

TESTIMONY AND SUMMARIES OF SESSIONS FROM THE PATIENT'S PERSPECTIVE

BY DIA PATIENT FELLOWS

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Patients' representatives, recipient of a DIA fellowship, have greatly valued their participation in this EuroMeeting. They have been enabled to enrich their knowledge on regulatory affairs and clinical trials as well as network with high-level healthcare representatives from pharmaceutical industry, national regulatory agencies, the European Medicines Agency and the European Commission.

Some DIA patient fellows expressed their interest in sharing their views on the EuroMeeting and summaries of sessions identified as "key" for their advocacy work. Please read their contributions below:

- Testimonies on patient representatives' involvement in DIA EuroMeeting
- "Is the patient adequately informed?"
- "Professionalization of patients and their advocates"
- "Evolutions in the EU Regulatory Landscape"
- "Can we merge two different worlds: regulatory review for marketing authorisation and HTA assessment for reimbursement decision?"
- Latin American Regulatory Session: "An update of the Pan American Network on Drug Regulatory harmonization (PANDRH) in Latin America – initiatives and current developments of regional countries (Argentina, Brazil, Peru, Mexico, others) on implementing regulatory harmonisation"

Testimony from Barbro Westerholm, AGE – Older People's Platform and Member of the Swedish Parliament.

I think it is absolutely necessary that representatives of patient organisations and organisations of older people take part in DIA meetings. The experiences and views of the "consumers" of health care has to be taken into account in the use of medicines. It became obvious during my session on rational use of medicines in the elderly but also in other sessions. Users can describe the quality of life while taking a medicine, physicians describe the effects on the disease.

It also became obvious that information about medicines on the website has to be tested among all readers, prescribers, other health care personnel as well as the users of medicines.

Testimony from Corinne Fournier, French Fragile X organisation

I am very happy to have been able to participate in this DIA EuroMeeting 2011.

For me, it was a great experience with many exchanges with all the participants: associations of patients, speakers, organizers and exhibitors.

We were well received during this meeting and I thank the organisers.

Maureen McGahan, for DIA, and Ariane Weinman, for Eurordis, were there to help us choose tutorials and sessions useful for us.

I could exchange directly with the organizers of the DIA and the various speakers, specialists in rare illness.

The tutorial was also very enriching and enabled patients to participate together with representatives from the industry and healthcare professionals, and to foster the dialogue with them.

The sessions helped better understand the role of patients in the development of a medicinal product. From the patient's perspective, it is important that investigators and patients meet and exchange their point of views. The both sides have much to learn from each other.

“Is the patient adequately informed?” – session summary by Lina Buzermaniene, European Federation of Allergy and Airways Diseases Patient Associations

The topic has been discussed from the three points of view: industry, regulators and patients.

Helen Darracott from The Proprietary Association of Great Britain gave an overview on how drug information to patient has developed over the years. She presumes that increasing load of information will be the largest factor in future health care issues.

Current challenges are: ensuring quality and usability of information; the information and promotion borderline; the trust challenge – credibility has to be earned. New formats of delivering information and interactivity raises new challenges too: the one who is providing information has responded to feedback accordingly and pharmacovigilance responsibilities appear.

The primary information about drug still is labelling and package leaflet.

Isabelle Moulon from European Medicines Agency introduced updated patient information leaflet template: more flexible, having more patient friendly elements, side effects section improved, with the new section on benefits and other sources of information. Guidance of pack design for over-the-counter (OTC) medicines is under development and will be published soon on EMA website and open for 3 months public consultation. Special attention in this guidance is paid to the use of symbols and pictograms.

Ilaria Passarini from The European Consumer's Organization (BEUC) stressed the right of patients to get information with no elements of promotional nature as defined in EU legislation and demonstrated examples of pharma companies obeying the law. BEUC was against the permission to link to product websites from package leaflets of OTC medicines, because sources of information should not be mixed and linking to product website may make patient think that website information is also validated by authorities. Ilaria also demonstrated few examples of not ethical approach trying to get to certain groups of patients via social web. There is necessary distinction of information which is intended genuinely to

inform patients and commercial communication designed to improve sales. Ilaria made an overview of opportunities and risks social technologies are bringing.

“Professionalization of patients and their advocates” – AGIHAS

This was my first meeting not devoted to a specific disease. During the presentations, I paid attention also to the question of informed patients and treatment advocates.

Still in the second half of the 20th century, patients used medicines that their parents have been using, or believed in advertisements. Only in 1990s, patient- oriented brochures started appearing. Now, in the 21st century the main source of information is internet.

It is even possible to buy medications via its shops. However, 50-60% of them are counterfeit. Besides, one can freely order around 90 different drugs there (e.g., Viagra etc.), which actually are prescription medicines. This poses great dangers.

Overall, to be able to distinct between scientifically proven and misleading information, patients and treatment activists need to be trained.

Besides, since many patients are following the medical information in mass media, journalists should get educated as well, but only in some countries there are special courses for journalists (on clinical trials, etc.).

Pharmaceutical companies have their own viewpoint on patient education. E.g., a „Hoffmann – la Roche” representative commented that it is a pity that pharma which has scientifically proven data is not allowed to inform European patients, who are often using unproven information from everywhere. Besides, treatment advocates are not allowed to have a dialogue with pharma. The only exception is AIDS activists, who have attained such a right.

Today’s patient should not only listen, but also be able to talk to the doctor as well.

So, the overall conclusion from the above is that patients and their advocates should get „professionalized” to become educated on regulatory and other affairs.

This may be achieved in many different ways, e.g., attending „Eurordis” summer schools etc. This was one of the „bring home” messages from this significant event.

Thanks to the Fellowship programme for letting treatment activists be part of it!

“Evolutions in the EU Regulatory Lanscape” – session summary by Maria Mavris, Eurordis

Session Chair: Kerstin Franzen (Pfizer, Sweden)

Speakers: Noel Wathion (EMA)

Susan Forda (Eli Lilly)

Rolf Bass (University of Berlin)

Bruno Flamion (University of Namur, Belgium) who replaced Tomas Salmonson (MPA Sweden) at the last moment

During this session several questions were raised by the panel for discussion and debate. The speakers represented three of the stakeholders involved and affected by the EU regulatory environment (regulators, industry and academia).

The issues raised and addressed included:

- i) the current model – is it appropriate (particularly timely after the Oxford debate of the opening Plenary session) and should new legislation be explored with new and emerging sciences;
- ii) antibiotics – how can academia and industry be stimulated to develop new antibiotics;
- iii) the patients' role in the EU regulatory landscape;
- iv) conflicts of interest;
- v) transparency.

One question (which was also addressed by Stephen Evans of the London School of Tropical Medicine and Hygiene) is **pragmatic clinical trials** (using larger trials with simpler design) versus **enriched design** (with staggered approval and strong surveillance post marketing authorisation) – would this speed up the regulatory process?

It was generally agreed that **new antibiotics were needed** and that incentives were also required to stimulate their development (possibly in the same way as was put in place for orphan drugs). At present, 2 large well controlled trials with at least 1500 patients each are required for antibiotics to pass the safety requirements and this can not be compromised.

With respect to the patients' role, it was generally accepted that in the **EU patients play a large role in the EU regulatory environment** with the recent addition of patients' involvement in safety announcements (2010). Patients have also been more involved in Scientific Advisory Groups of the European Medicines Agency (EMA) and patients will also be involved in benefit and risk evaluations.

When the time came to discuss **conflicts of interest and the revised policy**, we could feel a shift in the atmosphere with Noel Wathion, who is the person communicating these policy changes at the level of the EMA scientific committees taking a solid inflexible stance. The new EMA policy on conflicts of interest with no waivers aims to be a more robust system that can not be challenged.

Finally on the topic of **transparency**, most agreed that the new EMA website was more accessible and easy to use. However is there a gold standard for transparency on the industry side of things?

Final conclusions: For highest impact on the EU regulatory process, it is best to go via the informed professional, the informed patient, to exchange information and for best practices in work behaviour, usefulness and use of medicinal products. The EMA and the Heads of Medicines Agencies will meet at the end of April in Budapest to discuss access on company data. Lise Murphy, patients' representative and co-chair of the EMA Patients and Consumers Working Party, will attend and present at this meeting.

“Can we merge two different worlds: regulatory review for marketing authorisation and HTA assessment for reimbursement decision?” – session summary by Maria Mavris, Eurordis

Session chair: Wills Hughes-Wilson (Genzyme, Belgium)

Speakers: Andras Fehervary (Novartis Oncology, Italy)
Jiri Deml (Czech Republic)
Hans-Georg Eichler (EMA)

In this interesting session, the viewpoints, of Yes, Not Really and Maybe were expressed by the various speakers.

Not surprisingly Hans-Georg Eichler, Senior Medical Officer of the EMA, took the **‘yes’ position** – He developed the areas of:

- mutual interest, which include exchange of information (in particular the EPAR ‘usability’ project and confidentiality),
- parallel scientific advice (three pilots have been completed and two more coming up),
- debate of evidence requirements (particularly relating to endpoints although mutual input to guideline development possible too),
- relative efficacy assessments (this is an area of genuine difference as it is not an area for licensing although improvements in the presentation of data from regulatory assessments and the further development of standards and methodologies for indirect assessment of relative efficacy could be envisaged)
- post-marketing research activities(integration of benefit-risk and post-authorisation effectiveness studies. He expressed a need for harmonisation to enable a single post-marketing research plan)
- parallel review (as in the US and Australia – no EU experience at the moment) and
- managed market entry.

The ‘maybe’ viewpoint presented by Andras Fehervary was based on a perceived abandonment of Member States’ individual criteria and approaches to HTA and the understanding that they would accept, without question, results on clinical efficacy. He emphasised that currently the cost to bring a drug to market is between \$800 million and \$1.7 billion. He described a test model performed by himself and his colleagues of a mock drug and demonstrated the negative impact of international reference pricing and cost containment measures on potential revenues raised for that product.

The final presentation of **‘not really’** was presented by Jiri Deml of the Czech Republic, representing the national competent authority viewpoint. His talk focused on what we understand of the terms, regulatory, HTA and reimbursement, the objectives of these processes, the impact of possible synergies and views from the daily life of a national authority. His main points were that the HTA and Regulatory worlds were still different worlds without compatible legislation. His concern was that there was a potential risk for increasing the costs of development and delaying the process. He concluded by saying that the important thing in this debate was to increase the quality of life for patients.

At the end of this session, we were informed that changes will be introduced to the European Public Assessment Reports (EPAR) to include tabled information on every major clinical trial conducted. These will be introduced by the CHMP assessors. The benefit/risk ratio template

has been changed and further suggestions might be made based on EUnetHTA and EMA collaborations.

Latin American Regulatory Session: An update of the Pan American Network on Drug Regulatory harmonization (PANDRH) in Latin America – initiatives and current developments of regional countries (Argentina, Brazil, Peru, Mexico, others) on implementing regulatory harmonisation – session summary by Maria Mavris, Eurordis

Session Chair: Sergio Guerrero (Monterrey Intl Research Centre, Mexico)

Speakers: Martha Parra (Committee of New Molecules and Research, Mexico)
Agustina Bisio (Argentina)
Eduardo Johnson (Office of Clinical Trials and Bioethics, Chile)

This session was one of the regional perspectives sessions with a focus on Latin America. **My interest was to hear what if any comments were made on patients' involvement in regulatory processes, their attitude towards the Reflection paper on clinical trials in third countries, whether patients had access to drugs after clinical trials ended and what type of collaborations they had with Europe (EMA) and the US (FDA).**

Some interesting information was conveyed but not all my questions were answered.

The first speaker, **Martha Parra's organisation COFEPRIS is responsible for evaluating and authorising clinical trial protocols in Mexico.** Last year alone there were 5480 protocol submissions with the major pharmaceutical companies involved being Bristol Myers Squibb, Birmingham, Sanofi-Aventis and Glaxo Smith Kline and the primary areas of investigation being not surprisingly oncology, endocrinology, rheumatology and cardiology.

New guidelines have been developed for authorisation of ethics committees as third party reviewers and quality systems are under development with the PAHO (Pan American Health Organization) and WHO (World Health Organization). The Agency is currently developing a database and future challenges exist to authorise ethics committees in each state in Mexico and main referral centres. Inspection programmes for research sites and ethics committees need to be developed and new research sites still need to be included into the social security system.

Her conclusion was that Mexico with its large population was attractive for recruitment of patients for clinical trials.

The next speaker Agustina Bisio from Argentina detailed the process of authorisation in this country and explained in detail some of the directives and provisions involved in conducting clinical trials. She described the steps of the regulatory processes at 4 stages of clinical trials namely i) before submission – pre-presentation of protocol with pre-technical report, ii) prior to clinical trial commencement, iii) during the clinical trial and finally iv) at the end of the trial. These aspects were very regulatory and emphasised the increasing numbers of clinical trials since the collection of data by this department with approved clinical trials increasing from 80 in 1994 to 300 in 2010 and inspections of clinical trial sites from 10 in 1997 to 84 in 2010.

Importantly she mentioned that providing the medication post-trial was a challenge and that compassionate use programmes and extension studies were often used.

Inspections of sites are conducted in harmonisation with procedures used by the EMA and FDA and a database of clinical trial sites and Primary Investigators exist and that provisions were available for public consultation.

The final speaker Eduardo Johnson presented the Chilean perspective with an interesting introduction regarding his country. Apart from the interesting geography and demography, poverty that was at 40% in the 1990's has decreased to its current level of <10%. Similarly childhood mortality has decreased to its current rate of 8%. The population is 16 million.

As with Argentina and Mexico the number of applications for clinical trials has increased from 43 in 2002 to 100 in 2010 and once again the main areas of investigation were endocrinology, oncology, pulmonology, cardiology and rheumatology with > 70% of trials conducted being Phase III, approximately 25% being Phase II and 5010% being Phase IV. He stated that Phase I trials were not allowed in Chile but bioequivalence studies were performed.

The Chilean Institute of Public Health participates in the international conference entitled ICDRA – international conference on drug regulatory affairs organized by WHO. They are also involved in pre-qualification programmes for vaccines.

In addition they have elaborated a guide for the paediatric population on questions such as i) when to start a trial in children, ii) formulations to use, iii) timing of the trial and iv) exclusivity in the paediatric population.

Finally, he described the EAMI –Encuentro de Autoridades Competentes en Medicamentos de Ibero América consisting of 21 countries, 19 of which are Latin American in addition to Spain and Portugal, which meets 7 times every 2 years.

Conclusion: it was very interesting to hear from the medicines agencies and regulators from these Latin American countries. What was clear was that there were no working groups in any of their organisations for orphan drugs or advanced therapies and that collaboration with EMA and FDA is essential for guidance documents. The reflection paper in particular with respect to protection of patients and provision of medicinal products post-trial is also of utmost importance.