Recommendations for Involving Paediatric Patients in the R&D Process of Medicines

The research-based pharmaceutical industry aims to cure and alleviate the suffering caused by diseases in all age ranges. Children and young people also suffer from some diseases that are not present in the adult population, and therefore require efforts to provide the best possible treatments: better medicines that are adapted to the specificities and needs of the paediatric population. Children are not small adults; their metabolism, which is constantly developing, requires research into medicines specifically intended for them. Just as the case with adult patients, young patients deserve the opportunity to be actively involved in the R&D of medicines, thus guaranteeing that clinical trials take into consideration their rights, preferences and needs.

Thanks to publication in Europe of Regulation (EC) No. 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use, in recent years there has been a significant increase in the number of clinical trials in the paediatric population. This Regulation stipulates that a Paediatric Investigation Plan be conducted for all medicines developed that are intended for the adult population so that, in the event such a disease should become present within the paediatric population, the number of medicines being researched and those which can finally be marketed is higher. Likewise, there is increasingly more research and development of medicines for diseases only suffered by children or, more recently, developments being studied first within the paediatric population and later, when applicable, with adult patients.

In particular, over 500 clinical trials intended for the paediatric population have been conducted in Spain in the last five years (2016-2020), with 2016=107, 2017=109, 2018=119, 2019=144 and 2020=137). The main therapeutic areas were oncology (20%), vaccines (11%), infectious diseases (9.6%), haematology (8.6%), dermatology (7.7%) and respiratory conditions (7.5%). The vast majority of these studies (40-50% depending on the year in question) were focused on early-phase development of medicines (Phases I and II).

The outlook is hopeful in respect to the number of early-phases studies and developments in humans, but above all for research-based treatments. For the first time, health conditions which only affect children and lack any therapeutic option have more than one potential treatment being researched. Nevertheless, we must not lower our guard, and it is necessary to promote collaboration between all stakeholders involved in the research. There are still many health conditions which only affect the paediatric population, this being the case for 80% of rare diseases, for which an approved therapeutic option does not exist.

Children and young people are key players in this process. The pharmaceutical industry is aware that their collaboration is essential to the development of patient-focused clinical trials, counting on their participation throughout the process from early phases (identification of unmet medical needs) to the finalisation of the research initiative (publication of the clinical-trial results). Involving patients and guardians ensures a better experience for volunteers participating in the clinical trials and will influence the quality of research conducted*.

It is essential to take diversity into consideration when involving paediatric patients in the development of clinical-trial design. This must be understood from the biological level relative to the disease for which the treatment being researched has been developed, as well as in relation to socioeconomic and other aspects. The activities involved in the participation of paediatric patients should reflect the reality lived by the patients who may potentially participate in the clinical trial. Respecting inclusion of diversity in these activities is considered a principle of justice, fairness, and accessibility.

A critical component of this guide is the fact that its content has been designed in collaboration with paediatric patients, parents, and patient associations. It is intended to serve as a support resource for pharmaceutical companies based in Spain and

aims to help in the development of clinical-trial design that focuses on patients' needs. Children and young people are the key to unique and valuable knowledge, perspectives and experiences for research, and they deserve the same opportunities to participate as adult patients under conditions that protect their rights while at the same time helping them to become reality.

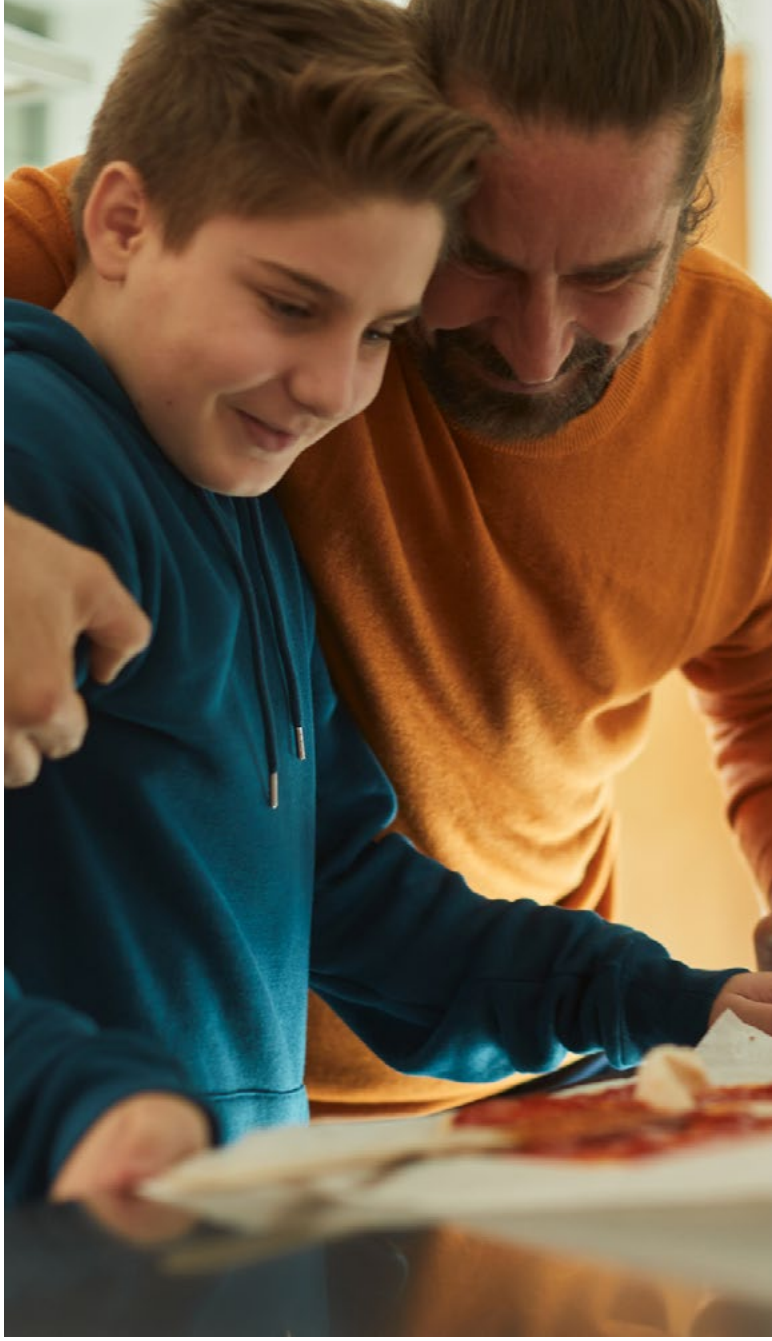
Children and young people, according to the Convention on the Rights of the Child (1989), shall have the right to freedom of expression (Article 12) and to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health (Article 24).

* In this respect, Article 9.3 of Regulation (EU) 536/2014, on clinical trials on medicinal products for human use, already establishes that at least one layperson shall participate in the assessment. Royal Decree 1090/2015, regulating clinical trials with medicinal products, Medicinal Research Ethics Committees and the Spanish Clinical Studies Registry, further states that, "The CEIm shall include a minimum of ten members, at least one of which shall be a layperson outside the field of biomedical research or clinical care, who shall represent the interests of the patients" (Article 15.1).

The key pillars upon which the content of this document is structured - and which serve to organise the recommendations therein - are the ethical guiding principles laid out in the Declaration of Helsinki (2008); Royal Decree 1090/2015, regulating clinical trials with medicines; Medicinal Research Ethics Committees (CEIm) and the Spanish Clinical Studies Registry; Regulation (EU) No. 536/2014 of the European Parliament and of the Council, on clinical trials on medicinal products for human use, and the aforementioned Paediatric Regulation (1901/2006); the 2012 European Union Charter of Fundamental Rights and Regulation (EU) (2016/679) of the European Parliament and of the Council, on the protection of natural persons with regard to the processing of personal data and on the free movement of such data; and Organic Law 3/2018, on personal data protection and digital rights guarantee.

This guide is the result of efforts made by a working group organised by Farmaindustria in which representatives from the Sant Joan de Déu Hospital of Barcelona (Grupo KIDS Barcelona and a parents' group), the Spanish Paediatric Clinical Trials Network (RECLIP), and the Spanish Paediatrics Association (AEP) all participated. The final version was open for consultation by patient organisations, pharmaceutical companies and paediatric research professionals. Serving as the basis for this guide are the strategic pillars defined in the guide for integrating the participation of adult patients, which was developed in collaboration with patient organisations and pharmaceutical companies (coordinated by Farmaindustria) and published in May 2020.

The objective of this guide is to provide recommendations to ensure an R&D process based on close collaboration with the pediatric patient



These efforts allowed for the development of a unique guide within the European context which **aims to provide recommendations shared by the different stakeholders which ensure a R&D process in the pharmaceutical industry that is focused on paediatric patients and is nurtured by close collaboration with them.**

The team involved in this initiative has concluded, among other findings, that there are at least **eight areas** in which patient participation and contributions to the biomedical R&D process can be integrated in an effective and valuable manner. The guide addresses the need for specific and distinguishable recommendations for the involvement of paediatric patients and their guardians as compared to adult patients, and it is for this reason that a separate, specific document is required in addition to the guide published in 2020.

The scope of activities covered in this guide are the following:

1. **Identification of unmet medical needs and definition of research priorities**
2. **Development of informational and patient-training materials on the R&D of medicines**
3. **Awareness outreach of paediatric medicines R&D for patients and the general public**
4. **Contribution to the drafting of paediatric clinical-trial protocols and informed consent for minors**
5. **Exploration and dissemination of clinical trials of interest by pathology**
6. **Contribution to the drafting of lay summaries of clinical trials**
7. **Collaboration in patient recruitment for participation in clinical trials**
8. **Interest of patient associations to participate in industry R&D activities**

01 Identification of unmet medical needs and definition of research priorities

01

Identification of unmet medical needs and definition of research priorities

Considered the first phase in the development of any research initiative, patient participation is critical as they can provide firsthand information about the illness. It is advisable that this information not only refer to the disease's biological impact, but also the societal and psychological aspects associated with the disease, which is vital to the paediatric population.

Participation of representatives from patient associations when beginning the research and development of a new medicine is increasingly more frequent in the context of the identification of unmet medical needs and the definition of research priorities in the pharmaceutical industry's activity. This is the case, for example, of patients participating - on a voluntary basis - on advisory boards alongside researchers, healthcare professionals and pharmaceutical company executives.

When referring to research in the paediatric context, these experiences are far more limited due to different conditioning factors:

- The right to protection of the minor and the confidentiality of their health and genetic data upon putting them in contact with certain professionals not involved in their care (researchers and healthcare professionals, pharmaceutical industry executives, etc.).

- The scarcity, to date, of experience with patient involvement in the identification of unmet medical needs (in its broadest sense) and in the definition of research priorities in the paediatric context - which will, thanks to this guide, present new opportunities to generate and communicate best practices.

- The need to develop methodologies which ensure that the objective, content and set-up of activities for gathering information on unmet medical needs and the definition of research priorities are suitable both to the needs and age range of children and young people.

With the importance of this phase in mind, it is vital that paediatric patients (when possible) or their parents or guardians participate in the appropriate forums to contribute their experience and preferences.

RECOMMENDATIONS

Considering that this type of activity is mainly carried out at companies' headquarters and at a multinational level, research-based pharmaceutical companies working within the Spanish setting should, to the best of their ability, facilitate the participation of representatives from Spanish paediatric organisations to help guide pharmaceutical companies requesting external counsel in their future research activity.

1 **Patient participation at this phase of the R&D process of a medicine for paediatric indication should be considered, in some cases, mandatory.** As the patient lives with the disease round the clock, their opinions are invaluable. When paediatric patients are unable to participate, be it due to their age (minors under 12 years of age) or their health condition, their parents or guardians should be consulted as they will look after the minor's best interests. Regardless, parent and guardian participation will always be valuable, as paediatric diseases impact the family as a whole and when a child or young person participates in a clinical trial, their experience will also affect the family as a whole.

2 **The definition of questions or areas to explore related to the experience with a disease and the detection of unmet medical needs is a key phase** prior to defining the best methodology for participation of patients and their parents/guardians. For certain diseases, it is advisable to create a list of ad hoc questions instead of using scales which measure the impact on quality of life which may not allow information to be gathered from a holistic point of view of the disease or are aimed at the patient or caregiver who will be involved.

3 Depending on the patient's age and the content to be explored, **both individual interviews and certain group dynamics can be considered as appropriate methodologies.** The facilitator's companiable yet objective role is important and advisable for both methodologies. The facilitator should not be directly involved in the research project and should have information-gathering mechanisms which allow for subsequent in-depth examination of the data collected if necessary. Both individual and group methodologies can complement each other and provide the research team with valuable information from a patient perspective.

RECOMMENDATIONS

4 **Patient associations play a key role in contacting patients or guardians interested in participating in this phase of research.** Professionals from healthcare centres in which clinical trials are conducted also play a key role in identifying patients or guardians on an individual basis, especially in the case of rare diseases with no representative patient organisation.

5 As an exception, when identification of unmet medical needs takes place on an international scale, patients or guardians must be proficient in English. In the event this impedes participation, and with the aim of guaranteeing equal opportunities to patients regardless of their country of origin, contracting simultaneous translation services is recommended in order to **design the most inclusive patient participation possible.**

6 **Use of digital teleconference platforms, when necessary, will allow patients or their guardians to make fewer trips,** while also guaranteeing that patients with reduced mobility may participate. These technologies also facilitate simultaneous translation into more than one language when necessary, and use of these technologies is therefore recommended as they guarantee a more inclusive and diverse patient participation. In terms of this recommendation as well as all others included in this guide, use of technologies and methodologies which facilitate universal accessibility should be promoted.

02 Development of informational and patient-training materials on the R&D of medicines

02

Development of informational and patient-training materials on the R&D of medicines

Considered a preliminary step to patient participation in the R&D process of medicines, it is **essential that representatives of paediatric patient organisations, as well as the patients themselves, their parents or legal guardians have sufficient training to understand the different phases of biomedical innovation**, the role they may play, and the roles of all others involved (AEMPS, CEIm, pharmaceutical companies, research centres, etc.).

In addition to patient and parent/legal-guardian groups, the presence of groups of young patient experts who have been trained by patient organisations or formed as a scientific council associated with paediatric hospitals conducting clinical trials is becoming more common in Europe. In Spain, the flagship group is KIDS Barcelona of the Sant Joan de Déu Hospital, created in 2015 in order to serve as expert counsel in the area of clinical research and health innovation. These groups contribute greatly to the activities related to the development of informative and training materials for patients. At present, existing European groups belong to the eYPAGnet Network (European Young Person's Advisory Groups Network), which is recognized by EnprEMA and allows for the development of patient participation activities at the international level.

Training patients and their guardians is key to empowering them through advisory roles in clinical-trial activities. There are materials designed to this end for adults, as is the case with the European EUPATI initiative, which has a specific section on the topic of clinical trials within the paediatric population.

Materials specifically geared toward the children and youth population are limited. The educational program YEAH (Youngsters Engagement in Health) coordinated by the Sant Joan de Déu Hospital is recommended as it is the only existing program currently at the national and European levels that is specifically designed for educating children and young people in the role they can play in the development of clinical-trial design.

RECOMMENDATIONS

Bearing in mind the need to empower children and young people as well as their parents/guardians, both in terms of general content on the R&D of medicines and paediatric clinical research focused on certain diseases, the following recommendations have been put into place for pharmaceutical companies to use in the development and publication of future content:

1 **Develop informative and training materials specifically for children and young people.** Materials for parents are also recommended, as these ensure that both groups are prepared to play an active role during the process of clinical-trial development.

2 **Involve children and young people in the design of clinical trials,** thus ensuring that both the content and format of the trial is appropriate for different age groups This recommendation is also applicable when materials are geared toward parents/guardians, encouraging them to participate in the process of developing the clinical-trial design. Participation of a group of expert patients or patient representatives will ensure the creation of appropriate materials both in terms of format and content.

3 **Accessible language.** Regardless of the format chosen, it is essential to use familiar language which is understandable to a non-expert audience and appropriately adapted to certain age ranges. Some general considerations that should be kept in mind when materials are geared toward minors are:

- Address the minor not as *patient* or *subject*, but rather as *child* or *young person*.
- In the event use of scientific terminology cannot be avoided, include a glossary of definitions. For written materials, it is best to include this information on the same page the term appears as this is more accessible. For other formats, such as multimedia, it is important to assess the best option for user-friendliness.
- Avoid overly lengthy texts which go into an unnecessary level of detail on the information for the child or young person's age.
- Cite sources and/or authors and ensure that the scientific content is approved by researchers or paediatricians with experience in the area of expertise the educational materials address.
- Illustrations, graphs, diagrams or other types of visual resources help make the written elements easier to understand.

Materials for parents are also recommendable, as these ensure that both groups are prepared to play an active role during the process of clinical-trial development

RECOMMENDATIONS

4 **Patient approval.** Informational or training materials for children, young people or parents/guardians should not be published without having first sought these participants' approval of these materials.

- Use of revision and approval tools for educational materials is suggested. These instruments can be designed based on the project so that everyone participating in the approval of the material in question can analyse and respond to the same items.
- It is important to consider the health literacy of the materials as this will help to ensure that the content is adapted to the age group in question. Use of the SAM scale (*Suitable Assessment of Materials*) is recommended, which is available in English and provides a guide for revising the level of readability and understandability of the written information on health content.

5 **Recognizable emblem.** Recognize materials that have been approved by patients through use of an emblem, which also helps build trust among families and patients. The most well-known recognizable emblem at the European level is *Patients Included*.

6 **Appropriate format.** Given that children and young people are digital natives and have been born into the era of images and micro engagement, using audiovisual formats is recommended when materials are geared toward them. It is important to be especially careful with recruitment materials that can be shared via social media, given the impossibility of controlling the extent to which they are shared. It is necessary to ensure that information included be as simple and intelligible as possible, and both the content and dissemination channels of these materials must always be approved by the Research Ethics Committee. Regardless of the format chosen, using colours, illustrations, diagrams and photographs will always help to make the written or oral text easier to understand. It will be important to evaluate whether different versions need to be developed depending on the age range of the patients or whether the material is geared toward parents/guardians. Online formats with the option to print (when possible) is recommended in order to make information more accessible to all audiences. When choosing the format, it will be key to take into consideration whether the materials are geared toward a special-needs group such as, for example, those with visual and/or hearing impairments. Adapt the format of the material (text, audiovisual, online, etc.) to the platform and channel chosen for its dissemination.

RECOMMENDATIONS

7 **Appropriate dissemination.** It is important to build a suitable roadmap for the material's dissemination which includes a timeline, a selection of external distribution platforms/channels (social media and company/association webpages) and internal distribution platforms/channels (mass mailing to target audience from patient associations or scientific societies involved).

- Using different dissemination channels to ensure that the target audience is reached is recommended: children and young people together with parents and guardians.
- Patient associations and paediatric hospitals should play a key role in dissemination and access to information.
- Patient registries can also help in disseminating not only clinical trials but also educational materials related to training patients in the R&D of paediatric clinical trials.

03 Awareness outreach of paediatric medicines R&D for patients and the general public

03

Awareness outreach of paediatric medicines R&D for patients and the general public

Biomedical research linked to the research and development of new medicines is a subject on which there is still much to be learned by the general public. Pharmaceutical companies, research centres and patient associations are making a tremendous effort in this regard, but these efforts have a long road ahead when it comes to dissemination of information on the R&D of medicines for the paediatric population – the goal being that children and young people understand the long process and efforts behind each and every medicine brought to market.

Creating social awareness on the relevance of research and development of medicines for the paediatric population is a particularly important, if not necessary.

> **Creating social awareness on the relevance of research and development of medicines for the paediatric population is a particularly important, if not necessary**

RECOMMENDATIONS

1 **An outreach and dissemination strategy aimed at children, young people, parents, guardians and the general public on the research and development of medicines** is recommended. This strategy should be carried out with the participation of relevant stakeholders, ranging from public authorities (Ministries, AEMPS, Spanish regions) and healthcare professionals or pharmaceutical industry researchers.

2 Should it be decided that opinion leaders participate in the design of information and awareness campaigns, it is important to analyse the impact the campaign may have in terms of value to the youth population.

3 **Schools can play a significant role** in dissemination efforts within the paediatric population by including content and activities in their academic curricula in various subjects (natural sciences, biology, ethics, etc.). This recommendation is supported by children, young people, and parent groups that participated in the creation of this guide.

4 **Research centres and other institutions linked to paediatric clinical research can promote informative activities geared toward schools.** Since 2016, Farmaindustria has organised the well-received *"Bringing Science into Schools"* programme which, in collaboration with hospitals, public institutions and high schools, entails an informative seminar geared toward baccalaureate students which details the process of pharmaceutical R&D.

5 From children and young people's point of view, **social media should also be considered a key channel** for dissemination efforts aimed at an age group that is undeniably digital.

6 **Primary care centres, hospitals and patient organisations,** in addition to the multiple apps and digital platforms offered to patients by the Spanish regions, were highlighted by parents consulted in the drafting of this guide as essential channels for the dissemination and development of informative campaigns on the R&D of paediatric medicines for patients, parents/guardians, and society in general.

Schools can play a significant role in dissemination efforts within the paediatric population

04 Contribution to the drafting of paediatric clinical-trial protocols and informed consent for minors

04

Contribution to the drafting of paediatric clinical-trial protocols and informed consent for minors

Once unmet medical needs are identified and research priorities are defined, it is essential that paediatric patients be able to participate in the design of clinical-trial protocols as well as the corresponding informed consent form for minors*. Collaboration in both activities will ensure that the protocol is adapted to patients' needs and priorities, and will therefore be easier to carry out**. Furthermore, it will help guarantee that the information included on both the informed consent form for minors (in Spain, patients over 12 years old) and the informed consent form (young adults over 18 years old and parents/legal guardians) will be understandable and accomplish its objective of providing information for decision-making.

Therefore, since the number is on the rise of young people with experience participating in the process of revision and approval of informed consent forms for minors, as well as parents/legal guardians as concerns the informed consent form they must sign, the track record of paediatric patient participation in the drafting/design of protocols is still quite limited. This is a key phase of clinical research for incorporating patient participation to ensure that the clinical-trial protocol design is as best adapted to the needs and preferences of paediatric patients as possible.

* Informed consent is understood as a patient's free and voluntary compliance to participate in activities affecting his/her health after receiving the appropriate information and being duly informed of its nature, significance, implications and risks. With regards to informed consent for minors, the following shall be required as provided for by national and European regulations:

a. Provision of information adapted to the minor's age and level of maturity by researchers or members of the research team who are trained in or have experience dealing with minors.

b. Request of signature of the document for patients 12 years of age and over, and in accordance with the minor's faculties and criteria of the researcher.

c. Respect for the express right of the minor, when they are capable of forming an opinion, to dissent or withdraw from the trial at any time.

In all situations, it is necessary to obtain prior informed consent of the minor's parents (who have not had their parental authority revoked) or legal guardian. Please also refer to the AEMPS' instruction document for conducting clinical trials in Spain.

** To this end, Regulation (EU) 536/2014, on clinical trials on medicinal products for human use, already establishes that the protocol should include a description of participation where patients were involved in the design of the clinical trial (Annex I, Article 17, Section E).

RECOMMENDATIONS

In this regard, the following is recommended:

1 **Incorporate patient associations representing the disease for which the trial is being developed into the development process of clinical-trial protocols** to ensure that they consider all useful aspects coming from the patients' point of view. These activities most commonly take place at pharmaceutical companies' headquarters at the multinational level, although there have already been instances of their taking place at the national level. Sponsors should support this participation both in Spain, when possible, and at the company's headquarters, when appropriate.

- The vast majority of illnesses affecting the paediatric population are rare diseases, and it is therefore not always possible that a patient organisation with expert professionals organising activities for the codesign of protocols exists. To this end, large hospital complexes with experience involving patients in R&D activities for the development of medicines are encouraged to pioneer the organisation of activities for incorporating patients or parents/guardians into the development of protocols.

- The task of designing activities which incorporate paediatric patients requires experience in similar activities, and it is essential that the methodology design not only facilitates the dynamic of participation, but also all matters related to the rights of minors, ethical principles of their participation in activities linked to clinical research and the compilation of results.

RECOMMENDATIONS

- In the context of activities which facilitate patient participation in the development of clinical-trial protocols, the following is recommended:

  – Organise group activities in which opinions can be freely expressed, with a moderator to help lead discussions as well as address questions about clinical research in general, the disease in question, and the design of the clinical trial. To this effect, the support of a researcher or doctor with the relevant knowledge is recommended.

  – Diversify, whenever possible, the paediatric patients or parents/guardians invited to participate in these kinds of activities. Diversity must be understood in a broad sense, taking into consideration exactly what the reality of patient participation will be at the time the clinical trial is conducted and therefore include different age groups (if applicable), cultures, genders, etc.

  – The three protocol sections considered most relevant by paediatric patients while consulting on this guide are:
  a. Medical tests during the clinical trial

  b. Inclusion and exclusion criteria

  c. Information on risks/benefits

  – In the case of protocols for decentralised and hybrid clinical trials, the opinion of the patient and parent/guardian will be key in ensuring adequacy and anticipating adherence issues in the use of remote patient monitoring devices or other aspects which may affect a patient's quality of life.

  – The main recommendations suggested by parents who have participated in the consultation on this guide are:

  a. Revision/validation of secondary results of the clinical trial is considered crucial as, sometimes, these provide information regarding quality of life, which is of utmost importance to the family.

  b. Offer opinions on scales measuring quality of life and/or patient-reported outcome measures (PROMs), given the importance of verifying that the items measured and response format (paper, electronic, etc.) are appropriate.

  c. Participate in the overall clinical-trial design. It is important that parents express their opinion in the event the study should involve a placebo arm or a comparator arm with natural history.

  d. Make suggestions for implementation of highly complex clinical trials. For example, suggesting the participation of a psychology professional in the team of professionals conducting the clinical trials, who will contribute to a better emotional experience for patients throughout the study.

Diversify, whenever possible, the paediatric patients or parents/guardians invited to participate in these kinds of activities

RECOMMENDATIONS

2 **Intensify revision by patient associations** of Annexes VIIIA and VIIB to the AEMPS' instructions concerning the **patient information sheet and informed consent form** for conducting clinical trials in Spain . It would be crucial to include the option for patient organisations to contribute to the revision of this documentation or, if this is not possible, to form an ad-hoc group of paediatric patients or parents/guardians. This would signify a considerable improvement in the overall process of informed consent for the minor and in the completion of patients' information sheet.

- Consulting of the following recommendation guides is suggested:
  - *Informed Consent in Paediatric Clinical Trials. Grupo Kids Barcelona.* Sant Joan de Déu Hospital.
  - *Assent/Informed Consent Guidance for Paediatric Clinical Trials with Medicinal Products in Europe*. EnprEMA.
- Having a mechanism in placefor the approval of content and health literacy, such as a rubric, would help to standardize the process and in the participation of various groups of patients or parents/guardians.
- The use of illustrations, diagrams, or other visual aids is quite helpful to paediatric patients' understanding of the material. This information will not replace the textual content, but rather help in understanding it.
- Audiovisual materials, videos or animations are preferred by paediatric patients. These are considered helpful in facilitating comprehension consent in paper format and are non-discriminatory.

RECOMMENDATIONS

3 Put together a glossary of terms and content included in the informed consent for minors, including visual aids.

4 Suggest that centres or researchers, prior to proposing participation in a clinical trial, use an informative video to explain to patients what clinical trials and informed consent are. The following links can serve as examples: link 1 y link 2.

5 Promote use of electronic informed-consent forms, as well as their implementation, in co-operation with the AEMPS, ethical committees, the pharmaceutical industry, and patient-organisation representatives.

Paediatric patients and parents/legal guardians who participated in the development of this guide attest to the benefits of using digital consent for minors in clinical trials, as well as for processes in which it is necessary that their consent be requested multiple times.

05 Exploration and dissemination of clinical trials of interest by pathology

05

Exploration and dissemination of clinical trials of interest by pathology

The Spanish Clinical Studies Registry (REec) is a free-to-use public online database that can be accessed through the AEMPS' webpage, who is responsible for its management. The REec has compiled all clinical trials authorised in Spain since January 2013. Its goal is to serve as a source for primary information on clinical trials for medicines and complies with the principle of transparency established to this end by Royal Decree 1090/2015, on clinical trials, which has been in force since 13 January 2016.

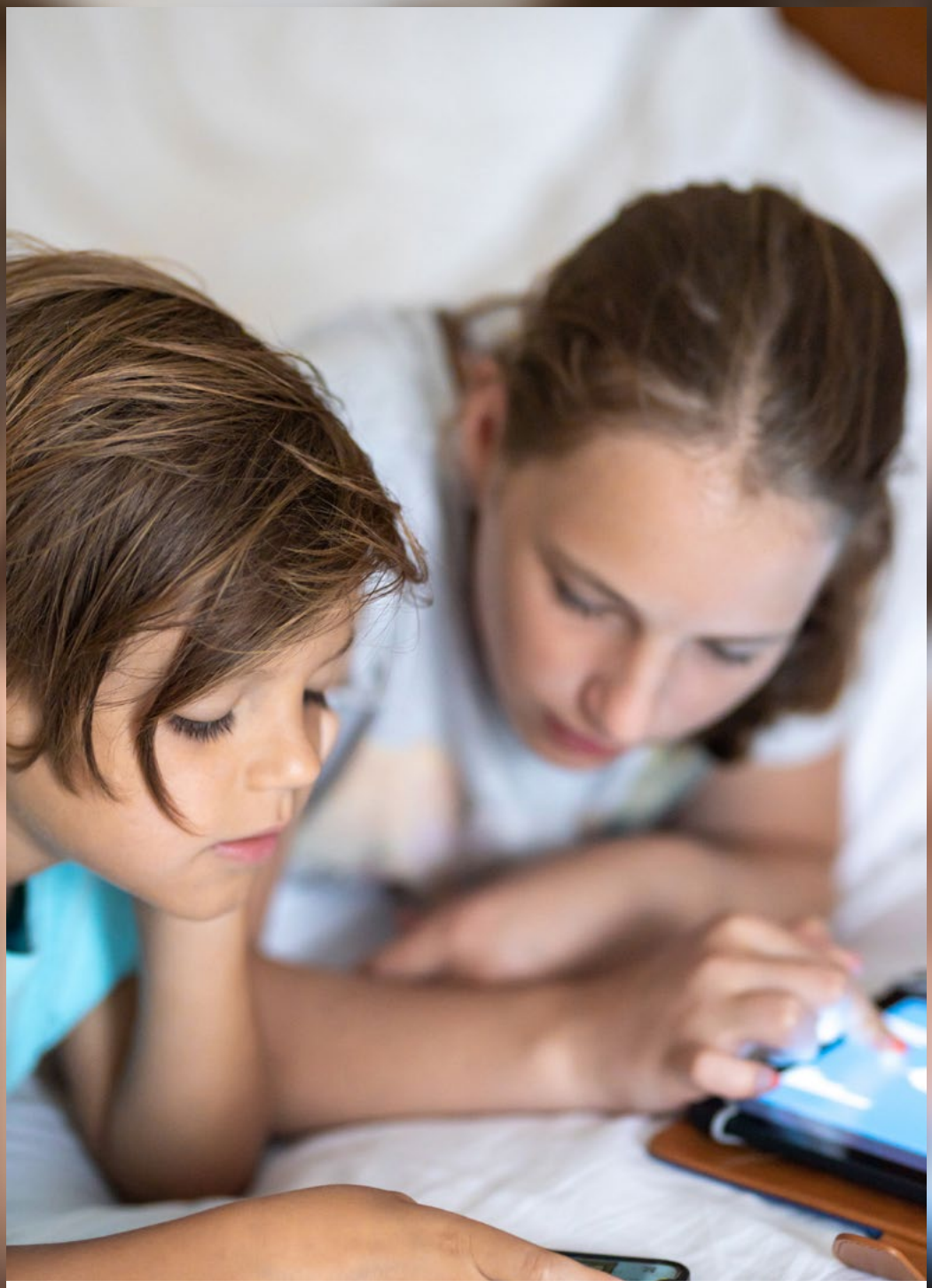
For every registered clinical trial (over 6,700), the REec offers information on the data compiled from application forms and the clinical trials' dates of progress sent by sponsors to the AEMPS. Moreover, differing from other registries, the REec includes a summary of the grounds for the clinical trial in easy-to-understand language and information regarding participating centres, as well as their status concerning recruitment of participants.

The REec is an invaluably useful tool that allows patient organisations to identify clinical trials of interest and make them available among their members. However, associations find that this repository lacks tailoring to patient profiles that make it more accessible and useful to patients and families when searching for information.

RECOMMENDATIONS

1. It would be ideal for the AEMPS to reinforce the **REec's accessibility and usability** in order to make this tool more user friendly and helpful in the tasks for which it is used by patients, their families and, in particular, the associations representing them.

2. Parents/guardians who have participated in the design of this guide recommend highlighting the importance of **making the REec more widely known** by dissemination through patient associations, health centres and hospitals throughout the country.



06 Contribution to the drafting of lay summaries of clinical trials

06

Contribution to the drafting of lay summaries of clinical trials

In accordance with the legislation regulating the content included in lay summaries and the guidelines for drafting them*, it is essential that this kind of document include the following:

- **Identification of the clinical trial** (including the title, protocol number and EUDRACT number)
- **Sponsor name and contact** information
- **General information of the clinical trial** (including where and when the trial took place, the trial's main objectives and the grounds for conducting the trial)
- **Population** (information about research subjects included at a local and global level, age and gender distribution, and the criteria for inclusion and exclusion)
- **Medicine being researched**
- Description and frequency of **adverse effects**
- **General findings** of the clinical trial
- **Comments** on the results found
- Determination of **future clinical trials,** if planned
- **Making resources for consultation** purposes available to find further information

* (EU Clinical Trials Regulation 536/2014, article 37. Phase 1–4 interventional studies with at least 1 site in EU. EU Guidelines on Summaries of Clinical Trial Results for Laypersons 26 Jan 2017 version 13.2)

RECOMMENDATIONS

Recommendations for the development of these documents as well as legal requirements, and with the intent of making them easier to understand for participating patients, are:

- **Including graphs and tables.** These are highly recommendable resources as they help better visualise the process and lighten the amount of text.
- **Using colours** throughout the document to highlight and separate content, always with the needs of the patients to whom they are aimed in mind.
- **Explicitly stating that the document only represents the results of a specific study** and does not represent an overarching knowledge of the medicine being studied. Likewise, it is advisable to specify that patients can consult their physician if they want or need further information.
- Identification of potential **dissemination channels of lay summaries:** physicians and researchers involved in the studies, REec platform, sponsoring company, patient association, etc.

In particular, paediatric patients emphasize the importance of:

- Including colourful tables, graphs and infographics that help to understand the information.
- Providing a video summarising the content included in the written version of the lay summary (always respecting criteria for the best accessibility possible) as visual formats facilitate the process of understanding information.
- Using different sources so that the lay summaries reach paediatric patients whether or not they have participated in the clinical trial. In the event they have participated, it is suggested that they be sent by email along with a thank-you letter.

It is also crucial to keep the following recommendations in mind:

- The objective of the lay summary is to inform society at large about the results of a specific clinical trial – not just participants – and the entire document should be drafted with this in mind.
- Removing the acknowledgement at the beginning, including instead only a note of appreciation at the end of the document addressed to the general population. In this regard, the following text is proposed: “Thanks to everyone who participated in this study, researchers have been able to answer important health questions that offer a greater understanding of the disease and contribute to the research of new medical treatments”.

The objective of the lay summary is to inform society at large about the results of a specific clinical trial – not just participants

RECOMMENDATIONS

To facilitate the process of creating and designing lay summaries - highlighting the value of patient involvement - consult the handbook titled “Good Lay Summary Practice” (GLSP). This handbook was co-created with the participation of various stakeholders (patients, academia, pharmaceutical companies, etc.) and has been approved by the European Commission’s Expert Group on Clinical Trials. The GLSP includes specific recommendations for paediatric clinical trials.

07 Collaboration in patient recruitment for participation in clinical trials

07

Collaboration in patient recruitment for participation in clinical trials

Although there have only been isolated collaborative initiatives by patient associations with the industry in recruitment efforts for clinical trials, these initiatives offer a very positive experience, and it would be worthwhile to universalise them according to a set of standardised recommendations.

The industry generally develops recruiting materials that come predesigned from headquarters that are then adapted and/or translated by national affiliates for their presentation to committees. These materials may be available from the beginning of the study, but in other cases they are designed after it becomes difficult to incorporate patients and the trial needs wider circulation. As claimed by patient organisations, their participation in the development and/or adaptation of these recruitment materials helps tailor them to the needs of the patients that may potentially participate in the trial, thus improving the accessibility of the content.

In the context of paediatric clinical trials, participation of patient and parent/guardian groups in the approval of recruitment strategies is considered extremely helpful as it contributes to achieving the objective of tailoring the strategy in question to the needs of a very specific group of patients. It is worth mentioning that it is not just the patients themselves who participate in paediatric clinical trials, but also their entire family.

In the context of paediatric clinical trials, participation of patient and parent/ guardian groups in the ap-proval of recruitment strategies is considered extremely helpful

RECOMMENDATIONS

A **model for patient-association participation** with the following components is suggested:

1. Involvement of associations from the beginning. Recruitment campaigns designed with the help of patients to better reach their collective.

2. Inclusion of hospital and health centre webpages among the dissemination channels to facilitate access to information and the recruitment process.

3. Revision and approval of information on clinical trials on web platforms or apps designed for consultation and access to information regarding clinical trials.

4. Joint development of strategy. Understanding of the project. Launch and dissemination.

5. Presentation of campaign materials and communication of patient associations collaborating in their drafting, revision and dissemination to the CEIm.

6. Consideration of different communication tools: print and electronic materials, seminars and presentations, workshops, forums, etc.

7. Involvement of centres' leading researchers by incorporating their participation into this collaboration. They should authorise the process as they will be the ones who receive patients referred by the association.

8. Research networks and scientific societies to which medical specialists belong, both at the national and international levels, are considered valuable channels for dissemination in efforts to facilitate equal opportunity to accessing paediatric clinical trials.

9. Promotion of trials through available channels from the association. Any interested patients will be able to directly contact the delegate (with their prior consent) from each health centre at which the trial takes place.

RECOMMENDATIONS

10 Collaboration ends after the study is concluded, not at the end of the recruitment process. Follow-up with the association is necessary until the study is finalised.

11 Delivery of results published in the REec to the association in order to conclude the process and share results with members.

12 Validation of the collaboration process between the association and the industry, giving it weight and credibility.

13 Evaluate the results of the joint campaign.

To avoid disruptions or delays the participation of associations could cause in the clinical-trial approval procedure, it is advisable to plan appropriately from the beginning of the collaboration as well as equip organisations with the necessary training relevant to their participation in this process, as well as the responsibility that comes along with it.

08 Interest of patient associations to participate in industry R&D activities

08

Interest of patient associations to participate in industry R&D activities

During the process of drafting this document of recommendations, it has become clear that associations and organisations representing patients have a strong interest in actively and efficiently taking part in the pharmaceutical R&D process. Keeping a list of organisations that have expressly stated their willingness to participate in these initiatives is recommended to manage this interest.

Along with patient organisations, involving expert youth groups, known as Young Person's Advisory Groups (YPAGs), is suggested. These groups, the Spanish counterpart being the Grupo KIDS Barcelona, have been formed and empowered with the aim of contributing paediatric patients' vision, needs and preferences to the context of clinical trials.

RECOMMENDATION

In order to facilitate participation of patient organisations in the R&D activities of the pharmaceutical industry, a non-exclusive, indicative online list of patient organisations, associations and YPAGs that show interest in forming part of this process should be created. In an initial phase, this list should only include organisations at the national level.

Interested organisations can sign up by writing to **participacion@farmaindustria.es.**

Those involved in putting together this document of recommendations would like to extend a sincere thank-you to all the children, teenagers, parents and guardians who participated by contributing to the progress of paediatric research. Their support is invaluable to the progress of fostering the development of paediatric medicines, which is the objective of this recommendation guide.

This guide has been put together by Farmaindustria, the Spanish Paediatric Clinical Trials Network (RECLIP), the Spanish Paediatrics Association (AEP), the Sant Joan de Déu Hospital, and the Grupo KIDS Barcelona, with participation of representatives from the following patient organisations, scientific societies, hospitals and pharmaceutical companies:

Patient organisations

Academia Europea de Pacientes EUPATI
Acción Psoriasis
Asociación Española de las Mucopolisacaridosis y Síndromes Relacionados (MPS España)
Asociación Nacional de Dermatomiositis Juvenil (ANADEJU)
Federación Española de Diabetes (FEDE)
Federación Española de Enfermedades Raras (FEDER)
Foro Español de Pacientes
Fundación Atrofia Muscular Espinal (FundAME)
Menudos Corazones
Plataforma de Organizaciones de Pacientes

Scientific societies

Asociación Española de Nefrología Pediátrica (AENP)
Asociación Española de Pediatría (AEP)
Sociedad de Psiquiatría Infantil de la AEP
Sociedad Española de Cardiología Pediátrica y Cardiopatías Congénitas (SECPCC)
Sociedad Española de Hematología y Oncología Pediátricas (SEHOP)
Sociedad Española de Infectología Pediátrica (SEIP)
Sociedad Española de Medicina de la Adolescencia (SEMA)
Sociedad Española de Neonatología (SENEO)
Sociedad Española de Neurología Pediátrica (SENEP)
Sociedad Española de Reumatología Pediátrica (SERPE)

Hospitals

Complejo Hospitalario de Navarra
Fundesalud – Complejo Hospitalario Universitario de Badajoz
Hospital Clínico Universitario de Santiago de Compostela
Hospital Clínico Universitario de Valencia
Hospital General Universitario Dr. Peset
Hospital General Universitario Gregorio Marañón
Hospital HM Montepríncipe
Hospital HM Puerta del Sur
Hospital HM Sanchinarro
Hospital Infantil Universitario Niño Jesús
Hospital Regional Universitario de Málaga
Hospital Sant Joan de Déu
Hospital Universitario 12 de Octubre (i+12)
Hospital Universitario Clínico San Carlos
Hospital Universitario Cruces
Hospital Universitario La Paz
Hospital Universitario Parc Taulí
Hospital Universitario Quironsalud Madrid
Hospital Universitario Ramón y Cajal
Hospital Universitario Reina Sofía
Hospital Universitario Severo Ochoa
Hospital Universitario Vall d'Hebron
Hospital Universitario Virgen del Rocío
Instituto Hispalense de Pediatría
Red de Salud Materno Infantil y del Desarrollo (RETIC SAMID)
Red de Investigación Transalacional en Infectología Pediátrica (RITIP)

Farmaceutical companies

Abbvie
BMS
Boehringer Ingelheim
GSK
Janssen
Lilly
Merck
MSD
Novartis
Pfizer
Roche
Rovi
Sanofi
Servier
UCB
Vifor Pharma

This document of recommendations has been reviewed by the Spanish Medicines Regulatory Agency (AEMPS).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Sant Joan de Déu
Barcelona · Hospital


RECLIP
Spanish Pediatric Clinical Trials Network


Asociación Española de Pediatría
AEP


KIDS
BARCELONA


MEDICAMENTOS
INNOVADORES


GOBIERNO
DE ESPAÑA
MINISTERIO
DE CIENCIA
E INNOVACIÓN