PHARMACEUTICALS

Russian drug law hinders clinical trials

Legislation to increase availability of new medicines has delayed approvals.

BY ALLA KATSNELSON

A law aimed at improving Russians' access to innovative medicines has backfired badly.

'On the circulation of medicines', a law that came into effect in September 2010, was intended to streamline the bureaucratic system for testing and registering new drugs in Russia. There were high hopes that it would also boost the nascent domestic pharmaceutical industry and attract foreign companies to run trials there. The law set a maximum cost and time limit for drug registrations, for example; mandated compensation for those injured during trials; and declared that drugs manufactured in Russia solely for export did not need to undergo registration.

But the law has actually hampered clinical trials and limited the number of drug approvals over the past year, according to a report from the Association of Clinical Trials Organizations (ACTO) in Moscow, which represents companies conducting clinical trials in Russia.

One problem is that medicines must now undergo local trials before they can be sold in Russia, regardless of whether they have already undergone trials or been approved elsewhere. The goal is to ensure that drugs are backed by high-quality trials that prove their effectiveness in the indigenous population. A few Asian countries have similar rules, but whereas some Asians are thought to metabolize certain drugs in a different way from Europeans, that is not the case for Russians, says Leonid Kokovin, a clinical-trials manager based in Moscow. "We are statistically like European and American subjects, so the argument for testing on our population isn't understandable," he says.

The law also raises ethical concerns because it subjects people to clinical trials that are not expected to yield extra knowledge, Kokovin notes. He suggests that medicines backed by suitable foreign trials should be approved by the Russian authorities, as long as they are tracked in post-marketing studies. "That would be much simpler, and wouldn't put such a barrier on the market," he says.

ACTO's report describes one (anonymized) European company's struggle to register a drug for preventing preterm delivery, a condition that affects about 5% of pregnancies. The medicine is already approved for this use in many Western countries, and for other uses in Russia. The cost of running a Russian trial was estimated to be €1 million (US$1.3 million), and patients in the control group would have to be asked to avoid the drug, raising their risk of preterm delivery. Furthermore, clinical trials on pregnant women are rare in Russia, so there are few accredited facilities that can screen participants.

Despite the difficulties, the company is going ahead with the trial. However, many others have been discouraged by a lack of detail about how to comply with the law. "No one can say — including, probably the regulatory agency — what kinds of trial specifically should be run," says Dmitry Margolin, co-chairman of ACTO's regulatory committee. "No one can give the guarantee that if you do these trials then the data will allow you to register the medicine." Margolin says he is aware of "several tens" of instances in which manufacturers had planned to seek registration fora medicine, but had been deterred by the requirement for fresh trials.

Russian pharmacies can't sell some internationally approved drugs, owing to a strict law.

S. KRASILNIKOV/ITAR-TASS

According to information from ACTO and the Ministry of Health and Social Development, which oversees the registration of medicines, just three repeat trials are under way for innovative medicines already approved outside Russia — two for hepatitis C and one for neuralgia — with two more set to start soon. "If the situation continues," says Margolin, "then a large number of new products will not be registered and will not reach Russian pharmacies."

On the basis of meeting summaries posted on the ministry website, ACTO also estimates that the ministry's Ethics Council rejects more than 30% of applications to run trials, mostly as a result of administrative or clerical errors in the applications. To avoid undue influence, Russia's new medicines law forbids the Ethics Council from directly contacting companies, so it cannot request that small errors are corrected. By contrast, in Germany, where the rejection rate is 1%, approvals are routinely conditional on small changes in the application. "It's one of the main flaws of the Russian regulatory system under the new law," says Sergei Lomakin, a senior associate at the Moscow office of the international law firm Baker & McKenzie. "The system leads to a bigger number of rejections than one that allows scientific dialogue" between companies and regulators, he says.

Another provision of the law — that medicines developed abroad cannot have their first clinical tests in Russia — is hampering foreign companies that are trying to develop products specifically for the Russian market. Ironically, many such companies have agreements with government-backed investors, such as the nanotechnology venture fund Rusnano, to develop new medicines in the country.

"These changes in the guidelines happened at the moment when the country had invested so much in innovative drug development that there were quite a few drugs which were around the corner from starting phase I trials," says Andrei Gudkov, chief scientific officer of Cleveland BioLabs in Buffalo, New York, which partners with Rusnano and is struggling to launch a Russian early-stage trial for one of its anticancer compounds. The Ministry of Health and Social Development did not to respond to *Nature*'s questions on the matter.

ACTO and others say that scrapping the requirement for local registration trials would be an important first step towards fixing the situation. Until that can be done, says Margolin, "companies for the most part are sitting and waiting". ■