

## Clinical Trials in Russia – Make the Right Choice

a report by

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### Russia as a Field for Successful Clinical Trials

Russia was ‘discovered’ by foreign pharmaceutical companies and contract research organisations (CROs) in the late 1980s. Since that time, the number of clinical trials in Russia has increased significantly. To quote Robert Rosen, the chief executive of the Association of the International Pharmaceutical Manufactures, “the potential of clinical research in the Russian Federation makes up \$200-300 million annually”.

CROs located in Russia often get the highest appraisal from their foreign colleagues who acknowledge Russian investigators’ expertise and work ability. Their achievements speak eloquently for themselves.

So what attracts foreign partners to Russia?

- population;
- healthcare system features;
- necessity of effective treatments;
- regulatory and ethics procedures;
- patients’ protection in local independent ethics committees (IECs);
- experienced investigators providing high recruitment rates with low drop-out rates; and
- local CROs.

### Population

The demographic setting in Russia is evaluated as ‘fast recruitment-friendly’. Approximately 150 million people live in the Russian Federation, and about one half of those live in town. There are more than 10 cities in Russia with a population exceeding one million people.

### Healthcare System Features

Russian’s system of healthcare is centralised. Almost all patients with diagnosed pathologies are registered in the databases of the regional healthcare administrations. Data about newly diagnosed patients is collected within these databases on a regular basis, at least annually.

### Necessity of Effective Treatments

Many patients in Russia require specific treatments that are beyond their reach. Sometimes, participation in clinical trials is a good opportunity for them to get the appropriate treatment for their disorder for a long period. There are also many drug-naïve patients with a wide range of pathologies. We should also consider the ethics issues arising in concern with these ‘dependent’ patients. Patient protection is noticeably strong in Russia.

### Regulatory and Ethics Procedures

Clinical trial regulatory packages are submitted to the Department of State Control of Quality, Efficacy, and Safety of Drugs at the Ministry of Health of the Russian Federation. They should contain the following documents:

- study protocol;
- investigator’s brochure;
- case report form and other data collection forms;
- information for patients and consent form;
- data collection forms for patients (diaries, questionnaires);
- insurance policy from a Russian insurance company; and
- other materials.

The documents should be translated into Russian in full (i.e. the protocol) or partly (i.e. the investigator’s brochure).

The Department officials prepare letters to one of the State expert committees (i.e. the State Pharmacological Committee) and to the National Ethics Committee at the Federal Body on the Control of Quality, Efficacy, and Safety of Drugs. These committees work in adherence to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) standard, which is acknowledged as a national standard. No clinical trial could be considered without the approval of these committees and the Department. The submission process usually does not exceed two to four months.



### Local IECs

Some words should be said about local ethics committees. Although not every hospital, out-patient clinic or medical university has its own institutional review board or ethics committee, the situation has changed remarkably since the early 1990s when there were no institutional review boards (IRBs) or IECs at all. Usually, today, there are one or more IECs in every region of Russia. They are usually located at medical universities or the biggest hospitals of the region. The members of these IECs are entitled to review and approve clinical trials in the regions where they work. The number of these committees rises constantly, and the professionalism and skills of their members improve continuously.

### Experienced Investigators

As recently as 10 years ago, only few physicians round the country could say that they were experienced in GCP-driven clinical trials. The situation has changed significantly since that time. According to the growth of a number of clinical trials, and the widening of their therapeutic areas in Russia, there is a noticeable increase in the number of experienced investigators, sub-investigators, study site co-ordinators and trial nurses.

Therefore, quality of clinical trials and data collection increases day after day. In addition, not only experienced study teams, but also newcomers are usually very effective in Russia due to the high reliability and professionalism of Russian doctors and nurses. Many of the investigators have undergone GCP training, so the main principles of clinical trial set-up, conduct and reporting are not novelties to them.

High recruitment of eligible patients is one of the specific features of the Russian investigators. Despite the high speed of recruitment, the number of drop-outs and data queries is insignificant in comparison with other countries.

Many Russian sites have been audited by sponsors, independent auditors and representatives of regulatory authorities (i.e. the US Food and Drug Administration (FDA)). There were no major findings during these audits.

### CROs

The companies occupying themselves with clinical trials in Russia should be mentioned. There are three types of companies:

- representative offices of medical departments of the pharmaceutical companies;

- representative offices of the international CROs;
- CROs of Russian origin.

The number of these companies has grown amazingly fast during the last few years, especially as a result of the companies in the third group. Making a choice, sponsoring companies have to take into consideration the experience and honesty of companies. Therefore, provided here is BTO's company profile, offering detailed information about the company.

### BTO Corporate Profile

#### Staff

All BTO employees have a university degree in Medicine, Biology or Pharmacology. We succeeded in forming a solid team of professionals who are competent in clinical trials to meet the international standards.

Regular training is our tool for improving the employees' skills.

#### Services

#### Therapeutic Overview and Potential Sites

Physicians of different specialties work for BTO. It is not a problem to hire an experienced physician as a part-time CRA or consultant for a trial in an exact therapeutic field due to our good relationships with doctors.

In our database, we have lists of potential sites and investigators. These are listed below. Most of the investigators took part in at least one international project, or even in a set-up process.

- Allergology and immune diseases – 14
- Anaesthesiology and intensive care – 12
- Cardiology – 123
- Dermatology – 32
- Endocrinology – 57
- ENT – 11
- Gastrointestinal disorders – 47
- General surgery – 21
- Gynaecology and obstetrics – 46
- Haematology – 11
- Infectious diseases – 28
- Neurology – 51
- Oncology – 103
- Ophthalmology – 14
- Orthopaedics – 18
- Paediatrics – 57
- Psychiatry – 34
- Pulmonology – 74
- Rheumatology – 16
- Urology and nephrology – 34

### **Trial Set-up and Conduct**

BTO offers:

- set-up and conduct of Phase I–IV clinical trials including bioequivalence studies and quality of life studies;
- full-time project management;
- study-related document translations;
- investigators' selection and site qualifications;
- set-up and conduct of investigators' meetings;
- central laboratory assistance;
- site start-up;
- routine monitoring;
- site closure;
- ensuring on-site record retention;
- contact with site staff; and
- thorough assistance to investigators and their collaborators.

### **Site Management**

BTO proposes:

- deployment of trained and experienced study nurses;
- provision of clinical sites with site managers;
- training of clinical research co-ordinators;
- assistance in maintenance and handling of study-related hi-tech equipment;
- assistance in patient recruitment;
- filling out CRFs; and
- tracking of AEs and SAEs.

### **Safety Monitoring and Reporting**

BTO provides:

- round-the-clock safety monitoring;
- timely safety reporting to sponsors, regulatory authorities and ethics committees; and
- active enquiry of investigators about new and on-going SAEs.

### **Data Management and Biostatistics**

We are ready to perform the following activities:

- data collection form design including CRF design;
- design of statistical sections of non-clinical and clinical protocols;
- data collection form distribution, retrieval and tracking;
- assistance in randomisation including IVRS assistance;
- fax and electronic data collection form transmittal;
- data collection form in-house review;
- database creation and tracking;

- query creation, resolution and tracking;
- retrieval and transmittal of radiology and ultrasound images, ECG printouts, central laboratory reports, etc.;
- status report creation;
- electronic data transfer;
- double key data entry;
- data validation;
- application macroprogramming;
- statistical analysis and reports;
- study data presentation; and
- NCR printing.

### **Medical Writing**

BTO suggests:

- clinical protocol compilation and review;
- study manual creation;
- presentation production; and
- study report writing.

### **Quality Assurance**

BTO performs:

- creation, maintenance, review, approval and archiving of all standard operating procedures (SOPs), both for the company and investigators' use;
- training of company staff in applicable regulatory documents and the company SOPs;
- routine quality control;
- internal and on-site audits and co-audits;
- issuance of reports of internal and external QA audits; and
- maintenance of the company master schedule.

### **Training**

We provide investigators and our employees with the following training:

- drug development overview;
- principles of GCP; and
- principles of project management.

### **Regulatory and Ethics Approval**

BTO executes:

- translations, back-translations and quality control of translations;
- collection, editing and formatting of investigators' CVs and other regulatory documents;
- preparation, filing and follow-up of regulatory submission packages;
- obtaining regulatory and ethics approvals and import/export licences;

- submission of safety updates and protocol amendments to local ethics and regulatory authorities; and
- safety reporting to ethics committees and regulatory boards.

**Logistics**

BTO offers:

- parleying and management of contracts and payments;
  - calculation and maintenance of pass-through costs;
  - travel arrangements;
  - legal support;
  - Customs clearance;
  - studies supplies shipment, storage, dispensation, return and destroy;
  - study-related document distribution and safe archiving;
  - co-operation with courier companies; and
  - assistance in set-up of toll-free telephone lines. ■
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