ISOP TRAINING COURSE IN BARCELONA

New Challenges in Clinical Safety, Pharmacovigilance and Vaccine Vigilance

On February 10-11 ISoP organised a challenging course about the new roles and responsibilities of Safety Staff in this new millennium. The course was structured to provide the attendees the opportunity to network with several and different parties, which showed their different point of view about several topics.

The first topic was WHO's 'policy on patients' safety. **Prof. Vladimir Lepakhin** gave a broad overview of the role of WHO looking after the safety of patients and how the international alliances could benefit the public health. He gave a very interesting overview of the global structure, role and activities of the World Health Organization (WHO); and described a detailed information about WHO's policy on patient safety; describing in depth the WHO's work on drug safety, including the WHO Programme for International Drug Monitoring.

The audience was then surprised with a very interesting topic: the new roles of a Drug Safety Officer in a HQ of a pharmaceutical company and in an affiliate.

Dr Irène Rebollo from Alcon Laboratories gave a comprehensive lecture on the state-of-the-art for a drug safety officer working in the European headquarters: how to interact with the whole organisation and at the same time satisfy the strict European and worldwide requirements within legislative pharmacovigilance framework, including the new responsibilities emerging from the new pharma review initiatives. She concluded that "the time of paperwork and useless bureaucracy are giving way to a much better understanding of the role of pharmacovigilance in public health protection".

Dr Maria A. Astorga from Sanofi-Aventis emphasized the critical role a subsidiary needs to play to look after the quality of the data to be included in databases: this is key to retrieve important and relevant information. She pointed out the difficult balance between the quality and the speed for reporting, and "how the pharmaceutical industry has become more responsible and more trained in pharmacovigilance… although PV Departments are always under budgetary constraints. The good function means no noise: to protect the patient and to protect the company".

The next topic related to the optimal pre and post authorisation conditions for a drug to be a successful candidate, related to the ICH E2E guidelines to be implemented in June 2005, was developed and discussed by 3 speakers: **Dr Ana Corrêa-Nunes** from INFARMED, **Dr Conxita Barajas** from Bayer Spain, and **Dr Peter Schulz** from Amgen HQ.

Dr Barajas gave an introduction to the topic remarking on the new responsibilities of drug developers to prepare a good pharmacovigilance plan and a meaningful risk management plan to introduce a drug in the market.

Dr Corrêa-Nunes showed the Regulatory Authority's point of view on this topic, remarking the importance of a new framework for the investigation, collection, presentation and discussion of safety data: "a new philosophy on planning pharmacovigilance activities to minimise risks for patients".

Dr Schulz reviewed the topics included in ICH E2E from a pharmaceutical company point of view. He said there are several methods to generate signals and to manage safety issues. There is a big trend in society to place more emphasis on pharmacovigilance, due to recent events. There is also a risk-conscious environment, and ICH has given us a legacy to establish several risk categories: concrete risk, contributory risk, hypothetical risk, unknown risk – but in any of these instances, the "Risk perception is driven by numerous emotional and cultural factors". In this sense E2E serves as a medium to formalise an approach to safety issues by use of different tools". Finally he opened a discussion with the audience where the importance to bring the risk profile to the prescriber, emphasising also that "Drugs can safely stay in the market by targeting the right patient groups through a coordinated safety and marketing strategy where revenue expectations that are consistent with what the safety profile supports".

During the lunch break there were several opportunities for networking and sharing best practices among the speakers and participants, with some room also for enjoyment and good mood.

The meeting was re-started punctually and the first topic was dedicated to Education & Training in pharmacovigilance. **Dr Jürgen Beckmann** (ex-BfArM Director of Pharmacovigilance, and currently Professor at Rostock University), explained that the 3 main goals of training of pharmacovigilance are to identify drug-related risks, to reduce them and mainly to enhance understanding of them. There are several training activities worldwide to be taken in consideration. At the same time ISoP is preparing an ambitious but achievable programme: ETP, taking advantage of the enhanced opportunities of bigger databases and modern technology, but also respecting the biodiversity of the worldwide 'pharmacovigilantes'.

Dr Beckmann explained that for organisational reasons it is convenient to divide the training material into eight chapters and the degree of intensity for this training will depend on the level of pre-existing knowledge and the work position. "Currently PV offers courses like the one run by the WHO Uppsala Monitoring Centre and others, covering large parts of this 8-chapters ISoP model. Considering this, the envisaged cooperation between WHO and ISOP and the public education in terms of avoidable and unavoidable drug-risks" may become fruitful and very worthy for public health.

Dr Tomás Moraleda (Medical Officer MSSO) transported the audience to the world of data-mining and coding in MedDRA Universe. He pointed out the importance of the clinical meaning of the adverse events: "Classification of data is only one part of the data management process, but the most important one is once the data has been codified, retrieve, sort and present it in the most understandable and reproducible way that makes sense for prescribers and patients: this is the spirit of pharmacovigilance: not just captured data, but produce useful information for the safest use of drugs".

The first day finished with a very relevant presentation on the Pharmacovigilance of Orphan Medicine Products (OMP). **Prof. Josep Torrent**, current Chairman of COMP prepared a very challenging presentation, where the terms 'big denominator' and signal detection based in big numbers lost their meaning.

He explained to the audience the current understanding of rare diseases and OMP as a EU Health Public priority and how the clinical evidence in these conditions follow a different clinical development plan, including the PV approach.

There are more than 6,000 identified Rare Diseases most of them affecting paediatric population. "They are life-threatening, serious and/or chronically debilitating, impairing QoL and causing long-lasting disabilities and dependences; the specific OMP regulation is needed because: Some conditions occur so infrequently that the cost of developing a medicinal product would not be recovered by the expected revenues. Therefore the pharmaceutical industry is unwilling to develop these medicines under normal market conditions. Finally he reviewed the special role patients and patients' associations play in this UNMET patient medical needs, where the Partnering with all stakeholders is very much needed, where the Biomedical research accounts for more coordinated public funds and incentives, where new methodologies and statistical approaches required to optimize clinical research in RD, and where long-term post authorization clinical investigations and patients views (risk perception) becomes crucial". He finished his speech remarking that "when providing information about this drugs, the transparency, objective, managing hopes and expectations should be done on scientific and ethical grounds".

Day 2 of ISoP training course started with a very provocative title: 'The Marketing of Pharmacovigilance', developed by **Dr Paula Marquez** (representing pharmaceutical companies), **Prof Giampaolo Velo** (representing academia) and **Prof. Vladimir Lepakhin** (representing WHO point of view and regulatory bodies).

Dr Marquez introduced the topic with a relevant introduction related to the 'negative' image that pharmacovigilance has had in the last decades, from the disaster of thalidomide following with the withdrawal of big blockbuster, "pharmacovigilance has been considered a difficult bureaucratic task that steals time and does not provide immediate reward. It has not been attractive for interested parties, with very scarce budget and very limited resources for the important mission to look after the safety of the patients taking drugs. However, this poor Cinderella has become a princess in the 21st century: in the communication era it is very important to involve and make partnerships with every stakeholder including patients and public media.

Two important meetings held in 1997 & 2004 about the effectiveness of Safety Communication: The Erice Declaration and the ISDB-Berlin Declaration showed the importance of renovating the way pharmacovigilance information is collected, analysed and communicated. More than ever pharmacovigilance is a shared responsibility, and ISoP has an enormous responsibility to help all stakeholders to work together with the common objective of the establishment of the safest use of drugs.

Afterwards Prof. Velo (Universita de Verona) gave the academic point of view of the marketing of pharmacovigilance. He said it is difficult for health care professionals to fill in a report and to send to any place: it's time consuming and there is no evident benefit. We should be able to explain to them this is the only way to obtain a better prescription. We should implement strategies to improve the drug use.

In this sense the media play an important role. In Verona 2003 there was a seminar on Drugs on the newspaper 'read all about it' where the main medical practice, drugs are an important part of modern therapeutic strategies. Since they are a component, within a broader treatment framework, communications concerning drugs should avoid terms such as 'miracle cure' or make claims for exclusivity. "Drug information (indications, counter-indications and adverse effects) about the molecule or class of molecules should be provided. Specifically, it should be remembered that if a drug has benefits, it also involves risks". Given the importance of the subject, the document may be signed by anyone who agrees with its contents.

The next topic was dedicated to Vaccinevigilance, an interesting matter with some similarities to drug vigilance, **Mrs Elisabeth Loupi** (sanofi pasteur) remarked vaccines are drugs presenting some particularities very important to consider their safety profile. Given its importance in the protection against infections and in the immunization programmes, the safety of" immunized people is mandatory.The various aspects of vaccinovigilance, from vaccine composition to risk

assessment including a review of the definitions and classification of the Adverse Events Following Immunization (AEFI) were addressed in the course with some special attention to the difficulties raised in doing case-by-case assessment.
Mrs Loupi further reviewed the different scenarios for reporting (VAERS system in the USA, Canada PPHB and other forms), the help brought by the Brighton Collaboration definitions, and explained the importance of Farrington studies in this discipline

Afterwards **Prof. Chalbi Belkahia** from the University of Tunisia showed the example of his national centre: the vaccines vigilance committee has a key role managing all the alerts emerging form the drug, the National Centre of Pharmacovigilance, the Health Primary Care (including paediatricians) and the Pasteur Institute: all of them interact and work together to prevent and counteract any risk from the vaccine therapy.

Also, **Dr Alejandro Roque** from the Finlay Institute in Cuba was invited to speak about vaccines, but unfortunately, after discussions with the Spanish Consulate, he was finally not able to attend our meeting due to severe visas restrictions.

The last topic of the course was dedicated to the pharmacovigilance of oncolytic drugs; **Dr Ron Meyboom** (from WHO) started the presentation remarking some differences of the pharmacovigilance of this class of drugs; the severity of the disease, the risk afforded for them, the speed to approve these drugs when there is no other alternative. However it will be important to work for a thorough knowledge of the delayed adverse effects of such a therapy, used chronically, in cycles, in combinations, with novel mechanism of actions, that may possibly have unidentified consequences.

The experience has shown that this type of class suffer a serious underreporting situation; new strategies, regulatory, scientific and financial, may be required in order to ensure rational and beneficial cancer chemotherapy.

The Friday afternoon was completely dedicated to practical exercises: data-mining with MedDRA and examples of good communications utilising Erice Declaration as a model to establish new strategies to improve communication skills in pharmacovigilance.
The attendees and speakers were divided into four groups and their conclusions are collected below; they constitute a starting point to develop future working groups within ISoP.

- It would be difficult to approach the patient by the pharmaceutical industry. They have websites, internet, toll free numbers and sometimes surveys with additional information but considered this communication tools insufficient to provide the patient with good information.
- Information coming from the pharmaceutical industry could be seen as a 'new' marketing tool.
- There is a new class of patients: those very well-informed by the internet sometimes knowing more than the physician or those in developing countries who could be helped with very simple leaflets in simple English about their diseases or drugs.
- Cultural differences should be considered for a worldwide approach. Maybe there is not one single standard approach. Besides that some patient are very interested in all risks (adverse events) and those who don't care.

The perception of risk is very different. Therefore the patient should be told by someone with knowledge: the physician/the health care professional: They should be very well informed about adverse event/risk information but also of their role as communicator to the patients thereof. We should include the nurses, pharmacists as information providers as well.

Anything that is used to inform should contain 'all' the information so that the physician can explain the risk properly.

Assessment Reports:

The audience was given a questionnaire to evaluate the course: 95% of them were very positive analysing the content of the presentations, the preparation of the speakers, the venue and facilities and the quality of lunch and coffee-break. This was a very international audience from pharmaceutical companies, regulatory bodies, and other (hospitals, etc).

Barcelona, Gaudi's dreamed city was the framework of a very interesting and successful course where all ISoP members crossed-up their minds to establish a very stimulating and inspiring framework where new and very relevant topics emerged from the Mediterranean to push and pull ISoP for the safest use of drugs worldwide in conjunction with WHO.