



# Clinical Trials in Ukraine

Untapped Potential  
& Proven Experience

## COUNTRY PROFILE

### Ukraine

- **Population**

45.4 million, on par with that of Spain

- **Urbanization**

Nearly 70% of the population live in urban centers, and five cities have populations of over one million

- **Main Cities**

Kiev (capital with 4 million), Kharkov, Dnepropetrovsk, Odessa, Lvov, Zaporozhye, which together represent over 20% of the population

- **Land Area**

Largest country in Europe (excluding Russia), roughly the size of Texas

- **Location**

Eastern Europe; borders Russia to the west; Belarus to the north; Poland, Slovakia, and Hungary to the east; and Romania, and Moldova to the south

- **Political Structure**

Independent state since 1991; governed by president, prime minister, and parliament

- **Economic Status**

Not yet part of EU, but adheres to EU values; Participates in Commonwealth of Independent States (CIS), but not formally a member

- **Health System**

Very well structured delivery system, which is funded by the government. Some private health insurance beginning as an option.

## Introduction: An Emerging Trials Market

Ukraine, the eighth largest European country by population, was often overlooked as a clinical trial site even before the political unrest and military actions that started in 2014. However, it remains an attractive location for those multinational companies astute enough to recognize its potential. The recent political unrest, which has been geographically confined, has closed off only about 7% of the country's more than 575 clinical trial sites to multi-national companies (MNCs) for research studies. (See Figure 1 on page 3)

Meanwhile, the country has a large population of modern-treatment-naïve patients and is far from saturated with clinical trials. Pharm-Olam's research has shown that only about 15% of the patient potential is currently being tapped. At the same time, it has the Clinical Trials legislation harmonized with respective EU Directives and Guidelines, educated, qualified and motivated investigators, infrastructure, systems, and capabilities to produce high-quality study results.

### Among Ukraine's Advantages for Clinical Studies Are:

- Recruitment rates that are higher than those of the U.S. or EU countries
- Two decades of experience in overseeing and running international clinical trials, with the number of trials steadily rising to 233 in 2013 (and 216 in 2014, as of September)
- An experienced, clinical community trained in Good Clinical Practices (GCP) that produces high-quality data
- A centralized system of healthcare that aids recruitment
- A relatively efficient approval process that compares favorably to other countries in turnaround time
- A low-cost structure. Grants to Principle Investigators are on par with those in Belarus, Georgia, and Russia, and the contracting process is well defined.



**Figure 1:** The region shown in red (Donetsk and Luhansk) and Crimea are the only areas not currently open to clinical trials. The affected sites represent only 7% of those in Ukraine.

### The Impact of Political Unrest On Clinical Trials

Political unrest began in Ukraine in November 2013, with peaceful protests (largely in Kiev) related to the Government's rejection of the Ukraine-EU Association Agreement. The protests spread to the Donetsk and Luhansk regions, where they became violent. For some months, these activities had no effect on the smooth operation of clinical trials in the region. Patient visits, laboratory tests, and courier services proceed unimpeded.

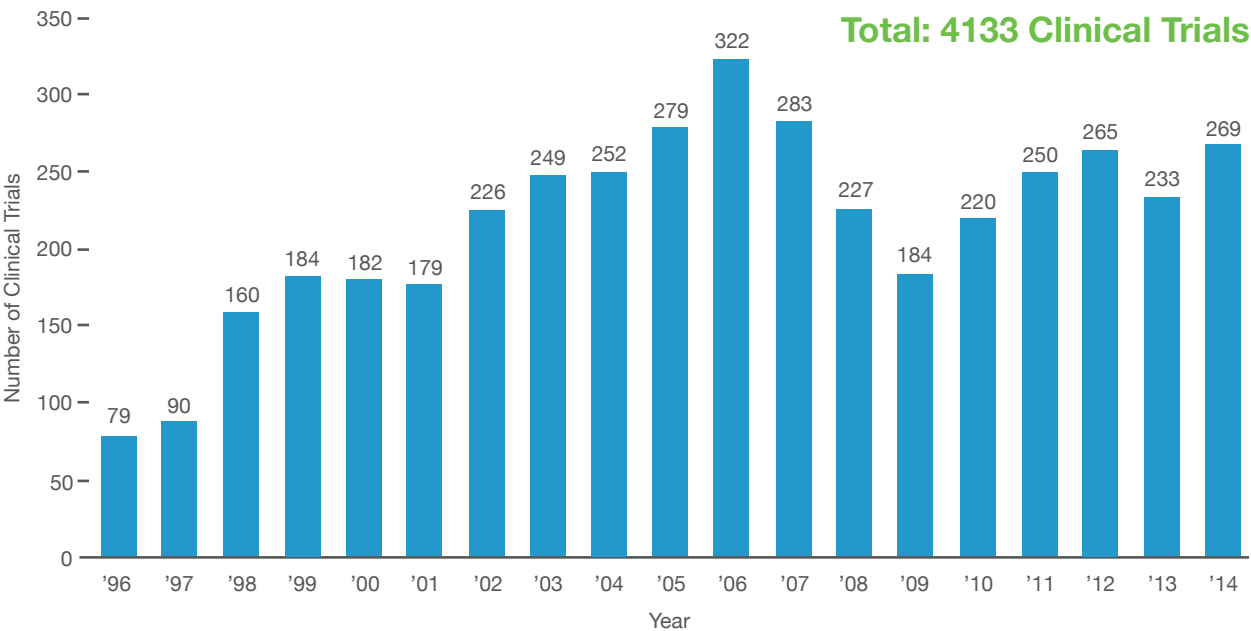
In May 2014, Crimea fell under Russian jurisdiction, and CROs/Sponsors took individual decisions regarding continuation of the sites participation or transferring them for monitoring by Russian local offices.

Meanwhile, military activities, which had begun in Donetsk and Luhansk areas, in March 2014, eventually led to the interruption of trial-related services in those areas in May. The Ministry of Health recommended that the sites in the small area of conflict be closed to clinical trials and that enrolled patients be transferred to nearby, unaffected sites. (In our experience, most patients chose to continue their trial involvement by switching sites.)

As the current military conflict contained to a very small geographic area, it has not affected the rest sites in the country. In fact, it appeared that the number of trials in Ukraine approved in 2014 exceeded the number from 2013.

Figure 2: Clinical Trial Volume

Displays the number of trials conducted in Ukraine since 1996. The number for 2014 is on track to match or even exceed that of 2013, suggesting that the political unrest and military actions have not affected the attractiveness of the country.



The Healthcare System

Ukraine’s healthcare system is one in transition with a growing market for modern treatments. The constitution provides for free, universal healthcare for all, which is funded by citizens’ social security contributions. In reality, only basic medical care is covered by the State, so patients are very motivated and compliant to take part in clinical trials providing access to modern treatment.

Care is provided through a very strong state-run system of outpatient facilities for primary care, general hospitals for secondary care, and large, specialized university hospitals for tertiary care. The number of physicians is high at 35.2 per 10,000 people, compared to 25 per 10,000 in the U.S., for example.

However, the government facilities and diagnostic capabilities are not always state-of-the-art, and the standard of care provided does not always include the most advanced treatments and frequently requires long wait times. For these reasons, many patients seek treatment at better equipped private institutions, where they must cover the cost themselves. To support this practice, private health insurance is on the rise.

The list of medications covered by the state health insurance is not extensive, which is one reason that patients are motivated to participate in clinical trials where they have the potential to receive the latest advances in medications.

## Understanding and Navigating Approvals

### The Legislative and Regulatory Environment

In 1996, the Pharmacological Committee within the Health Ministry of Ukraine organized a subdivision to develop, introduce, and monitor regulations on the use of medical products in the country—including clinical trials. Since then, the country has participated in 4,080 trials<sup>1</sup>. The Committee, formally called the Clinical Trials Coordination Department, is now referred to as the State Expert Center (SEC). It is responsible for running clinical trials at the state level. This means that it not only approves trial submissions, but also conducts inspections and offers training on GCP at various levels.

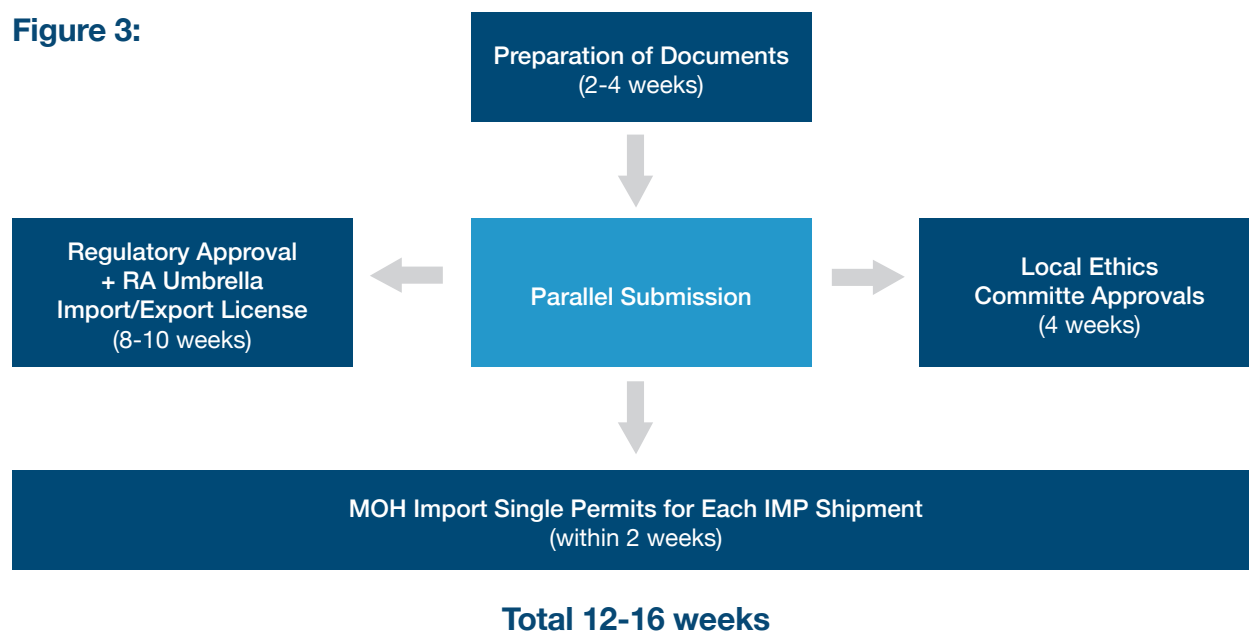
Ukraine's clinical trial regulations are harmonized with the directives, guidelines, and bylaws of the EU and are in compliance with the Declaration of Helsinki and the ICH (the International Conference on Harmonization). The country's laws pertaining to clinical trial practices are widely recognized as the most advanced in the Commonwealth of Independent State (CIS) countries and of other Eastern European Countries as well.

In June of 2014, despite being closely aligned with the EU, Ukraine signed its Association Agreement signaling, that in time, all clinical trial legislation will be fully aligned that of the EU.

### Approval Process for Conducting A Trial

Ukraine's approval process for clinical trial applications is relatively efficient, and much improved over its former sequential process. Today, two entities review submissions dossier in parallel: the State Expert Center and the Local Ethics Committee (LEC) associated with each investigational site. (See *Figure 3.*) The State Expert Center is to complete its review within 60 days, and the LECs in 30. The entire start-up process normally takes 12 – 16 weeks.

**Figure 3:**



Total start up period takes about 16 weeks (comparable to most EU countries)

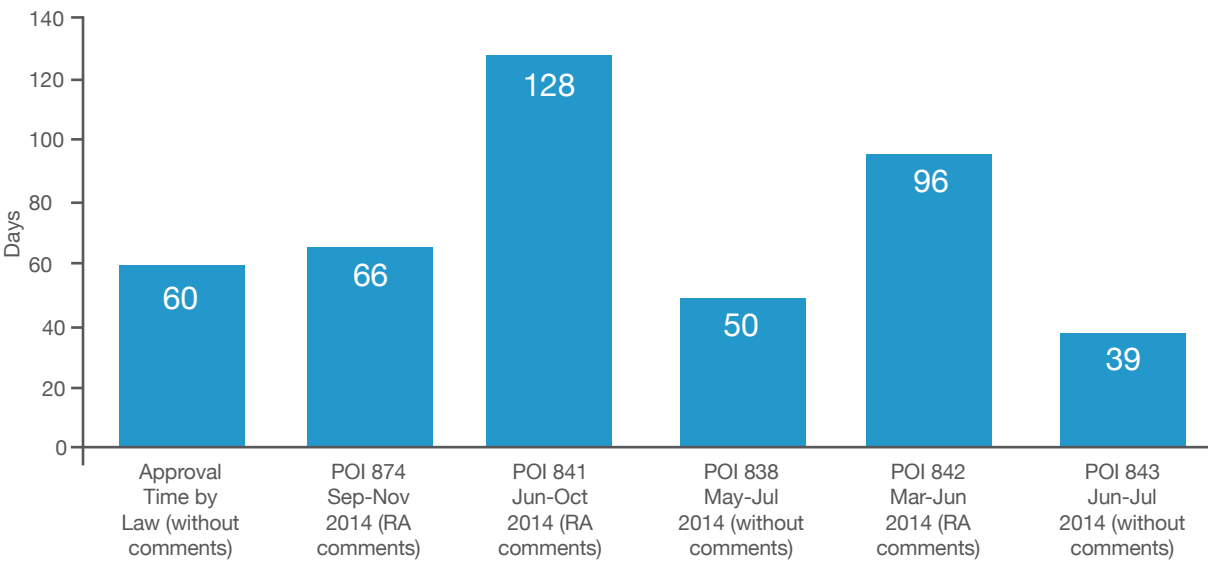
<sup>1</sup> [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

The State Expert Center requires an Investigational Medicines Product Dossier (IMPD), in keeping with EU requirements. Indeed, Ukraine has made a conscious effort to mirror EU standards and procedures wherever possible.

The LECs require fewer documents and focus their review on the protocol and the patient consent process. The application package includes a subset of those documents required for the regulatory authority submission. While there is less need for translation in Ukraine than in many countries, those materials prepared for patients must be translated into both Ukrainian and Russian.

As in most countries, as soon as one of the reviewing bodies asks the sponsor for more information or clarification, the clock stops. Once the sponsor’s response is received, the deadline countdown resumes. Also, the authorities can issue comments only once. Response may be provided informally, or in a formal letter. If there are no enquiries, it is possible to achieve full approval in 50 days, on average. However, when queries are involved, approvals take much longer. (See Figure 4)

**Figure 4: Number of Days to Achieve Regulatory Approval**



It is worth noting that the authorities are not very amenable to first-in-man studies, wanting to prevent the population from being subjected to early-stage experimentation.

## Import/Export Licenses

Following regulatory authority approval of the trial application, Sponsors/CROs must apply for an import/export license to cover shipments of the investigational and comparator products only; other trial supplies are excluded. The importation and customs clearance procedure and timelines are much improved since early 2012. It is a two-step process:

- An umbrella import license is required and may be sought in parallel with regulatory authority approval
- A single import permit is required for each shipment and is generally received within two weeks of application.

Customs clearance, at one time a time-consuming process has now been dramatically improved so that there is no delay in getting time-sensitive products through Ukrainian customs. Also, customs duties have been reduced to 7%.

## Study Implementation

### Contracts With Investigator Sites

In many countries, contracting with investigational sites is a protracted—even painful—process. In the EU, this step is the leading cause of delayed study starts. While contracts are required in Ukraine, they are less of an issue in the country than elsewhere. The law has defined three types of contracts:

- Between the sponsor (or CRO) and the hospital site
- Between the sponsor (or CRO) and responsible investigator
- Tripartite contract between the sponsor (or CRO), the scientific/educational establishment, and the hospital site

These contracts do not need to be signed at the time of the approval submission; that can be done on the basis of contract templates, which speeds the entire process.

### Patient Recruitment

The current structure of the healthcare system in Ukraine facilitates patient recruitment for trials, and existing healthcare practices make for both enthusiastic investigators and willing subjects.

The centralized hospital system means that large populations are treated by affiliated networks of primary care and specialist physicians. And the large hospitals accommodate multiple sites under one roof.

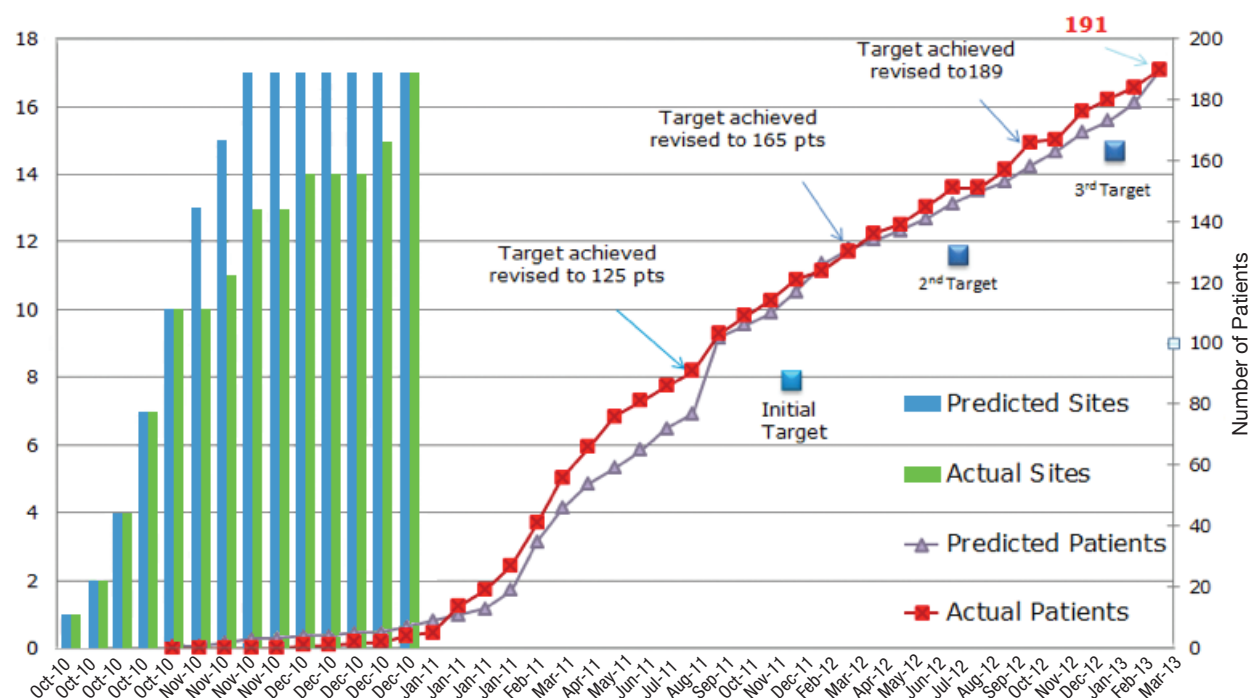
Because the standard of care within the socialized healthcare system has not always included the latest, most advanced treatment, it is still relatively easy to find patients who are modern-treatment naïve. Indeed, patients generally view late-stage trials as an opportunity to take advantage of more advanced diagnostics, closer physician monitoring, and breakthrough treatments. Ukrainian physicians, too, are generally eager to participate in investigations for the sake of their patients and to be on the leading edge of medical practice.

Meanwhile, the number of trials in Ukraine, while steadily increasing, is still far fewer than the population should support. Our experts have estimated that only about 15% of the country's patient enrollment potential is currently used.

All of these factors contribute to strong recruitment rates in Ukraine—generally at least three times higher than in the U.S. and EU.

## Figure 5: Recruitment for Hypertension Study

Illustrates that in a recent study for pulmonary hypertension, recruitment in Ukraine ran ahead of schedule.



## Data Quality

Ukraine has earned a reputation for conducting high-quality studies, in part through the training in GCP that the State Expert Center provides and in part through the active inspection schedule that the Ministry of Health maintains. (Note that the SEC no longer certifies sites or investigators.)

Results of audits by the U.S. Food & Drug Administration (FDA) have reinforced the reputation. Of the 17 inspections the agency conducted from 2009 through 2013, 7 resulted in Voluntary Action Indications, while the remainder resulted in No Action Indicated. The Ukrainian regulatory authority also conducts its own inspections, and completed 66 in 2013.

## Strategies For Success

- Tap the knowledge of local experts in guiding the application through the approval process
- Seek support from local staff who have experience in working with regulators in order to gain customs clearance
- Train sites during investigator meetings and site evaluation visits



## Conclusion

Ukraine is a favorable market for clinical trials with great potential for sustained growth. While it is certainly not “undiscovered” by drug sponsors, it remains underutilized. It offers an easily accessible, modern-treatment-naïve population, eager and well trained investigators, and practices that conform to international quality standards.

Recent improvements include:

- Faster regulatory approvals
- Application documents that are similar to those in the EU
- A faster, simpler import/export process

In spite of political unrest in a very small fraction of the country, Ukrainians are looking to the future with confidence as their development continues in line with EU regulations. The country as significant global support for its development and conflict resolution, and the country’s attractiveness to investors increased in July and August of 2014 after declining in the first half of the year.

Sponsors should, of course, work closely with an organization that has a history of working from within Ukraine, tapping its knowledge of, and relationships with, local regulators and the medical community.

### 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.

For more information on planning successful trials within the Ukraine, contact [info@pharm-olam.com](mailto:info@pharm-olam.com).



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