



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Public Hearing on Valproate

First experience and
lessons learnt



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Introduction

The European Medicines Agency (EMA) held its first public hearing on 26 September 2017 in the context of an ongoing [safety review](#) on measures to reduce the risks of valproate medicines in pregnancy. The full recording of the public hearing is available [here](#).

This document provides an assessment of the entire public hearing process, based on feedback from the parties involved. Learning what went well and what needs to be improved will help to optimise the conduct of future hearings.

The following annexes are included:

Annex 1: List of questions and summary of safety concerns for the hearing

Annex 2: Agenda for the hearing

Annex 3: Public hearing attendees' survey results

Annex 4: Public hearing PRAC members' survey results

Background

The EMA's safety committee, the PRAC (Pharmacovigilance Risk Assessment Committee) can convene public hearings during safety referral procedures that fall under Article 20 of Regulation (EC) 726/2004 or Articles 31 and 107i of Directive 2001/83/EC.

Members of the public are able to attend a public hearing and express their views to the PRAC on specific questions related to the assessment of a particular medicine. Hearings give the PRAC another means to gather the public's views and concerns, particularly where regulatory actions need to be considered in a wider public health context. Hearings are held where the PRAC determines that the views of the public can bring added value to its review.

Patients, consumers and healthcare professionals from across the European Union, as well as industry members, can register to attend as observers or speakers; members of the media can also attend as observers.

To prepare for public hearings, EMA devised specific procedures and materials; these include [rules of procedure](#) on the organisation and conduct of public hearings, a [video](#) and a [guidance for public participants](#). A simulated public hearing with EMA staff on 5 July 2016 tested the procedures.

This report is based on experience gained from the first hearing on valproate medicines and it includes feedback from those involved. All participants, including PRAC members, were invited to respond to a feedback survey two days after the hearing; 43 of the 65 (66%) public participants responded to the survey (16 speakers and 27 observers), and 35 out of 37 (95%) PRAC members responded.

PART A: IMPACT OF PUBLIC HEARING ON THE ASSESSMENT AND ADDED VALUE

- The outcome of the first EMA public hearing was instrumental in recommending new measures to avoid exposure of babies to valproate in the womb:
 - further restrictions on the use of valproate in women
 - a new pregnancy prevention programme
 - a new risk acknowledgement form
 - a visual warning in the outer packaging
- The public hearing was part of a series of consultations with patients and healthcare professionals which lie at the core of the valproate safety review. Firstly a written consultation with stakeholders took place in March 2017, and after the public hearing in September 2017, two meetings of scientific advisory groups (SAGs) on psychiatry and neurology were held in October 2017. These were followed by a large stakeholder meeting on 13 October 2017.
- The public hearing helped to identify the real problems in clinical practice and provided valuable insight and information which otherwise would have not been provided.
- The information gathered from the public hearing contributed to the agendas of the subsequent meetings and shaped the questions that the PRAC asked to the SAGs and at the stakeholder meetings.
- Speakers provided valuable information and insights from a range of different viewpoints which will contribute tangibly to the overall assessment and outcome of the review of valproate.
- The view of the patients and healthcare professionals steered the PRAC into looking into the issue from a different perspective and identifying areas where more focus should be placed.
- Suggestions and recommendations from the public hearing were considered during the assessment of the issue, and further elaborated during the expert meetings which followed. Furthermore, the input used directly for the final recommendations
- Issues were identified at the public hearing that go beyond the remit of the PRAC. Those were taken also into consideration, exploring possibilities for influence.
- The public hearing identified new important themes and information. The assessment report, which will be published once the review is complete, explains how the outcome of the public hearing has been considered during the PRAC's assessment of the issue. It identifies the themes/elements which come directly from the public hearing such as:
 - Lack of communication of the risks to women being treated – one of the key issues identified at the hearing
 - The need for a visual warning in the outer packaging
 - The need for regular reviews for all women treated

Feedback from participants

- In the feedback survey when the participants were asked whether they "*felt that the public hearing would make a difference to the Committee recommendations on valproate*", 88% said YES.
- 100% of respondents (43) indicated that they felt "*the hearing was a positive experience*".

Feedback from PRAC members

- The majority of members reported that “they learnt something new” from the hearing and 79% said that it would “make a difference to the assessment of valproate”.
 - However, much of the discussion related more to healthcare professionals’ actions and less to what the PRAC can influence. Furthermore it was mentioned that several of the issues under consideration needed to be implemented at national level, rather than by EMA.
- *“The hearing ran very smoothly and was most valuable... it was an important opportunity for healthcare professionals, patients and industry to hear one another’s’ views but equally important for all PRAC members to gain this important insight”.*
- *“Overall, a very well run event, a welcome addition to take on the views of the public. I hope that this will continue and views will be sought on other aspects where appropriate. ”*
- *“Bravo and well done on the first public hearing. The voice of the patient in particular is what we need to incorporate into our well-intentioned plans”.*

PART B: ORGANISATIONAL ASPECTS

1) Before the public hearing

1.1 Decision to hold a public hearing

- During its meeting in March 2017, the PRAC discussed the need for a public hearing to feed into its ongoing assessment of valproate. The PRAC concluded that a public hearing should be held *after* an initial assessment. The criteria were met as follows:
 - **Feasibility to hold a public hearing in light of the urgency of the matter:** A hearing could be organised within the assessment timelines.
 - **Nature and extent of the safety concern justifies the need of a hearing:** There is a high risk of teratogenicity (10%) and neurodevelopmental disorders (30-40%) in children exposed to valproate in utero. Despite regulatory efforts to prevent teratogenicity and neurodevelopmental disorders, children were coming to harm as a result of valproate use during pregnancy.
 - **Therapeutic effect of the medicine/class of medicines and availability of therapeutic alternatives:** Valproate medicines are used in the treatment of epilepsy and bipolar disorders and for preventing migraine in some member states; alternative treatments are available but in some cases valproate may be the best treatment.
 - **Potential high impact of possible regulatory actions on therapeutic practice and availability of treatments:** Women may need to consider alternative treatment and any use in pregnancy may need special measures.
 - **High level of public interest:** There is a high level of public interest, seen in the 2014 PRAC safety review, continued media reporting and also patient organisations expressing concerns about the use of valproate.
- During its meeting in June 2017, the PRAC decided to hold the public hearing on 26 September 2017.
- At its meeting in July 2017, the PRAC agreed a list of questions on which the public's views would be sought, together with a summary of the safety concerns. See Annex 1.
- These decisions were recorded in the PRAC highlights and PRAC minutes published on the EMA's website ([here](#)).

Analysis

- Based on the valproate review, the criteria for deciding to hold a hearing are appropriate; they form a good framework for decision-making.
- Publication of information on the hearing in the highlights and minutes of the PRAC meeting provided transparency over the decision to hold the hearing.

Recommendations

- Maintain the current criteria and process for identifying the need for a public hearing (recognising that they may need to be revised with further experience and more cases).

1.2 Questions to be addressed at the hearing and summary of safety concerns¹

Analysis

- The questions to be addressed at the public hearing were simple and focused. They were drafted to encourage the speakers to bring their own perspective.
- The preparation of the questions and the summary of safety concerns benefitted from the input of professional medical writers to help ensure it was appropriately written in simple, lay terms.
- Considering how focused most interventions were, it can be assumed that the public understood the issues and what the PRAC wanted from them.

Feedback from PRAC members

- The majority of PRAC members reported in the feedback survey that the questions were very useful in eliciting valuable and relevant insights (one member felt they were not, but did not explain why).

Recommendations

- Keep questions simple, focused and limited in number (ideally no more than 3).
- Involve professional medical writers in the preparation of the questions and summary of safety concerns.

1.3 Announcement of the public hearing and its dissemination

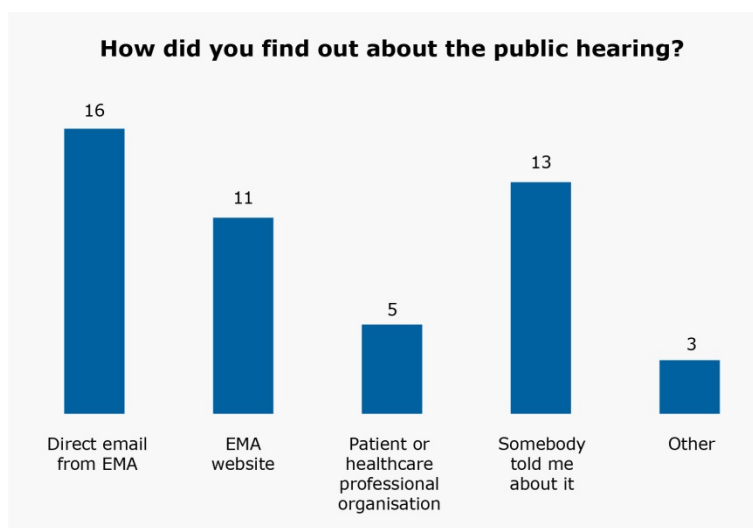
- On 11 July 2017 the hearing was [announced](#) on the EMA website, together with:
 - A summary of safety concerns and the 3 questions on which information from the public was sought.
 - Information on location, date and time of the hearing.
 - Registration information, including the deadline by which participants could register to attend the hearing as speakers or observers.
 - Option to request translation for speakers.
 - Guidance for participants at the public hearing.
 - EMA's dedicated email address for the public hearing.
 - Information about live broadcast on the EMA website.
 - EMA's press release, which was shared with a wide list of journalists.
- This information was published in English on the *Public hearings*, *Valproate* and *PRAC meetings* webpages. Also, a banner about the public hearing featured on the EMA homepage for the duration of registration period.
- The announcement was disseminated via Twitter with a specific logo.
- The announcement was also sent by email (over 300 emails) to the following groups:

¹ The list of questions and the summary of the safety concerns as adopted by the PRAC are presented in Annex 1.

- Pertinent organisations representing patients, healthcare professionals and academia, identified through the EMA network of organisations, as well as those identified by the PRAC members.
- Affected families and individuals previously in contact with EMA.
- The EU Medicines Regulatory Network using the so-called ‘Early Notification System’.
- Specific media groups.

Analysis

- The public hearing featured on social media extensively before, during and after the hearing.
- Twelve visual items and one video were published on twitter. In total, they generated more than 10,000 engagements (likes, comments, retweets, clicks) and 327 link clicks to EMA webpages about the hearing.
- Three visual items and one video were published on EMA’s LinkedIn page, which triggered more than 1000 link clicks to relevant EMA webpages about the public hearing.
- From the survey responses (see below) many participants learnt about the hearing via direct EMA emails, others heard about it by word of mouth and some from the EMA website.



Recommendations

- Use a variety of tools to announce the hearing to ensure the widest possible outreach.
- Increase engagement with organisations representing patients, consumers and healthcare professionals to reach the widest possible audience.

1.4 Registration for the public hearing

- Registration remained open until 25 August 2017 (6.5 weeks); participants were asked to complete and submit an electronic application form (in English) with the following information:
 - Name of the individual.
 - Capacity (i.e. patient, healthcare professional, academic or pharmaceutical industry).

- Affiliation (i.e. name of the organisation/pharmaceutical company that the individual represented), if applicable.
- Contact information (postal address, e-mail address, telephone number).
- For speakers, an outline of their planned presentation (how it addresses the PRAC's questions) and the time requested for the presentation.
- An email address (publichearings@ema.europa.eu) was set up, not only to receive the application forms, but also for general enquiries.
- The application form included a data protection statement explaining how EMA was to process personal information submitted by applicants to the public hearing. This information was also provided in the guidance document.

Analysis

- All applicants were able to complete and submit the application form, although some participants found it cumbersome and asked for technical assistance with the form. This is because the application could not be completed and submitted online; users had to save it and attach it to an email.
- From EMA perspective, the form effectively captured all the information needed to determine whether applicants were suitable for participation in the hearing.

Feedback from participants

Although most people found it easy to complete and submit the application form (see annex 3), several found it challenging and needed help. Some had technical problems in sending the form.

“There was a link to the online form but it was not possible to complete and submit online. It had to be printed then scanned and sent as an email”

Recommendations

- Explore the creation of a more user-friendly application form, which can be completed and submitted online.
- Keep the *content* of the form because it is effective for gathering the information needed from participants.

1.5 Selection of speakers and observers

- It was decided in advance that 12–16 speaker slots could be accommodated. The chosen room could seat up to 100 additional participants (observers).
- In total 89 requests for participation were received: 32 speakers and 57 observers. These were grouped per:
 - Speaker or observer request.
 - Patient/family, healthcare professional, academic or pharmaceutical industry.
 - Therapeutic areas (bipolar disorder, epilepsy, migraine).

- Participant's organisation, if applicable.
- Geographical location.
- All 57 requests for participation as observers were accepted.
- In order to select speakers, each application was reviewed and the following aspects were considered:
 - The relevance of their proposed presentation to the PRAC's questions.
 - Their affiliation (e.g. if and which organisation they represented).
 - Which group they fell in (e.g. patient, healthcare professional).
 - Geographical distribution.
 - Disease area (uses of valproate).
- The overall objective was to achieve good representation across all the groups.
- After review, 25 speaker requests were selected (7 were not accepted as they either did not fully address the PRAC questions or the applicants did not live in the EU; however these applicants were invited to attend as observers and 3 attended).
- It was clear that the planned duration of the hearing (13:00 to 16:00) could not accommodate 25 presentations. Therefore, to give the opportunity to speak to as many as possible, it was decided to:
 - Extend the timing of the hearing by two hours until 18:00.
 - Allocate 7 minutes to each speaker slot.
 - Request speakers with a similar background and proposed presentation to combine their points into one presentation delivered by a member of the group. This allowed for a broader range of views in fewer presentations.
- This approach resulted in 25 speakers being grouped into 16 speaker slots which, at 7 minutes each, could be reasonably accommodated within the time available.
- Those not selected to speak were assured that their written contribution would still be passed to the PRAC for consideration in the assessment, and that their contribution would be published on the EMA website.
- An overview of applications and outcome is provided in the tables below:

SPEAKERS				
General public (patient representatives, carers, families, etc.)				
Disease area	Country	Applied	Refused	Attended
Epilepsy	United Kingdom	8	2	5
	France	1	0	1
	Ireland	3	1	2
	Belgium	1	0	1
	EU-wide organisation	1	0	1
Bipolar	United Kingdom	1	0	1
Total		15	3	11

SPEAKERS				
Healthcare professionals and academia				
Disease area	Country	Applied	Refused	Attended
All (Pharmacy)	EU-wide organisation	1	0	1
Epilepsy	United Kingdom	9	1	4
	EU-wide organisation	1	0	1
	France	1	1	0
	Italy	1	1	0
Bipolar	United Kingdom	1	0	1
	Israel	1	1	0
Migraine	Italy	1	0	1
Total		16	4	8

SPEAKERS				
Pharmaceutical companies				
Disease area	Country	Applied	Refused	Attended
All (Company)	EU-wide organisation	1	0	1
Total		1	0	1

Total		32	7	20
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OBSERVERS		
General public (patient representatives, carers, families, etc.)		
Country	Applied	Attended
Belgium	3	3
Denmark	1	0
Germany	1	0
Greece	1	0
The Netherlands	1	1
United Kingdom	12	11
United States of America	1	0
Ireland	1	1
Switzerland	2	1
Total	23	17

OBSERVERS		
Healthcare professionals and academia		
Country	Applied	Attended
Belgium	1	0
Denmark	2	2
France	1	1
The Netherlands	1	1
United Kingdom	7	6
Italy	1	1
Total	13	11

OBSERVERS		
Pharmaceutical companies		
Country	Applied	Attended
France	3	3
Germany	1	0
United Kingdom	4	3
United States of America	4	4
Total	12	10

OBSERVERS		
Media		
Country	Applied	Attended
United Kingdom	9	7
Total	9	7

- Based on the applications, the first group of speaker slots were allocated to patient representatives or carers, followed by one slot to the company, and final slots to healthcare professionals and academics (see agenda in annex 2).
- Two requests for translation were received, both requesting translation from French to English.

Analysis

- All speakers requested to group their presentations were generally open and courteous to the proposal to join a 'speaker group'. However, this process required a sensitive and considerate

approach by EMA staff, to ensure good understanding of the reasons for forming a speaker group and to check that the speakers were content with their proposed grouping.

- Overall, each stakeholder group (i.e. patients, carers, healthcare professionals, academics and industry) was represented and the three disease areas – epilepsy, bipolar disorders and migraine – were covered (albeit the last to a lesser extent). Five speakers represented individual countries and three represented EU-wide organisations. Observers originated from 7 EU countries and 2 non-EU ones.
- There was a high proportion of participants from the UK, possibly due to EMA's location in London and the hearing being conducted in English.
- Most participants had an interest in epilepsy. This trend was already clear during the registration period. Outreach to engage organisations focusing on bipolar and migraine resulted in additional registrations including a bipolar representative speaker. In addition, a twitter campaign used images and messages to target patients and healthcare professionals in these disease areas.
- For any public hearing, the number and range of applicants is likely to depend on the topic and thus the level of public interest. EMA can strive to maximise outreach and awareness of the hearing but it has no control on who ultimately will register.

Feedback from participants

- *"Representatives from UK, Ireland, France, Belgium but none from southern, northern or Eastern Europe".*
- *"...there were only representatives of the British Epilepsy Association and the other countries were not represented. It is also a pity that there was only one Bipolar Association in England. The debate has been directed too much towards the problem in UK and not enough on Europe".*

Feedback from PRAC members

- 26 PRAC members who responded to the survey felt that the stakeholder groups were sufficiently represented; however, 9 felt that they were not and this is reflected in some of the responses.

- *"It was a pity that there were only very limited numbers of patients suffering from bipolar disorders and none for migraine"*
- *"The view of the currently practicing physicians could have been more represented."*
- *".. more details should be given by HCP representatives on whether their organizations exist in a high number of MS and the countries are represented enough especially as the legislation is different from a country to another in terms of medicines dispensation or prescription".*

- 70% of PRAC members felt that there could have been a broader representation of EU countries.

- *"UK was over-represented. This is to be expected to some extent as speakers from UK will find things easier in terms of travel and language, but may be something to consider in the future".*
- *"...A simultaneous translation of all the meeting should be arranged and publicised so that the speakers from non EN speaking countries would be comfortable to come and express themselves".*
- *"When possible, a wider representation from several MSs would be preferred".*

Recommendations

- Explore ways to increase awareness of the hearing and engage all EU countries and disease-specific groups. Work with the patients and consumers' and healthcare professionals' working parties to increase outreach.
- Explore ways of increasing participation from specific groups (e.g. general practitioners).
- Explain better that some participants were actually representing EU organisations covering a wide range of European countries.
- Explore options for involving the national competent authorities during the hearing.
- Routinely group participants with similar presentations to maximise participation and mention this in the guidance.
- Keep as the preferred order of presentation: patients first, followed by the pharmaceutical industry and healthcare professionals and academia at the end.

1.6 Contacting participants

- All participants were advised of the outcome of the selection process by email within 6 working days of the closing day for registration and they were advised they would receive an official invitation. They were recommended to read the guidance published on the EMA website: [Public hearings - guidance for participants](#).
- Official invitations were sent to those invited to the hearing. Speakers received reimbursement invitations (travel was covered by EMA), with the exception of industry speakers. EMA's Meetings Support Service booked main travel arrangements.
- The public hearing mailbox was constantly monitored. All 36 general enquiries received were responded to on the same day or the next day.
- The EMA public engagement team telephoned all speakers for a detailed briefing and to answer any questions. They were informed of their specific speaker slot (numbered 1–16; see agenda) and reminded of the importance of keeping to their allocated time.
- All speakers were asked to provide information in advance regarding any interests or links with pharmaceutical companies involved with valproate medicines. This was published with the list of speakers on the EMA website before the hearing.

Analysis

Feedback from participants

- 100% of the survey respondents reported that the guidance document was helpful.
- *"The full details and the high level of information provided before the event was very helpful and very reassuring. We also really appreciated having the full information so far in advance of the meeting to help plan for attending that day. The whole event felt incredibly well organised."*
- *"The detailed booklet about how the hearing would be conducted and advice how to prepare for it was exemplary".*

- When asked how satisfied they were with the background information and instructions provided before the public hearing, 90% of respondents indicated that they were *satisfied* or *very satisfied*.

- *“Excellent, clear and comprehensive information”.*
- *“All very well organised and planned. Really liked the idea of sending out the video of a hearing”.*

- In terms of EMA organising travel and hotel accommodation for speakers, most participants were *satisfied* or *very satisfied*; only one respondent was not satisfied.

Recommendations

- The need to individually call speakers to ensure their needs and expectations are well understood is critical to the public hearing’s success. Despite being resource-intensive and often needing additional follow-up, it is a fundamental step.
- Professional staff with experience in dealing with the public should be used to engage with applicants.
- Information provided to participants before the hearing worked well and should be made available in future.
- Ensure that participants inform EMA of any specific requirements (for example in case of disability).

1.7 Preparation for the public hearing

- During the initial preparation for public hearings an EMA taskforce was established comprising representatives from all EMA departments who would be involved in the organisation of a hearing.
- Internal guidance was prepared detailing all roles and responsibilities together with timelines.
- All members of the taskforce were kept up to date on the milestones for the preparation of the hearing by email as well as by regular taskforce meetings.
- PRAC members were also briefed on the progress of the preparation for the hearing at each plenary meeting leading up to the hearing.

Analysis

- Overall preparations worked well and no unforeseen or inadvertent event occurred that affected the hearing.
- The various EMA departments were kept up-to-date on key milestones within the hearing preparations and were therefore fully engaged.
- All tasks described in the EMA ‘roles and responsibilities overview’ were adhered to efficiently and in a timely manner.

Recommendations

- It is important that all relevant EMA departments are kept up-to-date on the preparations for any upcoming hearing.
- The taskforce should continue to coordinate preparations for the public hearing and to ensure everyone is informed and well prepared to contribute to the organisation of the hearing. Now that much of the groundwork on holding a public hearing has been done, the taskforce need not meet as frequently.

2) Public hearing conduct

2.1 Arrival, registration, security and welcome process

- The total attendance was 65: 28 patient representatives, 19 healthcare professionals and academics, 11 from the pharmaceutical industry and 7 from media.
- Additional security measures were put in place, including airport-style screening of personal possessions.
- All participants were asked to show a photo identification to receive an entry badge. Public hearing participants were identified by a grey lanyard, and speakers received a different cardholder colour.
- Participants were guided to a lounge where light refreshments were offered. They remained in the lounge until the start of the hearing.
- Participants were requested to tag and leave large items of luggage in the lounge area.
- The head of the Public Engagement department welcomed participants in the lounge and 15 minutes before the start of the hearing all participants were led to the public hearing room where PRAC members and EMA staff were already settled.

Analysis

- The whole arrival and registration process ran very smoothly; there were no hold-ups or queues for collecting badges or passing through the security screening.
- All the staff in the reception area were very attentive and helpful to the needs of the participants and were able to respond to all requests for assistance effectively.

Feedback from participants

- 93% of respondents were *satisfied* or *very satisfied* with the registration process at reception (2 were neutral). One person was *very unsatisfied* but did not explain why.
- The numbers were similar for the security processes; the majority was *satisfied* or *very satisfied* and one person was *very dissatisfied* (again, with no explanation).
- Some participants felt that the security measures were too extreme and asked if they were equally applied to all EMA visitors.

“All very efficient” and “Very polite staff”

- 11 out of 43 participants were not happy with the welcome area and refreshments in the lounge; no details were given, so it is difficult to understand the reason for their unhappiness.

Recommendations

- Arrange a similar friendly and coordinated approach from security and EMA staff to welcome participants in future hearings.
- Explore if the same security measures should apply to all visitors out of the context of a public hearing.
- Explore options for an alternative 'waiting area' and another format for the welcome introduction.

2.2 Press and media handling

- Press could request to attend the hearing using the same application form as other participants.
- 7 journalists participated in the hearing and were provided a table at the back of the room.
- Media requests for participation were received until the day before the hearing; some did not use the application form.
- Interviews were not foreseen but one interview with a patient representative was allowed.
- Several media representatives requested holding interviews before the hearing; this was handled by the EMA press office.

Analysis

- The system for registration was perhaps too rigid to accommodate media requests, which came even hours prior to the hearing.
- Several media teams arrived unexpectedly at the EMA premises wishing to interview participants. Because this was not agreed with the EMA press office beforehand, it created some difficulties for staff in the reception area.

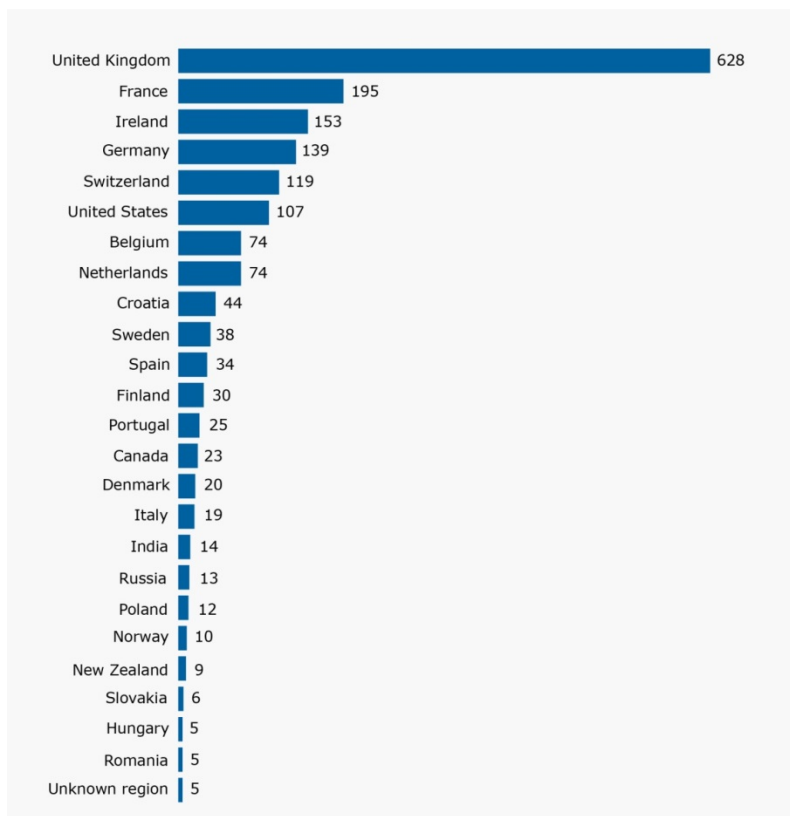
Recommendations

- Consider using a separate, more flexible registration system for media representatives as journalists may decide to attend the public hearing a few hours before the event.
- Allocate a more generous number of seats (around 10) to journalists.
- Decide, in advance of a hearing, whether journalists will be permitted to film interviews with hearing participants on the EMA premises.
- Make more staff available to welcome and accompany journalists to the hearing, taking into account possible arrival of several media representatives without prior notice.

2.3 Overall conduct of hearing

- The hearing began with a welcome from Guido Rasi (Executive Director), followed by a short address by Linda McAvan (member of the European Parliament for Yorkshire and the Humber).
- June Raine (PRAC Chair) chaired the hearing and Sabine Straus, the PRAC member leading the evaluation, gave an overview of the valproate referral procedure and explained how the hearing would feed into the overall evaluation.

- The introductory remarks were intentionally kept very short and did not exceed 20 minutes, so as to allow maximum time to speakers.
- The speakers were then invited to make their presentations. In the order of their allocated slot, speakers approached the central microphone, introduced themselves and gave their presentation. After each presentation, the chair invited PRAC members to ask questions to seek clarification.
- A summary of each participant's presentation is available [here](#).
- A coffee break after the first session of speakers (presentations 1 to 8) facilitated interaction between regulators and participants as well as between the different groups of participants. It helped to create a more relaxed atmosphere and also gave a necessary pause after the intense and often emotional interventions from patients.
- The company, then the healthcare professionals and academia presentations followed after the coffee break (presentations 9 to 16).
- At the end of the presentations, some additional time remained allowing the Chair to open the floor to anyone (including observers) to address the PRAC on the issues under discussion. There followed 9 short presentations.
- The Chair then summed up the hearing and the next steps in the procedure. At the end of the hearing all participants were led back to the reception lobby to collect their luggage, return their badges and leave the building.
- The hearing was broadcast live on the EMA website with around 1,900 people following it on the day and 420 views of the recording within 2 days of the hearing. To date there have been over 1,800 views of the public hearing recording. The geographical location of those tuning in on the day is shown below:



Analysis

- The entire hearing ran very smoothly; the speakers kept to their time limit and PRAC members were able to ask follow-up questions to speakers.
- The speakers' presentations mainly focussed on the PRAC questions.
- The presentations provided valuable information and insights on valproate and its current use. This helped to focus and define where the real problems in managing the risk of valproate are and also gave some indications for possible solutions.
- There was sufficient time to allow observers to make contributions, which was much appreciated and appeared to increase the hearing's standing and to foster trust.
- The web streaming went very well; feedback from those who joined online reported that the full hearing could be viewed and heard well.

Feedback from participants

- 99% of the survey respondents felt that the presentation introducing the hearing was very clear and useful. One participant taking a different view said that "the goals of the public hearing were not sufficiently elaborated in the presentation and the results of the public hearing do not make the objectives pursued self-evident".
- To the question "Do you think the public hearing was well conducted", 95% responded "yes", with 98% reporting that the "PRAC was listening and engaged".

- *"Partly, But it was difficult to know, because there were not many questions. ... it was not intended to start a debate, and therefore not many PRAC members said anything."*
- *"It would have been good for more PRAC members to ask questions of the speakers."*

- There were some comments relating to the seating and layout of the hearing. Several people could not hear or see all the proceedings fully.

- *"The observer area was not optimal because of the low chairs which prevented us being able to see the Committee. Also the screens didn't show any of the live camera feed."*
- *"I could barely hear some people talking."*
- *"As there were so many delegates it would have been useful to have the speakers and the PRAC members shown on the screens as and when they spoke."*

Feedback from PRAC members

- 100% of respondents indicated that they felt the hearing was well conducted
- Almost all PRAC members reported that the speakers' presentations were focused on the PRAC questions and 85% of survey respondents said they learnt something new.

- *"The practicalities were very good. Cannot be better."*
- *"I think it was very successful."*

Recommendations

- Follow the approach and structure used for the valproate hearing which ran very smoothly.
- Give a short (no more than 20 minutes) and clear introduction to the hearing.
- Plan for the PRAC Chair and members to ask questions for clarification after each presentation to fully engage with the hearing and to demonstrate that the PRAC is listening to the views presented.
- Allow more time for PRAC members to ask questions.
- Allow time for spontaneous interventions from participants at the end of the hearing.
- Use the same approach to chairing and summing up of the hearing as a model for future hearings.
- Use experience of the valproate hearing to inform the room layout, seating, audio arrangements and video monitors, particularly for EMA's new premises.
- Explore options for a location that allows participants to see and listen to the proceedings better, potentially using tiered seating and showing the presenters on screens around the room. Take these aspects into consideration when looking at EMA's new location.
- Include a coffee break as done in the valproate public hearing.

2.4 Time management

- The hearing duration was finally set at 5 hours and 15 minutes: 30 minutes for welcome and introductory remarks, 25 minute for a coffee break and almost 4 hours for speakers. The aim was to ensure that the majority of the hearing was dedicated to the speaker presentations to enable the PRAC to gather the broadest possible range of views.
- Giving about 7 minutes for each presentation would give sufficient time to convey key points to the PRAC, while still allowing a good range of presentations.

Analysis

- The number of requests for participants to speak could not be predicted and, therefore, it was important to allow some flexibility. Indeed, to accommodate as many speaker requests as possible, the timing of the hearing was extended by 2 hours.
- The hearing started and finished on time and most speakers kept to their allotted time.
- Feedback from participants and from PRAC members confirmed that the speaker time slots were optimal.

Feedback from participants

- When asked if the time allotted to speakers was adequate, 85% responded positively.
- Most respondents felt that the hearing duration was 'about right', with a few mentioning that it was somewhat too long (2 mentioned too short).

"I was very impressed by the pace and unhurried nature."

Feedback from PRAC members

- The majority of PRAC members felt that the time allotted to the speakers was about right and 90% felt that they had adequate opportunity to ask questions to the speakers.
- Most PRAC members felt that the overall duration of the hearing was optimal (three felt it was too long, one too short).

Recommendations

- Offer 7-minute speaking slots because this duration seems most appropriate for drawing out the widest range of points efficiently.
- Keep the timing format similar to this first experience in future hearings.

3) After the public hearing

3.1 Publication and dissemination of hearing summary and recording

- A summary of the public hearing was published on the EMA website after the hearing, together with the [recording](#).
- The link was sent by email to all participants of the hearing, who were also told that they would be informed of the PRAC conclusions as soon as they are issued.

Analysis

Feedback from participants

“The online information was great and the upload to YouTube invaluable but it would have been nice for EMA to upload each speech separately as well... These are ideal for sharing on social media and help raise awareness of the excellent work the EMA do. In a world of deregulation I feel it essential that you are able to promote the benefits of regulation.”

Recommendations

- Continue to broadcast public hearings.
- Explore the feasibility of putting up each presentation separately when publishing the video recording of the hearing.

3.2 Collection of feedback from participants and PRAC members

- All participants, including PRAC members, were invited to respond to a feedback survey 2 days after the hearing. The survey was open for 3 weeks and a reminder was sent 1 week before the deadline.
- Of the 65 public participants, 43 responded to the survey: 16 speakers and 27 observers. Responses were received from 14 patient representatives, 2 from charities, 1 representative of the patients' and consumers' working party, 4 academics, 12 healthcare professionals, and 10 from the pharmaceutical industry.

- Of the 37 PRAC members, 35 responded to the survey.

Analysis

- This is a useful way to collect feedback on the hearing which can be used to inform the organisation of future hearings. The responses were anonymous, allowing people to be honest in their responses.

Recommendations

- Continue to collect feedback from participants and PRAC members and encourage more detailed feedback where recommendations for improvement are made. This input will be used to monitor and continuously improve organisation of future hearings.

3.3 Personal data handling

- The personal data collected in the application forms were used by EMA staff only to assess the applications and to draw up the list of participants for the public hearing. For speakers, the appropriateness of their proposed oral presentation was reviewed, as well as affiliation and geographical location. For observers, only affiliation and geographical location were considered. For practical reasons, data on disability or mobility impairment were also processed. There was no further processing of personal data for any purpose outside the scope of the hearing.
- All the data were stored at EMA premises within a secure data centre which is password protected and only available to EMA staff.
- Only the names of speakers, including their affiliation, proposed oral presentation (as submitted in the form) and any declared interest were published on the EMA website; no contact details were published.
- In accordance with EU data processing regulation, and as agreed by the European Data Protection Service, the personal data of public hearing participants (both speakers and observers) will be deleted within two years of the public hearing. This also applies to members of the public whose requests to speak were declined.
- Administrative data of speakers for whom EMA covered travel expenses will be kept for the duration needed to comply with the provisions of the Financial Regulation, for auditing purposes, namely five years after discharge of the budget by the European Parliament.
- An internal process has been developed to track and ensure the appropriate and timely deletion of the data.

Recommendation

- The procedure as agreed by the European Data Protection Service was adhered to and should be maintained for all future hearings.

OVERALL CONCLUSIONS AND RECOMMENDATIONS

- From the moment the PRAC decided that it would be feasible and beneficial to hold a public hearing to inform the assessment of valproate, EMA put into action the procedures previously established in anticipation of its first public hearing.
- The overall feedback attests to the success of this first hearing, both from an organisational and scientific point of view;
 - Over 90 applications were received and almost all were accommodated.
 - Grouping speakers was a very efficient way to maximise the range of views and opinions presented at the hearing; these were augmented by written statements.
 - Considering the number of applications received and the complexity of the referral, the duration of the hearing as well as the time allotted to speakers was appropriate.
 - The level of support and guidance provided to participants was appreciated and was essential for the smooth running of the hearing.
 - The hearing was instrumental in providing insights and information to PRAC members that they did not have previously. It helped them learn the different views and positions of the various stakeholders and to enhance their knowledge about valproate use in routine practice. The presentations were of immense value to EMA and the PRAC.
 - As one participant summed up “it is a pity that a similar exercise cannot be applied, for obvious reasons, to all safety reviews, as the huge contribution given by the hearing gives the best quality output to the act of regulating medicines”.
- The main limitations relate to the representation of participants; there was a high representation from UK and for the epilepsy use of valproate. Outreach and awareness can be enhanced; however, registration is essentially dependent on the level of interest and availability of individuals and organisations. It will be interesting to see if this trend continues once the Agency holds further public hearings, especially in the new premises in Amsterdam.

In conclusion, the public hearing about concerns with the use of valproate in pregnancy provided a valuable opportunity for the PRAC to gather the views and experiences of the public. These views contributed to the assessment and final recommendations on the use of valproate.

Based on the previous analysis and all the experience acquired during this first hearing, we can conclude that the public hearing added value, improved quality of the assessment and fostered trust in the system:

- It led to better safety recommendations, tailored to meet the real needs and problems of patients, which were identified at the hearing
- It allowed different stakeholders to listen to and learn from each other
- It increased overall transparency and understanding of regulatory procedures in Europe

Regarding organisational aspects, they were successful as per the feedback received. However from the lessons learnt we can extract recommendations for process improvement will be implemented in subsequent hearings.

The public hearing is a resource intensive tool, and a decision to hold a hearing needs to be well balanced.

ANNEX 1

PUBLIC HEARING ON VALPROATE

Summary of safety concerns and List of Questions for the Public Hearing

Background and Summary of Safety Concerns

Valproate and related substances² (valproic acid, sodium valproate, valproate semisodium, and valpromide) are medicines that are currently used in Europe for the treatment of epilepsy, bipolar disorders and, in some Member States, to prevent migraine attacks.

For some patients with serious conditions, valproate may be the best or only treatment option. However, it has long been known that if taken during pregnancy it can affect the unborn baby and cause certain abnormalities.

Following a review in 2013, including consultation with patients and other stakeholders, the European Medicines Agency (EMA) recommended restrictions to the use of valproate. The product information was updated and educational materials were developed for healthcare professionals and patients. These included a guide for prescribers, a patient booklet, an acknowledgment of risk form and a letter to inform healthcare professionals.

However recent research carried out in France has suggested that these measures have not had the desired effect. The French medicines regulator (ANSM) therefore asked the EMA to review the current measures and to consider whether further measures are needed to minimise the risks of valproate in women who are pregnant or of childbearing age.

This new review began in March 2017 and EMA's safety committee (PRAC) felt it was essential to take into account the views and experiences of patients, affected families and the wider EU public. It therefore decided to conduct a public hearing.

The public hearing for valproate will be held on **26 September** at the EMA offices in London. The hearing will focus on the questions outlined below. Information about public hearings, including full details on how this hearing will be conducted and how interested individuals can participate, is available on EMA's [webpage for public hearings](#).

After the public hearing, the PRAC will continue its review according to the [published timetable](#). Once the assessment is finalised, the PRAC will publish a report on the safety of valproate and related substances which will set out its conclusions and will clearly explain how the information gathered during the public hearing has informed the Committee's recommendations.

² Marketed under the trade names: Absenor, Convival Chrono, Convulex, Delepsine, Depakin, Depakine, Depakote, Depamag, Depamide, Deprakine, Diplexil, Dipromal, Epilim, Episenta, Epival, Ergenyl, Espa-Valept, Hexaquin, Kentlim, Leptilan, Micropakine L.P., Orfiril, Petilin, Valepil, Valhel PR, Valpal, Valpro and Valprolek

Questions for the public hearing on valproate

Based on your experience with valproate treatment during pregnancy:

Question 1

What is your view of the risks of taking valproate during pregnancy, including its potential effect on the child?

Question 2

What are your views on the measures currently in place to reduce the risks of using valproate during pregnancy?

Question 3

What other measures should be taken to reduce the risks of using valproate during pregnancy?

ANNEX 2

Agenda

Agenda

Chair: June Raine (PRAC chair)

11:45 *Registration opens*

12:30 *Participants escorted to meeting room 3M*

12:45 **Welcome and introduction**

- ▶ **Guido Rasi** (EMA Executive Director)
- ▶ **Linda McAvan** (Member of European Parliament)
- ▶ **June Raine** (PRAC chair)

13:00 **Public hearing rules and background information on Valproate's ongoing assessment**

- ▶ **Juan García Burgos** (EMA Head of Public Engagement)
- ▶ **Sabine Straus** (PRAC rapporteur)

13:15 **Speakers interventions** (7 minutes per intervention)

General public (patient representatives, carers, families)

Speaker 1:

- ▶ **Catherine Cox¹**, Fetal Anti-Convulsant Support Association, UK
Janet Williams, Independent Fetal Anti-Convulsant Trust (In-FACT) & FACS Syndrome Association, UK

Speaker 2:

- ▶ **Marine Martin**, Association of Parents of Children with the syndrome anticonvulsant (APESAC), France

Speaker 3:

- ▶ **Karen Keely**, FACS Forum, Ireland

Speaker 4:

- ▶ **Clare Pelham**, Epilepsy Society, UK
Philip Lee, Epilepsy Action, UK

Speaker 5:

- ▶ **Nathalie Raemdonck**, Belgian Association of Victims of Valproate Syndrome (ABSVV/BVSVS), Belgium

Speaker 6:

- ▶ **Martin Brodie**, International Bureau for Epilepsy (IBE)

Speaker 7:

- ▶ **Josephine Tapper**, Patient, member of Bipolar UK

¹ For grouped interventions, the name in **bold** is the speaker

Speaker 8:

- ▶ **Joanne Cozens**, Organisation for Anti-Convulsant Syndromes (OACS), UK
Emma Friedmann, FACSAWARE.NET, UK
- ▶ **Branwen Mann**, Patient representing Anti-Convulsant Syndrome, OACS Youth Trustee

15:15 Coffee break

15:40 Speakers interventions (7 minutes per intervention)

Pharmaceutical companies

Speaker 9:

- ▶ **Eric Teo**, Sanofi

Healthcare professionals and academia

Speaker 10:

- ▶ **Jurate Svarcaite**, Pharmaceutical Group of the European Union (PGEU)

Speaker 11:

- ▶ **Helen Cross**, European Reference Network for Epilepsy (EpiCARE)
Timothy Barrett, University of Birmingham, UK
Daniel Hawcutt, Royal College of Paediatrics and Child Health (RCPCH), UK

Speaker 12:

- ▶ **Torbjörn Tomson**, International League Against Epilepsy (ILAE) (CEA)

Speaker 13:

- ▶ **Anthony Marson**, European Academy of Neurology (EAN)
Philip Smith, Association of British Neurologists (ABN)
Sanjay Sisodiya, Epilepsy Society, UK
Dyfrig Hughes, Centre for Health Economics and Medicines Evaluation, Bangor University, UK

Speaker 14:

- ▶ **Paolo Martelletti**, European Headache Federation (EHF), Department of Clinical and Molecular Medicine, Sapienza University, Italy

Speaker 15:

- ▶ **Kim Morley**, Epilepsy specialist midwife/ nurse practitioner, UK

Speaker 16:

- ▶ **Angelika Wieck**, European Psychiatric Association (EPA)/ Greater Manchester Mental Health NHS Foundation Trust

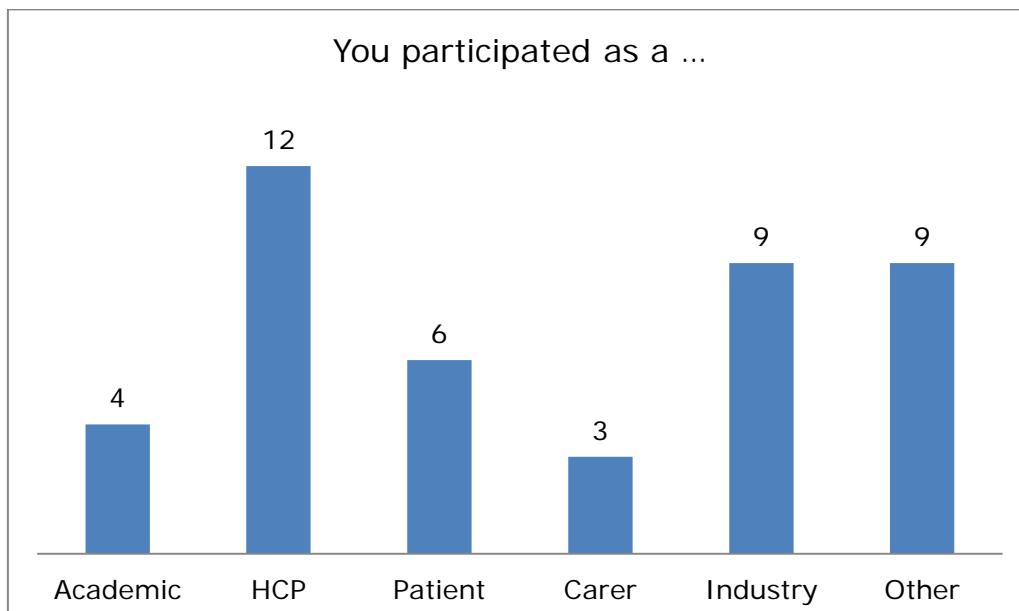
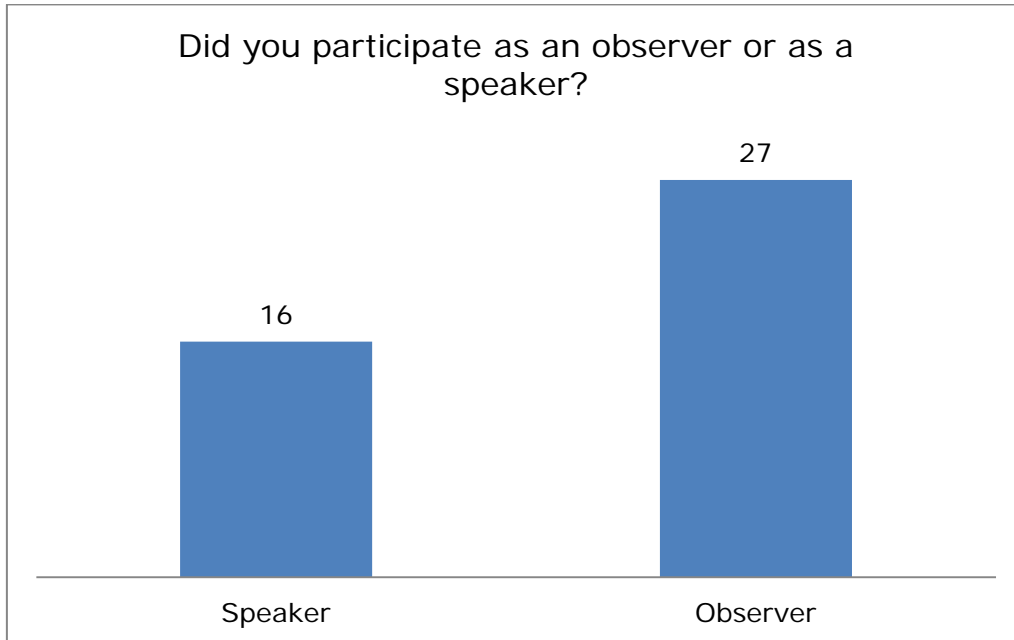
17:30 Wrap up, summary of interventions and next steps

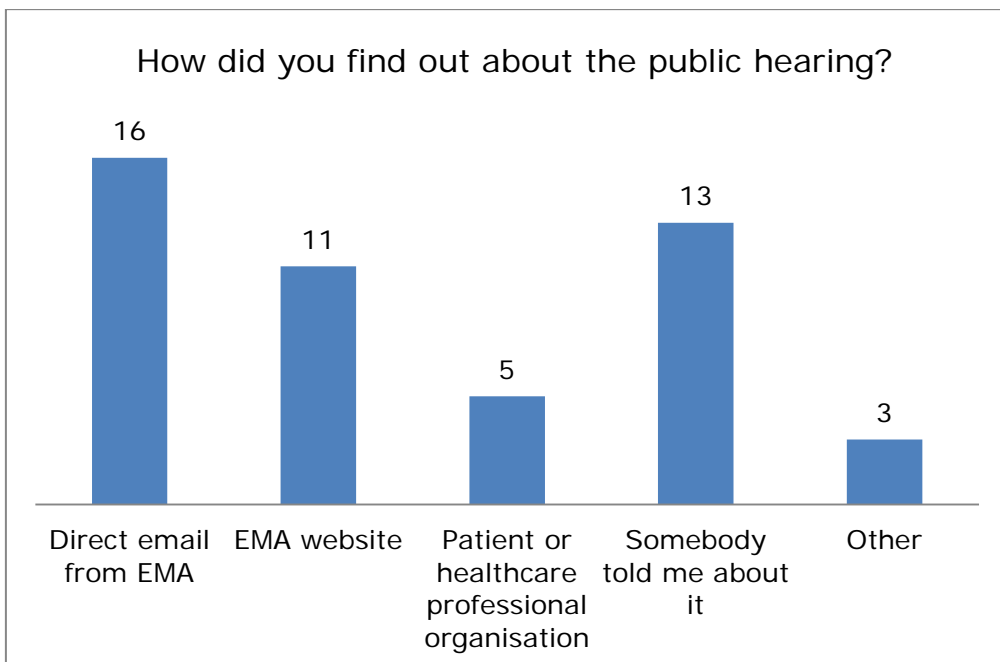
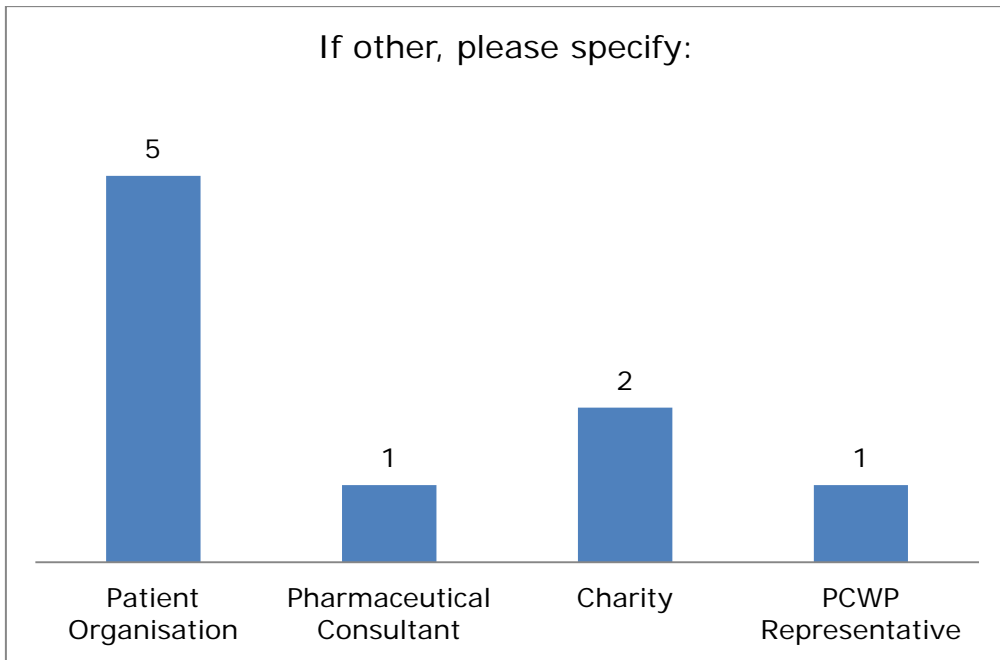
- ▶ **June Raine** (PRAC chair)

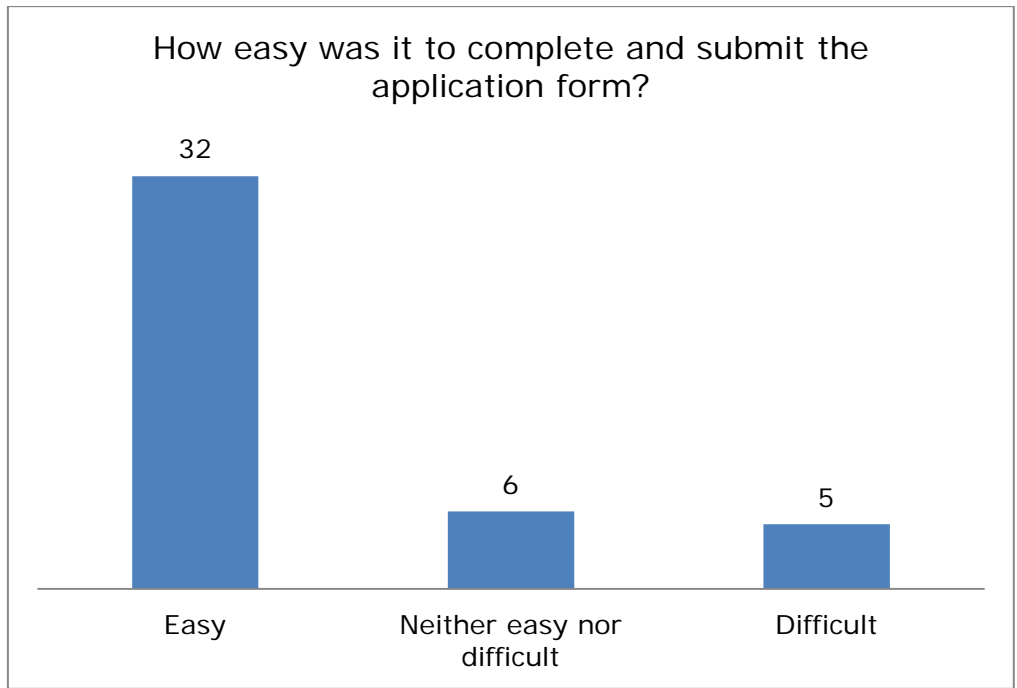
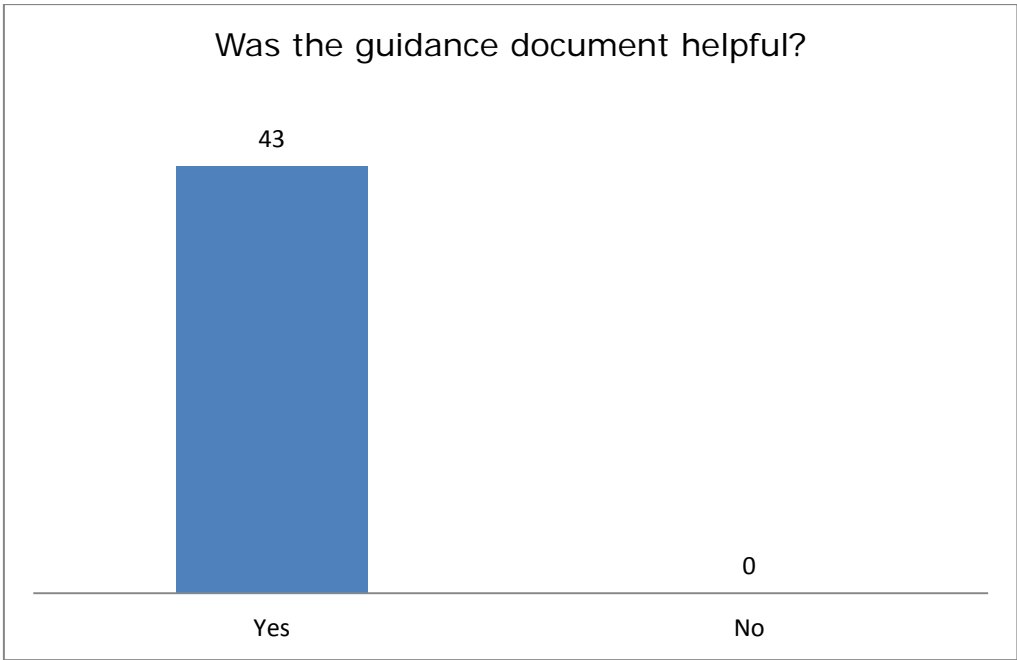
18:00 End of public hearing

ANNEX 3

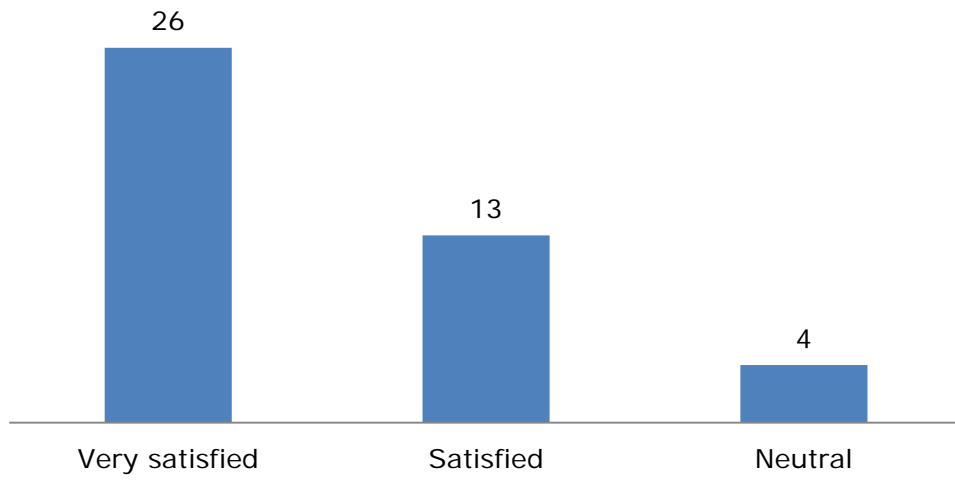
Public hearing attendees' survey results



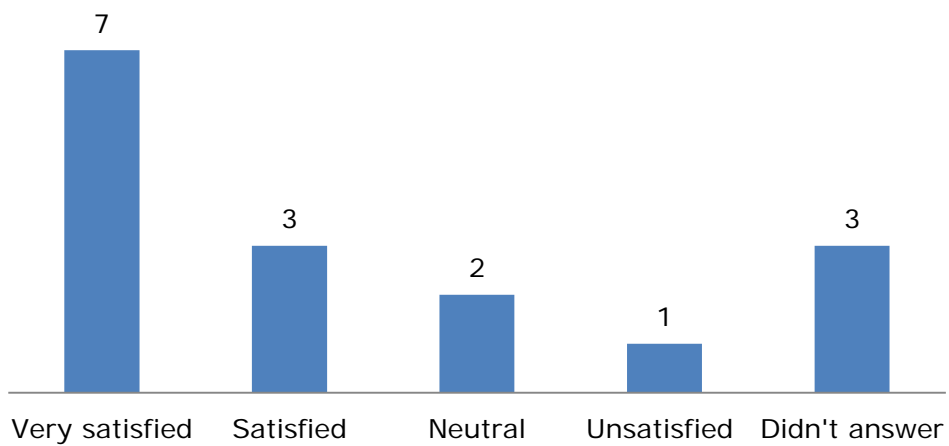


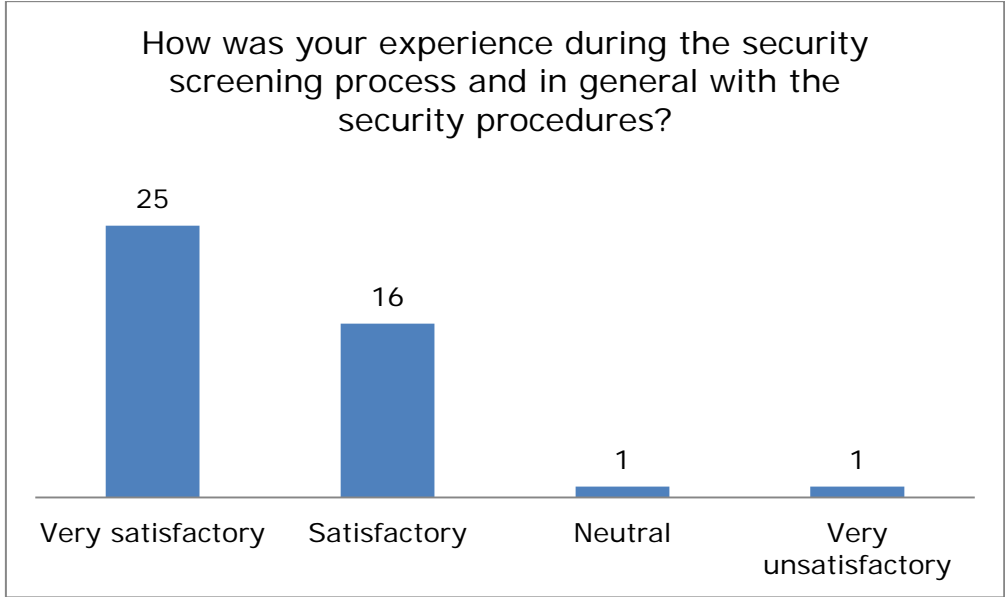
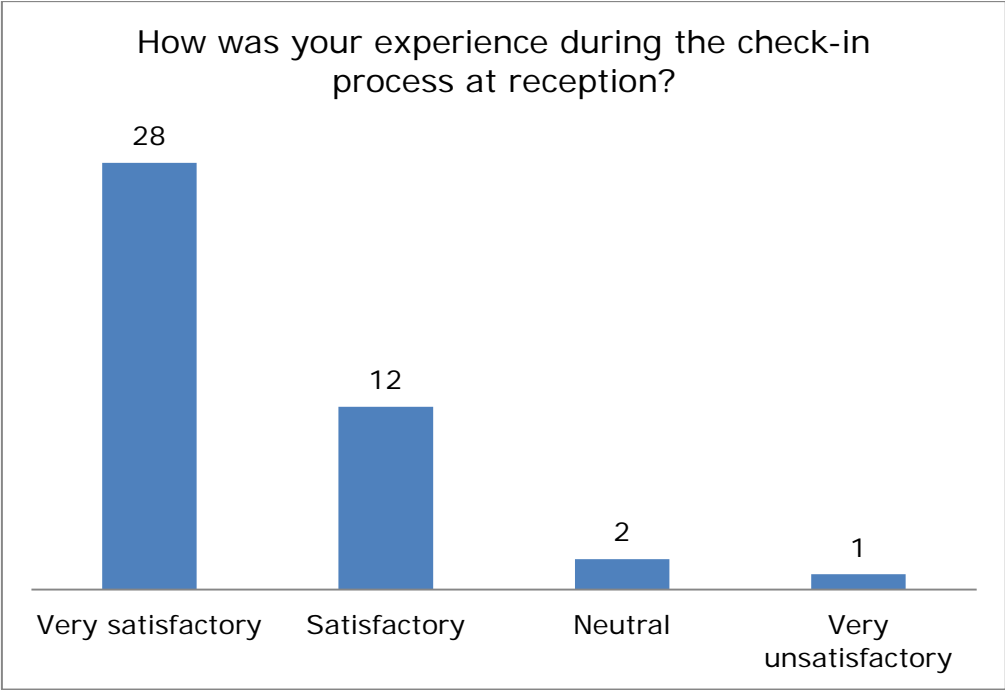


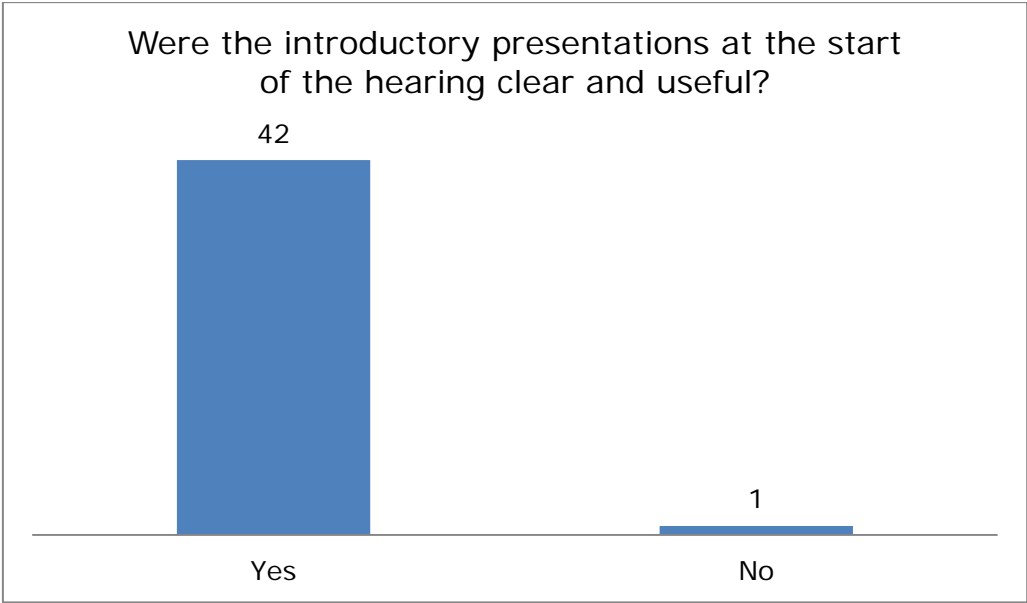
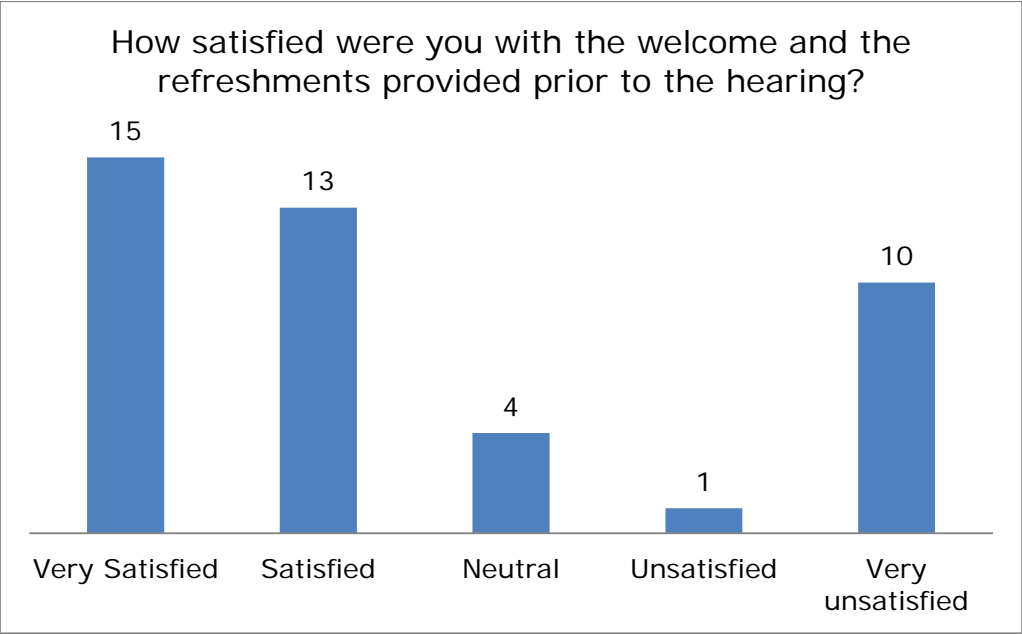
How satisfied were you with the background information and instructions provided before the public hearing?

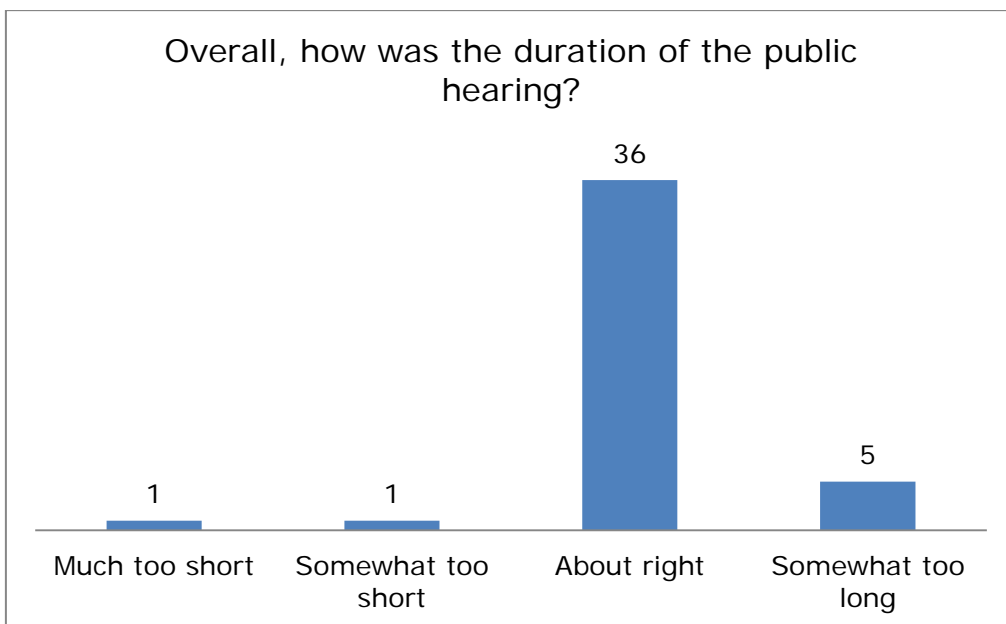
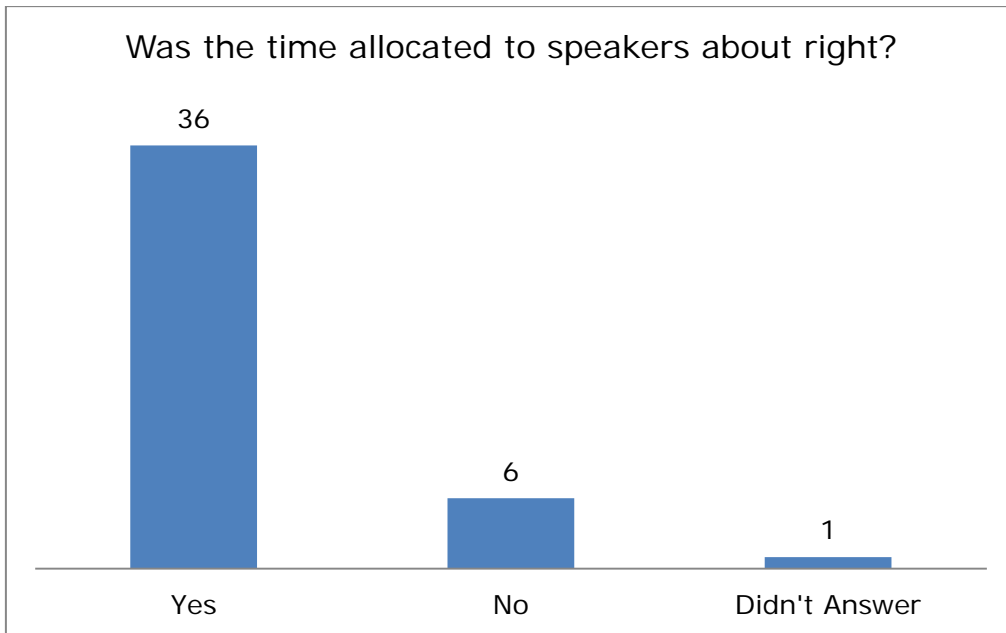


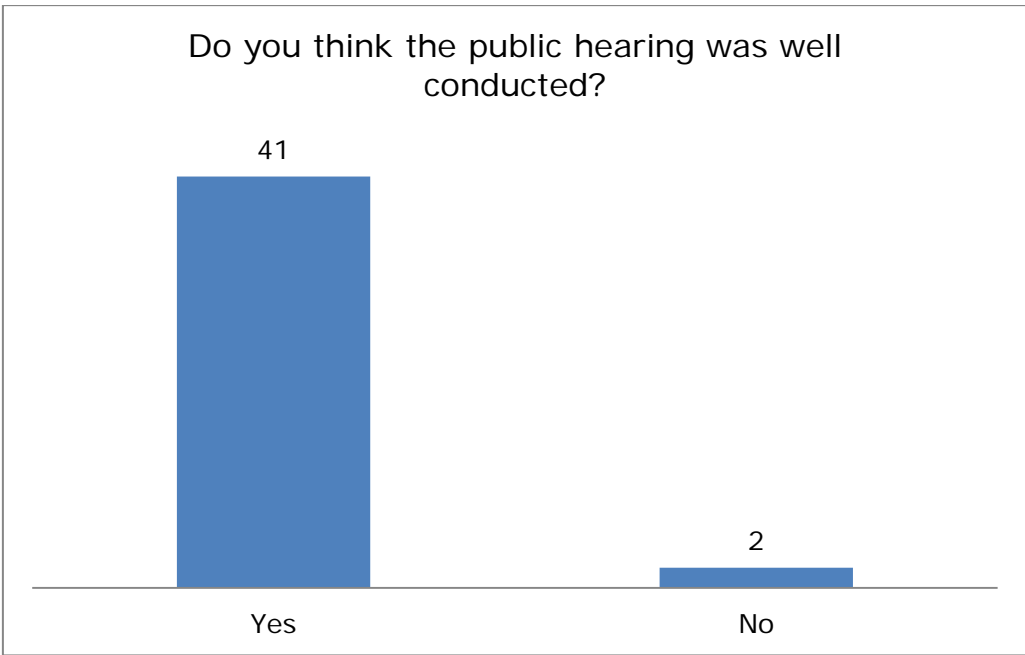
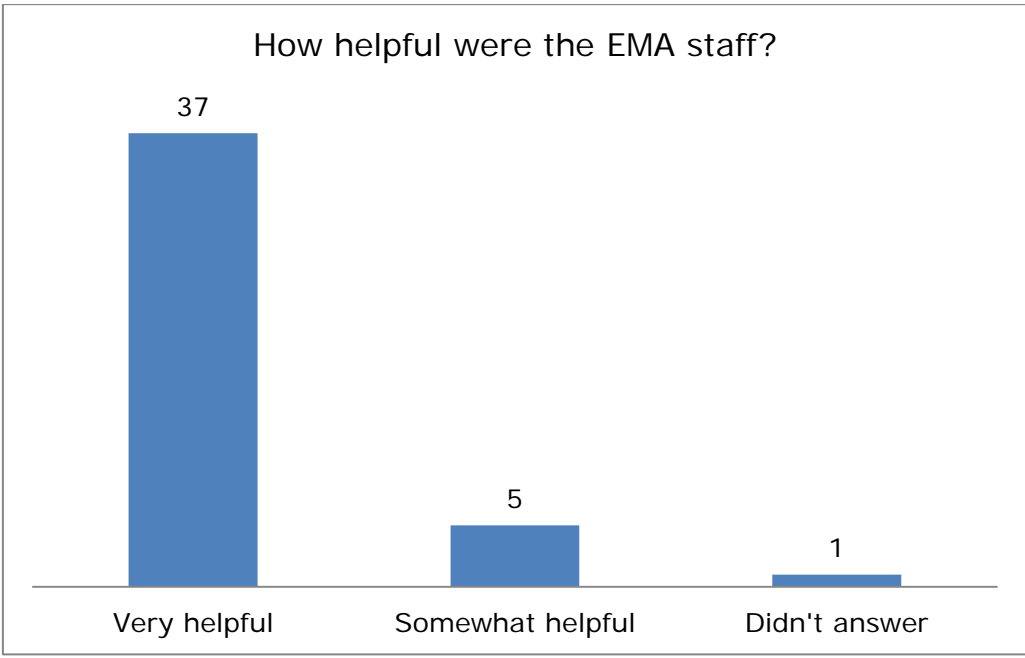
How satisfied were you with how your travel requirements were handled by EMA staff? (for speakers only)



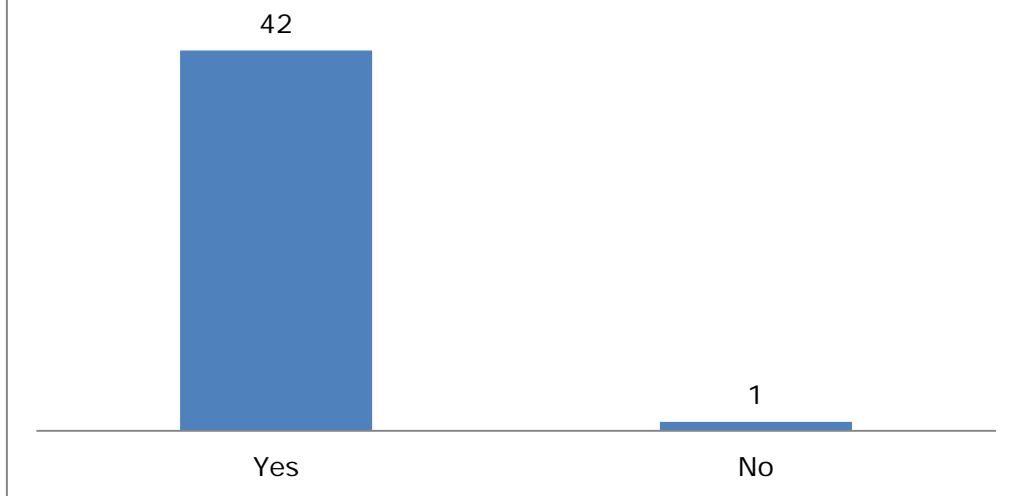




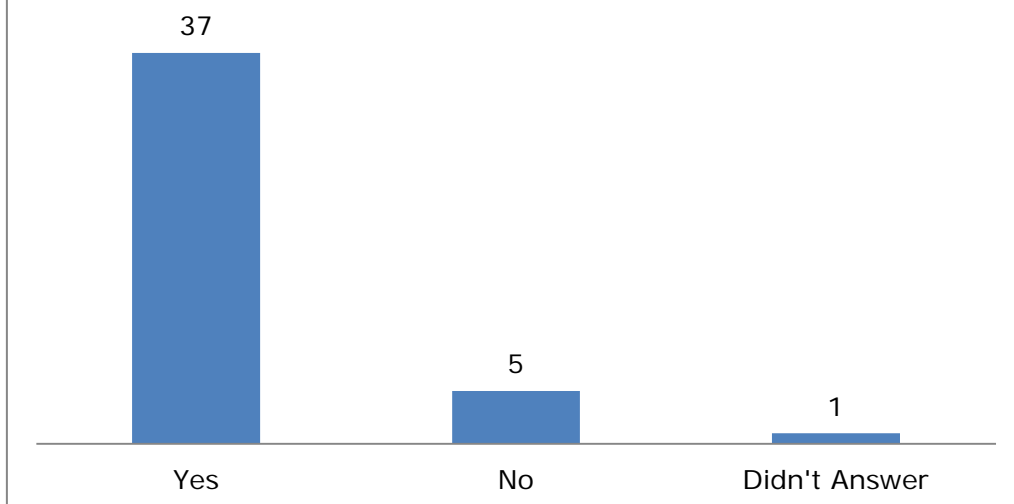


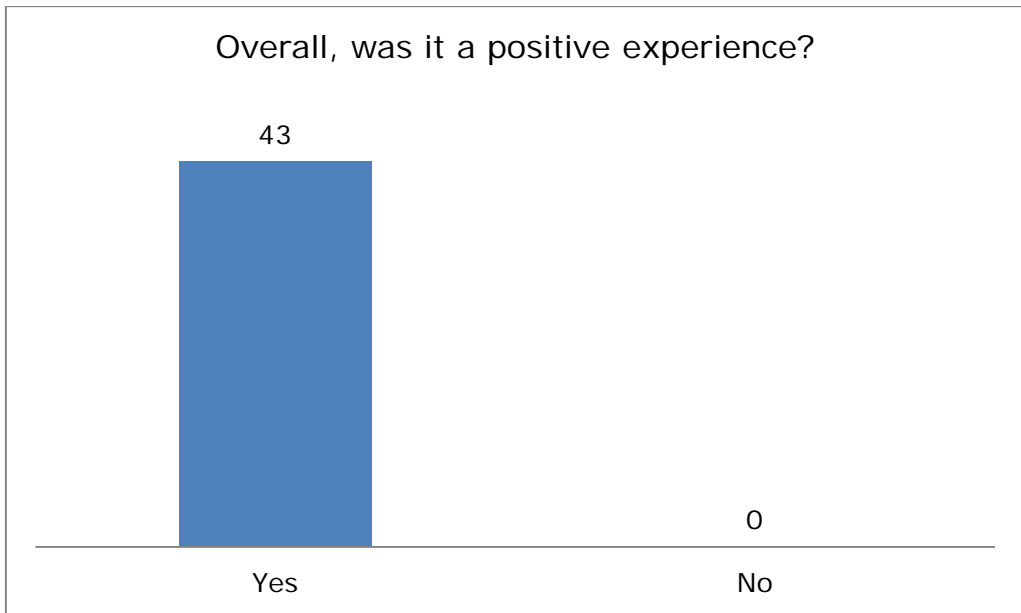
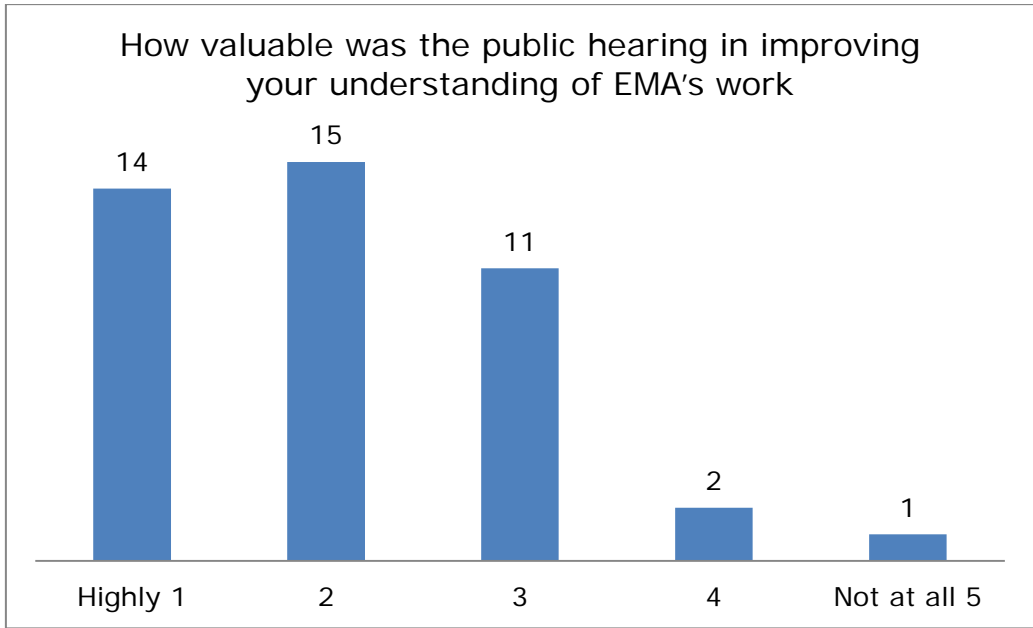


Did you feel that the Pharmacovigilance Risk Assessment Committee (PRAC) was listening and engaged during the hearing?



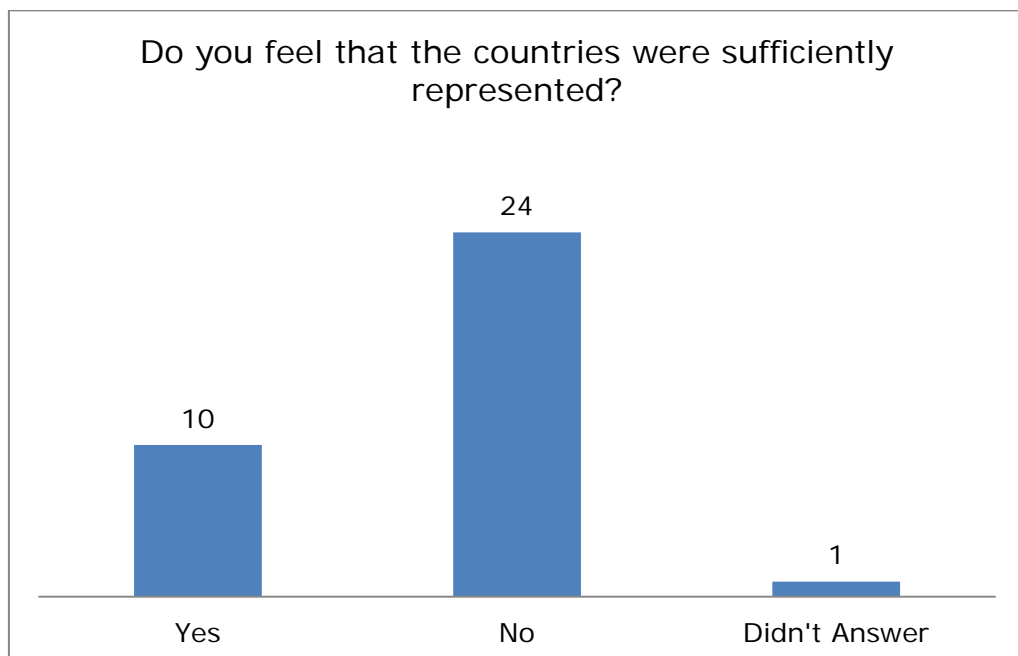
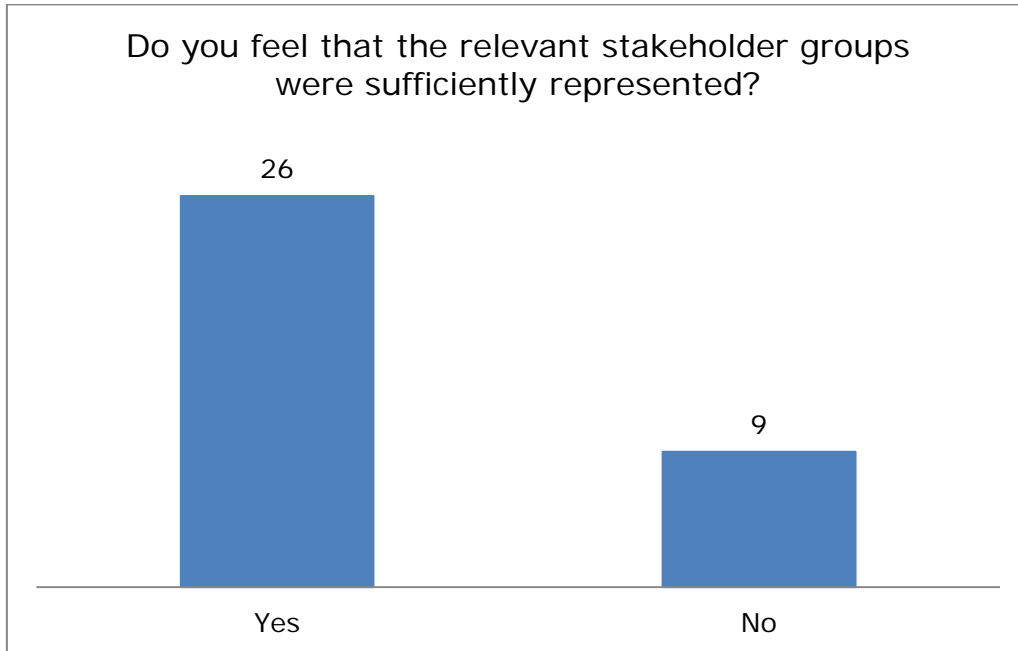
Do you feel that the public hearing will make a difference to Committee's recommendations on valproate?

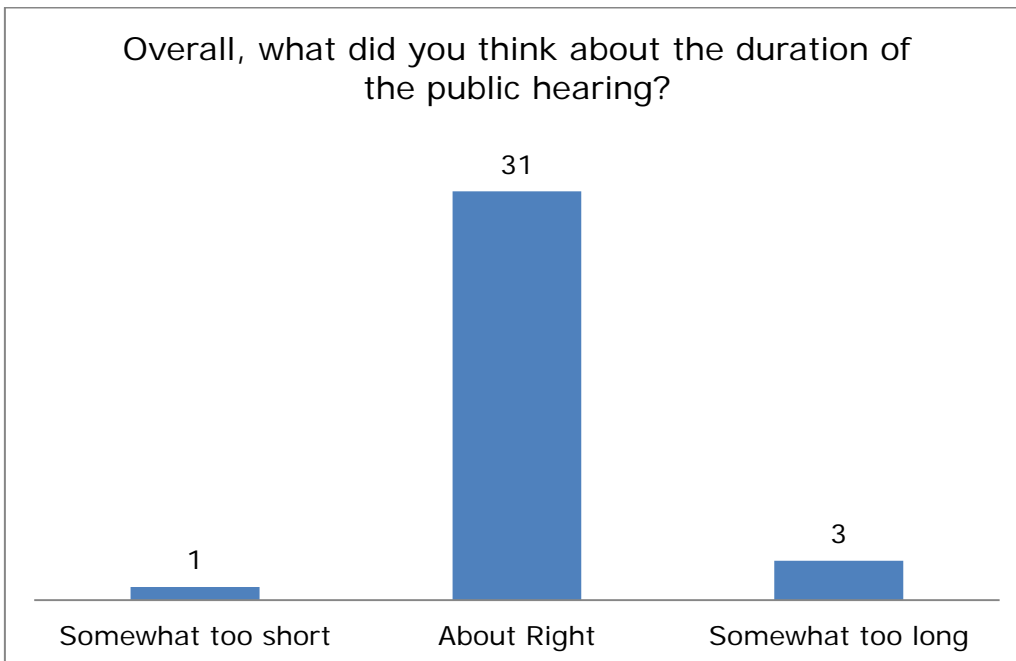
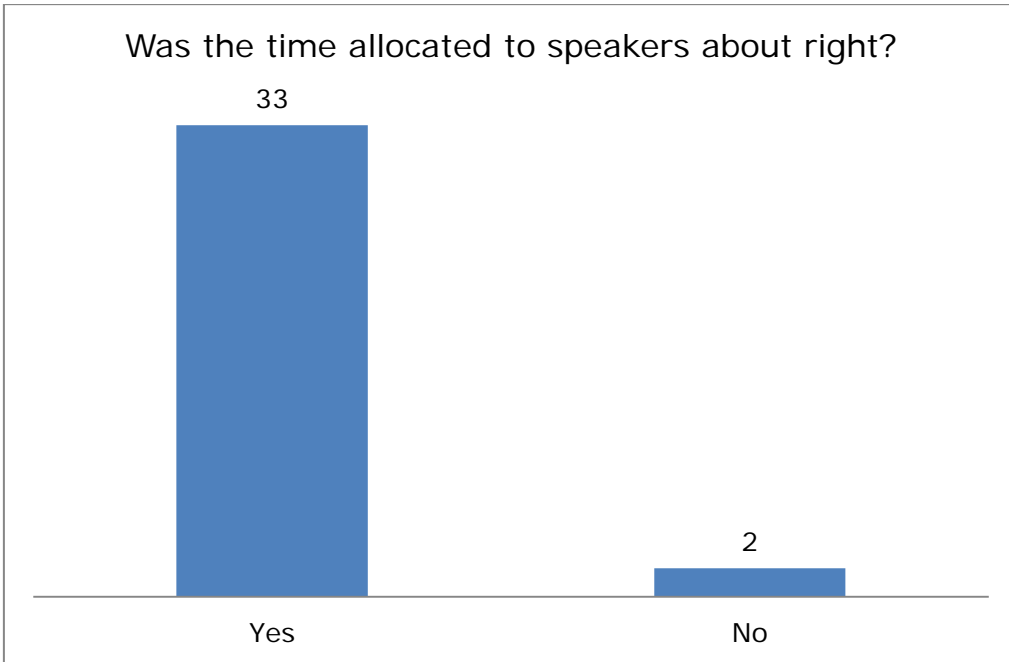


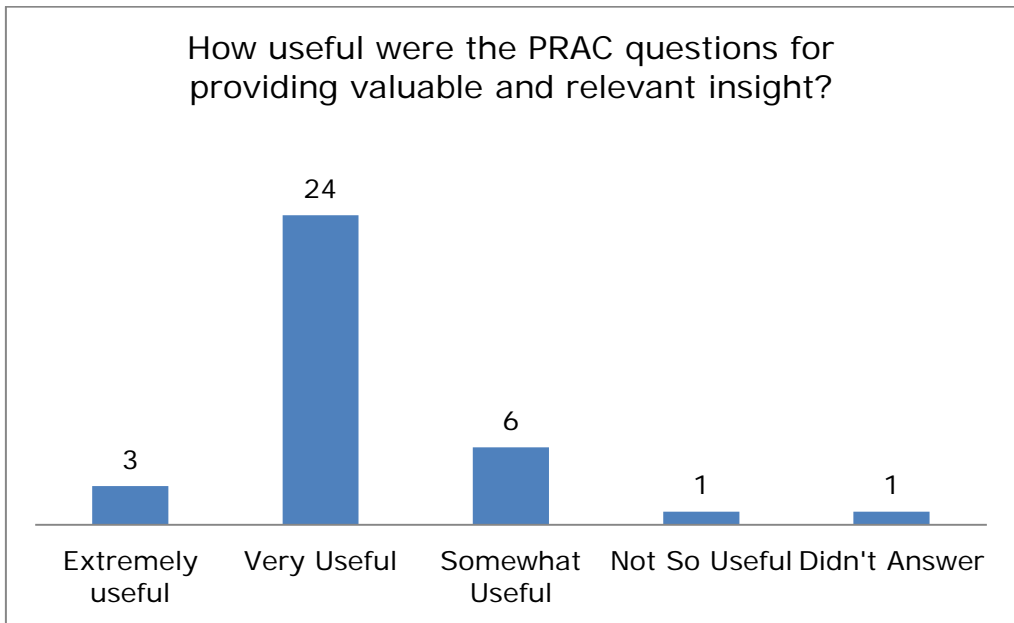
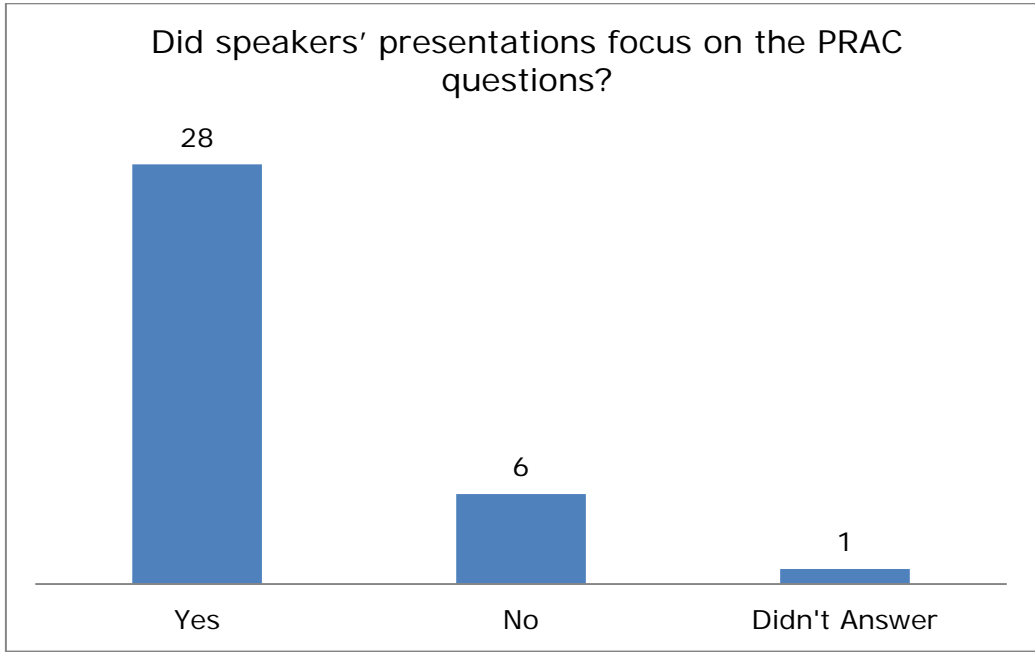


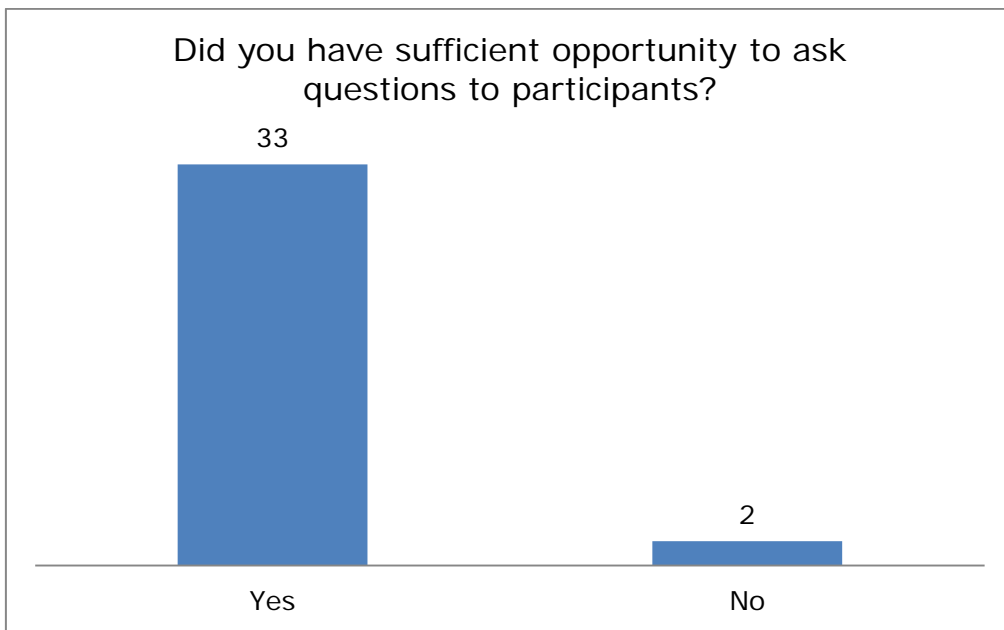
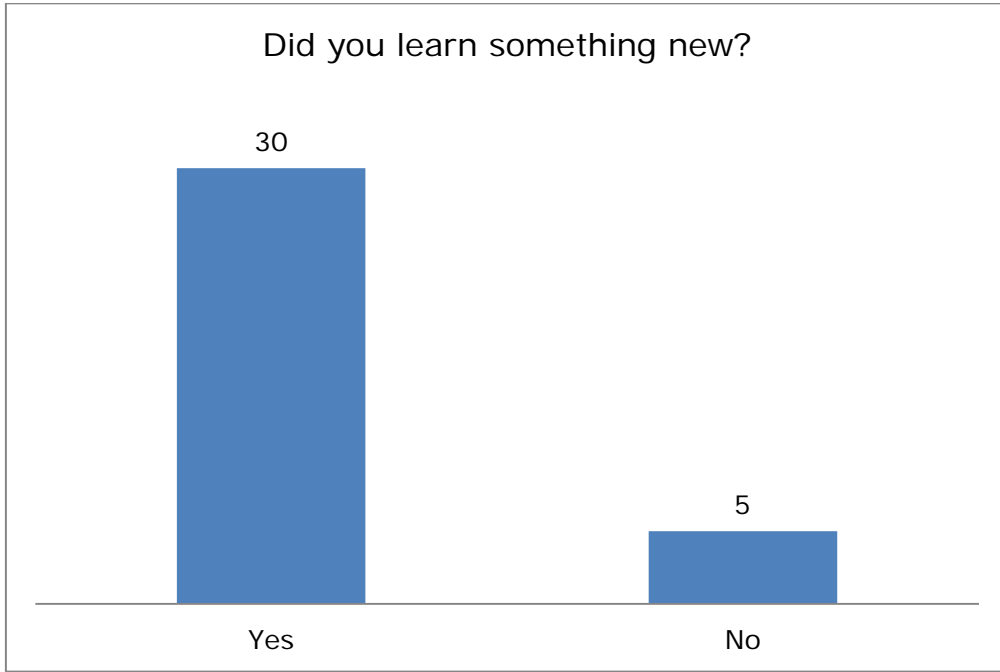
ANNEX 4

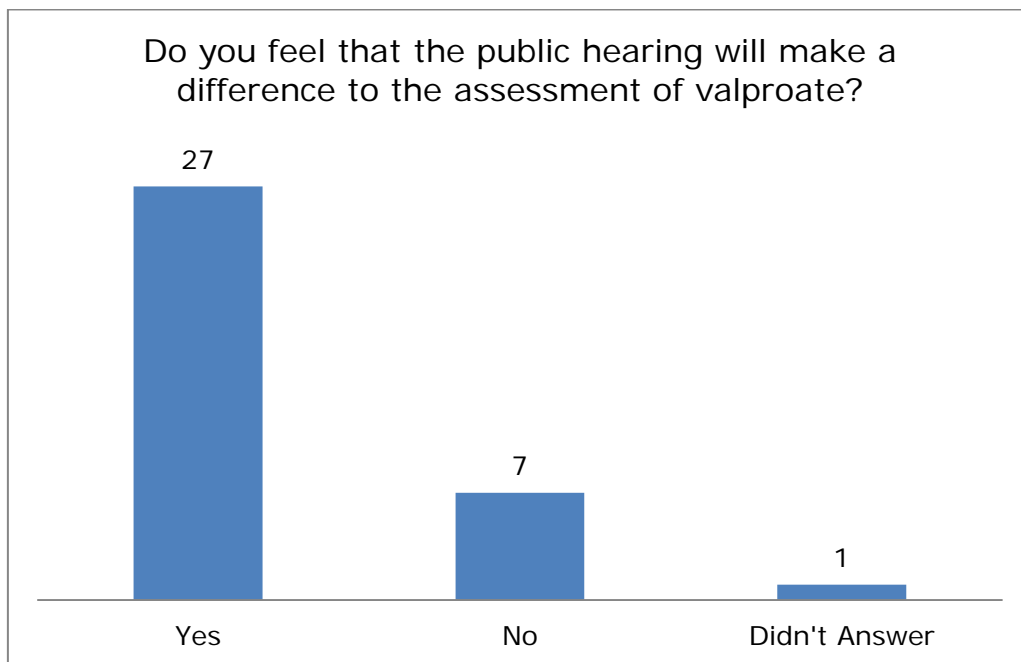
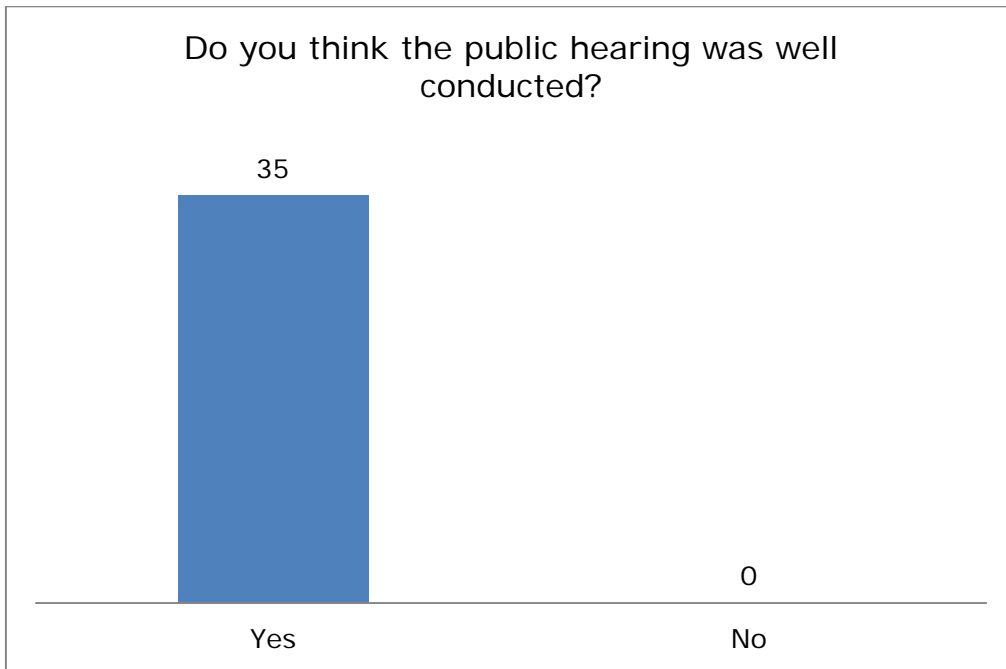
Public hearing PRAC members' survey results











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