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Recommendations for the Integration of Patient & Patient Associations' Participation in the Pharmaceutical R&D Process

The research-based pharmaceutical industry researches, develops, produces and commercialises medicines with the aim of curing diseases, alleviating the suffering they cause, and improving patients' quality of life. Its main activity is therefore performed with a focus on patients and increasingly involves the patients themselves.

Over the last few decades, this operating model has improved concerning patient participation in the research and development (R&D) process of new medicines carried out by the pharmaceutical industry. Patient participation in the R&D process has improved because patients and their families, through their associations and representatives, have asserted a greater capacity of influence and decision-making, as well as pharmaceutical companies' increasing appreciation for the added value that these groups contribute to their activities.

For several years, Farmaindustria has been working within the setting of patient participation in biomedical R&D: initially with the European initiative EUPATI[1], which develops training content for patient representatives in this field, and later, within the framework of the Spanish Technological Platform for Innovative Medicines' BEST Project. Under the Best Project, workshops have been held since 2015 for various patient groups to explain the value that the pharmaceutical industry's innovative activity can mean for their respective pathologies. At the same time, **Farmaindustria has worked in close collaboration with the Spanish Society of Clinical Pharmacology on the development of a thank-you letter template for participants in clinical trials** – something which to date had not been done. This template was published by the Spanish Medicines Regulatory Agency (AEMPS) and can be used by sponsors of clinical trials.

This cumulative experience has made it possible to identify two convergent interests: on one hand, pharmaceutical companies' willingness to incorporate the patient voice into their various R&D activities; and on the other, patient associations' intention to become an additional player in these R&D activities alongside authorities, ethical committees, researchers and companies.

The research-based pharmaceutical industry wants to rely on patients' insights and experience in order to better understand how they live with specific diseases. This information is invaluable in the identification of unmet medical needs, definition of research priorities and optimisation of clinical-trial design. Likewise, the patient voice should have more weight in the evaluation of clinical-trial outcomes and in the development of assessment criteria in order to obtain results that bring real improvement to patients' lives.

For patients and patient associations to play a key role in health management and the development of new therapeutic solutions, clinical research cannot be kept on the sidelines.

For several years, Farmaindustria has been working within the setting of patient participation in biomedical R&D.

[1] The European Patients' Academy (EUPATI) is an initiative implemented by the IMI from 2012 to 2017 and financed by the European Commission and EFPIA in order to create content and organise training activities on the R&D process of medicines. This training is geared toward representatives of patient organisations for training purposes and participation in R&D activities in Europe. The EUPATI consortium was able to gather 33 organisations -of which Farmaindustria has been a part since the project's inception- under the leadership of various patient collectives (with the coordination of the European Patients' Forum) and with the participation of academic institutions and pharmaceutical companies.

Through a working group formed by Farmaindustria with representatives from member companies, the Spanish research-based pharmaceutical industry has carried out an intense collaborative effort in recent months with various patient organisations including EUPATI (that provided expertise in the area of training patient representatives), as well as the Patient Organizations Platform and the Spanish Patients' Forum (which represents patient organizations in Spain). **This shared effort aims to establish a series of recommendations in order to channel the joint determination of promoting patient participation in the R&D activity of new medicines.** This document is the result of said collaboration.

The working group involved in this initiative concluded, among other findings, that there are at least eight areas in which patient participation and contribution in the biomedical R&D process can be articulated in an effective and valuable manner:

1. **Identification of unmet needs** and definition of research priorities

2. **Development of informational** and patient-training materials on medicines R&D

3. **Awareness outreach of medicines R&D** for patients and the general public en general.

4. **Contribution to the drafting of clinical-trial protocols** and informed consent

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** in participating in industry R&D activities

1 Identification of unmet needs and definition of research priorities

There is already proven track record of the participation of representatives from patient organizations in the starting point of the R&D process of new medicines, the identification of unmet needs, and the definition of research priorities in the activity of the pharmaceutical industry. This is the case, for example, with patients that are part of advisory boards alongside researchers, healthcare professionals and executives at pharmaceutical companies. It is evident that the participation of representatives of organisations of patients and their families in these forums brings a significant contribution to all parties involved.

Recommendations

While it is known that such activities are 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 contribution of representatives of Spanish patient organizations to help guide pharmaceutical companies requesting external counsel in their future research activity.

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

Considered a preliminary step to patient participation in the medicines R&D process, it is essential that representatives of patient organisations have sufficient training to understand the different phases that biomedical innovation entails as well as the roles played by those involved in it (AEMPS, CEIm[2], companies, etc.).

In order to achieve this, it is necessary to have accredited, accessible and high-quality informational and training materials. The EUPATI initiative is considered a remarkable starting point, and guaranteeing its continuity and sustainability over time is advisable in order to ensure updating and periodical revision of these materials.

Recommendations

Based on these materials, the following best practices have been put into place for pharmaceutical companies to use in the development and publication of future content:

User-friendly language. It is fundamental that these publications, regardless of the chosen platform, are written in a language that is adapted to the target audience (patient organisation representatives as well as patients, relatives and caregivers). To do so, working with a group of expert patients or patient representatives while drafting these materials is recommended.

Patient approval. Once the drafting is finished, have the materials revised and approved by a wide range of patients representing the pathology in question.

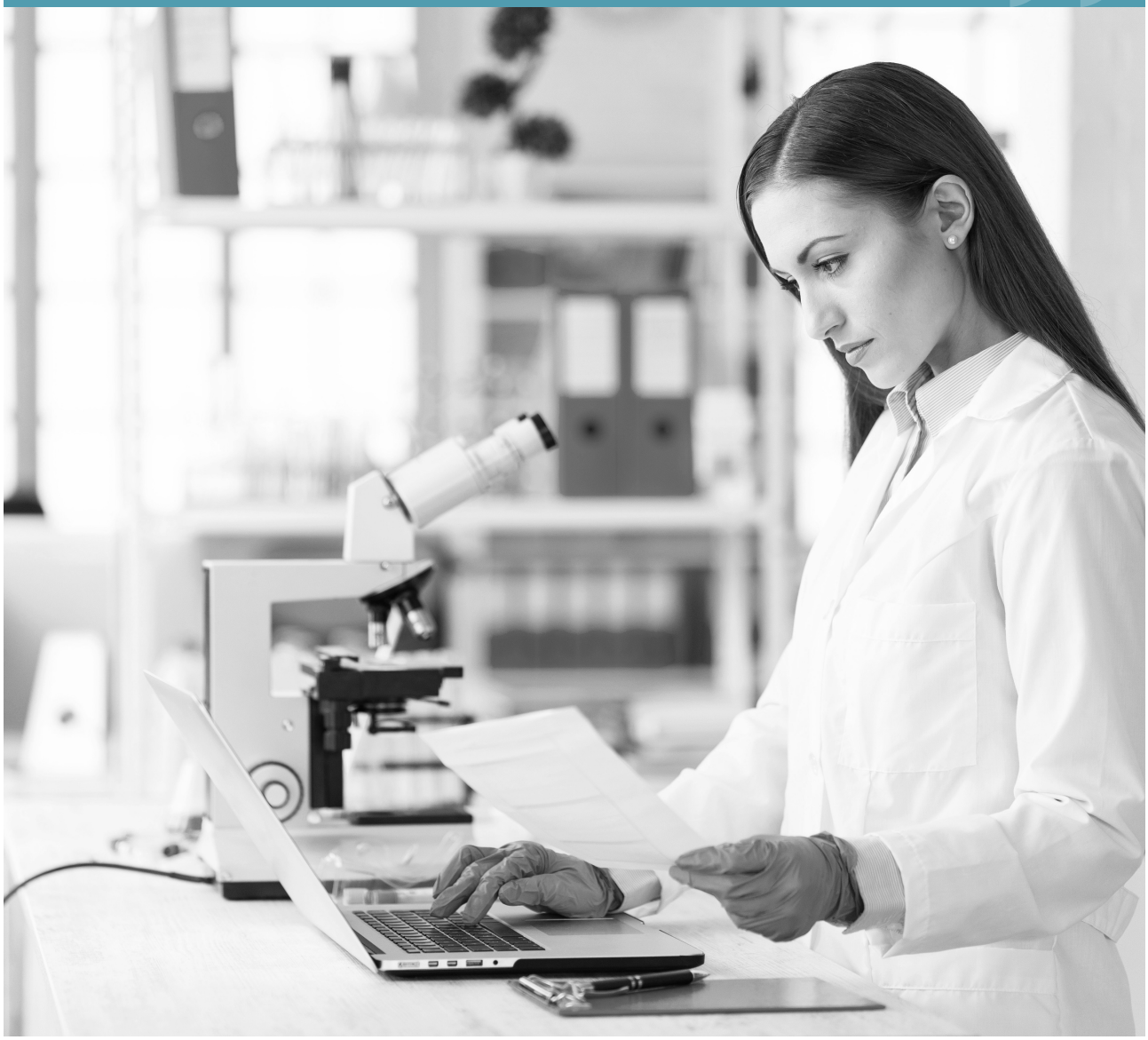
Guarantee of robustness and reliability of the content. The material should be approved by an accredited group of experts or a scientific society.

[2] CEIm is the Spanish Research Ethics Committees with Medicines.

Appropriate format. Adapt the format of this material (text, audio visuals, online, etc.) to the platform and channel that has been chosen for its dissemination.

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

By the same token, it is worthwhile to consider making materials which already exist as well as future publications available to special-needs groups (paediatric population, physical/mental disability groups, etc.).



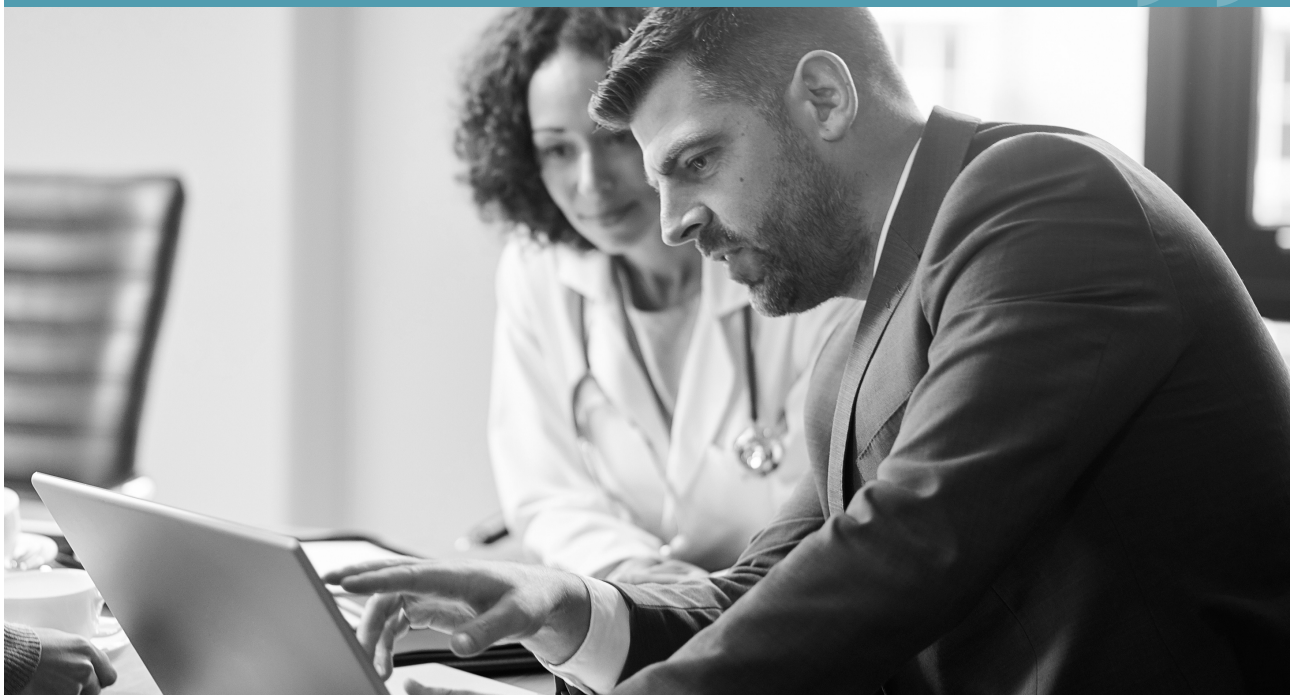
3 Awareness outreach of medicines R&D for patients and the general public

The value of biomedical research in general, and particularly the R&D of new medicines, is a matter that is little-known among patient organisations and within Spanish society in general. Workshops held in the last few years by Farmaindustria in this area have confirmed this lack of awareness not only among patient organisations and associations, but also among secondary-education students.

Therefore, the possibility of making the value and contribution of biomedical R&D known to the general public – especially patients, relatives and caregivers – is at present of particular importance, if not necessary.

Recommendation

It has therefore been recommended that the EUPATI National Platform in Spain, with the collaboration of as many interested patient organisations as possible, address the development of an informational outreach strategy on the R&D of medicines that is aimed at patients on an individual basis and society in general. This strategy should also be carried out with the participation of public authorities (ministries, AEMPS, Spanish regions) and healthcare professionals as well as with the help of the research-based pharmaceutical industry.



4 Contribution to the drafting of clinical-trial protocols and informed consent forms

In this field, participation by organisations of patients and their representatives is very important, as has been demonstrated by the experience gained in recent years.

Recommendations

To this effect, the following is recommended:

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

> Intensify revision by patient associations of Annexes VIIA, VIIB and VIIC of the AEMPS' instructions relating to patient information sheets and informed consent for conducting clinical trials in Spain. It would be crucial to integrate the option that patient associations can contribute to the revision of this documentation with their suggestions, as it would entail a considerable improvement in the overall process of informed consent and in the completion of the patient's information sheet.

> Make a glossary of terms and content included in the informed consent, including visual aids. Some available examples are attached as an annex. The aim is to reach a consensus to then share with the AEMPS and could be included as part of the instructions. It would be of great help in creating an informed-consent form template with a maximum of 15 pages, as suggested by the AEMPS.

In this regard, the model in discussion by the IMI Do-It[3] Consortium could be considered and thus validated at the national level.

> Suggest that centres or researchers use a video to explain to patients what clinical trials and informed consent are prior to proposing they take part in a trial. The following links can serve as examples.

https://bit.ly/2m0UhyK

https://www.youtube.com/watch?v=PrQDYNk4CU0

> Promote use of electronic informed-consent models in cooperation with the AEMPS and ethical committees.

[3] The IMI DO-IT Project is a Coordination and Support Action (CSA) for the IMI 2 Program called Big Data for Better Outcomes (BD4BD), in which 37 different stakeholders from the pharmaceutical industry, patient associations, academia, hospitals and research centres are working. Work package 4 of the project aims not only to agree on a comprehensive informed consent for participating in clinical trials that meets biomedical research needs for promotion, aligned with the new rights and principles established by Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 (as relates to the protection of natural persons with regard to the processing of personal data and on the free movement of such data), but also to develop a series of materials which aim to explain to patients and health professionals the possibility that future use of patient data will not be solely based on a specific consent, except for scientific research (Article 9.2 as well as the guarantees in Article 89 of the Regulation). **https://www.imi.europa.eu/projects-results/project-factsheets/do-it**

5 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 from the AEMPS's webpage who is in charge of its management. The REec has gathered all authorised clinical trials in Spain since January of 2013. Its goal is to serve as a source of primary information on medicines' clinical trials and complies with the principle of transparency established for this matter in the Royal Decree for Clinical Trials1090/2015 (which has been in effect since 13 January 2016).

For every registered clinical trial (over 4,000) the REec offers information on the data compiled from applications forms and the dates of progress in the trial that promoters send to the AEMPS. Moreover, differing from other registries, the REec includes a summary of the grounds for the trials in a user-friendly language and information regarding participating centres as well as their status concerning participants' recruitment.

The REec is an invaluably useful tool that allows patient organizations to locate clinical trials of interest and make them available among their members. However, associations find that this repository needs to be more tailored to the patient profile with the purpose of making it more accessible and useful to patients and their families when searching for information.

Recommendation

t would be ideal that the AEMPS reinforces the REec's accessibility and usability in order to make it more user-friendly in the work that patients, their families and in particular the associations representing them can do with these tools.

6 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[4], it is essential that this kind of document include the following:

a) Identification of the clinical trial (including the title, protocol number and EUDRACT number)

b) General information of the clinical trial (including where and when the trial took place, the trial's main objectives and the grounds for performing the trial)

c) Population (information about research subjects at a local and global level, age and gender distribution, and criteria for inclusion and exclusion)

d) Medicines being researched

e) Description of side effects and their frequency

f) General findings of the trial

g) Comments regarding results

h) Determination of future trials, if planned

i) Making available resources for consultation purposes in order to find further information

Recommendations

Recommendations for the development of these documents, in addition to legal requirements, and the intent of making them us-friendly for participating patients, are:

Including graphs and tables. They are highly recommendable resources as they help better visualise the process and lighten the text.

Using colours in order to highlight and separate content.

[4] 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

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, also specify that patients can consult their physician if they want or need further information.

Identification of potential dissemination channels of the lay summaries: physicians and researchers involved in the study, the REec platform, promoting company, patient association, etc.

After having analysed the models shared by the various promoters, the working group considers the best models those published by CISCRP (The Center for Information and Study on Clinical Research Participation **https://www.ciscrp.org/communicating-trial-results/**), to which the following modifications are suggested:

> The objective of the lay summary is to inform society at large of the results of a specific clinical trial, not just the participants, and the wording of the entire document should be written under this premise.

> It is recommended that the acknowledgment at the beginning be eliminated, instead including only a note of appreciation at the end of the document addressed to the general public. 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." This proposal is in line with the template for thank-you letters recently published by the AEMPS for clinical-trial participants.

7 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 generalise them according to a set of standardised recommendations.

The industry generally develops recruiting materials that come predesigned from headquarters which national affiliates then adapt and/or translate for their presentation to committees.

These materials may be available from the beginning of the study, but in other cases they are designed after the incorporation of patients into the trial becomes difficult and it 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.

Recommendations

A patient-association participation model with the following features is suggested:

- Involve the associations from the beginning. Protocol should be thorough concerning recruitment methods. Campaigns should be designed in collaboration with patients in order to best reach their organizations.
- Jointly develop a strategy. Understand the project. Launch and dissemination.
- Present campaign materials and communicate the collaboration of patient associations in the drafting, revision and dissemination to the CEIm.
- Consider different communication tools: print and electronic materials, seminars and presentations, workshops, forums, etc.

Involve the leading researchers of the centres by making them participants in this collaboration. They should authorise the process as they will be the ones who receive patients coming from the association.

Promote trials through available channels from the association. Any interested patients will be able to directly contact the person in charge (with their prior consent) at each health centre where the trial is to take place.

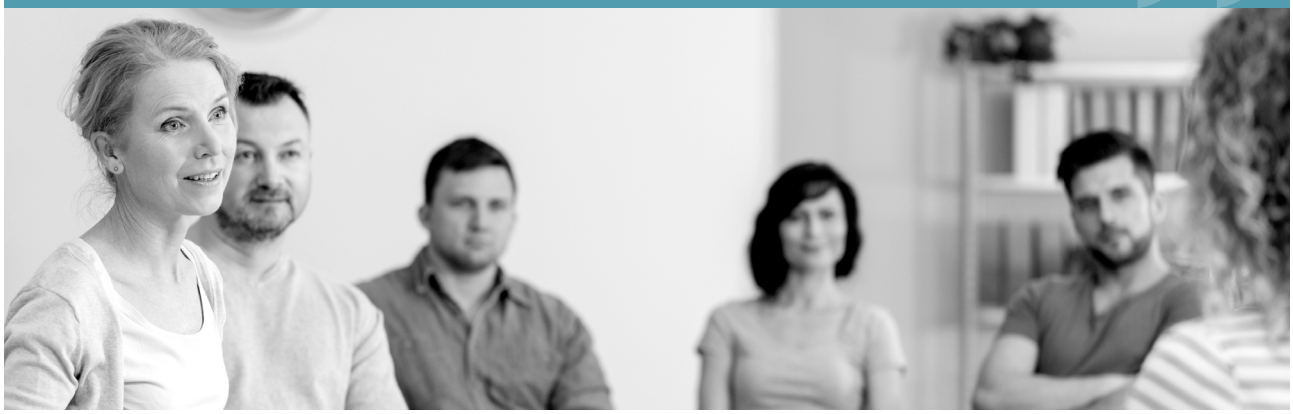
Collaboration ends after the study is concluded, not at the end of the recruitment process. Follow up with the association is necessary until the study is finalised.

Deliver results published in the REec to the association in order to conclude the process and share results with members.

Validate the collaboration process between the association and the industry, giving it weight and credibility.

Evaluate the repercussions of the joint campaign.

To avoid disruptions or delays that the participation of the 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 and the responsibility that comes along with it.



8 Interest of patient associations in participating in industry R&D activities

During the process of drafting this document of recommendations, it has become clear that the 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 in order to manage this interest.

Recommendation

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

Interested organisations can sign up at participation@farmaindustria.es

The list is available for consultation through the following link:
https://www.farmaindustria.org/servlet/fiPublic/docs/ListadoEntidadesID.pdf

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This document of recommendations has been put together by Farmaindustria with the contribution of representatives from the following patient associations and pharmaceutical companies:

EUPATI, Patient Organisation Platform (POP), Spanish Patients' Forum, Acción Psoriasis, Confederación ACCU, ConArtirtis, Federación Española de Diabetes (FEDE), Lung Cancer Europe, Lupus Madrid & Unimid.

Abbvie, MBS, Boehringer-Ingelheim, GSK, Janssen, Lilly, Merck, MSD, Novartis, Pfizer, Roche, Rovi, Servier, UCB and Vifor Pharma.

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