Zsuzsanna Fürst – President, Ethics Committee for Clinical Pharmacology, Hungary

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Dr. Zsuzsanna Fürst, President of the Ethics Committee for Clinical Pharmacology, elaborates on the role and activities of the ethics committee, shares her insights on structural framework of the application process for clinical trials, and the future outlook of clinical research in Hungary.

Can you give insights on the structure of the Ethics Committee for Clinical Pharmacology and how it fits in the bigger framework of the country?

The Ministry of Human Capacity (EMMI) is the overarching governmental body that oversees the activities of the Medical Research Council (ETT). Within the ETT there are four ethical committees for clinical research; the Scientific and Research Ethics (TUKEB), the Ethics Committee for Clinical Pharmacology (KFEB), the Regional Research Ethics Committees (RKEB), and the Human Reproduction Commission (HRB). Furthermore, there are three theoretical committees for basic research; the Committee on Research and Development (KFB), the Clinical Research Committee (FDI), the Board of Forensics Experts in the Field of Health (ISZT). All these bodies operate as advisors to the EMMI which report to the State Secretary of Health – unlike most countries, there is no stand-alone Minster of Health in Hungary.

The Ethics Committee for Clinical Pharmacology (KFEB) is an independent body that has 30 members which are appointed by the Minister of Human Capacity (EMMI) by the recommendation of Semmelweis University, and the Academy of Science. Our members cover 24 different medical professions and include six laypersons: two theologists, lawyers, and nurses. Their expertise is welcomed when dealing with subjects such as General Data Protection Regulation, or when assessing the ethical and practical implications of clinical trials. Within the committee, quorum meetings are organized regularly involving a minimum of five members, among them two laypersons at least, who have the power to assess and pass decisions on bioequivalence, phase IV studies, substantial amendments, and other urgent matters related to the National Competent Authority (NCA). Each and every application, both initial applications and protocol amendments, are assessed by KFEB from professional and ethical points of view – our focus is the benefit of the patients.

How is the clinical trial regulation structured in Hungary?

The trial applications pass through the NCA and then are forwarded to the KFEB. Once the assessment is completed by the ethics committee, our decision is returned to the NCA. The NCA and KFEB both must accept the whole of the application documentation in order for the trial to get authorized.

The Ethics Committee for Clinical Pharmacology has tri-weekly meetings which are determined in January for the rest of the year. The quorum meets on a weekly basis to evaluate and amend clinical trials that have been submitted. There is a 60-day deadline for the evaluation process to take place – 30 days for initial applications and another 30 days for amendments. This timeframe also includes the time the sponsor needs to answer the deficiencies. However, the NCA has 15 more days for their decision to be taken.

This lengthy process has been a sore point for companies. However, this process is being reviewed and changed in preparation for the upcoming EU Clinical Trial Regulation No 536/2014 which is anticipated to go into effect in the upcoming year. Under the recommendations of the Clinical Trial Facilitation Group (CTFG) and the Voluntary Harmonization Procedure (VHP), the regulation is being implemented in parallel to the existing application process to streamline the assessment of multinational clinical trial applications.

The VHP procedure is a potential model for the clinical trial authorization procedure before the implementation of the EU Clinical Trial Regulation No 536/2014. In most countries, this procedure

reduces the time period required for the authorization of multinational studies. Nevertheless, according to the Hungarian regulation, the authorization period for Hungary is 75 days for the national phase compared to the 10 days given in the VHP Guidance document. The reason for this is that the national phase authorization procedure in Hungary includes the ETT and KFEB evaluation as well. In order to decrease this long authorization period and to prepare for the new Clinical Trial Regulation, Hungary offers the possibility for applicants to submit national documentation (patient and site documentation) in parallel to the VHP Plus (VHP+) procedure. This means that Part I and Part II of the evaluation can be done in parallel, reducing the time required for the assessment to 10-15 days.

What are the trends associated with clinical trials?

Over the past decade, clinical trials in Hungary have been relatively stable, ranging between 320 and 390 new trials evaluated every year. However, the number of amendments made have been increasing yearly, which is related to the growing complexity of the active components that are being assessed. In Europe, the number of clinical trials has been decreasing, whereas in the United States, it has been increasing. Hungary on other hand, has remained unaffected by these changes.

Nevertheless, we have noticed an increase in the number of clinical trials in the field of oncology and hematology. This reflects a global trend, where cancer rates are increasing, and it is an area with still substantial groundwork to cover. In our committee, we have three hemato-oncologists which allows us to evaluate these specific trials in depth. Interestingly, cardiovascular is an area that has been decreasing, despite there still being a need in Hungary. On the other hand, we see interesting fields of study like analgesia, inflammatory diseases, autoimmune disease indications, and application of biologicals as drug candidates in any of those fields. However, biological compounds are expensive to produce, and once a trial is completed, treatments may not continue for patients who benefit from the therapy applied; lack of funding enhances this problem.

What are the strengths and weaknesses of the clinical pharma landscape in Hungary?

The strengths of Hungary’s educational and medical institutional network, alongside the practitioners’ competency, make the clinical pharma landscape in the country attractive for pharmaceutical companies. Medical universities like Semmelweis, or organizations like the Institution of Experimental Medicine, are just two examples amongst many that have a historical

leadership and strong international ties. The collaboration with international entities permits an exchange of best practices, both in theory and in practice. Hence, the doctors that we have are very knowledgeable and competent, which makes them sought after. Unlike most countries, Hungary has an occupation called clinical pharmacologist who are specialists in the clinical field. They have to be the head of the institution and/or principle investigator (PI) where the trials are conducted. This is very attractive for international clients. Consequently, personnel are sought after from this environment and we are all exasperated by the fact that Hungary suffers from a brain drain.

Although Hungary has such strengths, competition to attract trials remains very high and there is only a limited amount of funding available in the country. Many hospitals, university clinics, small and unknown organization scramble for the finances and medical equipment necessary to conduct their trials. This affects also the talent search, as the best qualified doctors go where the best economic prospects are for them. Infrastructure is also another issue which we have raised with the NCA as they inspect trial facilities. They follow the Good Clinical Practices (GCP) guidelines, but they do not necessarily align with our recommendations as well take into consideration a wider range of factors.

What stages of the clinical trial are Hungary most prolific?

We receive most trials in the third phase, as there are a greater number of patients participating in them. Hungary is ranked first in Europe in terms of accessibility and availability of trials per capita, which is another factor that makes us attractive to the international market. First phase trials are not frequent but are only performed by facilities accredited by the NCA, thus high quality of their performance may be expected. In this case head of the site, as well as the PI have to be qualified as clinical pharmacologist. In further phases PI has to have recent GCP credit and qualified in the clinical profession corresponding to the indication of the trial. Phase two trials are more demanding in terms of clinical science. We have a fair share of those as well, probably owing to the good reputation of the best Hungarian clinicians.

How is the committee collaborating with the government and the industry?

Clinical trials are a very sensitive area and we must exercise caution as to not allow radical ideas to disrupt the system, which is apparently functioning: it is also part of the committee’s role. The

committee is not directly involved with government but is through the connections with the NCA, that we collaborate with the state. Nevertheless, there is always collaboration with the industry and the government, as it is in everyone’s interest for a smooth process.

How do you see the clinical trial environment evolve in the next five years?

With a new Pharmacovigilance Hub opened by Roche this year, it might be an indication of a heightened interest in Hungary as a pharmaceutical market. Potentially, this could be a sign of new foreign direct investments to come, which would infuse the pharma landscape with much needed funding and dynamism.

We plan to enhance the influence of our ethics committee, to create a favorable legal framework for clinical trials, to improve the current IT system, to increase the number of Secretariat operative staff, in order to facilitate faster decision-making, and to increase the effectiveness of control, both in terms of facilities of sites and suitability of the investigators. The final purpose is to make Hungary an attractive place to bring in clinical trials in increasing number, and to make Hungary increasingly attractive to applicants as a country for effective and reliable clinical trials.

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