Interview with Svetlana Zavidova, Executive Director, Association of Clinical Trials Organizations (ACTO)

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Tags: Association of Clinical Trials Organizations (ACTO)

The primary objectives of this association are to promote Russia as a clinical trial destination, optimize the regulatory and legislative environment, and promote the interests of ACTO members. Can you give us an overview of the current clinical trial environment in Russia, and explain why a unified organization like ACTO is necessary?

Clinical trials in Russia are a very interesting area for international sponsors. First of all, we have a large, diverse population of naive patients, and high rates of patient enrollment in trials. Second, we have a great standard of quality, because our doctors are highly skilled. Russia is quite competitive amongst the BRICs as an attractive destination to conduct clinical work.

Of course, we have some problems with our legislation—doubtless, many will agree. But I hope that given time, we will resolve any issues plaguing the market.

Before last year, the rate of clinical trials conducted in Russia was on the rise. Subsequently, due to regulatory difficulties, 2010 saw a decrease in the number of trials. Nonetheless, we expect that within half a year to a year, this problem too will be resolved and the rate will rise again.

In the Russian market, we have many different associations in the pharmaceutical sector—the AIPM, the ARPM, etc. But the reason for the organization of the ACTO is that our field is rather narrow, and specific. If we look, for example, at the aims of the AIPM, we see that they have many broad interests, mostly related to product marketing. Due to the specificities of our field, it

demands special attention; and it needs a body that can facilitate expedient decisions and has the ability to understand niche problems. Therefore, pharmaceutical organizations that conduct clinical trials in Russia, and contract research organizations (CROs), decided to organize this organization.

One of the problems that provided the stimulus for our creation was related to the 2007 ban on biosample exports. At the time, there was no agency that could bring a unified voice on biosample exports into meeting rooms with officials. For large associations like the AIPM, this was a relatively minor issue—but for interested companies, it was of course significant, because to ban exports of this kind seriously hindered their clinical activities. It became apparent that an organization was necessary to speak on behalf of these parties.

We established the ACTO at the end of 2007, and began to rise rather quickly. Today, we have 26 members, including both pharmaceutical players and CROs.

What are the current items on your agenda for this year?

One of our main priorities is to establish good practices within the environment created by the new law on Circulation of Medicines. The new regulations beg many questions. First of all, the legislation stipulates that local clinical trials must be conducted for all new medicines being registered on the Russian market. We at the ACTO see this legislation as problematic. On the one hand, this regulation helps to increase the number of domestic clinical trials. But on the other hand, the quality of such local trials may not be as stringent as international trials—and our first priority is to proliferate international-level trials in the Russian territory, and to provide good clinical practices (GCP). Our mission is greater quality. Further, the law is a significant barrier to medicine registration. Thankfully, at this point, we have hope that in the future, we can change the situation.

There are a number of other challenges in the market: for example, requirements for principal investigators. The new law stipulates that principal investigators need five years of experience in clinical trials. Previously, the requirement was two. This means that in Russia, the number of eligible principal investigators has decreased. We are worried that demand will now outpace supply, and this will pose a problem for companies. Again, we have reason to believe that the situation will soon be resolved, because the demand for principal investigators is first of all an issue for local manufacturers. With the onset of Pharma 2020 and demands for innovation, local companies need to conduct clinical trials more and more. It will be difficult for them to locate principal investigators in competition with multinational companies, if the pool of investigators is significantly decreased. We hope to speak to the Minister of Health regarding this issue.

The key difficulties on this market are less problems of legislation—because although we have had many legislative changes, I would not say that they are particularly dramatic. At this time, our core problems are within the regulatory system. We did not have any transition period to adjust to novel regulations. For example, there are now new challenges related to the timeline of approvals of clinical trials from the Ministry of Health, etc. However, we believe the regulatory system should be assimilated and stabilized within a year—because in the wording of the law itself, there are good timelines for approvals; I believe they are quite comparable to the E.U.

Let’s look a bit more closely at the legislation requiring local clinical trials. An article by the ACTO has noted that firstly, these trials are repeats of those already conducted in other countries—hence making them unethical from the standpoint of patients. Furthermore, Russia put a provision in the law that allows for mutual recognition of clinical trials with other nations—something the ACTO says has no legal precedent and is likely impossible. Can you delve more deeply into these issues?

You are correct. Our law has a provision that says that Russia may agree to mutually recognize clinical trials with another state. In Russian, we call this kind of provision a “dead rule.” It cannot be used. Mutual recognition of clinical trials is legal nonsense! Mutual recognition is possible in, say, official inspections, etc.—but not in clinical trials as such. Because clinical results are the products of work done by private companies, not the government.

I think the discussion of mutual recognition is a bit of a play by officials, because their decision to require local clinical trials was unethical, difficult for industry, and against the interests of patients. The authorities’ reasoning for enacting this rule is that we need to look at the safety and efficacy of drugs specifically within the Russian population—as if we have some special characteristics! Their reasoning is difficult to understand and to explain. First of all, we do not quite understand what they mean by the Russian population, because we have so many different nationalities.

At the time of drafting, this rule was actively criticized, and the provision for mutual recognition was a sign of compromise from the government. But again, we view this as a play—they are misleading the industry. Soon after the announcement was made regarding mutual recognition, Minister Golikova held a number of discussions with the European Committee, and with the Indian Minister of Health. This was an interesting moment. After the negotiation, documents issued by the European Committee noted nothing about this discussion. On the Russian side, however, there was quite a bit of material expressing how close we were to implementing mutual recognition!

ACTO sent a request for clarification to the European Committee. Their response was that there is no such thing as mutual recognition of clinical trials between countries.

What can be the way forward? Is it feasible that this law will be repealed?

In May, the Presidential Committee for Modernization discussed this problem. A presidential order was issued to resolve the matter. However, this order is rather ambiguous. It says that we must change our legislation, and that we must recognize clinical trials that were conducted in the USA and the E.U. But the second point of this order is again about mutual recognition! I believe that it is at least a good sign that these problems were discussed at high levels, and with time, I hope that we will be able to change our legislation. As it stands, it is a significant challenge for our industry.

As we have discussed, Russia is fundamentally an appealing location for clinical work—but this seems mostly due to population demographics and the quality of scientists. In terms of the legislative framework, you have mostly mentioned numerous challenges. Would you say that the government is doing anything to incentivize clinical trials here?

I am afraid not. Currently, I believe that our legislation has no special stipulations that would make clinical trials attractive. However, there are government programs—for example, Pharma 2020, and so on—that are not specifically about clinical trials, but nonetheless, in their drive toward innovative development in the pharmaceutical sphere, indirectly incentivize clinical trials as well.

Companies sponsoring trials have two options: they can run the trials in-house, or contract out to a CRO. What is usually the case in Russia?

10 years ago the majority of clinical trials were conducted by pharmaceutical companies themselves. Now, I believe that the greater part is overseen by CROs. However, there are a number of companies that have very strong in-house clinical research programs in Russia. For example, Janssen, Servier, GlaxoSmithKline, MSD, and so on. They have strong teams and experienced R&D departments.

In Russia, multinational companies mainly conduct phase III trials. What is your assessment of why we see very few earlier phase studies?

I would say, first of all, that there are a significant number of Phase II studies done in Russia, as well. Our new legislation places barriers for international companies against conducting phase I trials. They do not want foreign players using our health volunteers in potentially dangerous studies. As ACTO, we cannot understand this rule!

However, if we look at previous years, when our legislation did not include these barriers, we saw low numbers of early phase trials anyway—so the problem is perhaps not one of legislation. I believe the reason is more closely linked with the financial decisions of international sponsors. The

first phase is rather small, and for them, it is simply easier to conduct it closer to home.

What is the state of GCP in Russia?

We are not members of the ICH. Nonetheless, we have a national standard that is equal to ICH GCP. In approximately half a year, we will have common rules for the Customs Union—based, again, on the ICH standards.

Do Russian companies adhere to the same level of standards that multinationals follow?

I am afraid that this is not always the case, unfortunately. It is not a problem of clinical trials, but rather a problem of drug registration. Currently, we have a double standard for Russian and foreign players, in terms of registration. If we compare what is necessary for a registration dossier, the requirements for Russian companies are far more lax. International companies must present the results of international trials, a plethora of statistics, and so on. Local manufacturers need only present the results of a limited number of Russian clinical trials, on a limited population set.

To change this situation, we need to, first of all, make ICH standards mandatory for local manufacturers. We also need to create new rules for registration. If it is stipulated that registration will only be approved if Russian players conduct pre-clinical trials according to GLP, and clinical trials according to GCP, then can we ensure a higher benchmark.

We can, of course, ensure the quality of international clinical trials. We have a strict inspection framework that includes inspections from the FDA. Compared to other countries, Russia is at a good level in this sense.

Unfortunately, again, we cannot say the same for our own companies.

You have said throughout the interview that perhaps we will see improvement quite shortly.

We certainly hope so. The pharmaceutical industry is experiencing a challenging moment in Russia. We cannot understand many of the seemingly adverse decisions of our government. We hope that soon, they will make note of some of the practical barriers they have created—for example, with registration—and laws will be amended.

There are many patient groups that have begun to struggle for their interests. Our government must listen. In some time, the situation will improve.

What do you believe are the benefits for Russia of having a strong clinical research base?

It means investment into the healthcare system. We can see the concrete effects of such investment in individual clinics: for example, if a particular clinic does not have certain equipment, a pharmaceutical company using this facility for a trial will provide this equipment. The clinic then retains the equipment after the trial.

The investment is not only financial, but is also an investment into local science, and local doctors. It gives our specialists the opportunity to work at the highest levels.

Finally, clinical trials are very beneficial for our patients—especially those with serious diseases such as AIDS and cancer.

What is your final message to the international readers of Pharmaceutical Executive?

In spite of any challenges, we believe in Russia!

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