



Clinical Trials in Russia

The Promise and the Approach

- Discover the benefits of including Russia in your clinical trial
- Gain an understanding of how to navigate the legislative & regulatory environment
- Obtain tips to implement an optimal strategy for study success

COUNTRY PROFILE

Russia

- **Population**

143 million (2010 general census data), 73% urbanized

- **Main Cities**

Moscow (capital), St. Petersburg, Novosibirsk, Yekaterinburg, Nizhny Novgorod, Samara, Omsk, Kazan, Ufa, Chelyabinsk, Rostov-on-Don, Perm, and Volgograd

- **Political Structure**

Federation

- **Health System**

Follows European model.

Centralized Healthcare system comprising very large hospitals and university clinics, each specializing in a therapeutic area. Over 9,500 health care institutions and nearly 22,000 polyclinics. Supported by 4.31 physicians per 1,000 patients (nearly double that of U.S., with a ratio of 2.42).

Introduction: Why Russia? Why Now?

Since 1990, Russia has garnered a strong reputation for clinical research as the country's resources have become more available to international customers. The number of clinical trials performed has grown rapidly, from 292 in 2002 to 932 in just the first six months of 2013. Russia's population of more than 140 million and its centralized healthcare system of more than 9,500 health care institutions and nearly 22,000 polyclinics are just part of why the country is conducive to clinical trials. Other advantages include:

- A highly educated and motivated medical staff, well trained in Good Clinical Practices (GCP), and the application of Western medicine. Regulations require that Principle Investigators have at least five years of trial experience and be certified specialists in the classification of diseases.
- Strong patient recruitment and retention rates resulting from Investigator experience. Patients are highly motivated to participate in trials in order to gain access to free therapy (medicines are not covered by insurance in Russia) and to gain access to treatment and supervision from qualified doctors who are readily available. As a rule, clinical trials in Russia are performed in big hospitals/university clinics where qualified staff are concentrated.
- Access to facilities for conducting studies, including academic centers and specialized hospitals for all therapeutic areas. Sites must have permission from the Ministry of Health (MoH) to conduct trials and follow GCPs.
- Key opinion leaders who can identify leading physicians in any therapeutic area.
- Access to treatment-naïve or modern-therapy-naïve patients, minimizing study bias.
- Relatively fast regulatory approval.
- Fewer competing studies.
- Low patient relocation rates.
- Hospital costs generally provided by the State.

Such benefits often translate into greater cost advantages due to lower investigator fees compared to the U.S. and Western Europe.

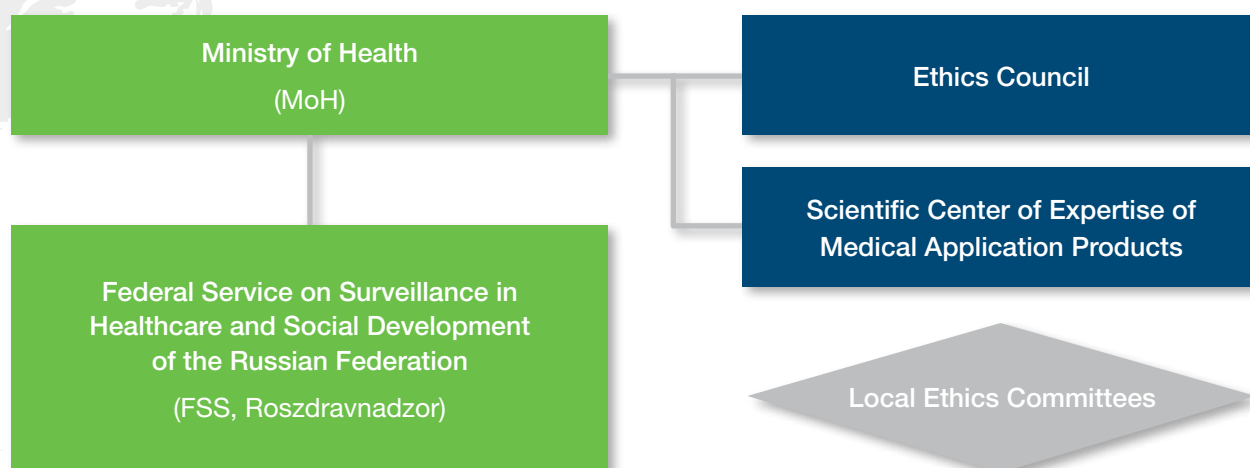
Understanding & Navigating Requirements

The Legislative & Regulatory Environment

Clinical trials in Russia are conducted in accordance with international standards and local legislation, including Federal Law No. 61-FZ “On Circulation of Medicines” from 2010 and the Guidelines “Evaluation of Drug Product Bioequivalence” of 2008. Documents for primary and additional submissions must be submitted to the Ministry of Health (MoH), the main regulatory authority for clinical trials. Operating within the MoH are the Ethics Council and the Scientific Center of Expertise on Medical Application Products.

The Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation (Roszdravnadzor) is responsible for safety issues and all types of safety reporting. All safety documentation must be provided to both the MoH and Roszdravnadzor.

Documents are reviewed both by the Ethics Council that is part of the MoH and by Local Ethics Committees (LECs), in some cases in parallel, in others in succession.



Drugs Registration

Data on studies with Russian patients is required for marketing approval in Russia. To sell a drug in the Russian market, a company must either:

- Include Russia in international studies during phases II-III.
- Conduct a local study in advance of seeking marketing authorization. Bioequivalence studies require a minimum of 18 subjects; simple comparative studies require no less than 100 subjects.

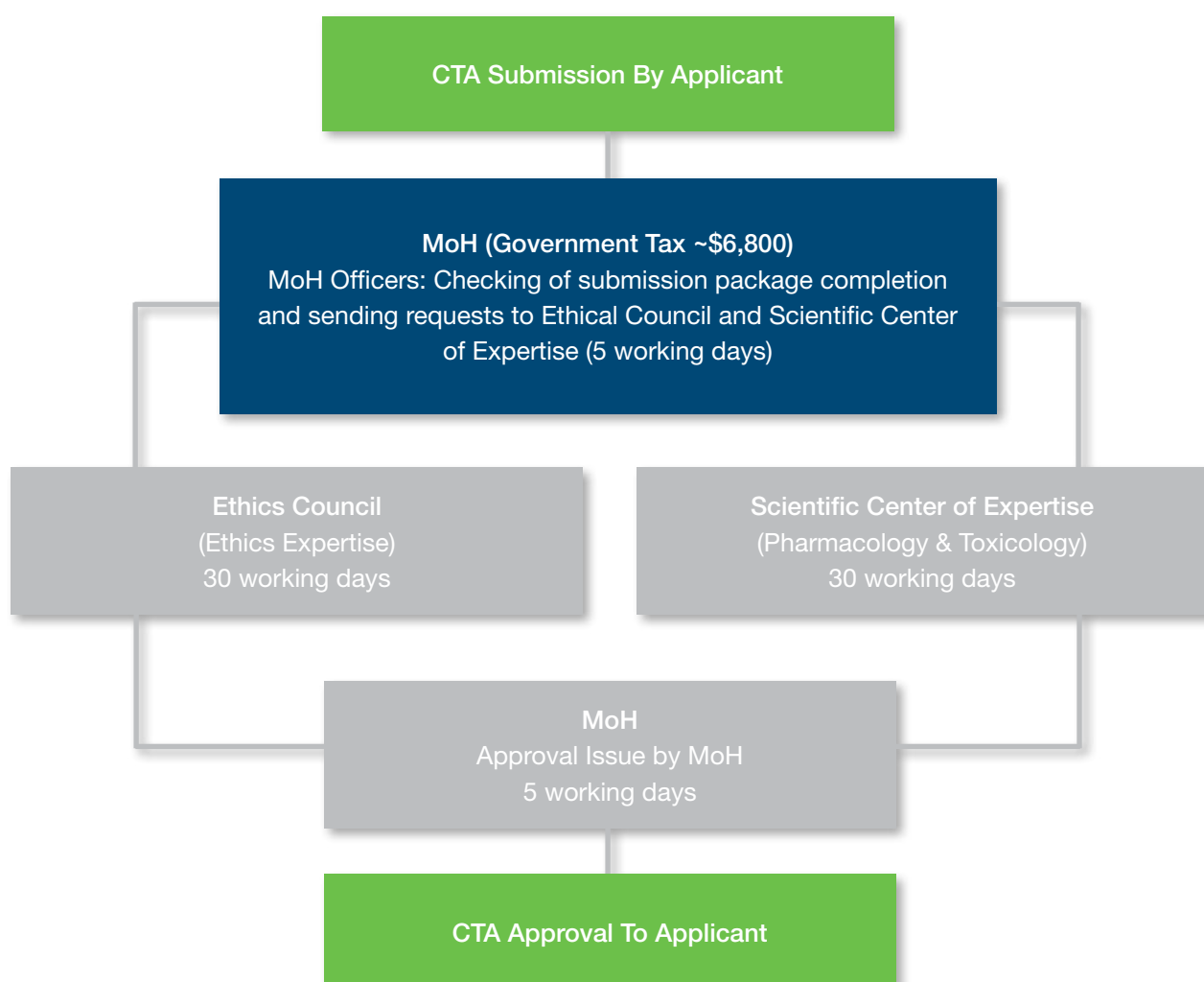
Process Flow and Timeline for Approving the Conduct of a Clinical Trial

Conducting a clinical trial in Russia requires a multi-tier process to secure approval to run the study. The Ethics Council and the Scientific Center for Expertise on Medical Application Products (both part of MoH) must sign off on the

application, which must include a list of sites and Principal Investigators. The application then goes to Roszdravnadzor. Finally, it is forwarded to Local Ethics Committees (which perform a simultaneous review only in some circumstances).

The average time to gain approval for conducting a clinical trial in 2012 was 115 calendar days (with a minimum of 16 calendar days), according to the Association of Clinical Trial Organizations. This varies from the timeline stipulated by current legislation, totaling 40 working days.

The total cost involved in submitting to the MoH is approximately \$6,800. LEC review costs vary from \$0 to \$600.



* Timelines provided on the scheme are the timelines per current legislation

Maximizing the Advantages

Patient Recruitment

Relatively fast and high recruitment rates in Russia typically offset the rather complicated approval process. Strong recruitment rates and retention stem from referrals from polyclinics and hospital outpatient departments. When self-directed patients seek consultations at clinics, physicians are able to discuss clinical trial participation with them.

Data Quality

As of February 2012, 91 U.S. Food and Drug Administration (FDA) inspections have been conducted in Russia. Comparisons of inspection results for Russia and the U.S. indicate a relatively low number of required actions in Russia.

It is likely that high data quality is directly related to the competency of the study teams, with a large percentage of MDs and PharmDs certified in the relevant indication and having a minimum of five years of experience. Site audits conducted by Pharm-Olam International and sponsors indicate generally high levels of quality.

An Optimal Strategy for Study Success

To ensure the success of a clinical research study, an organization should:

- Develop a protocol design with a consistent patient population across all countries in the trials.
- Incorporate contingency plans (site identification and qualification, thorough training, co-monitoring visits, site audits, increased monitoring, and central rater/rater surveillance).
- Train sites during Investigator meetings and site evaluation visits.
- Rely on highly qualified staff, with MDs serving as Clinical Research Associates (CRAs), Lead CRAs, and Project Managers whenever possible.
- Monitor sites, minimize travel costs, and increase quality by relying on local offices.

Conclusion

Russia shows every indication of sustaining its growth trajectory in clinical research, and organizations in the pharmaceutical and biotechnical industry appear eager to continue to tap the country's potential. The Russian market offers advantages that outweigh the challenges of its regulatory process. This gives companies more options for conducting studies cost effectively with the assurance of data quality in a broad range of therapeutic areas and phases of development.

PHARM-OLAM INTERNATIONAL

Helping Create a Healthier World

Your clinical trials are critical stages of a major research and development investment and hold the promise of bringing relief, better health, a more effective therapy, or longer life to patients across the globe. Pharm-Olam - founded by a physician in 1994 - understands the stakes for your company and the investment that rides on this next important phase in your quest for regulatory approval.

Pharm-Olam began by focusing on the emerging markets of Central and Eastern Europe, but has now expanded its services to more than 40 countries across five continents, including North America, Western, Central & Eastern Europe, Latin America, Asia, and Africa. This global reach allows Pharm-Olam to conduct global studies by seamlessly integrating team members across international boundaries.

Pharm-Olam has dedicated staff in three offices in Russia (Moscow, St. Petersburg, Novosibirsk) and also in Georgia, Kazakhstan and the Ukraine. Most Pharm-Olam clinical staff in this region have medical degrees, and many are certified specialists in particular therapeutic areas including oncology, cardiology, pediatrics, ophthalmology, and dermatology. In addition to highly qualified clinical staff, Pharm-Olam has local regulatory, logistics, and drug storage facilities to initiate and effectively manage studies.

All Pharm-Olam drug storage and distribution processes meet Good Manufacturing Practice, GDP, and local requirements and practices, with Standard Operating Procedures (SOPs) in place, written in English. The Clinical Supply Unit in Russia is equipped with:

- Storage of Investigational Medicinal Products (IMPs) and other clinical trial materials at room temperature +15+25°C
- Storage at +2+8°C and subzero temperatures (up to -90°C)
- Humidity and temperature monitoring system (in case of any temperature and/or humidity deviations Clinical Supply Unit staff are notified by email and text messages)
- Power outage alarm and power generator
- Storage agreements with outside companies
- Security system and program support

To learn more about Pharm-Olam, visit www.pharm-olam.com or contact us at info@pharm-olam.com.

Would your clinical trial pipeline benefit from expanding into Russia?

To learn more on how Pharm-Olam can help you tap into the potential the Russian market offers, please be sure to contact us at info@pharm-olam.com.

About Pharm-Olam International

Pharm-Olam International is a global contract research company with a presence in over 40 countries, offering a wide range of comprehensive, clinical research services to the pharmaceutical, biotechnology, and medical device industries. From Phase I to Phase IV, Pharm-Olam focuses on delivering the highest quality data, achieving targeted enrollment, and meeting projected timelines.



Pharm-Olam International

450 North Sam Houston Parkway E., Suite 250
Houston, TX 77060
T: 713.559.7900
F: 713.559.7901

Pharm-Olam International (UK)

The Brackens, London Road
Ascot, Berkshire, SL5 8BJ, UK
T: +44 (0) 1344 891121
F: +44 (0) 1344 890335

www.pharm-olam.com