

A Pocket Guide to Clinical Research in Poland & Romania

Grzegorz Litynski & Dr Ramona Nicolescu

Reporter: Joanne Towing

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Grzegorz Litynski and Dr Ramona Nicolescu provided two very informative and entertaining presentations on clinical research in Poland and Romania, respectively. Poland is becoming an increasingly popular destination for clinical trials and Grzegorz provided an overview of the clinical trial environment in Poland, highlighting some recent changes and current trends in Polish clinical trials. Ramona then provided an understanding of the clinical research process in Romania, including the regulatory and ethics committee requirements and the Romanian legislation on clinical trials.

Clinical research in Poland

Grzegorz began by highlighting that Poland is actually in Central Europe, rather than in Eastern Europe as is commonly believed. With a total area of 312,680km², it is the 69th largest country in the world. Poland has a population of 38.6 million (figures from 2004) with 66% concentrated in urban areas. It's easy to see why Poland is chosen to conduct clinical trials: with one language, a centralized health system and a high prevalence of particular disorders, it's an attractive option. Access to the national health system is limited and medication is expensive, so with the offer of better medical care, free drugs and diagnostic procedures, patient recruitment is very high in Poland. In fact, when comparing various trials running simultaneously in Western and Central Europe, Poland regularly came at the top of recruitment scales. Increased benefits for patients participating in clinical trials leads in turn to highly motivated investigators, as they can see the benefits in the work they do more than their colleagues in Western countries. Poland can also offer good quality data and highly educated clinical research staff.

Grzegorz then went on to explain the approval process in Poland. Poland became

a member of the EU on 1st May 2004; the country started implementing the EU Clinical Trials Directive in April 2004 and has now completed the process. Ethics committees are set up in the same way as they are in Germany, with the medical universities and medical chambers each having their own ethics committee. The approval process is similar to most countries in that approval is required from the competent authority (CA). This is authorised in Warsaw, and takes approximately 60 days. However, in Poland a test article import license is also required, which can take an additional 10 working days after receiving CA approval. The import license can be applied

for at the same time as the CA approval, but will be received outside the 60-day period, once the Ministry of Health is satisfied with the documentation. Trials that have received CA approval cannot begin until they have received the import license and Poland has very strict regulations preventing companies from shipping

drugs into the country, even from within the EU. Despite these constraints, the approval process in Poland has been improved, with the Minister of Health issuing an ordinance on 3rd January 2007, which introduced the unification of submission forms for ethics committee approval.

Setting up clinical trials in Poland does come with challenges. The extensive set-up period is much longer than in other countries and if it is essential to run a trial at a medical university then it can take months to receive approval. The length of time required to sign the contracts is a limiting factor, as they need to be received from all sites before submitting them to the CA. There are other challenges beyond the administrative constraints. There is difficulty in identifying experienced CRAs and other clinical research staff. There are also serious logistical considerations, with the



Grzegorz Litynski

poor condition of the roads and only a single motorway running through Poland. It is for these reasons that Grzegorz believes local expertise is crucial in the successful conduct of clinical trials in Poland.

Clinical research in Romania

We then moved on to hear about clinical research in Romania. Many of us are familiar with some images of Romania: the gymnast Nadia Comaneci and of course Count Dracula; however, Dr Nicolescu also showed us some lesser-known figures in Romanian history. Romania is located in South East Europe and has a population of 22 million. Ten percent of the inhabitants are located in Bucharest, which is the sixth largest city in the EU. Romania is certainly a thriving location, and figures taken from 'World Bank: Doing business in 2006 report', which compared 155 countries in Europe and Central Asia, showing that Romania is the 3rd quickest place to start a business (11 days) and requires one of the lowest number of procedures to start a business (five). Furthermore it is one of the cheapest places to start a business, taking only 5.3% of Gross Domestic Product (GDP) per capita. According to the European Investment Monitor (2001-2005), Romania accounts for 40% of regional FDI (foreign direct investment), with 285 projects directed there. It's a promising destination, according to the South East Europe Attractiveness Survey, with Romania being perceived as the most attractive country for potential productivity increase and site availability.

Romania signed the Accession Treaty to the EU on 25th April 2005 and became an EU member in January 2007. The legislation on clinical trials is harmonised with the EU and the EU Clinical Trials Directive was transposed into national legislation in July 2004. This was followed by the implementation of the guidelines on many aspects of setting up and conducting clinical trials, including:

- The request for authorisation of a clinical trial to the competent authorities
- The application format and documentation to be submitted in an application to an ethics committee
- GCP inspections and the archiving of clinical trial documents
- The import, export and manufacturing of products



Ramona Nicolescu

With regards to the regulatory environment, clinical trials in Romania are under the supervision of the National Medicines Agency (the CA) and the National Ethics Commission (for multi-centre trials). Clinical trial documents can be submitted simultaneously to both authorities and the review of these documents is done in parallel, making the system transparent and relatively fast. The examination of an application submitted

in the correct format should take no longer than 60 days. This has clear

advantages for Romania, and this is shown in the increase in the number of clinical trials conducted there. Figures taken from the regulatory authority show that in 2001, 78 trials were submitted for approval, while in 2005 they received 180 applications. There have been a limited number of inspections on Central and South-Eastern European sites,

but an FDA inspection conducted in 1998 in Romania concluded that no action was needed, which gives a good indication of the quality of data. So, with big, centralised hospitals, a large and compliant patient population and a number of GCP-trained investigators and medically qualified monitors, it is clear to see why there has been an upsurge in interest in this country. Dr Nicolescu concluded by suggesting that with the enlargement of the EU membership, the traditional research boundaries will have to extend eastwards.

Discussion

Questions focussed on the time it takes to approve clinical trials in Poland and it was understandable that the audience were keen to find out the implications of this process taking longer than 60 days. One audience member asked that with the contract negotiation delaying the overall start of the trials, whether there was any evidence of clinical trials moving out of Poland. Grzegorz presented some figures which clearly showed that clinical trials were not moving out of Poland. In 1995 the competent authority received 50 applications for trials, but at present this is now up to 500 applications a year. For trials that have a very aggressive and short recruitment period he would not recommend Poland, but if the trial has a long and steady recruitment period then Poland would be an excellent choice. Another question followed on from this and asked that

if the CA was inundated with applications, were they still meeting their 60-day deadline? Grzegorz said that deadlines were being met by the competent authority, but with the validation process and import license it is advised for the sponsor to allow 90 days. Yet he was keen to point out that although the clinical trials approval process takes on average an extra 25-30 days in Poland, the recruitment for trials is four times higher than in Western countries.

It was interesting to compare clinical research in these two countries, which have both become members of the EU in the last few years. Both are thriving places to conduct clinical trials and although several members of the audience were concerned at the length of the approval process in Poland, figures show this is not deterring sponsors. Interest in Romania is steadily growing and the provisions they have in place means it won't be long before they too become inundated with applications for clinical trials.

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Risk Management in Clinical Trials

Rebecca Hastings

Reporter: Jon Milton MICR

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Cast your mind back to 1995 and the fall of Barings Bank. Could the demise of one of the oldest and most reputable banks in the UK have been avoided? Thankfully, and owing principally to the fact that I am largely unqualified in the realms of finance, my remit does not stretch to answering this question in significant detail. I can, however, plant the seed and offer an opinion. Personally, I would go with a resounding yes. In fact, based on Rebecca's excellent and interactive presentation, it is clear that risk management could almost certainly have helped circumvent the downfall. So, risk management is important, that much is clear. Moreover, and despite not having a prescriptive standard, it is a universal concept. It effortlessly transcends the world of finance to simple everyday tasks (should I cross the road as this bus hurtles towards me?) and, inevitably, into the pharmaceutical arena. Indeed, it was one of the five initiatives in the US Food and Drug Administration's five-part strategic action plan

of 2003. Therefore, please take a few moments to discover how risk management can improve the conduct of clinical trials. By doing so, you will also learn how you can adopt a few simple steps in your everyday work, in order to help embed this culture firmly within your company and the industry as a whole.

Definitions

Risk can be succinctly defined as the product of the probability of an event and its consequences. Risk management encompasses the identification of a risk and its subsequent handling. Often overlooked is the fact that risks can be positive (advantageous opportunities for a company) as well as negative (potential threats to triumph). The overarching objective of risk management, therefore, must include both the good and the bad, ie, a strategic measure to ensure maximum benefit is derived from each undertaking.