27th Workshop of the EURORDIS Round Table of Companies (ERTC)

Patient engagement in the product life-cycle and Community Advisory Boards (CABs)

Tuesday, 16 October 2018
Hospital Sant Pau Recinte Modernista – Barcelona - Spain

PROCEEDINGS

The 27th Workshop of the EURORDIS Round Table of Companies (ERTC), gathered 143 participants from 16 countries including patients and patient advocates, healthcare industry representatives, EURORDIS staff and a sprinkling of HTA experts and regulators.

Overarching context

For most of history, medical science has evolved with little to no input from the people being studied. CABs change that, and help to design, carry out and communicate on studies that are more rational and inclusive from a patient's point of view. By doing so, a bond of trust between the patient and scientific community is formed.

More than ever, patients and the patient perspective are seen as a way to make medical research and clinical studies more impactful, possibly quicker and certainly more efficient.

Patient Community Advisory Boards (CABs) are groups established and operated by patient advocates. They facilitate discussions (in a neutral setting) on the latest developments and challenges related to medical research and procedures in a disease area, with the company or body conducting the research.

A CAB is a group of patients who offer their expertise to sponsors of clinical research. For example, by being involved before a clinical study starts, patients help ensure that clinical studies are designed to take into account their real needs, resulting in higher quality research.

CABs, with anywhere from seven to 20 patient advocate members, are involved in scientific as well as policy-related issues (ie, access). They provide expert advice to all stakeholders involved in the research, development and service provision of medical treatments.

Workshop Objectives

- Understand the best practices EURORDIS promotes for working with patients to develop orphan medicinal products
- Understand the objectives and outcomes of PARADIGM and how patient engagement fits within the product life-cycle
- Learn about the concept of CABs including the method, contractual implications, limits and financial model

- Learn about the value that companies can get from CABs
- Learn from the experience of existing CABs
- Take-away key information to share with colleagues and advocate internally to invest in CABs
- Understand how EURORDIS can advise and provide guidance to facilitate the creation of a CAB (and what is outside of EURORDIS' scope)

Morning Session Outcomes

Engaging with patients: *from ticking a box to real value for business and patients*

Co-Chairs:

Fabrizia Bignami, EU Medical Lead at Bluebird Bio

Jonathan Pearce, Regional Director Europe of the Lymphoma Coalition, a global patients group.

Speakers:

Yann Le Cam, CEO, EURORDIS - Rare Diseases Europe

Yann emphasized the importance of this Workshop as the opportunity to learn how CABs are contributing to meaningful medicines development and create synergies with fellow participants.

Merlin Williams, Consultant, Executive Insight

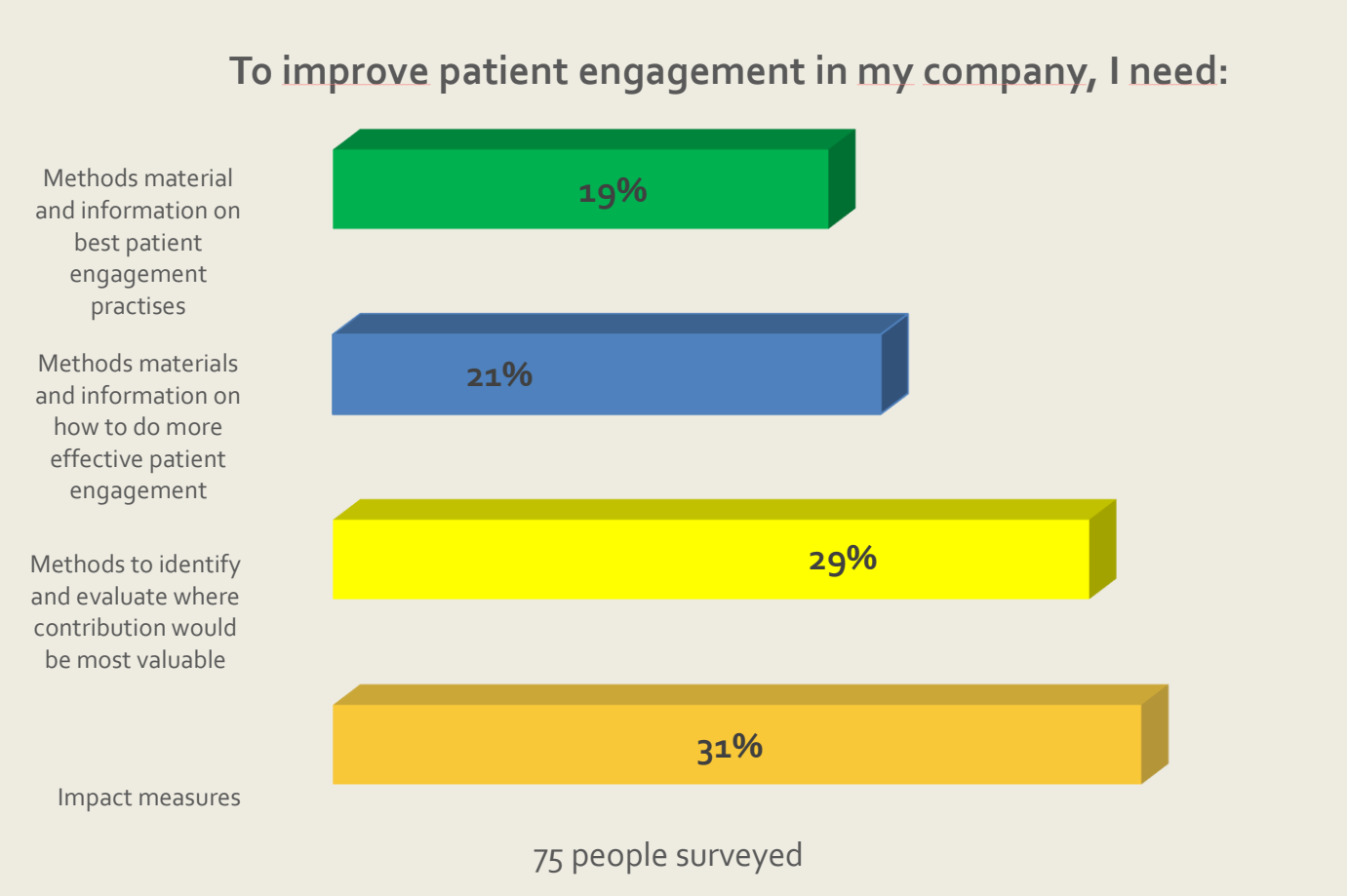
Merlin presented conclusions of his Master's thesis investigation on the different perspectives of patient engagement, both from the pharmaceutical industry and the patient association perspective:

- Patient engagement does not slow down drug development, because engagement aids development
- Some challenges include compliance, one achievable tool is more training for patients, while pharmaceutical companies need to provide the necessary investment (in a mind change, including their own training) to work towards a truly patient-centric paradigm
- Overall, both groups need to continue working together towards a collaborative future. One philosophy that Merlin heard during the day that makes a lot of sense to him is, "companies should not wait to engage with patients when they think that they are ready, patient engagement should be carried out when patients are ready."
- Merlin also agrees that metrics need to be "developed and put in place to measure the value of the impact of collaborating."

Luciana Ballini, Senior HTA Researcher, Italy, (Regione Emelia-Romagna)

Luciana presented about patient involvement in the lifecycle of HTA and the importance of multi-stakeholder early dialogue that aims to inform the formulation of safe, effective health policies that are patient-focused and achieve best value.

Luciana also raised the question whether we should consider patients as a stakeholder vs. as a decision maker, a concept that provoked a lot of reflexion among the public. According to Denise Dunne and Anne Marie O'Dowd from Cystinosis Network Europe, Luciana was one of "the most thought-provoking speakers from our perspective, who gave insight into the HTA process. Her description of patient advocates as decision makers rather than stakeholders will have a significant impact on our perspective of our own work into the future."



Graph taken from on-site voting at the 27th Workshop in Barcelona

Nathalie Morgensztejn, The French Agency ANSM

Nathalie shared her experience as a Drug Regulator being involved with patient representatives in the field of HIV infection as a critical model of patient representative engagement in early drug access for patients with an unmet medical need and the challenging benefit/risk assessment in drug regulation.

Nathalie further concluded that TRT5, a French patient group who worked with companies, was a critical model of patient representative engagement, with major achievements in the therapeutic management of HIV-infected patients for decades.

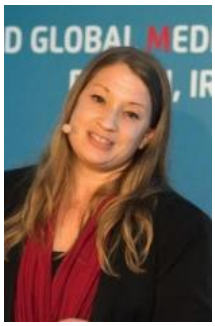
Vinciane Pirard, Public Affairs, Sanofi-Genzyme

Vinciane gave an overview on PARADIGM, an IMI project that EURORDIS is participating in. PARADIGM's aim is to firstly: develop tools and resources to allow the effective and systematic inclusion of patients. Secondly, it aims to design an innovative roadmap to ensure long-term sustainability of patient engagement, in three key decision-making points in medicines development:

- Research priority setting
- Clinical trial design
- Early dialogue with regulators and HTA bodies.

She stated that the project is still in its early stages but the intended outcomes are to:

- ✓ Strengthen a better understanding of stakeholders' needs and their expectations for engagement
- ✓ Ensure maximum synergies with similar initiatives
- ✓ Develop a workable suite of tools, including a sustainability roadmap with metrics
- ✓ Strengthen systems-readiness



Joëlle Rebetez, Global Patient Advocacy, Actelion

Joelle talked about the benefits to industry of engaging patients early, systematically and directly across all aspects of drug development and treatment. These enhanced relationships help them to generate solutions that better meet patients' needs and they are already seeing results. J&J/Actelion base their approach on four elements:

- ✓ Embed patient engagement into everything, within a cross-functional team across all areas.
- ✓ Proactive dialogue and sharing of tools and processes, enabling them to take a systematic approach to gathering and implementing patient insights, early and often throughout the entire lifecycle of medical product development (from a pill's colour, size and flavour to frequency of doses and the shape of a device) to best serve people who will ultimately receive the treatment.
- ✓ Accountability, by measuring progress and ensure that they gather feedback directly from patients and act upon them as needed that encourages them, industry, to change by showing the business value of patient engagement.
- ✓ Being dynamic, constantly working to address evolving patient needs, ensuring patients the access and transparency they deserve.

Their goal is to engage systematically with patients early and often in the drug development process as it has a wide range of benefits, like the ability to reduce clinical trial protocol amendments. Likewise, drug development can be accelerated, solutions can reach patients faster, and resources can be freed up for future R&D.

Finally, she showed the benefits of an early engagement with CABs, which resulted in innovative trials with 2 of their experimental compounds, that resulted in products with better safety profiles and easier administration, as well as faster acccess to new products for patients. After this positive experience, the company will set up other CABs for other diseases.

Carla Fladrowski, European Tuberous Sclerosis Complex (E-TSC)

Carla described E-TSC's involvement in the creation of a disease registry called TOSCA, a collaboration of Novartis, patient representatives and TSC experts. The objective was to understand the impact of TSC on the lives of patients both in terms of quality of life and burden of the illness.

TOSCA is a multicentre international disease registry designed to collect data from patients with TSC across many countries worldwide and to address the gaps in understanding the clinical course of the diseases and therapeutic outcomes. Around 2000 individuals with a diagnosis of TSC participated, with 250 sites across more than 30 countries worldwide. Carla supported this large-scale international registry as a model, and encouraged to plan similar registries for other rare diseases. She did emphasize the need for planning so a registry will continue after any one of the partners needs to leave.

"We need practical tools to implement patient engagement on the different stages of R&D, and how to measure its effect"

- A Workshop Participant

Serge Smeets, Medical Director, Rare Diseases, Novartis

Serge reinforced the importance of the patient input into clinical trial protocols, patient safety, data transparency, data integrity, and early access to medicines. He focused his presentation on the autoinflammatory diseases, specifically SJIA's (Systemic Juvenile Idiopathic Arthritis) burden of disease project for patients and caregivers. He also shared Novartis' initiative *'Living with Periodic Fevers'* website (www.periodicfevers.com), which aims to provide comprehensive and accurate information about autoinflammatory diseases, to help adults and children with these diseases as well as their families, to cope with the day-to-day challenges of the condition and find expert help. This was achieved through a multi-stakeholder collaboration involving patients, Policy Action Groups (PAGs) and health care providers using a positive and innovative approach to portrait patients' lives by combining a storytelling narrative with digital experiences.

Rob Camp, Patient Engagement Senior Manager, EURORDIS

Rob dedicated his presentation to introducing the CABs concept, how they have been created and the collaborative relationship between patients and industry.

- ✓ CABs started in the mid-1990s by people living with HIV to help shape clinical research, and now is being applied to the rare disease area. CABs are based on collaboration between different decision-makers, by signing a *Memorandum of Understanding,* which provides guidelines about the form and objectives of the collaboration. In addition, a *Charter for Clinical Trials* that outlines a collaboration based on trust and transparency, and a commitment between the sponsor to work together with patient networks throughout the research and development process.
- ✓ CABs give input on topics agreed to by both parties, including: real-life constraints, quality of life questions and measurements; patient-reported vs patient-relevant outcomes and how to measure them; patient involvement in designing the true questions that are of importance to the end user; inclusion/exclusion criteria; selection of the sites; interim analyses and the writing up of results.
- ✓ Overall, CABs are contributing to meaningful medicines development and to creating synergies with fellow participants.

Rob also talked about a series of articles recently published in the journal Nature on "co-creation" of research in many areas of science including medical sciences. He ended with a reminder that the terms "patient engagement", "patient involvement" and "patient centricity" etc. need to be better defined and adhered to in order to get the most out of them. He used the example of Leann who blogged that "I am not your partner", who as a clinical trial participant did not consider that she was anyone's partner, except perhaps if it were an abusive relationship. We need to carefully measure our words. And the relationship that develops will be much richer if the stakeholders (decision-makers) are on equal footing. According to Cathelijne van Doorne of Euro-Ataxia, "co-production is exactly what CABs are".

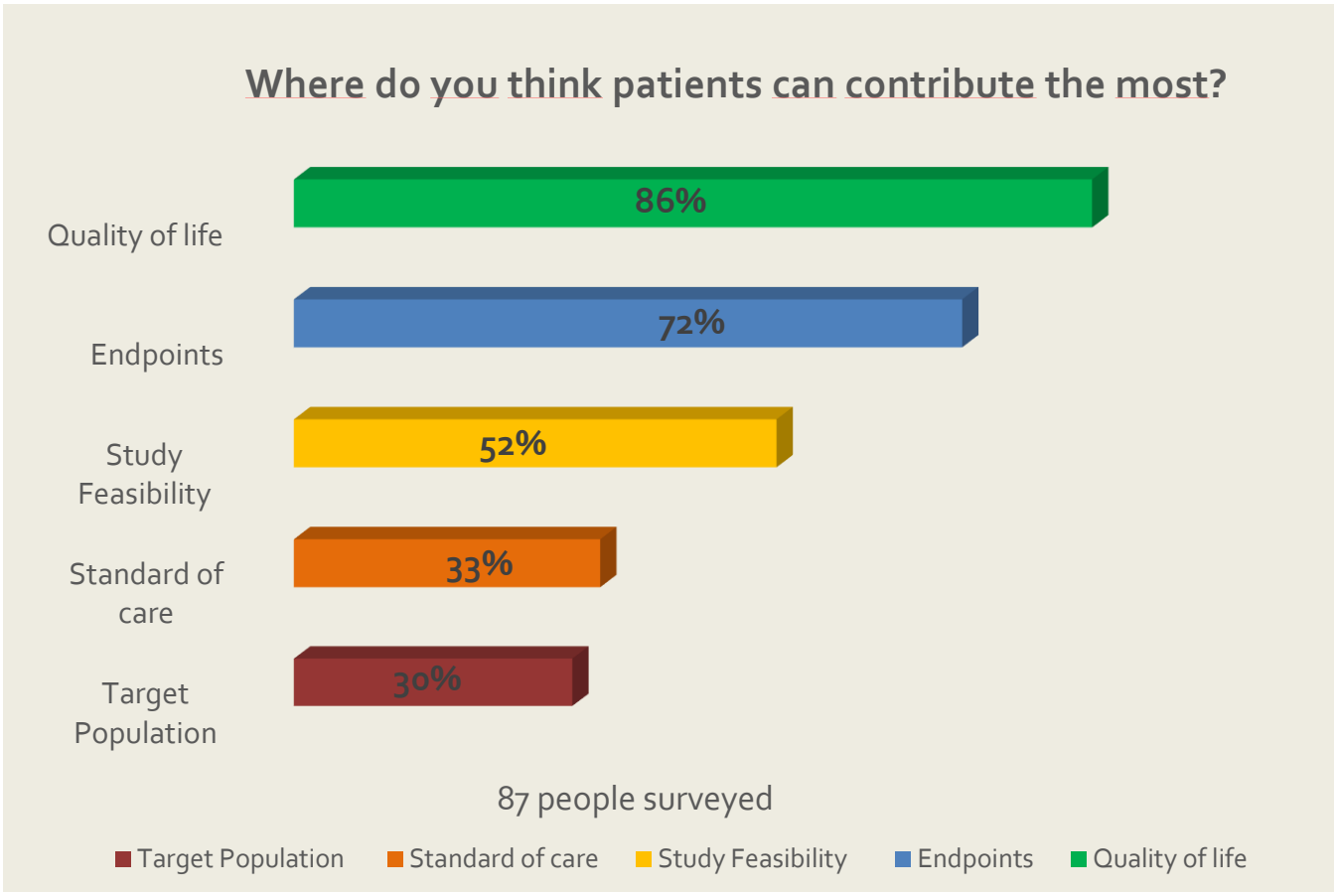
François Houÿez, Treatment Information and Access Director and Health Policy Advisor, EURORDIS

François focused his presentation on how to participate in a CAB by giving an example of an HIV CAB in the late 90s that helped design a pivotal trial for a drug that made a sea-change in the HIV epidemic for patients because harsh side effects were better controlled by lowering the dose. At the same time, the manufacturer saw a surplus sale of $500 M at year 2 compared to their most optimistic models forecasted. He also informed about the ongoing CABs for rare diseases, and their positive outcomes.

François, illustrated the EuroCAB programme by explaining:

- ✓ Guidance provided by EURORDIS on how to operate, Declaration of Interests…
- ✓ Code of conduct, transparency, independence
- ✓ Mentors such as patients advocates, along with health care professionals' input, HTA & regulatory advice
- ✓ Trainings like EURORDIS' Open Academy (Summer and Winter Schools), EUPATI
- ✓ GPEP (Good Patient Engagement Practices)

He emphasised the importance of early engagement and the main steps such as identification of disease areas where CABs are needed, matchmaking with industry and mentoring. The CABs model will be presented at the EMA this December.



Graph taken from on-site voting at the 27th Workshop in Barcelona

Afternoon Session Outcomes

From Concept to Reality

Co-Chairs:

François Houÿez, Treatment Information and Access Director / Health Policy Advisor, EURORDIS

Wiebke Sauter, Senior Clinical Research Scientist, Boehringer Ingelheim

The first session in the afternoon focused on recent CABs that are active or in creation from the patient organisation and the pharmaceutical companies' perspectives.

Speakers:

Flaminia Macchia, Director, EU Government Affairs and Public Policy, Vertex

Flaminia shared Vertex's perspective on how the Cystic Fibrosis Europe (CFE) CAB has benefitted them:

- ✓ Offering a space where they have the opportunity to get feedback on their pipeline
- ✓ If/how the portfolio meets the needs of patients
- ✓ They receive the patients' perspective which informs the clinical development process and the post-approval data generation plan;
- ✓ It establishes a two-way dialogue and builds trust
- ✓ They get expert advice on endpoints, PROMs, Quality of Life, etc.

She emphasised the need to create the CAB as early as possible. To Flaminia, key success factors are:

- ✓ The selection of motivated participants, with different skills and background
- ✓ The representativeness of disease heterogeneity
- ✓ The training and mentorship offered by EURORDIS

Hilde De Keyser, Cystic Fibrosis Europe

Cystic Fibrosis Europe represents CF patients on the European level, working together with all stakeholders in the field. The CFE CAB works as a group totally independent from any company or other organization, with patients from across the EU. They make their expertise available in a structured, transparent way and have an impact on all stages of medicine development as well as access to treatments, etc.

Their mission is to improve CF patients' understanding and knowledge of scientific research across the EU and to facilitate their ability to partner with physicians and researchers, so that the patient perspective is taken into account. To ensure patient access to innovative therapies by integrating the evidence required for reimbursement into the development process, contribute to research and regulatory aspects of legal, policy, and ethics issues and to build awareness among researchers, policy-makers and regulators around the needs of CF patients.

She concluded remarking how important CABs can be for all stakeholders and the need to continuously improve training programmes and representativeness of the CAB members.

Sally Hofmeister, World Duchenne Organization

Sally gave her perspective on the Duchenne CAB, which was created in 2018 and is based on confidentiality, transparency, sharing to promote exchange of ideas, knowledge, best practices and data. In order to accelerate global drug development, optimisation of research and development and a joint plan to streamline cooperation between stakeholders, de-risk development and decrease cost from basic research to clinical trials, market approval and access in a global environment.

Some challenges were identified such as:

- ✓ communicating the advantages of early interaction with the CAB in order to "make a difference" in a rapidly developing field,
- ✓ selecting meaningful outcome measures and appropriate clinical trial designs,
- ✓ demonstrating to regulators which outcomes are meaningful to patients.

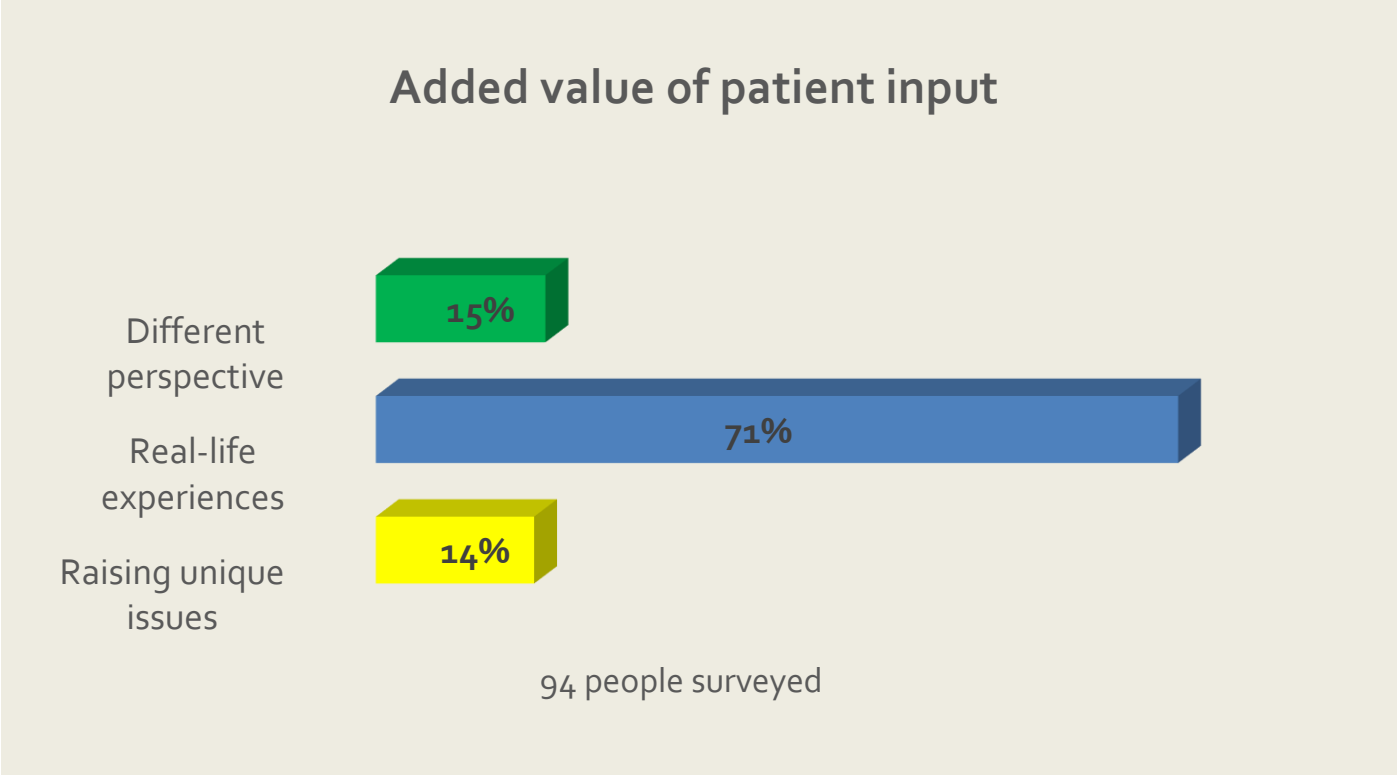
Overall, Sally emphasised pricing, accessibility and TIME!

She expressed the desire of the companies involved in the Duchenne CAB to continue working on patient needs and expectations in research and development.

Elena Zhuravleva, Patient Partnership Director, Roche

Elena presented the opportunities that the Duchenne CAB has brought to Roche, such as access to expert advisors from across the EU and the US. There are challenges, like the specific country compliance regulations.

She pointed out some issues discussed like the different perspectives between countries on the barriers to study participation and the communication strategies in different countries (similarities as well as differences). Study design (ie, duration, placebo use) and endpoints (novel ways of capturing endpoints from patient/observer perspectives) are important learnings. Elena underlined the commitment of CAB members, especially in terms of time dedicated and valuable input.



Graph taken from on-site voting at the 27th Workshop in Barcelona

Russell Wheeler, LHON Society UK

Russell brought us a different perspective from a small disease group of patients where a CAB is also possible, although a more flexible and creative approach might be needed. He presented his personal experience on trying to group various rare eye diseases to build a common CAB, and the difficulties when it comes to a small disease group where not everyone is able to, for example, communicate well in English. According to Russell, "the keywords are flexible and creative. If I add to that "open-minded" then I think we have the start of a (decent) conversation on this topic."

- A workshop participant

"CABs need more collaboration with industry to address some of the hurdles (legal/compliance.)

He remarked on the changing of the landscape where new treatments are starting to cross the old classification boundaries, and the needs of sponsors to engage with multiple patient groups resulting in a greater utility and efficiency for industry partners, as well as a broader perspective and sharing of expertise among patients. This multi-disease approach, he feels, as a collaborative model, could prove very attractive to patient groups and companies alike. For companies like Spark and Novartis the ability to have all patient advocates for a wider disease group in one-space offers far more by way of synergy than it might suffer from any perceived lack of focus.

Russell also used the example of collaboration within ERN-EYE as a perfect example of this, whereby "all of us" have to represent all the diseases under ERN-EYE's remit and not just focus on one particular area. The possibility of a Rare Eye CAB being a conduit for industry to establish a link to the ERN itself was also something not lost on the audience.

"The perspective of Russell on the need to look outside our own, possibly very strict, interpretation of where we should engage was a useful challenge to consider.

- Anne Marie O'Dowd and Denise Dunne

Afternoon Session Outcomes

Breakout session 1: Enterprises, non-profits and/or patients' organisations as sponsors of clinical trials

CABs of a different colour, one might say, with small sponsors, ultra-rare diseases, or broader scope than a typical CAB.

Moderator: François Houÿez, Treatment Information and Access Director / Health Policy Advisor, EURORDIS

Rapporteur: Carol Pitcher Towner, Vice President, International Regulatory Affairs, Alnylam

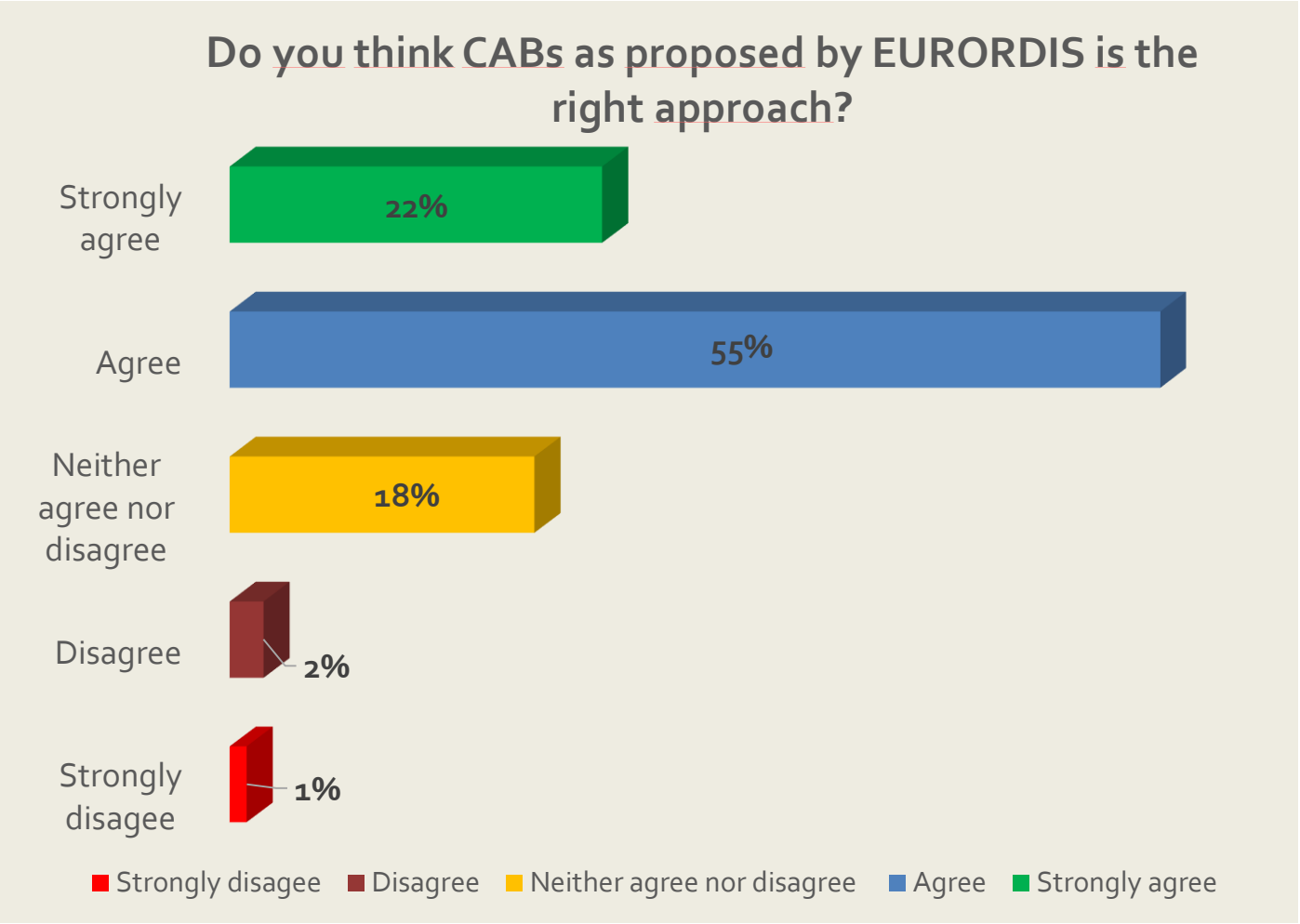
Contributor: Virginie Hivert, Therapeutic Development Director, EURORDIS

Some of the issues that need to be clarified are that sponsors might need to consult with a group of patients in urgent situations, or with limited resources. In this case, could there be a CAB lead, again to answer in time-sensitive situations? In an "emergency" situation, the CAB Chair and CAB liaison might facilitate the process.

Can there be mixed models with company-driven advisory boards still existing? For example, a CAB may be "in creation" but in the meantime can a light consultation, online via an e-meeting to review a consent document, for example, happen? F2F meetings are the optimal practice but virtual interactions, interviews by phone, etc, all have their value. Flexibility may be useful in the CAB activities to be created. In some diseases like Ataxia, the same with San Filippo, it makes sense to group them together providing they can identify where the differences are when they discuss with companies.

Can sponsors work with the patient community when there is not yet a CAB? To form a CAB, perhaps speaking with clinicians and/or RareTogether and others to find such a group. In the case of EUROCABs, transparency is paramount. There should be some follow-up after the F2F meeting, teleconferences, collaboration in between the meetings, milestones met etc. The CAB members themselves will decide on the format, and time that they can contribute in-between meetings. The CAB steers the agenda along with the sponsor. A Best Practices document needs to be developed, for example, on contacting CAB members outside the meeting.

EUROCAB still needs to convince EMA that CAB members are valuable and should be able to contribute to being a patient representative, for example, in a Committee; can CAB members be considered "patient investigators"? And of course, time varies, discussion on endpoints requires more time than to review a consent form.



Graph taken from on-site voting at the 27th Workshop in Barcelona

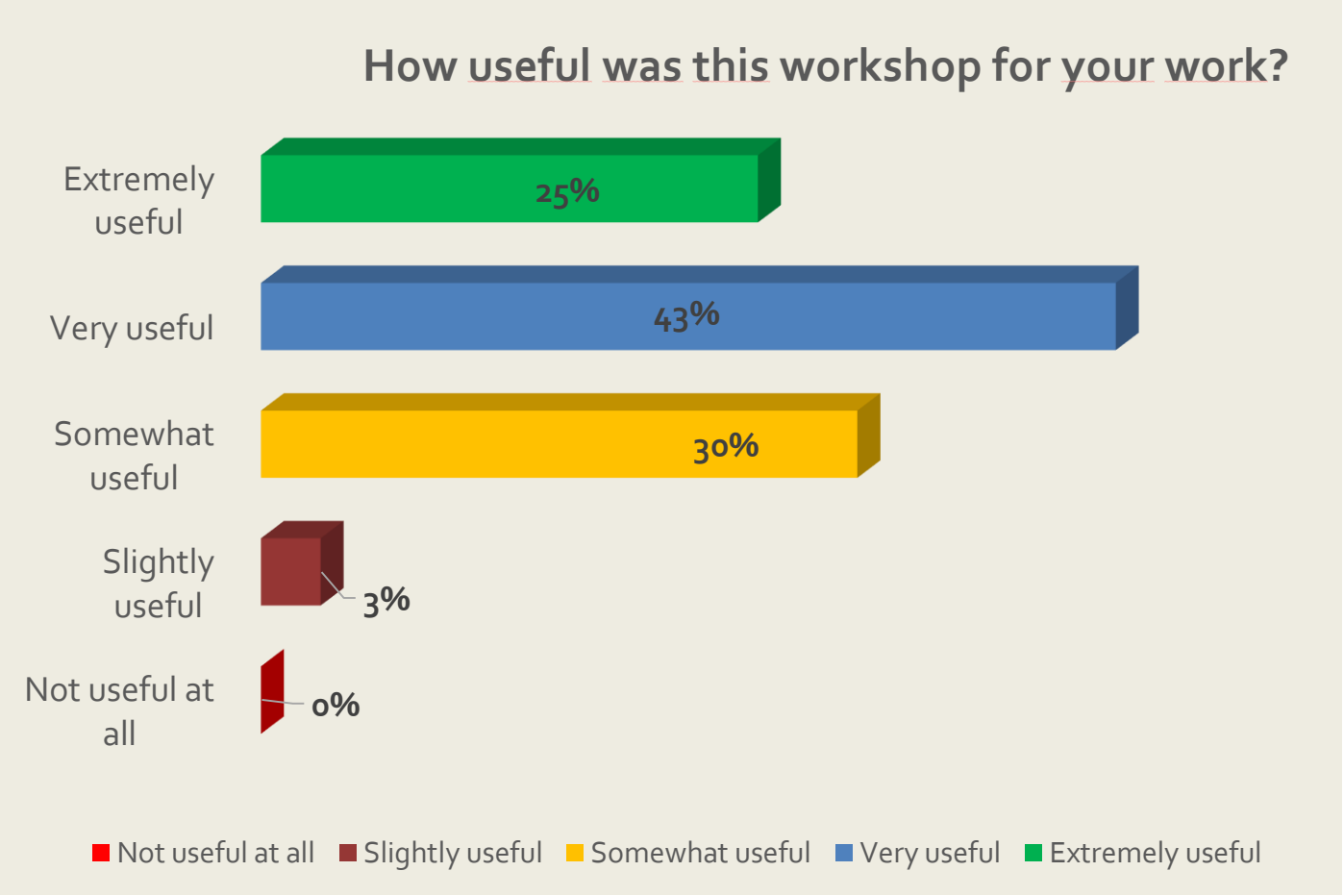
Breakout session 2: Research projects that require cooperation between competitors

Moderator: Alexandre Mejat, EURORDIS Board Member and Scientific International Affairs Manager for AFM-Téléthon

Rapporteur: Jennifer Wilson, Head of Patient Advocacy – International, Amicus

In this breakout session the discussion was very focused on CABs, pre-competitive research and selection/development/adaptation of PROs between different companies and collaborative insights.

In addition, comments on the creation/management of disease registries were addressed, such as personal experiences given by the participants where data ownership was the main issue. There are still some misunderstandings regarding who owns the data (the patient, pharma, etc), the quality of the data and how this is all collected and managed related with the new GDPR. It was agreed that the industry should share the data in pre-competitive research and selection/development/adaptation of PROs between different companies and patients for the benefit of the patients.



Graph taken from evaluation survey in the 27th Workshop Barcelona 2018

Breakout session 3: Outstanding issues

Moderator: Rob Camp, Patient Engagement Senior Manager - CABs, EURORDIS

Rapporteur: Fatima Scipione, Senior Director, Patient Advocacy, Takeda Oncology, USA

Contributor: Elisa Ferrer, Patient Engagement Senior Manager, EURORDIS

In this breakout session, the participants worked on practical and logistical issues. The main focus was the EURORDIS Charter of Clinical Trials, a non-legally binding voluntary agreement. It could be interpreted as a contractual agreement. Perhaps it might be called a letter or declaration of intent?

- ✓ The Memorandum of Understanding is agreement between a company and the CAB; it is also non-legally binding, but sets out the collaboration in a milestone/timeline way. It is a 100% adaptable roadmap of the specific research project on hand.

- ✓ Perhaps some of the compliance concerns can be put aside after the WECAN, MPE, PFMD set out their "reasonable legal agreements". Also to keep a close watch on PARADIGM. Everyone agreed to add a sentence on 'What is a CAB?'
- ✓ Other non-resolved issues: Do we need a better definition of EURORDIS' role in selection, monitoring of CAB members? Now it is not included in the Charter, but in another guidance document, but could be referred to in the Charter.
- ✓ CAB members are not allowed to be in committees at EMA: the *patient investigator* category is being explored. Patient experts work at EMA level. CABs are not perceived as biased by regulators. Industry advisory boards are.

"I was impressed by the companies' interest in setting up a working group for things like contracts and confidentiality agreements. I hope this can move forward!"

- Sally Hofmeister, Duchenne CAB

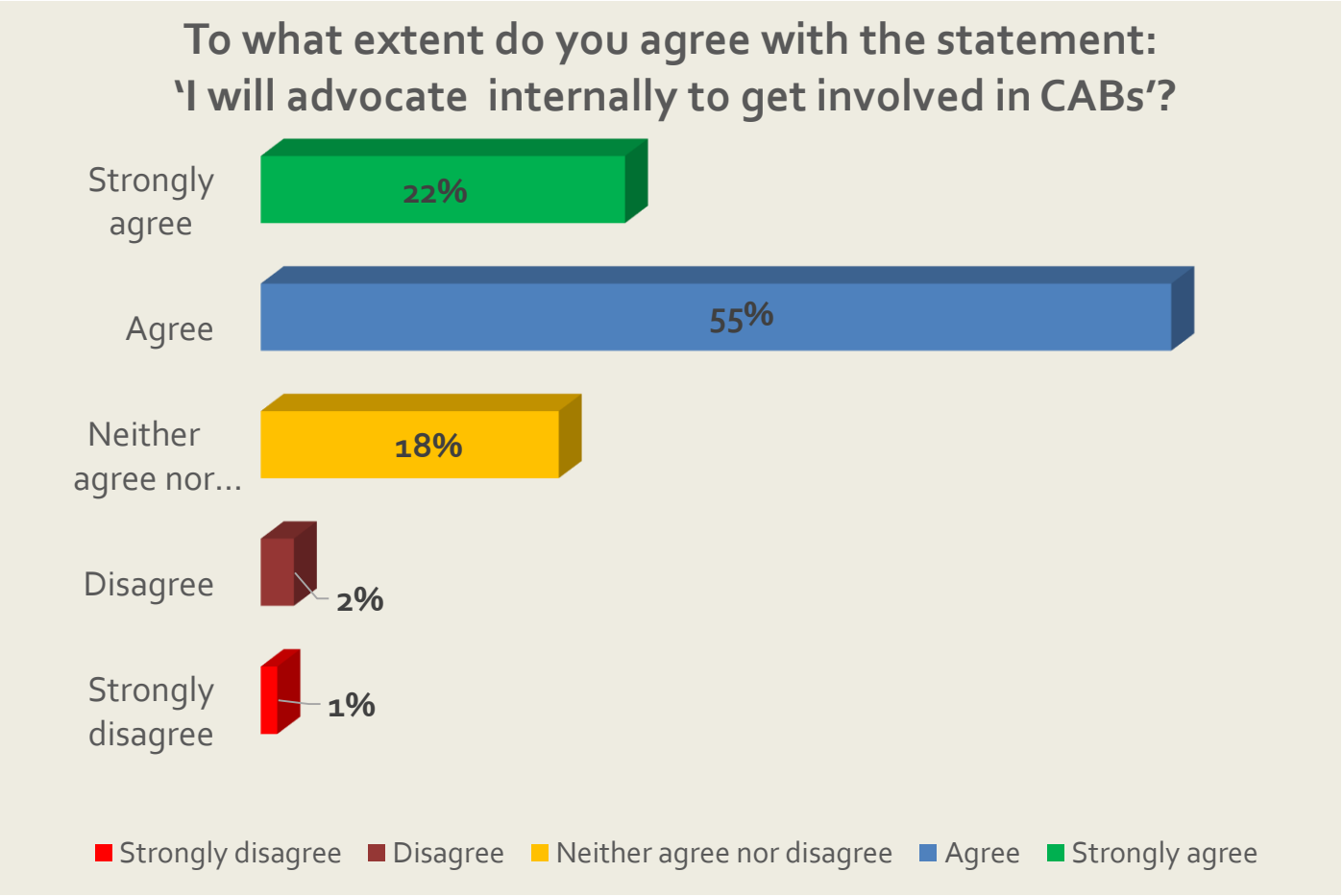
- ✓ From company perspective, company functions involved in the CAB cannot be interacting with trial participants
- ✓ The Charter should be kept as simple as possible and add guidance documents to get into the details. To make it as general and applicable as possible.
- ✓ Can EFPIA or EUCOPE be used as platforms for discussion?
- ✓ Will CAB members be considered from a legal perspective as patients (and could still be considered a promotional activity)? This needs to be clarified. Does being part of the CAB prevent one from participation in a clinical trial? We leave it up to the patient network organizing the CAB to decide (and declare it). This is especially important for RD patient communities. Definition of patient advocate would be useful to have it included in the charter. It needs to be clear that this is a non-promotional activity.
- ✓ There is already some protection in the set up that EURORDIS has constructed: companies are not selecting the patients, patients are helping to set the agenda, etc.
- ✓ CAB members need to be part of an organization. Money needs a structure (patient org) to be transferred.

Conclusions

Yann Le Cam, Chief Executive Office, EURORDIS, provided the conclusions and take-home messages at the close of the workshop.

For the **patient organisations**, he underlined the value of being trained and how EURORDIS can address this by F2F meetings, online trainings, webinars, etc. and underscored what needs to be the essentiality of the CABs within their organisations.

To the **sponsors**, he encouraged participants of the workshop to share the information on EUROCABs within their companies and sign the Charter, so that they will benefit from early and consistent interactions with patients, as well as a stronger and "common-sense" alignment throughout the industry space.



Graph taken from evaluation survey in the 27th Workshop Barcelona

More information

If you are interested in finding out more information about CABs or launching a CAB, please contact rob.camp@eurordis.org.