICIPANT FEEDBACK

5- Completion of the study

When the study ends, the participants must be notified and informed of the treatment assigned to them (if applicable) as well as the associated results, in accordance with the agreed incidental findings policy.

All information about the treatment assigned, the procedures carried out and the associated results should be registered in the participant's medical records. If the participant expresses that they do not want their results to be recorded, this must be taken into account.

In addition to these, i-CONSENT recommends:

1. Thanking participants for taking part

A thank you letter (or another form of communication) expresses gratitude from the research team and the sponsor when the participant has finished their involvement. Thank you letters are a good opportunity to highlight the importance of participation in research and the objectives that each participant helped in reaching. It should include information about the study, and a summary of the available results.

2. Including participants in the first steps of result dissemination



Participants may be included in different dissemination events addressed to them. A summary of results understandable to laypersons must be provided.

3. Asking participants for feedback on the process

Feedback should be obtained at all stages, including at the end of the study.

RELATED FACT SHEETS:

TOOL II. HOW TO GAIN PARTICIPANTS' FEEDBACK

TOOL III. GUIDANCE ON CREATING "THANK YOU" LETTERS

TOOL IV. CREATING A SUMMARY OF THE RESULTS FOR LAYPERSONS

1.2 DESIGNING CONSENT WITH STUDY PARTICIPANTS

When Barbara Balik, BS and MS in nursing and doctorate in educational leadership, talks about how to deliver patient- or family- centeredness healthcare, she explains that the process can be characterized in 3 different stages: the "doing to"; "doing for"; and "doing with" stages. This can be also applied to the informed consent, where we need to shift from an approach where the informed consent is done TO the potential participant to one in which the informed consent is done WITH the potential participant.

Informed consent has to move from the "doing to" perspective, where the sponsor or the investigators decide what information the potential participant should receive, to a "doing for" perspective where potential participants are asked about their experiences and are considered when designing the informed consent. We should finally arrive at

a "doing with" perspective, where potential participants are involved in the design of the informed consent, making them central to the process.

i-CONSENT proposes a "doing with" perspective for the informed consent process in three steps (see Figure 2) where sponsors and investigators seek to understand their target population (Understand), and incorporate them in the design, development and review of the informed consent (Co-create), to ensure materials are more inclusive and tailored to potential participants' actual needs and preferences (Outcome).

Some key design points are relevant during all the consent process. General i-CONSENT recommendations are provided here:

Figure 2. How to improve consent materials by placing potential participants at the centre of the design process

UNDERSTAND

Know your target population, study them and identify their needs and preferences

CO-CREATE

Design, develop, and review consent with a diverse sample of potential participants.

OUTCOME

Consent materials that are better suited to potential participants' needs

1. Balik B. Patient- and Family- Centredness: Growing a Sustainable Culture. Healthcare Quarterly. 2012; Vol.15 Special Issue:10-12



UNDERSTAND

Use interdisciplinary quantitative and qualitative methodologies to learn about your study population, their interests and needs

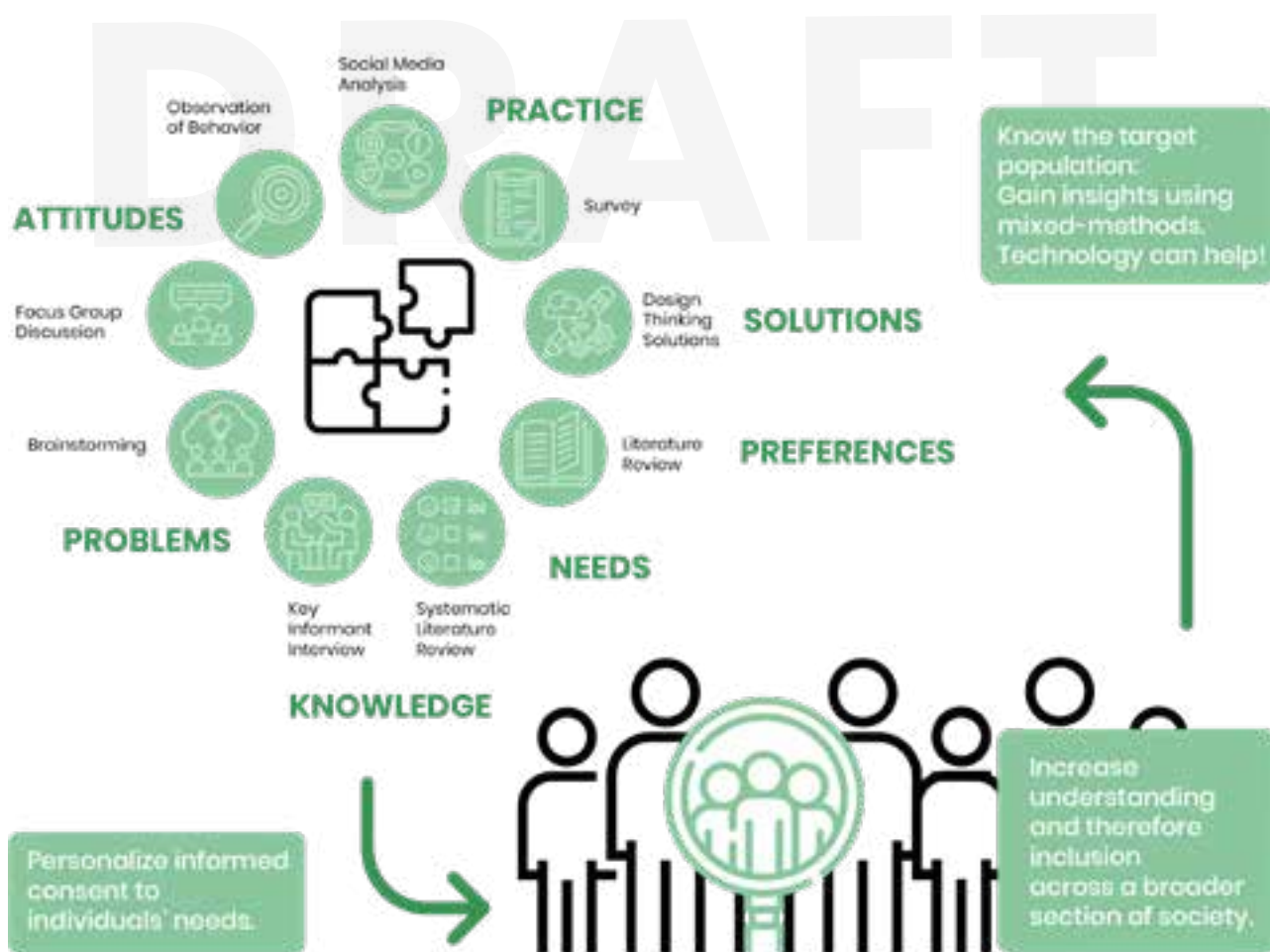
When obtaining consent, an understanding of the target study population is essential to ensure that information is provided in a way that is appropriate to their needs.

Insights on needs can be obtained using a variety of methods (Figure 3). It may be useful to explore the available literature on the target population (e.g. systematic or narrative literature review); ask the target population directly (e.g. interviews; surveys; design thinking); seek advice from

experts (e.g. key informant interviews; brainstorming...); observe the target population; and/or analyse their interactions on social media and blogs.

Technology provides new opportunities to help gain insights from society (for example, analysing their interaction on social media and blogs or doing electronic surveys) and personalize informed consent to users (such as using a layered approach for presenting the information in a website), while new methods from other disciplines (for example, design thinking) help us turn insights into action.

Figure 3. Methods that can be used to better understand your target study population



CO-CREATE

It is important to consider the way in which the potential participants experience the consent process. They should play a central role, together with other stakeholders, in all design phases (Figure 3). While many qualitative and participatory research methodologies can be used to gain insights for the consent design process (TOOL 5), there is also a lot to learn from disciplines such as Human Centred Design (HCD).

The points of view and expertise of other stakeholders (such as investigators or ethical and legal experts) should

also be taken into account when preparing informed consent materials.

It is highly recommended that consent materials are tested with representatives of your target population before their use.

RELATED FACT SHEETS:

TOOL V. METHODOLOGIES AND TOOLS
TO INCORPORATE THE PARTICIPANTS'
PERSPECTIVE

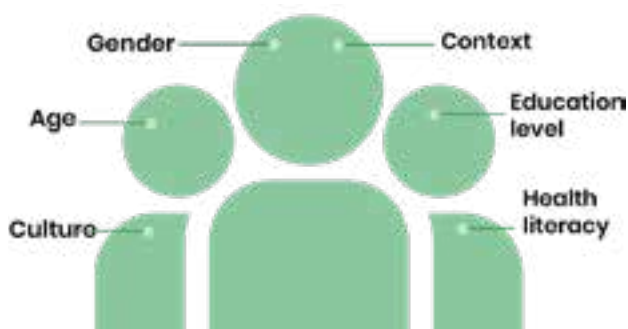
OUTCOME

Provide clear and concise information.

Ensure that the information is:

- Relevant: according to the nature of the study (objectives/ type of study/ phase...) and to your target population.
- Complete: to ensure that potential participants do not need to seek additional information from other sources.
- Easily understandable: use plain language, avoiding the use of jargon and acronyms. Throughout the consent process, all information provided to research participants should be tailored to their health literacy level.
- Neutral/balanced: Information should be presented using impartial and transparent language. It is important not to mislead the participant into having unrealistic expectations or therapeutic misconceptions.

Figure 4. Individual factors that may influence potential participants' needs during the consent process.



Provide inclusive information and consent tailored to individuals' circumstances

To be inclusive, the information provided should meet the diverse needs of the potential participants, in their specific context. Potential participants' preferences for consent are unique and influenced by multiple factors, some of which are represented in Figure 4. Needs may also change throughout a person's lifetime, for example a woman's needs may change when pregnant or breastfeeding.

The discussion between the potential participant and investigator provides an ideal opportunity to address the participant's individual needs. Recommendations include using a layered approach for presenting information, and providing different channels and formats to receive information or communicate with the research team. Technology also provides new opportunities to tailor informed consent to participants (such as presenting the information in a website using a layered approach).



1.3 TAILORING THE CONSENT PROCESS TO THE TARGET POPULATION

The Clinical Trial Regulation ([REGULATION \(EU\) No 536/2014](#)) establishes that, unless otherwise justified in the protocol, the subjects participating in a clinical trial should represent the population groups that are likely to use the medicinal product investigated in the clinical trial, for example gender, age or ethnic groups. If a specific group is excluded from or underrepresented in the clinical trials, the protocol should include an explanation of the reasons and

justification for these exclusion criteria. This representation criterion is also recommended for other clinical studies.

In this section we give recommendations for consent processes with a gender perspective; and for studies with specific populations (pregnant, breastfeeding or fertile women; minors; people from different cultural and religious backgrounds; low-income populations).

1.3.1 The gender perspective during the consent process for clinical studies

A lack of participation by women in clinical studies may produce a source of gender inequality. A gender perspective must be included during the consent process to ensure it is inclusive and to avoid stereotyping.

International Ethical Guidelines for Health-Related Research Involving Humans, Commentary ([CIOMS, 2016](#)) on Guideline 18 (Women as research participants) highlight that despite the current general presumption that favours the inclusion of women in research, in many societies women remain socially vulnerable in the conduct of research. For example, they may suffer negligence or harm because of their submission to authority, their hesitancy or inability to ask questions, and a cultural tendency to deny or tolerate pain and suffering. When women in these situations are potential participants in research, researchers, sponsors and ethics committees must take special care in the research design, assessment of risks and benefits, and the process of informed consent, to ensure that women have the necessary time and appropriate environment to make decisions based on the information provided to them.

Differences between sex and gender and how they influence the informed consent

The informed consent process may be influenced by sex and gender differences.

- “Sex” refers to the biological condition and anatomic differences between males and females.
- “Gender” refers to the psychological, social and cultural dimensions that influence men and women’s behaviours and roles.

Based on sex:

Female and males are biologically different, so:

- They may have different responses to medications.
- Fertile, pregnant and breastfeeding women require specific protection measures, as stated in the Clinical Trial Regulation ([REGULATION \(EU\) No 536/2014](#)). In these specific cases, information should be adapted to women physiological conditions (section 1.3.2).

Based on gender:

Gender differences are **socially constructed**; they differ from one society to another and they can be **changed**.



The ones presented here come from different studies that indicate the existence of different behavioral trends between women and men (most of them included in i-CONSENT's deliverable 1.2). They only show general

trends may vary, **they are not categorical**. To apply a gender perspective it is important to understand the five characteristics of the concept of gender (Table 2): relational; asymmetric/hierarchical; historical/changing; contextual specific; institutionally structured.

Table 2: Characteristics of the concept of gender

Relational	Gender refers to the relationship between women and men, not to them in isolation.
Asymmetric/hierarchical	These relationships often privilege one group. They usually give more value to the characteristics and activities associated with the masculine, contributing to produce unequal power relations
Historical/Changing	It is based on historical traditions and practices that evolve and change over time and space. They are susceptible to changes by interventions
Contextually specific	Gender's relationship and characteristics change depending on the multiple identities women and men have (age, ethnicity, sexual orientation, social and cultural stratum, etc.). They differ in all contexts due cultural traditions and practices
Institutionally structured	It refers not only to relationships at the individual and private level, but also helps to perpetuate gender-related beliefs through infrastructure such as laws, religion, politics, etc.

Sources: Escuela Andaluza de Salud Pública ² (2010) and World Health Organization³ (2011)

Gender differences that may influence the consent process are of varied nature:

- Societal: as Cassese and Zuber⁴ point out, women generally have less free time to participate in clinical studies, since they tend to take on “Double burden” (paid jobs and household chores) more than men.
- Preferences and use of ICT: men and women tend to

evaluate and use technology differently: generally women use the internet more as a communication tool ⁵ while men as an information seeking tool⁵ and overall women and men use different styles and strategies in online discussions^{6,7}. There are also gender-based differences in eye tracking behaviour^{8,9}.

2. García Calvente, Mdm (ed.). Guía para incorporar la perspectiva de género en la investigación en salud. Spain: Escuela Andaluza de Salud Pública; Observatorio de Salud de las Mujeres. 2010.

3. Gender mainstreaming for health managers: a practical approach. Facilitators' guide. Participant's notes. WHO 2011.

4. Cassese M, Zuber V. Clinical trials and gender medicine. Ann Ist Super Sanità. 2011; 47(1): 100-3.

5. Jackson LA, Ervin KS, Gardner PD, Schmitt N. Gender and the Internet: Women Communicating and Men Searching. Sex Roles. 2001;44(5/6):363-79.

6. Tsai MJ, Liang JC, Hou HT, Tsai CC. Males are not as active as females in online discussion: Gender differences in face-to-face and online discussion strategies. Australasian Journal of Educational Technology. 2015; 31(3).

7. Caspi A, Chajut E, Saporta K. Participation in class and in online discussions: Gender differences. Computers & Education. 2008;50:718-24.

8. Alt64, AIMC. Estudio Eyetrack Medios España: Análisis del comportamiento visual de los internautas y la efectividad de la publicidad online. España; 2005.

9. Mueller SC, Jackson CP, Skelton RW. Sex differences in a virtual water maze: An eye tracking and pupillometry study. Behav Brain Res. 2008;193(2):209-15.



- Relationship and communication between investigator and participant (and vice versa): differences may be due to the gender of the investigator, the gender of the participant and how they interact in different contexts.
- Motivations and decision making procedures: scientific studies suggest that women tend to be more health conscious¹⁰; are more likely to thoroughly read the informed consent document, more information seeking, more cautious to avoid manipulation¹¹; and are more likely to decline participation in clinical studies^{12,13,14}.
- Disparities in experience and treatment: Hoffmann and Tarzian¹⁵ indicate that “women who seek help are less likely than men to be taken seriously when they report pain and are less likely to have their pain adequately treated”. Due to this gender-based bias,
- Male patients are consistently given more time and attention from medical professionals than female patients with the exact same symptoms.
- Communication:
 - There are more similarities than differences in the communication between men and women, and the differences are not categorical.
 - Male and female communication styles are often influenced by gender stereotypes¹⁶.
 - Male and female communication styles are not attributable to men and women respectively. Men and women use characteristics of both communication styles and change from one to another depending on the circumstances. For example someone may take on

characteristics usually attributed to the feminine style (more conciliatory) when talking with his/her boss or to a police officer who is rebuking him/her, and may take a more masculine style (more authoritarian) when speaking with his/her subordinate. In these cases, the position will have more influence on communication style than the sex of the speaker.

- As well as gender, other factors influencing communication must be taken into account. They may include age, cultural and religious backgrounds, socioeconomic status or cultural patterns, among others.

Recommendations for a gendered approach

- Take into account the ways in which gender influences health needs and concerns, including the different roles and interests of women and men, as how health messages are received.
- Ensure materials are inclusive. Test and retest messages, concepts, and intended program formats with women and men to ensure that they work well for both. Adapt consent materials by gender only when the strategy or study is directed to a single sex group (for example, when only male participants or pregnant and/or breastfeeding women are recruited to a study).
- Use multiple communication strategies to ensure that services, supplies, and practices of the chosen media do not reinforce gender stereotypes.
- Adapt the informed consent process, especially during the interview, to the characteristics of the participant

10. Friesen LR, Williams KB. Attitudes and motivations regarding willingness to participate in dental clinical trials. *Contemp Clin Trials Commun.* 2016 Jan 12;2:85-90. doi: 10.1016/j.conctc.2015.12.011. eCollection 2016 Apr 15.

11. Knepp MM. Personality, sex of participant, and face-to-face interaction affect reading of informed consent forms. *Psychol Rep.* 2014;114(1):297-313.

12. Knepp MM. Personality, sex of participant, and face-to-face interaction affect reading of informed consent forms. *Psychol Rep.* 2014;114(1):297-313.

13. Petty DR, Zermansky AG, Raynor DK, Vail A, Lowe CJ, et al. “No thank you”: why elderly patients declined to participate in a research study. *Pharm World Sci.* 2001 Feb;23(1):22-7.

14. Simons-Morton DG, Chan JC, Kimel AR, Linz PE, Stowe CL et al. Characteristics associated with informed consent for genetic studies in the ACCORD trial. *Contemp Clin Trials.* 2014 Jan;37(1):155-64.

15. Hoffmann DE, Tarzian AJ. The Girl Who Cried Pain: A Bias Against Women in the Treatment of Pain. *J Law Med Ethics.* 2001;29(1):13-27.

16. See Cameron D. Gender. In: Brown K, editor. *Encyclopedia of Language & Linguistics (Second Edition)*. Oxford: Elsevier; 2006. 733-9 p.; Griffin E. A first look at communication theory. 8th ed. New York: McGraw-Hill; 2012.



(considering gender). Good communication between the investigator and participant is key.

- Provide opportunities for participants to discuss the trial with friends and family members, but consider whether the family group or the larger community network may unduly influence the woman's decision on whether to participate.
- In the case of women coming from different cultural backgrounds, consider using a cultural mediator with a

gendered approach in order to bridge communication gaps. Permission to participate from the woman's partner cannot replace the individual informed consent of the woman herself.

- If possible, foster the role of women as research actors (as investigators; representatives of patient associations; and members of ethics committees) who can also contribute towards a better understanding of the needs of women enrolling in clinical studies to enable their participation.

1.3.2. Adapting the informed consent process to fertility, pregnancy and breastfeeding

Women could be vulnerable in research during pregnancy and breastfeeding. These specific circumstances may require special protections, as stated in the Clinical Trial Regulation ([REGULATION \(EU\) No 536/2014](#)). Article 33 of the Regulation addresses the issue of clinical trials on pregnant and breastfeeding women.



It is important to note that pregnancy and breastfeeding do not affect a woman's capacity to decide on their participation in research studies after having received adequate information.

When recruiting fertile women into a clinical trial, the informed consent process should include:

- That the clinical trial may put the foetus at risk, so during the trial and for some time after it has ended (specify how long), the woman should avoid pregnancy.
- The need to verify the absence of pregnancy through pregnancy tests during the trial.
- Respect for the woman's choices and moral or religious convictions regarding how to avoid pregnancy during the clinical trial, including abstaining from sexual intercourse.
- Information about risks related to contraception.

When recruiting pregnant women:

- The informed consent should include a clear description of the risk for both, the mother and the foetus.
- A close follow-up of the pregnancy, foetus and child is essential and should be clearly communicated during the informed consent.

When dealing with breastfeeding women:

Remember to inform about:

- The risks concerning the health of both the woman and the newborn.
- The possible excretion of the experimental drug into human milk. This should be monitored and the duration of exposure should be adapted according to the level of risk. This should be clearly communicated during the consent process.

Partner involvement during pregnancy, breastfeeding or when the trial can affect fertility:

- The woman should involve her partner in the informed consent process. Permission from the woman's partner cannot replace the individual informed consent of the woman herself.
- Men participating in research which is potentially toxic for gametes or foetuses should receive clear and detailed information on the risks of their participation, and involve their fertile or pregnant partners in the consent process.



1.3.3. The informed consent process in clinical studies involving minors

Ensuring the best interests of the child is of fundamental importance. Children should be involved in the decision-making process, according to their age and maturity.

Research involving minors requires special protection for them because minors may be vulnerable in relation to age, maturity and development. These reasons will affect their ability to understand, appraise and express their opinion, and that should be treated with special care.



Consent process in clinical studies with minors

- A clinical trial study with minors can only be conducted when informed consent by their legally designated representative has been obtained.
- It is important to ensure that children are involved in the decision-making process, according to their age and maturity.
- Minors should be informed about why the study involves minors; the nature and the purpose of the research; related risks and burdens (discomforts); and expected benefits (direct or indirect). They should also be given the opportunity to ask questions and express an opinion on whether or not they would like to participate (assent). Information must be given in accordance with the maturity of the child.
- A minor's wish not to participate should be considered binding if the minor is mature. Parental consent, without the minor's assent, is sufficient only if a direct benefit is expected to be obtained (for the best interests of the child), risks and burdens are minimal and the minor is not sufficiently mature to express a valid objection.
- A participant reaching the legal age to consent (according to national legislation) during the research will need to sign the consent for the first time for their participation.

NOTE:

Clinical Trial Regulation (REGULATION (EU) No 536/2014), Article 32, indicates the requirements and conditions that must be met in clinical trials with minors.

How to adapt the information to the minor's age and maturity

Figure 5. How to adapt the information to the minor's age and maturity



1.3.4 The informed consent process in clinical studies involving people from different cultural and religious backgrounds

Cultural differences between investigators and potential participants in clinical trials can result in communication barriers, which are likely to hinder awareness about possible risks/benefits and therefore pose challenges to the informed consent process. In order to avoid this possible obstacle and to ensure that the process respects cultural practices, it is important to:

- Adopt procedures that incorporate an intercultural sensitive approach, which includes a deeper understanding and respect for people's cultural and religious backgrounds, to improve fairness and equity in research participation.
- Provide information in an easy-to-understand and culturally appropriate language.
- Promote the participation of trained cross-cultural professionals in the study.
- When appropriate, a translator and/or a cultural mediator should be available during the process of obtaining informed consent. They should be familiar with medical terminology and experienced in the relevant language, social habits, culture, traditions, religion and particular ethnic differences.



- Deliver a translated informed consent form in a language and using terms understandable to the participant in order to provide trial related information adapted to the specific needs of families with a different cultural background. Particular attention should be focused on the appropriate use of local dialects and investigation-related terminology. Another challenge in presenting information to culturally diverse populations can be related to perceptions about the body, causes or prevention of diseases and different understanding of risks and benefits. Cultural differences could also impact upon a participants' perception of altruism, autonomy, risk aversion, etc.
- Use a participant-centred approach to communication

which takes into account the needs and preferences of research participants. This also ensures respect for the cultural and religious values of the participant, fosters a good relationship between the participant and investigator, and builds long-term relationships between the community and the research team.

3 key steps to adapt consent process in different cultural contexts:

1. Be aware that key concepts can be understood differently
2. Empathize/Sensibilize
3. Where possible, adapt the consent process

1.3.5 The informed consent process in clinical research involving low-income population

Special caution is needed when low-income populations are enrolled in clinical studies in order to ensure they have not been coerced (through social conditioning, pressures by medical staff or the research team) or unduly influenced to participate (financially, by offering better healthcare or by their family). It is important that these aspects are not underestimated due to other priority interests.

Investigators should ensure that potential participants with low literacy levels have fully understood all the benefits and risks relating to their enrolment in clinical research. Investigators should pay special attention to ensure that people from vulnerable social contexts have willingly consented to participate.

OTHER RELATED FACT SHEETS:

FACT SHEET II. PRESENTING STUDY INFORMATION

FACT SHEET IV. INFORMATION TO GIVE TO POTENTIAL PARTICIPANTS DURING THE INFORMATION PHASE

FACT SHEET V. INVESTIGATOR-PARTICIPANT RELATIONSHIP DURING THE CONSENT PROCESS

FACT SHEET VI. HOW TO ASSESS PARTICIPANT COMPREHENSION

FACT SHEET IX. THE INFORMED CONSENT PROCESS IN CLINICAL RESEARCH INVOLVING HEALTHY PARTICIPANTS

FACT SHEET X. INFORMED CONSENT AND THE USE AND STORAGE OF BIOLOGICAL SAMPLES AND DATA.



2. CHECKLIST

A STEP-BY-STEP GUIDE FOR CONDUCTING THE CONSENT PROCESS

This step-by-step guide includes key points for good practice in clinical studies. Use of the guide can assist investigators and organisations to fulfil the requirements of regulatory, funding and other bodies and ensure that important issues have not been overlooked.



2.1 STEP 1: FIRST CONTACT WITH THE POTENTIAL PARTICIPANT

The first contact is the beginning of the recruitment process for potential study participants. This initial stage aims to provide essential information about the study, and explain the nature of participation and what it would involve, before the continuation of the full recruitment process. However,

before an individual has the option to decide whether or not to participate, they must be aware that the study is being conducted. Investigators may therefore need to think beyond traditional recruitment techniques to ensure their target audience is reached.

Points to consider when designing a recruitment strategy:

- Have you identified your target group?
- Have you considered which methods you will use to identify the needs of potential participants?
- Have you considered what methods / professionals you will use for the first contact with potential participants?
- Have you included all the basic information in the first contact? (see FACT SHEET III)
- Have you ensured that information is presented in a neutral way?
- Has everyone who can participate had access to the information?
- Have you considered the use of different formats/ channels for the first contact? Have you considered the appropriateness of that media/format from a social, methodological, legal and ethical point of view?
- Have all your recruitment materials and methods been approved by an Independent Ethics Committee?



2.2 STEP 2: PROVISION OF INFORMATION

It is important to consider the provision of information in written or digital formats as complementary and not a substitute for face-to-face discussions between the potential participant and investigator. Evidence suggests that simple and shorter consent forms and increased dialogue between potential participants and study team members may improve understanding.

People typically show lower levels of comprehension when

information is presented in long consent documents. In order to increase participant knowledge and understanding, use short and enhanced consent forms, translated into simplified documents (paper or electronic formats) with improved design. Consider text style, images/graphics, summary sections, booklets or leaflets, page layout, revised language, shorter sentences, improved readability, non-technical words, bullet points, different fonts, etc.

Points to consider when preparing study information:

- Have information materials been prepared taking into account the target population?
- Have you tested your communication materials with representatives of your target population? Have you tested it with men and women (if applicable)?
- Is the information clear and concise? (see FACT SHEET II)
- Is the information relevant and complete? (see FACT SHEET IV)
- Has it been presented in a neutral/balanced way?
- Have you provided references to reliable sources of information? (see FACT SHEET I and TOOL VI)
- Does the study include placebo control? Have you informed participants about the details of its use and the placebo effect? (see FACT SHEET XI)
- Have you informed participants about the incidental findings policy? (see FACT SHEET X)
- Have you considered a range of media channels/platforms/formats?
- Have all the information materials been approved by an Independent Ethics Committee?

2.3 STEP 3: DISCUSSION AND DECISION MAKING

For a well-designed consent process, interaction between the potential participants involved in clinical studies and investigators is essential. The consent process should be adapted to meet the particular needs of individual study participants (see Section 1.3) and it should involve an ongoing, interactive conversation between the participant and the investigator, throughout the process. Establishing

a relationship of trust, having good communication skills and cultural sensitivities (if applicable to the study) can improve the interaction between the research team and the participants.

A member of the research team must be available to explain the information and answer questions raised by potential participants.



The discussion must clarify:

- all risks and benefits (direct or indirect) of participation
- what participation will involve (in terms of time commitments, procedures and the responsibility of participants).

Ensure that the potential participant has fully understood the information presented and the process, has adequate time to consider the information received and decide whether or not to participate, and has not been coerced.

Points to consider during the discussion and decision making process:

- Has the participant had appropriate time in a suitable environment to process the information?
- Have you checked that the participant understood all the information before signing the informed consent? (see FACT SHEET VI)
- Have you offered the potential participant a decision aid tool? (see FACT SHEET VII)
- Have you offered alternative communication channels between the participant and investigator to resolve any doubts about the study?
- Has informed consent been obtained before enrolling the participant in the study?
- Have you asked participants for feedback? (see TOOL II)

2.4 STEP 4: INTERVENTION AND FOLLOW UP

At this stage of the process, the research team should:

- be easily available to respond to any questions and concerns research participants may have;
- share any new and relevant information which becomes available;
- and provide study updates.



Points to consider during the intervention and follow up:

- Is the participant happy with their participation? If not, are they aware that they can withdraw at any time, without consequences?
- Have participants who become adults during the study consented to their continued participation?
- Have you ensured that participants know how to contact the research team?
- Have you checked if the latest version of the informed consent is being used? (see FACT SHEET VIII)
- Can the participant have access to the information used during the recruitment process?
- Have you asked participants for feedback? (see TOOL II)



2.5 STEP 5: COMPLETION OF THE STUDY

Participants should be taken into account when disseminating the results and a lay-language summary of the finding should be accessible to them. The participants should be informed about when the summary is expected to be available and how they can access it (see TOOL IV) through a range of media.

The method of sharing information with participants, such as information about the treatment group assigned (in blinded clinical trials), must be planned in advance and offered to participants in a range of media channels/platforms/formats.

Points to consider once the study has been completed:

- Have you delivered the thank you letter to the participant? (see TOOL III)
- Have you asked participants for feedback? (see TOOL II)



3. FACT SHEETS AND TOOLS

The fact sheets deal with aspects directly related to the informed consent process, while the tools include aspects that do not strictly belong to the informed consent process but are useful for its better development.

3.1 FACT SHEETS

- FACT SHEET I. Communicating at the appropriate health literacy level for participants
- FACT SHEET II. Presenting study information
- FACT SHEET III. Advertising the study
- FACT SHEET IV. Information to give to potential participants during the information phase
- FACT SHEET V. Investigator-participant relationship during the consent process
- FACT SHEET VI. How to assess participant's comprehension
- FACT SHEET VII. The use of decision aid tools
- FACT SHEET VIII. When is re-consent needed?
- FACT SHEET IX. The informed consent process in clinical research involving healthy participants
- FACT SHEET X. Informed consent and the use and storage of biological samples and data
- FACT SHEET XI. Ethical considerations of using placebo control in clinical trials

3.2 TOOLS

- TOOL I. How to become a good communicator
- TOOL II. How to gain participants' feedback
- TOOL III. Guidance on creating "thank you" letters
- TOOL IV. Creating a summary of the results for laypersons
- TOOL V. Methodologies and tools to incorporate the participants' perspective
- TOOL VI. Fake news and the reliability of sources



FACT SHEET I.

COMMUNICATING AT THE APPROPRIATE HEALTH LITERACY LEVEL FOR PARTICIPANTS

Introduction

For many people in society, complex health concepts can be difficult to understand. Health literacy refers to the degree to which individuals have the capacity to comprehend, access and apply health information in order to make an appropriate health decision. Study information should be adapted to the health literacy level of the potential participant to enable them to make an appropriate decision about whether or not to take part. Participants'

comprehension of the information provided through the informed consent process is one indicator of its quality. To enable comprehension, appropriate, accurate and relevant information should be provided in a language and format that is understood by participants. New technologies can be useful for communicating consent information. Investigators should ensure the accuracy of the information provided and the suitability of its communication.

Recommendations

Some practical tips for increasing health literacy include:



Use a glossary of terms to explain the more complex concepts. The use of dictionaries and links to "further information" is also recommended.



Ask open questions to assess understanding.



Provide information at a level of at least three years of education less than the average level of the target population. See FACT SHEET II.v



Employ multimedia tools for a specific objective, always taking into consideration the characteristics of your target population.



Use storytelling formats when appropriate, e.g with children.



Train your participants to improve their digital and health literacy. Critical thinking skills can empower citizens to freely decide which sources of information they prefer and what they share on social media.

FACT SHEET II. PRESENTING STUDY INFORMATION

Use clear and concise information

Use a layered approach for presenting study information:

- In the first layer, provide a concise and non-technical summary of the study which provides the essential information that participants need to make an informed decision about whether or not to take part.
- In the second or further layers, include more detailed information.

Present information taking into account the interest of the potential participants, in an orderly manner. For example, a workshop with patient group representatives (i-CONSENT deliverable 1.6) revealed that ethical approval should be placed at the beginning of the document to reassure prospective participants that the research has been appropriately reviewed.

- Describe the purpose of the study early in the document.

Include the key points in booklets, leaflets or a flowchart to facilitate understanding.

Use graphics to complement information

Include graphics to facilitate processing and enhancing comprehension, independently of an individual's health literacy level. Graphics might include:

- Diagrams
- Pictures
- Icons
- Infographics

Provide information in different formats

Alongside with a personal and face-to face interaction, consider the use of digital tools or multimedia components, such as:

- Video with voice over
- Webpage with hyperlinks
- Mobile App

Give potential participants a choice of more than one format for receiving information.

Ensure written information is easily readable

Use plain language and avoid technical jargon:

- There are some guidelines or toolkits that can help. "The [PRISM Readability toolkit](#)"¹⁷, for example, includes strategies, real-world examples and related resources to help investigators create easy to understand materials.

Measure the readability of a text by using validated indexes or TOOLS designed for that language, such as:

- Dutch: Leesindex
- English: Flesch Kincaid Index and Reading ease score
- French: Kandel and Moles Modified Flesch Reading ease score
- German: Hohenheim Comprehensibility index
- Italian: GULPEASE index
- Spanish: Fernández Huerta index
- Swedish: Lasbarhets index

Jubelirer et al. indicate that "consent forms and other health education materials should be written at least three grade levels lower than the average educational level of the target population"¹⁸.

Ensure legibility: use appropriate font styles, sizes and colours; use images, tables and graphics properly.

- Some tools, such as the [CDC's "Simply Put](#). A guide for creating easy-to-understand materials", provide guidance on this.

Include an easy to understand glossary of difficult to understand or technical terms

OTHER RELATED FACT SHEETS:

FACT SHEET IV. INFORMATION TO GIVE TO
POTENTIAL PARTICIPANTS DURING THE
INFORMATION PHASE

17. Ridpath JR, Greene SM, Wiese CJ; PRISM Readability TOOLkit. 3rd ed. Seattle: Group Health Research Institute; 2007.

18. Jubelirer SJ, Linton JC, Magnetti SM. Reading versus comprehension: Implications for patient education and consent in an outpatient oncology clinic. *J Cancer Educ.* 1994; 9(1):26-29.



FACT SHEET III. ADVERTISING THE STUDY

The first contact with potential participants may be carried out in several ways, such as in person, by letter/ email, telephone call, via an advertisement, etc. The method you plan to use must be appropriate from a social, methodological, legal and ethical point of view. All materials and methods selected for the first contact with potential participants must be approved in advance by an Independent Ethics Committee.

During the first contact:

- Provide information to potential participants in simple language.
- Avoid using content or language that could lead to misconceptions or promises of non-proven benefits.
- Ensure that any information about the study (such as explanations of the methods, scope of the study, etc.) is presented in an accessible way.
- Design the information to account for a possible lack of health literacy of the potential participant.

Considerations for different forms of communication

In person	Plan in advance what will be said to the potential participant to ensure that they are provided with all the necessary information. Rehearse the conversation beforehand.
Letter/email	Check if you are authorised to carry out the first contact. Decide in advance how you will manage non-respondents (if you will re-contact them, specify this in your first letter/email). Avoid including personal and confidential information as letters may be opened by someone other than the potential participant. Be cautious with the personal information included, as emails and letters can be unsecure channels.
Telephone	In order to protect the privacy of potential participants, this method is not recommended if there has not been previous contact with them. Plan what will be said to the potential participant and rehearse the conversation in advance.
Advertisement	Choose the most appropriate format (flyers, newsletters, websites, social media posts, posters, etc.) for your intended audience. Be aware of the language you use. Avoid inducement and use neutral language.

The information provided in the first contact with the potential participant should include:

- The purpose of the research, the importance of the study and expected duration.
- The target population with some inclusion and exclusion criteria (e.g. pregnant women between 18-40 years old).
- A brief description of the relevant study procedures (e.g. a routine blood sample).
- Contact person at the study site.

OTHER RELATED FACT SHEETS:

FACT SHEET II. PRESENTING STUDY INFORMATION

FACT SHEET IV. INFORMATION TO GIVE TO POTENTIAL PARTICIPANTS DURING THE INFORMATION PHASE PARTICIPANTS DURING THE INFORMATION PHASE



FACT SHEET IV.

INFORMATION TO GIVE TO POTENTIAL PARTICIPANTS DURING THE INFORMATION PHASE

The European Clinical Trial Regulation (CTR) [\[REGULATION \(EU\) 536/2014\]](#) specifies the type of information potential participants must be provided with before they decide to enrol in a clinical research study, and this can be complemented by major international ethics guidelines¹⁹.

The information elements to provide potential participants with can be arranged into four broad categories: (i) information about the research study; (ii) information about participants' rights; (iii) information about data protection; (iv) general information.

Information elements about the research study

- Aims and purpose
- Inclusion and exclusion criteria
- Methods and procedures, including planned genetic test
- Experimental aspects in the research and uncertainties related to the experimentation
- Approximate number of participants
- If other hospitals/research centres are involved
- Expected duration of participation
- Sponsors and funding sources
- Possible reasons for early termination
- Anticipated direct/indirect benefits
- Foreseeable risks or inconveniences
- Risk minimisation
- Alternative procedures of treatment
- Treatment options in case of harm
- Gratuity of participation
- Reimbursement for expenses related to study participation
- Limits of compensation in the event of injury or harm
- A copy of the ethics committee approval should also be made available to potential participants.
- Trial registration number (indication of when results available)
- Limits of compensation in the event of injury or harm
- A copy of the ethics committee approval should also be made available to potential participants.
- Trial registration number (indication of when results available)

19. WMA, Declaration of Helsinki – Ethical Principles for Medical Research Involving Humans, 1964, latest revision 2013, art. 26; CIOMS, International Ethical Guidelines for Health Research Involving Humans, 2016, Appendix 2 "Obtaining informed consent: essential information for prospective research participants"; ICH, Good Clinical Practice (E6), par. 4.8.10, provides a list of required contents for the informed consent form



FACT SHEET IV.

INFORMATION TO GIVE TO POTENTIAL PARTICIPANTS DURING THE INFORMATION PHASE

Information elements about participants' rights

- Right to receive information
- Right to ask additional questions or for clarification
- Right to receive any new information about the research
- Right to refuse participation

Information elements about protection of data

- Measures to protect confidentiality of medical health records
- Procedures for accessing personal medical health records
- Data collection, storage and/or the reuse of biological samples and further processing of previously collected personal data
- Consent for sharing or disclosure of data to third parties and for what purposes
- The storage of biological samples and possible further reuse of biological samples and personal data
- Conditions for disclosure of incidental findings

General information

- Identification of study as research
- Differentiation between research study and medical treatment
- Explanation of research methodology (e.g. randomisation, placebo, blinding etc.)
- Institutional affiliation of investigator(s)
- Contact details of investigator(s)

Sources:

WMA Declaration of Helsinki (2013), Regulation (EU) 536/2014, CIOMS International Ethical Guidelines for Health-related Research involving Humans (2016), ICH E6 (R2) Guidelines for Good Clinical Practice (GCP) (2016).



FACT SHEET V.

INVESTIGATOR–PARTICIPANT RELATIONSHIP DURING THE CONSENT PROCESS

Written documents, such as information sheets and/or booklets are an essential feature of the informed consent process, however the importance of the relationship between the participant and research team should not be overlooked. Effective investigator-participant relationships not only aid comprehension of complex medical

information but can also help identify when a person's emotions, perceptions or expectations may interfere with their decision about participating in the study. Moreover, effective communication can result in a positive impact on study recruitment and retention and can help alleviate concerns a participant might have about clinical research.

Study comprehension	A positive relationship between investigator-participant is essential in ensuring that participants feel comfortable to ask questions, and can clarify their understanding, without feeling pressured to participate. Participants can sometimes feel overwhelmed after reading extensive and complex study information, but such effects can be reduced through clear and open communication.
Managing participants' expectations	Trustworthy and clear information is important to ensure that any person considering taking part in a trial is aware of what their participation will entail. Investigators are in a unique position to provide such information. Investigators should receive appropriate training to ensure that verbal communication is delivered in a balanced and complete manner. This communication contributes to create trust.
Children's assent and family dynamics	For clinical studies involving children, the importance of good communication and trust is even further emphasised. Research teams need to establish good relationships with both the child and parent. The ideal scenario would be the investigator, child and parents working as a team. Emphasis should be placed on all parties, including the child. All parties should share and discuss their concerns in order to agree on a decision that is in the best interests of the child.
Gender	Gender-based communication differences may affect the participant-investigator dynamic, both in the way investigators communicate and the way in which participants interact with the investigator. In research of a more sensitive nature (e.g. trials of vaccines against sexually transmitted diseases) it may be beneficial if the investigator in contact with the potential participant is of his/her same sex. However, the major focus should be on connecting with the individual participant, rather than making gender-based assumptions.



FACT SHEET VI. HOW TO ASSESS PARTICIPANT'S COMPREHENSION

Comprehension is a key element of the informed consent process, directly determining its quality and how ethical principles are applied.

The best way to ensure that the potential participant has understood information about the study to make an informed decision, is through a conversation with the investigator. If the investigator does not have adequate communication skills, it is recommended that he/she seeks to improve them.

Additionally, there are some tools and methods that can be used to assess comprehension. Their use may, however, cause the potential participant to feel as if they are being evaluated or examined. As a result, these methods should not be the first choice to assess comprehension. Among these tools or methods we find:

<p>Interview</p>	<p>The investigator should plan the interview in advance and include questions to assess participant understanding.</p> <p>The following method may help to assess potential participant's understanding:</p> <ul style="list-style-type: none"> • Teach-back method: asking potential participants to describe in their own words their understanding of what they have been told by the investigator.
<p>Questionnaires</p>	<p>The following proposed tools are validated questionnaires that can be used to assess a potential participant's understanding of the information:</p> <ul style="list-style-type: none"> • Quality of Informed Consent (QuIC) ²⁰ • Deacones Informed Consent comprehension test (DICCT) ²¹ • Brief Informed Consent Evaluation Protocol (BICEP) ²²

Source: own elaboration

Consider any therapeutic misconceptions or unrealistic optimism that participants may have when disclosing information, as this can prevent a person from understanding the risks and benefits and may prevent them from being able to properly evaluate the information they need.

NOTE: For investigators with good communication skills, natural conversation is the best option. Be careful not to give the impression of examining the potential participant.

OTHER FACT SHEETS RELATED:

FACT SHEET V. INVESTIGATOR-PARTICIPANT RELATIONSHIP DURING THE CONSENT PROCESS

20. Joffe S, Cook EF, Cleary PD, Clark JW, Weeks JC. Quality of Informed Consent: a New Measure of Understanding Among Research Subjects. *JNCI*. 2001;93(2):139-47.

21. Miller CK, O'Donnell DC, Searight HR, Barbarash RA. The Deaconess Informed Consent Comprehension Test: an assessment TOOL for clinical research subjects. *Pharmacotherapy*. 1996;16(5):872-8.

22. Sugarman J, Lavori PW, Boeger M, Cain C, Edson R, Morrison V, Yeh SS. Evaluating the quality of informed consent. *Clin Trials*. 2005;2(1):34-41.



FACT SHEET VII. THE USE OF DECISION AID TOOLS

What is a participant decision aid?

A tool that helps a potential participant make an informed decision. It describes the decision to be taken, the options available, and the outcomes of these options (including benefits, risks and uncertainties) based on a careful review of the evidence.

They are available in a variety of formats (i.e. online, paper based or video). Their purpose is to:

- Provide a structured method for potential participants to evaluate the available options.
- Encourage active engagement with the decision-making process.
- Help prospective participants reflect on their own values and preferences.

Ideally, potential participants should be given sufficient time to work through the decision aid. They should be given the opportunity to discuss the use of the tool with the clinician, before reaching their final decision.

Key benefits of using decision aid tools:

- To place the focus on the prospective participant. Although participants may expect the clinician to advise on the best option, ultimately, this decision must be made by the participant.
- To provide an accurate explanation of the risks.
- To present the information clearly and without bias.
- To allow the use of icons and other visual aids to help distinguish the pros and cons.
- To go beyond providing information, and seek to help people consider their own values.

Decision aids support prospective participants to:

- Improve their knowledge and understanding of the information given and their options.
- Make choices that are consistent with their values.
- Participate more actively in the decision making process.
- Have more accurate and realistic expectations of benefits and risks.

Pros
of the study



Cons
of the study

Further resources in: [International Patient Decision Aids Standards \(IPDAS\)](#); “[Development and evaluation of decision aids for people considering taking part in a clinical trial: a conceptual framework](#)” and “[A systematic development process for patient decision aids](#)”



FACT SHEET VIII. WHEN IS RE-CONSENT NEEDED?

Consent is ongoing but can be withdrawn at any time and dissent should always be respected. Under certain circumstances during the study, it may be necessary to re-affirm participants' willingness to remain in the study. This is referred to as "re-consent".

Circumstances that require participants to re-consent

- A substantive change in the conditions, procedures or protocol of the research.
- New information becomes available that could affect the willingness of participants to continue, for example, a new treatment alternative
- In the clinical study, new elements appear regarding the use of data which were not stated in the original consent document.
- The original consent document has been improperly signed or documented.



Consent for the first time

It is the case of a participant initially unable to give consent, who reaches the capacity to consent.

- A minor participant reaching the legal age to consent (according to national legislation) during the research will need to sign the consent form.
- Alongside with consent for the first time, participants should be given the opportunity to give consent to the storage and use of his/her biological samples or data (if applicable).

Consent for a different use

The protocol for every study using stored human biological materials and related data must be submitted to the independent ethics committee, which must ensure that the proposed use of the materials falls within the scope specifically agreed to by the donor, if the donor has given broad informed consent for future research.

Re-consent is necessary:

- If the proposed use falls outside the authorized scope of research
- If the initial consent does not cover purposes for future research.

New consent must be approved by an Independent Ethics Committee (IEC) or an Independent Ethics Committee (IEC).

Sources: elaborated from Resnik D (2009)²³; Dixon-Woods M et al. (2017)²⁴

23. Resnik D. Re-consenting human subjects: ethical, legal and practical issues. *Journal of medical ethics*. 2009;35(11):656-7.

24. Dixon-Woods M, Kocman D, Brewster L, Willars J, Laurie G, Tarrant C. A qualitative study of participants' views on re-consent in a longitudinal biobank. *BMC medical ethics*. 2017;18(1):22.

FACT SHEET IX.

THE INFORMED CONSENT PROCESS IN CLINICAL RESEARCH INVOLVING HEALTHY PARTICIPANTS

What is a healthy participant/volunteer?

The Royal College of Physicians²⁵ defines a healthy volunteer as “an individual who is not known to suffer any significant illness relevant to the proposed study, who should be within the ordinary range of body measurements such as weight, and whose mental state is such that he is able to understand and give valid consent to the study.”

Four points to be aware of:

1. Coercion and influence must not be used when obtaining informed consent.
2. Participants should be reasonably reimbursed for costs directly incurred during the research, such as travel costs, and compensated reasonably for their inconvenience and time spent.
3. It should be clear that there is no financial compensation for the participation in a study. Ensure that participants are not influenced by economic reasons.

4. The participants' understanding of the risks should be carefully assessed. Investigators should be able to identify any healthy participants that are not fully aware of the risks of the study.

Key issues

Ensure that potential participant:

is not taking part in another clinical trial at the same time and is not motivated by reimbursement;

- understands the risks, the benefits and the absence of therapeutic benefits;
- understands all key features of the study, that participation is not compulsory and that they can withdraw at any time.

To achieve this, the information should be adjusted to meet the needs of those with low literacy levels.



25. Royal College of Physicians. Research on healthy volunteers. A report of the Royal College of Physicians. J R Coll Physicians Lond. 1986;20(4):243-57.



FACT SHEET X.

INFORMED CONSENT AND THE USE AND STORAGE OF BIOLOGICAL SAMPLES AND DATA

Biological samples are often stored in biobanks in clinical research. Informed consent for the biobanking and re-use of biological samples and data has to be obtained in addition to consent for participation in clinical research. Remember that research participants and donors:

- must be previously informed about the collection, storage (time, place) and possible future uses of their biological samples;
- must be provided with a description of any planned genetic test;
- must be provided with the option of: consenting (or not) to research on biological samples for research directly related to the trial; and of consenting (or not) to the use of biological samples for research not directly related to the original trial;
- should be given the opportunity to withdraw from research, and to be assured of the removal and destruction of any stored samples and/or information;
- should be given the option for their biological samples to be 'anonymized' or 'pseudonymized' (or codified). With the first option the link between the biological samples and personal/clinical data of the participant is removed (this option, on the one hand undermines the meaning of research, while on the other guarantees privacy); the second option maintains the link between the samples and participant data, through a key under the investigator's custody (this option guarantees a measure of confidentiality, but this is not complete), but it is vital to building trust and enhancing involvement in research activities. "Pseudonymization" is in line with the [European General Data Protection Regulation 679/2016](#). Participants should also be given an explanation of the advantages/disadvantages of each option;

- should be informed about data storage, risks of confidentiality and disclosure in certain circumstances.

Investigators should be transparent and inform participants and donors about the methods and goals set for the use of samples, drawing a clear distinction between research and therapeutic applications as a possible option. Participants who reach the legal age to consent during the research should be given the opportunity to give informed consent to the storage and use of their specimens or data.

The establishment of ethics committees in every biobank, who are in charge of supervising research and ethical conditions, carrying out surveillance on ethical standards and compliance with donors' consent is considered relevant.

ISSUES RELATING TO INCIDENTAL FINDINGS

An incidental findings policy between investigators and potential participants should be agreed through informed consent.

- Donors should be informed of expected or possible unexpected results, with regard to information relating to the diagnosis of ongoing diseases, the susceptibility/predictability of possible future diseases, also involving family members.
- Findings should be fed back when they are of immediate clinical relevance from a preventive, diagnostic and therapeutic level, and for reproductive choices. Adult participants should be given the opportunity to agree or decline this information and decide whether this information should be disclosed to family members. Investigators should ensure this even if the biobank has no diagnostic purpose.
- In the case of minors: parents should receive information relevant on a preventive, diagnostic and therapeutic level, and for reproductive choices. Communication about late-



FACT SHEET X.

INFORMED CONSENT AND THE USE AND STORAGE OF BIOLOGICAL SAMPLES AND DATA

onset disease should be discussed and included in the informed consent, also giving the option of the results being communicated only to the physician.

ISSUES RELATING TO CONFIDENTIALITY

Protection of personal data is required to guarantee the individual's right to confidentiality, through the anonymization, codification or pseudonymization of stored information that can be carried out on biological samples, tissues and/or collected health data stored for clinical practice purposes.

Data protection reduces the risk that information can be used for discriminatory purposes (i.e. in the field of insurance or employment), minimizing the possibility that stakeholders other than donors, family members, investigators and the scientific community might access personally identifiable information collected and stored for scientific purposes.

Confidentiality of health data is mandatory and should also be assured within the family in some circumstances, although information should not be shared with parents about minors if not necessary.

OTHER RELATED FACT SHEETS:

FACT SHEET IV. INFORMATION TO GIVE TO POTENTIAL PARTICIPANTS IN THE INFORMATION PHASE.



FACT SHEET XI. THE USE OF PLACEBO IN CLINICAL TRIALS

Placebo is a very complex concept which means it should be clearly explained to the participants.

What information should be given to potential participants when the study includes the use of placebo control?

- Short description of placebo control and its use in clinical research
- Short description of possible placebo or nocebo effects
- Describe the procedures related to placebo control (possibility that not all the participants will receive the drug that is being tested, how many participants will receive placebo and how they will be selected, etc.)
- Describe any further possible risks
- The use of placebo in a research protocol is approved by the Independent Ethics Committee (IEC).

EXAMPLE OF INFORMATION TO DELIVER:

What is placebo?

[Medline](#) defines placebo as “An inactive, non-drug compound that is designed to look just like the test drug. It is administered to control group subjects in double-blind clinical trials (in which neither the researchers nor the subjects know who is getting the drug and who is getting the placebo) as a means of assessing the benefits and liabilities of the test drug taken by experimental group subjects.”²⁶

What is placebo effect?

An apparent result of a drug that occurs due to the patient's expectation of having received it, even though they have not. These effects can be positive (based on the expected effect of the drug) or negative (based on the expected side effects).



26. [Glossary \[Internet\]. United States: The National Multiple Sclerosis Society. \[cited 2021 February 23\]. Available from: https://www.nationalmssociety.org/Glossary](https://www.nationalmssociety.org/Glossary)

FACT SHEET XII.

INFORMED CONSENT, CLINICAL RESEARCH AND COVID-19

Clinical research is crucial in facing the health impact of the COVID-19 pandemic. However, even in the emergency setting due to the pandemic, scientific, ethical and legal requirements of biomedical research must be respected.

Despite the urgent need for quick advances in COVID-19 treatment, the ethical imperative to obtain informed consent remains. No matter how extreme the conditions, informed consent must be taken into account to ensure that those who decide to participate in the research can effectively understand risks and potential benefits, and make informed decisions.

Clinical trials during the COVID-19 pandemic

Even in the context of the pandemic emergency, the general ethical criteria of clinical trials should be respected, as should the relevant legal regulation:

- the scientific justification of the validity of the trials
- the balancing of risks/benefits
- the protection of health, safety and well-being of the patient/participant
- the informed consent process
- the informed consent process related to the use of biological samples
- privacy and data protection requirements
- the study review by independent ethics committees
- the absence of any conflict of interest from of all personnel involved in the study

So called “regulatory flexibility” aims to guarantee the achievement of all these requirements, while accelerating as much as possible the process for scientific and ethical evaluation of clinical protocols concerning treatments for and vaccines against COVID-19. This has been instituted

at international and national level, for example establishing scientific, regulatory and ethical bodies with the specific task of evaluating clinical studies related to COVID-19 at both a scientific and ethical level.

A trial of therapeutic treatments for COVID-19 must not exclude any subject, unless there is an unfavourable risk / benefit ratio. The exclusion of particularly vulnerable people from the trial is contrary to the principle of justice, as it deprives them of the same possibility of treatment, as no safe and effective treatment is currently available. Fundamental rights and freedoms, in particular the right to privacy, must be guaranteed.

The impact of the Coronavirus pandemic needs to be considered on both ongoing trials and new clinical trials. Participants should be informed regarding the impact the situation might have on the trial protocol, with possible changes in the risk/benefit balance and possible interruption of trials.

At every stage, it is very important for participants to be kept informed of changes to study and other plans that could impact their care. Since trial participants may not be able to visit the site for the protocol specific visits and investigations, sponsors should evaluate whether alternative measures such as virtual visits, alternative locations for assessment, including imaging centres and labs, could suffice, while ensuring the safety of the participant. This is important for trials that include participants who need additional safety monitoring.



FACT SHEET XII.

INFORMED CONSENT, CLINICAL RESEARCH AND COVID-19

Information regarding relevant therapeutic alternatives (if any)

Informed consent for clinical research also requires information to be provided about relevant alternatives that might be beneficial to the individual. It is the responsibility of the physician to properly inform the patient of any alternative clinical trial that would be a good option for patients. Clinicians may also be asked to make recommendations between multiple clinical trials, given the proliferation of COVID-19 studies.

Experimental protocols, vulnerability and the information process to the patient/participants

It is essential that researchers realistically balance the potential benefits and risks for research participants:

- avoiding trials in which the risks outweigh the possible benefits;
- evaluating risks and benefits considering the specific conditions of the patient, including situations of particular vulnerability;
- communicating risks and benefits in a clear and transparent way to potential participants;
- communicating scientific uncertainties related to the still scarce existing scientific knowledge about COVID-19.

Researchers have the responsibility to manage the information process and to carefully inform patients on the above mentioned aspects.

In particular, in trials for COVID-19 treatments, the best available standard of care should be guaranteed to all the patients participating in the trial. The identification of the standard of care, although difficult to determine, is a crucial ethical requirement for the study design and therefore for the information to the patient. In this specific context, randomized controlled trials are ethically controversial when offering participants randomization into a placebo arm that could produce serious harm including additional suffering, or even death. Adaptive and pragmatic clinical trial designs are the only methodological alternative, even if ethically challenging.

Researchers must consider the particular condition of vulnerability in the pandemic context and always evaluate the best interest of the patient, despite the possible request of patients to participate in a COVID-19 trial for therapeutic purposes.

Furthermore, researcher must consider informed consent in the context of the development of the disease (there are many decisions to be made at different times), choosing the appropriate time for the patient, considering their ability to understand and their emotional condition.

Despite the external pressure to start/conduct clinical trials, it is of paramount importance to respect the participant's decision-making process, considering – when there are uncertainties - that fear and discomfort can compromise confident and effective participation.

In addition, considering the existing general pressure for accelerating research in order to obtain useful results to combat the COVID-19 pandemic as soon as possible, researchers should carefully balance communication through social media of partial or in-progress scientific results. This is recommended in order to avoid the spread of so called fake-news that can result in disinformation or even in slowdown of research itself (for example because of the confusion generated by fake news amongst study participants).



FACT SHEET XII.

INFORMED CONSENT, CLINICAL RESEARCH AND COVID-19

Adaptive and pragmatic clinical trials

- Adaptive and pragmatic clinical trials search for a balance between the needs of clinicians to save lives and the needs of the medical and scientific community to obtain evidence of sufficient quality and scientific rigour.
- Pragmatic and adaptive trials designs produce true “experimental evidence”, based on a methodology of pragmatism and adaptation: Pragmatism means that physicians continue to treat their patients without the restricted limitations of protocols, obtaining a rapid recruitment of a broad population without a precise standard of care defined at the beginning, which is likely to change during the trial; Adaptation means flexibility, considering possible change from the initial design as more data becomes available, considering the evolution of data.
- Adaptive and pragmatic designs can balance the rapidly changing standards of care with speed and agility.

Information process in the case of adaptive and pragmatic clinical trials

- Participants as patients should be correctly informed about the design of trials and how they differ from traditional trials, explaining the necessity of adaptation and pragmatism.
- Physicians/investigators should inform that participation in research encompasses uncertainties because of lack of knowledge about the best treatment: the absence of a standard of care should be mentioned explicitly in the informed consent and correctly explained to patients. This means that the patients should gain awareness that a pharmaceuticals considered beneficial at the beginning of the trials, could become harmful during the trial or at the end of the trial.
- It follows the obligation for the doctor to provide comprehensive, clear and comprehensible information with an empathic attitude.
- The shared purpose (of both physicians and patients) is to allow the patient to make an informed decision appropriate to the situation with proportionate and realistic expectations. Maximum transparency and clarity is required of the doctor especially if the possible side effects and potential harmful effects of the therapy are not known, so as to allow the patient to exercise their autonomy.
- This intense situation can produce an atmosphere of mutual pressure between patient and doctor: one expects a remedy at any cost and the other aspires to provide it in any way. The proportionality of the information should lie in the difficult relationship between the maximum expected benefit and the least foreseeable harm.

Informed consent and digital/other ways of consenting in a pandemic

Information provided by the researcher must also be transparent in the clarification of uncertainties: it is necessary to verify the participant’s understanding, being

aware that, in the context of the pandemic, the perception of risks has decreased, in face of expectations that are not always reasonable.



FACT SHEET XII.

INFORMED CONSENT, CLINICAL RESEARCH AND COVID-19

According to ethical and legal requirements for informed consent in an emergency situation:

- In compliance with health protocols in relation to SARS-CoV-2, exceptions to traditional written consent are allowed with the use of digital consent or oral consent in the presence of witnesses. In the latter case, it is important to confirm the patient's consent through third parties, that is, a person external to the health team and possibly to the health structure; also, where possible, the patient's consent should be confirmed with relatives on video call.
- When a patient is not able to receive and understand the information, but s/he is affected by pathological conditions without alternative treatment and it is not possible to promptly consult the trustee or a legal representative, for the authorization to prolong participation in a trial with potential direct benefits, consent should be obtained when it is reasonably possible to do.
- The doctor must comply as far as possible with the indications of any "advance treatment arrangements" or "shared care planning", and the indication of a trustee.
- In case of changes in protocols, which are frequent due to the evolution of the pandemic, consent must be, to the extent possible, requested again with the appropriate changes.
- Where it is not possible to obtain informed consent in the usual form (written consent), due to movement restrictions or patient isolation, alternative procedures should be considered, but as soon as the situation permits it, informed consent must be obtained.

Alternative procedures for obtaining consent can include:

- **oral or photographed/videotaped consent** in the presence of witnesses (selected according to impartial criteria justified by the investigator);
- **deferred consent**, according to ethical requirements (see the box below);
- **e-Consent**, using digital technologies for informed consent (avoiding paper and improving and speeding up information for patients), according to ethical requirements (see the box below).

Potential benefits of e-Consent

- It allows for enhanced infection prevention and control;
- Potential research participants can utilize Internet-connected device to virtually discuss the trial with researchers and access the informed consent document (advantage over paper consent forms, where the transmission of COVID-19 is possible);
- It facilitates a consent discussion with a patient who is not physically in the hospital. E-Consent also expands participations to populations traditionally not afforded clinical research opportunities through 'remote enrolment';
- Enhanced understanding, as e-consent often make use of boxed text and flexible text size, and incorporates multimedia tools that increase readability, engagement and retention. Ensuring critical information is available online enhances transparency and traceability, and verification of the regulatory process.



FACT SHEET XII.

INFORMED CONSENT, CLINICAL RESEARCH AND COVID-19

Off-label and compassionate use of drugs during the COVID-19 pandemic

In the context of the COVID-19 emergency, given the rapid spread of SARS-CoV-2, the severity of the clinical situation of some patients, the lack of resolutive care and the urgency of treatments for the protection of individual and social health, there is a strong push towards:

- **off-label** use of drugs: the use of a drug for clinical conditions that differ from those for which drug marketing has been authorized,
- **compassionate use** of drugs: the use of an experimental drug outside a clinical trial already in progress, for a single patient or for patients, for whom it is believed there may be a clinical benefit, on the basis of a defined clinical protocol or on a nominal basis for a single patient.

In both situations, patient(s) should be clearly informed about possible risks. Access to unvalidated therapies by compassionate use of drugs should never consist of a hidden experimental protocol, or a “shortcut” to accelerate the pace of research. Access to unproven therapies should not be a “hidden” trial, which, by means of compassionate use, obtains results by bypassing the usual lengthy trial procedures and authorization.

Furthermore, the public health threat posed by the pandemic does not justify coercive treatment.

Remember that:

- consent must be suitably informed, covering the uncertainties, the limits to hope and possible harmfulness or even lethality;
- risk-taking should always be personal;
- off-label/compassionate use of drugs results should be always documented, to benefit from the results for the progress of clinical/scientific knowledge;
- a need to re-consent may be required in case of a newly approved therapy for COVID-19 (which would present an alternative to participation) or of new information on the therapy offered in the trial, discovered during treatment of prior subjects. With rapid changes in understanding of the disease, and hundreds of weekly publications focused on the topic, it may also be unclear how often such disclosure and re-consent should take place: this aspect should be carefully assessed.



FACT SHEET XIII.

THE USE AND STORAGE OF BIOLOGICAL SAMPLES AND DATA IN CLINICAL RESEARCH IN THE COVID-9 PANDEMIC

Biological samples

Informed consent must always be required for the acquisition of biological samples, even in the case of serological tests and swabs.

- It should be specified whether they are taken for diagnostic and/or research purposes;
- As required in clinical research in general, consent must specify the time, place, storage methods of the samples and the purposes of the research, specifying whether it is directly related to research on COVID-19, as well as any subsequent use of samples for compatible purposes;
- In any case, the security of storage and the protection of privacy with pseudonymisation must be guaranteed in a manner that must be specified in the consent, to avoid any abuse and to be able to trace the identity of the subject in the event of results of clinical relevance;
- In the case of biological samples taken from minors, consent must be given by the parents and, upon reaching the age of majority, a new consent must be requested from the subject for their conservation and use, unless they are anonymized.

Considering the urgency and importance of biomedical research for humanity in the context of the pandemic, it is important to encourage the use for clinical research purposes of biological or clinical material residual from previous diagnostic or therapeutic activities.

This should be done defining homogeneous criteria for the use of biological samples, taking into account the procedures for accessing and acquiring the patient's consent on the subsequent use of the sample taken. It is to be hoped that the consensus on biological samples in the context of the COVID-19 pandemic will be broad, that is, open to future uses of the samples for research.

The legal status of biological samples has been problematic since their storage became possible. One of the central issues that has been discussed is that identity is biological as well as relational (so should be the legal status of these samples, some argue).

Should donation then be casually permitted? Given that each biological sample is also linked to our relationships (family, ethnic group, etc.) this is problematic and strongly connects the notion of informed consent to the concept of relational autonomy.

Another delicate issue is whether or not we should have a right not to know. Once more, the response to such a question is related to the interpretation we give to autonomy.

- A first interpretation is that of negative liberty – the freedom from interference from others.
- A second interpretation sees a moral agent that must always have sovereignty over their life/body but needs to know as much as possible -this means a duty to know.
- A third interpretation focuses on the importance of existential freedom (authenticity).

The first and third options allow for the right not to know, while the second does not.



FACT SHEET XIII.

THE USE AND STORAGE OF BIOLOGICAL SAMPLES AND DATA IN CLINICAL RESEARCH IN THE COVID-9 PANDEMIC

Privacy, blanket consent and data

Clinical experimentation in emergency situations also concerns the issue of privacy. At a European level, the relationship between clinical trials regulation and personal data protection regulation (which tends to place less emphasis on the importance of individual informed consent) has become closer than previously -and COVID-19 has had an impact on that. For example, the GDPR has “freed” research in a sense (with broader and more all-encompassing consents called “blanket consent”) and this seems to be more and more the way forward for clinical trials. We can give broad and selective consents (giving consent for e.g., public research, etc.), but in a less all-embracing way that would slow down or interrupt research.

With the advancement of technology, the collection of data can now be done remotely as well as on site and, obviously, the former option has increased drastically due to COVID-19. For example, in the US the FDA requested their employees to move their working time from on site to remote. To make such a change is important in times of pandemic, but we also need to understand what this shift can imply for the scientific validity of the trials.

Hacking is the main threat. In the case of a trial with multiple sites, we should make sure that each site can follow new protocols, because otherwise there is a risk of losing data or control of data if some sites are not able to comply with the requirements. If, for example some sites have outdated, unstable internet connections or easily hackable computers, this could put privacy at risk.

Finally, Data philanthropy (where private individuals or companies share data for the public good) opens the door to clinical trials and beyond as the whole paradigm of owning one’s data will change further as a result of the pandemic.

Data sharing -the practice of sharing data used for research (scholarly, marketing or otherwise) to other investigators- has recently gained attention, in particular in relation to the issue of transparency (or lack thereof) concerning such sharing. Data sharing might also come under stress within the EU as different countries could have different levels of security and this aspect has become particularly relevant in relation to privacy.



FACT SHEET XIV.

COVID-19 CLINICAL TRIALS AND PATIENTS' VULNERABILITIES

Minors

- In COVID-19 minors have been less affected, and those infected less seriously ill, so that the need for trials were not as urgent as in adults. However some children developed severe disease, so completely excluding these vulnerable populations from clinical trials, could exclude them from therapies.
- Multicenter coordinated trials should be prioritized. These would support sufficiently powered studies to test therapies for sicker, hospitalized children and facilitate analyses amongst subgroups with specific predisposing conditions. Existing trial networks like the Pediatric Trial Network could be enlisted. Some therapeutics trials in adults could be extended to include children, as a small number of studies are already doing. Joint studies also would enable resource sharing, alleviating pragmatic barriers to pediatric trials.
- Children receiving drugs for COVID-19 should at least be offered the opportunity to participate in prospective observational studies. Although these studies are limited in their ability to establish efficacy, they would allow prospective data collection on clinical and virological and drug-associated adverse effects. It would also permit comparative subgroup analyses between groups of children with varying risks for adverse outcomes. Conducting controlled, coordinated pediatric trials is the only way to learn whether the potential benefits of these drugs outweigh their risks.

Women

- The “protection by exclusion” of pregnant women from drug development and clinical therapeutic trials, even during pandemics, is not unprecedented. Even during the Ebola virus epidemic, pregnant women were excluded from all therapeutic and vaccine-development trials. This automatic disqualification denies pregnant women the potential for benefit given to other patients.
- The lack of data specific to pregnancy will negatively affect the health of pregnant women and their access to interventions in the current pandemic and beyond. This will create a knowledge gap concerning the safety and efficacy of any drugs or interventions that may emerge from current COVID-19 research. Although fetal safety is the most cited reason for the exclusion from research studies of pregnant women and those who could become pregnant, it is unethical to automatically preclude them from carefully designed clinical therapeutic research studies.
- Pandemics are underlining a cultural shift within the research community to view this population as in need of more evidence, particularly in pharmaceutical research. Pregnant women should be permitted to determine their eligibility and entry into a research study, always based on the principle of informed consent.
- Although one must consider the safety of a drug in pregnancy, it is equally important to consider the risks of not treating or inadequately treating pregnant women. Similarly, the risk of treatment to the fetus needs to be weighed against the risk of inadequate treatment, given that many of the conditions that affect the mother will ultimately adversely affect the fetus if not treated.



FACT SHEET XIV. COVID-19 CLINICAL TRIALS AND PATIENTS' VULNERABILITIES

Patients coming from different cultural backgrounds

- Recruitment strategies and information provision approaches that work for the majority population may be ineffective for minorities. Interpreters, translators and cultural mediators could be needed, along with culturally sensitive recruitment methods.
- Ensuring research is culturally and linguistically accessible and inclusive requires the commitment and resources of researchers from the start. The COVID-19 pandemic has exposed a problem that has been known for a long time.
- Results of research must apply to everyone in the community who will be a candidate for treatment or prevention; researcher should ensure that groups, which are in the minority in a country because of their ethnic origin or some other way are not excluded. If research fails to engage all those who could benefit, there is no guarantee that the results will apply to populations not included in the research.



TOOL I. HOW TO BECOME A GOOD COMMUNICATOR

Effective communication is a skill all healthcare professionals need. It matters not only “what” is said but also “how” and by “whom”. In a single day, healthcare professionals may speak to people of varying educational, cultural and social backgrounds and they must do so in an

effective, caring and professional manner to convey the message and contribute to a participant’s autonomy and understanding of the process.

Here are some key elements to consider:

<p>Consider your environment</p>	<p>Time and place</p> <ul style="list-style-type: none"> • Approaching a participant in a confusing area with lots of people can hinder communication, and therefore participant’s comprehension of the delivered information • Being in a chaotic place may require you to raise your voice which may have a negative impact: intimidation/lack of effective communication and consequently altering free consent • If you are going to be asking personal questions, finding a more private environment is essential to safeguard the privacy of the participant.
<p>Building rapport</p>	<p>Listen and ask questions.</p> <ul style="list-style-type: none"> • Listening without interrupting is vital, as it conveys interest and respect for another’s point of view. Maintain eye contact to keep attention. • Use questions beginning with ‘why’, ‘what’, ‘when’, ‘where’ and ‘how’. Open-ended questions provide the most effective way of understanding another person. • Use the valuable time you have to open the discussion slowly.
<p>Body language & non-verbal communication</p>	<p>Use positive body language</p> <ul style="list-style-type: none"> • Eye contact is important. • Keep your hands and arms in front of your body, without crossing them. • Relax your facial expressions to prevent from grimacing, twisting or pursing your lips, lifting your eyebrows, or scowling. • Tone can help de-escalate a distressed and angry participant. This is referred to as the ‘emotional contagion effect’, where your emotional state can affect how another person feels.



TOOL I. HOW TO BECOME A GOOD COMMUNICATOR

Inclusive communication

- Be patient: It is essential to always respect the participants and dedicate the right amount of time to allow them to express themselves, so to get the whole story.
- Be mindful of your language: Using complicated medical terminology, or 'jargon', is not an effective way to communicate with any participant. Try to use language that is simple, clear and non-threatening, while remaining accurate. Base your language on the questions asked to you and the cognitive ability of the patient you are speaking with.
- If an adult is not able to consent and the consent is given by a family member, their assent must always be respected.
- Take into account participants' age and their level of understanding, and tailor your explanation to meet their needs.
- Regarding older adults: Including the family is often a big part of communicating with older participants. Always try to keep them involved in the conversation.
- Regarding children: Although the parents/guardians may ask most of the questions, it is important to include the child and obtain their assent when talking about procedures and their health.

Some recommendations about what to do and not to do during the consent process, from a communication perspective:

DO:	DO NOT:
<ul style="list-style-type: none"> • Establish a positive relationship with the participant • Make sure the participant feels comfortable to ask questions and clarify their understanding • Provide trustworthy and clear information • Use a plain and understandable language • Use short sentences • Receive appropriate training to ensure that verbal communication is delivered in a balanced and complete manner • When children are involved, focus in both, the child and the parents. 	<ul style="list-style-type: none"> • Overwhelm potential participants with extensive and complex study information • Make gender-based assumptions • Encourage participation, using undue influence (offering an excessive, unwarranted, inappropriate or improper reward or another overture for participating) or unjustified pressure (when people in a position of authority or with influence urge the subject to participate). • Use coercive language (presenting intentionally threat of harm to obtain compliance) • Employ vague expressions • Use exculpatory language • Use too technical or complex terms

Note:

Remember to be careful to use neutral language when communicating with the participant.



TOOL II. HOW TO GAIN PARTICIPANTS' FEEDBACK

The experiences and opinions of potential and current participants can be useful in identifying unforeseen situations and ensuring that the informed consent process is adapted to the informational needs of the participants. This helps to define and improve the process of both ongoing and future studies, making informed consent a dynamic and evolving process.

It is recommended to have a de-briefing session with your team about the consent process using this information. Doing this after the study may help to improve the consent process of future studies, while doing it during the study may help improve the process of the current ones.

How to get the feedback?

- Consider different ways of obtaining feedback from study participants such as via surveys or comment boxes, both in electronic or physical formats. The tool used, and the conditions of its use, must be included in the study protocol and receive approval by the ethics committee.
- Choose the most appropriate mechanism by considering factors such as the participants' personal and social situation and their daily schedule.

- Feedback should be obtained at all stages, i.e. about the experience before starting the study (to get during the first month), during the study (to get during trial progress) and at the end of the study (to get during the last visit).
- Feedback should be obtained in a way that avoids overloading investigators and/or participants.
- The chosen tool should be made available in the participant's language, and the participant should also be allowed to give feedback in their native language.
- Include some free-text boxes so the participant can add any further information they consider relevant.

Example

If you do not have your own questionnaire, i-CONSENT recommends the use of the following toolkit:

- [The Study Participant Feedback Questionnaire toolkit](#) (by Transcelerate Biopharma)²⁷: includes three short, validated surveys designed to capture feedback from participants anonymously at the beginning, during and end of the trial.



27. [Study Participant Feedback Questionnaire Toolkit - TransCelerate](https://www.transceleratebiopharmainc.com/assets/patientexperience/study-participant-feedback-questionnaire/) [Internet]. TransCelerate BioPharma Inc. [cited 2021 February 23]. Available from: <https://www.transceleratebiopharmainc.com/assets/patientexperience/study-participant-feedback-questionnaire/>

TOOL III. GUIDANCE ON CREATING “THANK YOU” LETTERS

A “Thank You” letter expresses gratitude from the investigation team and the sponsor. It is recommended that letters are prepared by the sponsor together with the investigators.

HOW TO PREPARE A THANK YOU LETTER?

- Personalise the letter.
- Highlight the importance of participation in research and the objectives that each participant is helping to reach.
- If possible, include information about the study and a summary of the available results.
- Explain how and when they will be informed about which treatment they received (if applicable).
- Remind participants of their right to access study results: inform them about how to access this information and approximately when it will be available.
- Provide contact details to the participant, in case they would like further information in the future.

WHEN AND HOW TO DELIVER IT?

- Usually, the principal investigator is responsible for sending the letter to the participant, on behalf of all the staff involved and the study sponsor, at the end of their participation in the study.
- It should not be delayed by the results of the study, as it can take several months for results to become available.
- It may be delivered in a number of different ways, such as in person, sent by postal mail, electronic mail or via a notification within a mobile application for the study; always taking into consideration the appropriateness from a social, methodological, legal and ethical point of view.

EXAMPLE:

There are templates in English and other languages such as the ones developed by [Transcelerate Biopharma](#) or by the [Agencia Española de Medicamentos y Productos Sanitarios \(AEMPS\)](#).



TOOL IV.

CREATING A SUMMARY OF THE RESULTS FOR LAYPERSONS

The EU Clinical Trial REGULATION (CTR) [\[REGULATION \(EU\) 536/2014\]](#) requires sponsors to provide summary results of clinical trials in a format understandable to laypersons. This is good practice for all clinical studies and not only clinical trials.

Specifically, participants in clinical studies want to know about the results of the studies they have contributed to, for themselves, their quality of life and society in general. The delivery of this information may influence their satisfaction with the study and their likelihood of participating in future studies.

Contents

The summary of the results of the clinical trial for laypersons according to Annex V of the CTR shall contain:

- 1 *Clinical trial identification (including title of the trial, protocol number, EU trial number and other identifiers);*
- 2 *Name and contact details of the sponsor;*
- 3 *General information about the clinical trial (including where and when the trial was conducted, the main objectives of the trial and an explanation of the reasons for conducting it);*
- 4 *Population of subjects (including information on the number of subjects included in the trial in the Member State concerned, in the Union and in third countries; age group breakdown and gender breakdown; inclusion and exclusion criteria);*
- 5 *Investigational medicinal products used;*
- 6 *Description of adverse reactions and their frequency;*
- 7 *Overall results of the clinical trial;*
- 8 *Comments on the outcome of the clinical trial;*
- 9 *Indication if follow up clinical trials are foreseen;*
- 10 *Indication where additional information could be found.*

Tips to prepare the summary

- Write the summary and reflect data and findings in an objective way (e.g. instead of “this study proved...” use “this study found that...”; or instead of “X is better than Y” use “# of people with treatment X experienced Y”
- Involve participants, patient groups or members of the public in the development and review of the summary. Incorporate health literacy concepts.
- Consider other formats, as well as written, for providing a summary and choose one that best suits the characteristics of the target population.
- The EU also provides [recommendations](#)²⁸ for the implementation of cited Regulation.
- TransCelerate has developed an [implementation guide](#)²⁹ for preparing Layperson Summaries of Clinical Trials

OTHER RELATED FACT SHEETS:

FACT SHEET II. PRESENTING STUDY INFORMATION

TOOL V. METHODOLOGIES AND TOOLS TO INCORPORATE THE PARTICIPANT PERSPECTIVE

TOOL VI. FAKE NEWS AND THE RELIABILITY OF SOURCES

28. [Summaries of Clinical Trial Results for Laypersons Recommendations of the expert group on clinical trials for the implementation of Regulation \(EU\) No 536/2014 on clinical trials on medicinal products for human use. 2018. \[cited 2021 February 23\]. Available from: \[https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf\]\(https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf\)](#)

29. [Layperson Summaries of Clinical Trials: An Implementation Guide \[Internet\]. TransCelerate BioPharma Inc. \[cited 2021 February 23\]. Available from: \[http://www.transceleratebiopharmainc.com/wp-content/uploads/2017/02/Implementation-Recommendations_20Jan17_Final.docx\]\(http://www.transceleratebiopharmainc.com/wp-content/uploads/2017/02/Implementation-Recommendations_20Jan17_Final.docx\)](#)



TOOL V.

METHODOLOGIES AND TOOLS TO INCORPORATE THE PARTICIPANT'S PERSPECTIVE

To gain insights from the community, the i-CONSENT project used a variety of interdisciplinary, mixed research methods, which ensured that the informed consent process was co-created by a team that included representatives from all the different roles in the recruitment process, particularly potential participants.

1. Why is it important to include the participant perspective?

As highlighted by EFPIA³⁰, in the past, decisions about participants in medical research were taken without their involvement. This led to inefficiencies in process and outcomes. Therefore, many companies are now developing new ways to incorporate participants' insights and to collaborate with them in an ethical way. This has improved trials, engagement, communication and participants' experiences.

2. How to include the participant's perspective for a better informed consent?

As part of the i-CONSENT project, the team has created a series of consent materials, with input from participant representatives. Feedback has been collected in the following ways:

- 1 Social media analyses: combining the skills of communication specialists, data scientists, and epidemiologists to analyse:
 - Facebook users opinions and feedback through posts on an OPBG hospital page and Facebook paid advertisements.
 - Public comments on news stories on vaccination were analyzed both qualitatively and quantitatively, using Natural Language Processing.

2 Online survey: We polled an extended network of clinical trial investigators to gain insights on their attitudes and practice on the use of informed consent

3 Design Thinking: We engaged patients and their families, investigators, social scientists, and cultural mediators from the initiation of the design process to:

- Identify the problem
- Define it
- Develop ideas to solve it
- Develop prototypes of the solution

All of these methods provided insights that complement the existing knowledge base gained from relevant literature and helped to design and create the consent materials. A mixed method approach for gaining participant perspectives is recommended to adapt the informed consent process to the local community.

3. Where to get more information?

- About how to work with patient groups:
 - EFPIA provide some useful guidance: [Working together with patient groups.](#)
 - For a summary about how mixed-methods research can help you expand your evidence base:
 - Shorten A, Smith J. Mixed methods research: expanding the evidence base. *Evidence-Based Nursing*. 2017;20:74-5.
 - For guidance on analysing information from different sources in a way that adds value:
 - Hussein A. The use of triangulation in social sciences research: Can qualitative and quantitative methods be combined? *Journal of Comparative Social Work*. 2009;1:1-12.
 - i-CONSENT experience using [Design Thinking](#).

30. EFPIA Patient Think Tank. Working together with patient groups. 2017.



TOOL VI.

FAKE NEWS AND THE RELIABILITY OF SOURCES

Fake health news can have dramatic consequences for participants and is a significant concern in today's society. It can have negative consequences, particularly in the fields of politics and health, and impact individual and societal perceptions and actions.

There are different definitions and classifications for the expression "fake news". A much-quoted classification is by media professor Melissa Zimdars of Merrimack College³¹, who groups "fake news" into four categories, although each can be grouped in more than one category:

- Fake, false, or regularly misleading websites, pictures, videos or articles shared on social media.

- Websites, pictures, videos or articles circulating misleading and/or potentially unreliable information or presenting opinion pieces as news.

- Websites, pictures, videos or articles that sometimes use hyperbolic or clickbait headlines and/or social media descriptions, but which circulate reliable and/or verifiable information at other times.

- Satire/comedy sites, pictures, videos or articles that have the potential to be shared as actual news.

This factsheet offers a tool that investigators can use to prevent participants from being misled by "fake news" and help them to improve their health literacy.

10 tips for identifying "Fake News" or unreliable sources

10 CLUES TO IDENTIFY 'FAKE NEWS'

- 1 Check the domain**
 - Check the URL of the site/link
 - Some fake news includes a link, supposedly, to an official website but the hyperlink goes to a fake domain that imitates the original one
- 2 Look for the author**
 - Check the authorship
 - Search through previous articles to see if he/she is a legitimate journalist or has a history of hoaxes
- 3 Publication date**
 - Check the publish time stamp
 - Story may not be completely fake but a distortion of a real event
 - The publication may be current but the event is old
- 4 Emotional responses**
 - Be aware of those articles that appeal to emotions
 - If an article makes you angry probably it has been designed to do so
- 5 Compare with other sites**
 - Read several sources of information to compare the data
 - Collect a variety of viewpoints and media frames to contrast the information
- 6 Read beyond headline**
 - Continue reading after a provocative headline
 - Sometimes the headline doesn't reflect the content of a story
- 7 Source of information**
 - Don't trust information without a clear and reliable source
 - Be aware of fake links
 - Be cautious of shocking or suspicious quotes
- 8 Verify photos**
 - Pay attention to fake pictures
 - Do a reverse image search to check if the image already existed and where and when the image originated from
- 9 Check if it is a joke**
 - Some articles have been created for satirical purposes
 - The type of information is usually clearly labelled, but not always
- 10 Ask an expert**
 - For any health-related question, ask a health professional
 - False health news can have dramatic consequences for you



31. Zimdars M. False, Misleading, Clickbait-y, and/or Satirical: "News" Sources.; 2016 [Available from: <http://d279m997dpfwgl.cloudfront.net/wp/2016/11/Resource-False-Misleading-Clickbait-y-and-Satirical-News-Sources-1.pdf>; Last visit: 4th of October 2020]

4. LIST OF I-CONSENT'S SCIENTIFIC DELIVERABLES & PUBLICATIONS

“Scientific deliverables and publications’ elaboration was ongoing when the guidelines were released. Find the full scientific deliverables and publications list at [CORDIS](#)”

Deliverables

- WP1: A multi-layered approach to informed consent
 - D1.1. Report on guidelines, standards and initiatives for improving informed consent in the healthcare context. (<https://i-consentproject.eu/wp-content/uploads/2019/01/D1.1-Report-on-guidelines-standards-and-initiatives-for-improving-informed-consent-in-the-healthcare-context.pdf>)
 - D1.2. Report on gender and age-related issues associated with the acquisition of informed consent. (<https://i-consentproject.eu/wp-content/uploads/2019/01/D1.2-Report-on-gender-and-age-related-issues-associated-with-the-acquisition-of-informed-consent.pdf>)
 - D1.3. Ethical and legal review of gender and age-related issues associated with the acquisition of informed consent. (https://i-consentproject.eu/wp-content/uploads/2019/02/D1.3_EthicalLegal_20171030_FINAL.pdf)
 - D1.4. Ethical issues concerning informed consent in translational / clinical research and vaccination. (<https://i-consentproject.eu/wp-content/uploads/2019/01/D1.4-Ethical-issues-concerning-informed-consent-in-translationalclinical-research-and-vaccination.pdf>)
 - D1.5. Legal issues concerning informed consent in translational/clinical research and vaccination. (<https://i-consentproject.eu/wp-content/uploads/2019/01/D1.5-Legal-issues-concerning-informed-consent-in-translationalclinical-research-and-vaccination.pdf>)
 - D1.6. Patient group insights on improving guidelines for informed consent, including vulnerable populations, under a gender perspective. (<https://i-consentproject.eu/wp-content/uploads/2019/01/D1.6-Patient-involvement-in-vaccine-research.pdf>)
 - D1.7. Socio-cultural, psychological and behavioural perspectives toward informed consent process. (<https://i-consentproject.eu/wp-content/uploads/2019/01/D1.7-Sociocultural-psychological-and-behavioural-perspectives-towards-informed-consent-process.pdf>)

32. More deliverables and papers will be published in the framework of the Project after the publication of the guidelines. Find them in: <https://i-consentproject.eu/results/> or <https://cordis.europa.eu/project/id/741856/results>



Papers

- [Monographic BioLaw Journal, Special Issue 1/2019: 1-149.](#)
- L. Palazzani. Why informed consent requires attention once more?
- J. Fons-Martínez, C. Ferrer-Albero, R. Russell, E. Rodgers, L. Glennie, J. Díez-Domingo. i-CONSENT: presentation of the project and the importance of participants' perspective in the informed consent process
- L. Palazzani. Informed consent, experimentation and emerging ethical problems
- F. Macioce. Informed consent procedures between autonomy and trust
- J. Fons-Martínez, F. Calvo Rigual, J. Díez-Domingo, L. Nepi, L. Persampieri, C. Ferrer-Albero. Contents of the minor's assent in medical research: differences between the scientific literature and the legal requirements
- L. Nepi. Ethical issues concerning the informed consent process in paediatric clinical trials: European guidelines and recommendations on minor's assent and parental permission
- L. Persampieri. Gender and informed consent in clinical research: beyond ethical challenges
- A. Garcia, M. Garasic. Interreligious perspectives on Informed consent in the light of Human Rights
- L. Palazzani, F. Macioce, M. Daverio, V. Ferro, L. Persampieri. New strategies for increasing participation of patients from diverse cultural and religious backgrounds in clinical trials
- M. Daverio. Informed Consent in translational/clinical research. Ethical issues according to international guidelines
- V. Ferro. The impact of socio-cultural and religious background in the ICP. Implications for sensitive recruitment of multicultural participants in CT
- [Studia Bioethica. \(2019\). 11\(2\): 3-57.](#)
- E. Zhang. Informed consent – A Critical Response from a Buddhist Perspective
- L. Palazzani. Multicultural and interreligious perspectives on informed consent. The Christian perspective
- M. Garasic, A Garcia. New Considerations on Informed Consent
- R. Fan. A Confucian View of Informed Consent and the Issue of Vaccination
- A. Padela. Reflecting and Adapting Informed Consent to fit within an Islamic Moral Landscape and in Muslim Contexts
- D. Heyd. Informed Consent and Clinical Trials - A Jewish Perspective
- A. Lavazza. A Neurobioethical Perspective on Informed Consent
- E. Sirgiovanni. Agency, autonomy and consent: cues from the neuroscience of self-control
- [Medicina y Ética 2019. 30\(2\): 621-635.](#)
- A. García Gómez; M.D. Garasic; M. Cubillo Díaz-Valdés. Ethical issues concerning informed consent in translational/clinical research and vaccination bias and informed consent.
- [Biolaw journal 3/2020:323-335.](#)
- L. Palazzani. Consenso informato alla ricerca clinica nell'ambito della pandemia CoViD-19: tra bioetica e biodiritto
- [Frontiers in Pediatrics 2021. 8:520803.](#)
- Jackson SM, Daverio M, Perez SL, Gesualdo F and Tozzi AE. Improving Informed Consent for Novel Vaccine Research in a Pediatric Hospital Setting Using a Blended Research-Design Approach.
- [BMC Medical Ethics](#) volume 22, Article number: 18 (2021)
- Francesco Gesualdo, Margherita Daverio, Laura Palazzani, Dimitris Dimitriou, Javier Diez-Domingo, Jaime Fons-Martínez, Sally Jackson, Pascal Vignally, Caterina Rizzo & Alberto Eugenio Tozzi. Digital tools in the informed consent process: a systematic review



Chapters in books & Books of Abstracts.

- 5º Congreso de la Asociación Nacional de Comités de Ética de la Investigación (ANCEI): Los Comités de Ética de la Investigación: conjugando la utilidad social de la investigación, los cambios normativos y las nuevas tecnologías. Valencia, Spain, May 17-18, 2018. (<https://ancei.es/wp-content/uploads/2019/10/Libro-de-ponencias-y-comunicaciones-V-CONGRESO-ANCEI-2018.pdf>)
 - J. Fons-Martínez, F. Calvo Rigual, J. Díez-Domingo, L. Nepi, L. Persamperi, C. Ferrer-Albero. Contenido del asentimiento del menor en investigación médico: diferencias entre la literatura científica y el requisito legal. Pp. 129- 133.
 - F. Calvo Rigual, J. Fons-Martínez, J. Díez-Domingo, C. Ferrer-Albero. La comprensión de los documentos de asentimiento en investigación con menores: una revisión sistemática. Pp. 189-194
- 6º Congreso de la Asociación Nacional de Comités de Ética de la Investigación (ANCEI): Trabajando juntos para mejorar el debate ético en la investigación biomédica. Tarragona, May 30-31, 2019. (<https://ancei.es/wp-content/uploads/2019/10/Libro-de-ponencias-y-comunicaciones-VI-Congreso-ANCEI-2019.pdf>)
 - J. Fons-Martínez, C. Ferrer-Albero, R. Russell, J. Díez-Domingo. Proyecto i-CONSENT: desarrollo de guías para mejorar el proceso de elaboración de consentimientos informados implicando a todas las partes interesadas en el proceso de investigación. Pp. 3-8.
 - J. Fons-Martínez, A.J. Quesada, E. Fernández de Uzquiano, M. Ugalde Díez, A. Hernández Gil, M. Cubillo Día-Valdés. El uso de las redes sociales para el reclutamiento de participantes en ensayos clínicos: perspectiva de los comités de ética (CEI/CEIm). Pp. 77-82.
- J. Fons-Martínez, M. Cubillo Día-Valdés, C. Ferrer-Albero, J. Díez-Domingo. La perspectiva de género en el proceso de consentimiento informado en investigación médica. Pp. 145-150.
- J. Fons-Martínez, M. Cubillo Díaz-Valdés, R. Russell, C. Ferrer-Albero, J. Díez-Domingo. El proceso de consentimiento informado en investigación clínica: propuesta del proyecto i-CONSENT. Pp. 151-156.
- 36th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID). Malmo, Sweden, May 28-June 2, 2018 (<https://keneswp.azureedge.net/wp-content/uploads/sites/21/2018/08/ESPID-2018-Abstracts.pdf>)
 - C. Ferrer-Albero, F. Calvo-Rigual, J. Fons-Martínez, J. Díez-Domingo. Information, Comprehension and Competence: Key elements in children's assent for vaccine research (ESP18-0781)
- 38th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID). Virtual Meeting, October 26-29, 2020 (<https://keneswp.azureedge.net/wp-content/uploads/sites/77/2020/11/ESPID-2020-Abstracts.pdf>)
 - D. Dobreva, J. Fons-Martínez, C. Ferrer-Albero, S. Jackson, J. Díez-Domingo. Design thinking as a process to improve the communication of information to children (P0441 / #1444)
- III National Congress of Young Researchers in Biomedicine. Valencia, April 24-26, 2019.
- J. Fons-Martínez, J. García-Bayarri, J. Díez-Domingo. How to strengthen the recommendations for the informed consent process in health-related studies: The i-CONSENT project methodology. Pp. 59. (https://i-consentproject.eu/wp-content/uploads/2019/05/BookOfAbstracts_ConBioPreVal2019.pdf)



- Good Health, Quality Education, Sustainable Communities, Human Rights: the scientific contribution of Italian UNESCO Chairs and partners to SDGs 2030 (https://www.fupress.com/archivio/pdf/3951_20122.pdf)
- A. García Gómez, M.D. Garasic. Dilemmas of informed consent process in clinical research from a multireligious perspective. Pp. 47-56.
- XII Congreso Internacional de la Asociación Española de Bioética y Ética Médica. Valencia, Spain, October 25-26, 2019. (<http://aebioetica.org/revistas/2019/30/100/331.pdf>)
- M. Cubillo Díaz-Valdés, C. Ferrer-Albero, J. Fons-Martínez, R. Boceta Muñoz, O. Martínez Casares, D. Dimitriou. El concepto terapéutico errado en ensayos clínicos. Cuad Bioet. 2019;30(100):341.

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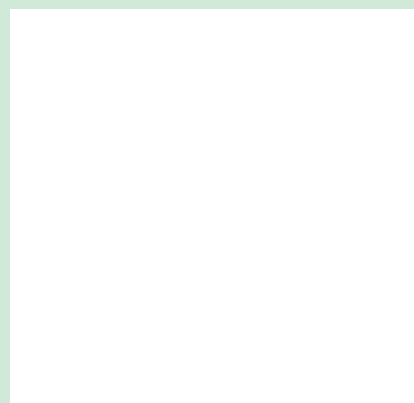


GUIDELINES FOR TAILORING THE INFORMED CONSENT PROCESS IN CLINICAL STUDIES

Improving the guidelines for
informed consent, including
vulnerable populations under a
gender perspective



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