



Clinical Trials in Canada

A Primer for Sponsors

COUNTRY PROFILE

Canada

- **Population**
35.3 million, 80+% in urban areas
- **Land Area**
3.8M sq. mi., second-largest country in the world
- **Location**
North of the United States
- **Main Cities**
Toronto, Montreal, Vancouver, Ottawa, Calgary, and Edmonton. Each of these cities has a population of more than one million and the Greater Toronto Area has more than six million.
- **Political Structure**
A constitutional monarchy and parliamentary democracy consisting of the Crown (Elizabeth II, the Queen of Canada), the Senate and the House of Commons.
- **Economic Status**
According to the Heritage Foundation, "...Canada remains one of the worlds' most stable business climates and an attractive investment destination."⁴ The country's inflation rate to date in 2015 is .9%⁵. The U.S. is Canada's largest trading partner—and vice versa.
- **Clinical Trials**
Currently, there are 1,843 clinical trials that are active, but no longer recruiting patients and 3,953 open studies. The most popular provinces in which to conduct clinical trials are Ontario, Quebec, British Columbia, and Alberta, in that order.

A Separate, but Familiar Venue

Sponsors looking for early sites in which to launch Phase I-III trials often turn to the United States, although they can also look to Canada for similar reasons and with equal success. In fact, perhaps Canada's greatest recommendation as a clinical trial location is that is often cited as the country most like the U.S.; sponsors familiar with operating in the U.S. will find familiar ground in Canada.

Canada boasts one of the world's shortest clinical trial approval timelines (30 days or less), and its medical community and facilities meet the highest international standards. Other benefits include several large metropolitan areas where recruitment can be concentrated, a largely English-speaking population that is generally amenable to trial participation, and financial incentives via the exchange rate and government tax credits. Finally, Canada is not "saturated" with trials, at least as compared to the U.S. The number of open trials per capita is .0089 in Canada and .021 in the U.S.

The most limiting factor is that the country is geographically vast, so that trials conducted across multiple areas will require long-distance travel.

Country Demographics

Canada, by area, is the second largest country in the world, second only to Russia, and the largest country in the Western Hemisphere. It measures 3.8 million square miles (compared to 3.7 million square miles for the U.S.) and has the longest coastline of any country.

Population-wise, Canada, with 35.5 million people, is slightly larger than Iraq (with 37.4 million people). So, while Canada is slightly larger than the U.S. in terms of territory, it has only 11% of the population. Canada's population is growing at a little over one percent per year, owing largely to immigration.

Roughly 75% of Canadians live within 100 miles of the U.S. border. Over 80% live in urban areas, and 43% live within the country's six largest cities, each of which has over one million people: Toronto (with over six million people), Montreal, Vancouver, Ottawa, Calgary, and Edmonton.

Canada is a multi-cultural society with a "visible minority"¹ of 19.1% of the population. Roughly 28% are of British descent, 23% are of French descent (concentrated in Quebec), and 2% are aboriginal peoples. Other minorities include Italians, Germans, Ukrainians, and Chinese.²

The life expectancy of a Canadian born in 2009 is 81.1 years, and ischemic heart disease, bronchus, lung cancers, and cerebrovascular disease are the leading causes of premature death in the country.³



¹ Canada's Employment Equity Act defines visible minorities as "Persons, Other Than Aboriginal Peoples, Who Are Non-Caucasian in Race or Non-White in Colour."

² <http://travel.nationalgeographic.com/travel/countries/canada-facts/>

³ www.healthdata.org/sites/default/files/files/country_profiles/GBD/ihme_gbd_country_report_canada.pdf

⁴ www.heritage.org/index/country/canada

⁵ www.Inflationcalculator.ca

The Healthcare System

Canadian citizens receive universal healthcare coverage (via the Canada Health Act) for preventative care, medical treatments and dental surgery. Excluded are prescription medications, dental services, optometry, and home care. Provinces and territories are responsible for administering and delivering healthcare and must meet the minimum requirements set by the federal government. Because individual provinces may provide coverage for some medical expenses above and beyond what is covered by Health Canada, there are slight variations in coverage from one province to the next.

Employers typically offer private health insurance plans to supplement the country's universal insurance with coverage for prescription drugs, vision care and dental care. Individuals can also purchase insurance from private providers.

Canada has more than 750 hospitals (particularly in Toronto and Montreal, several are teaching hospitals), and approximately 77,000 physicians, which equates to 2.2 physicians per 1,000 people, very comparable to the U.S. doctor-to-patient ratio. Patients are free to choose their own primary care physicians, although it can sometimes be difficult to find a physician that is taking new patients.

One tradeoff that Canadians make for having universal healthcare coverage is enduring longer wait times than in the U.S. For example, in Canada, it is not unusual to have to wait several months for an MRI, depending upon the indication. As a consequence, private clinics are beginning to spring up in Canada, and these facilities are generally able to provide services more quickly than public providers.

Regulatory Structure

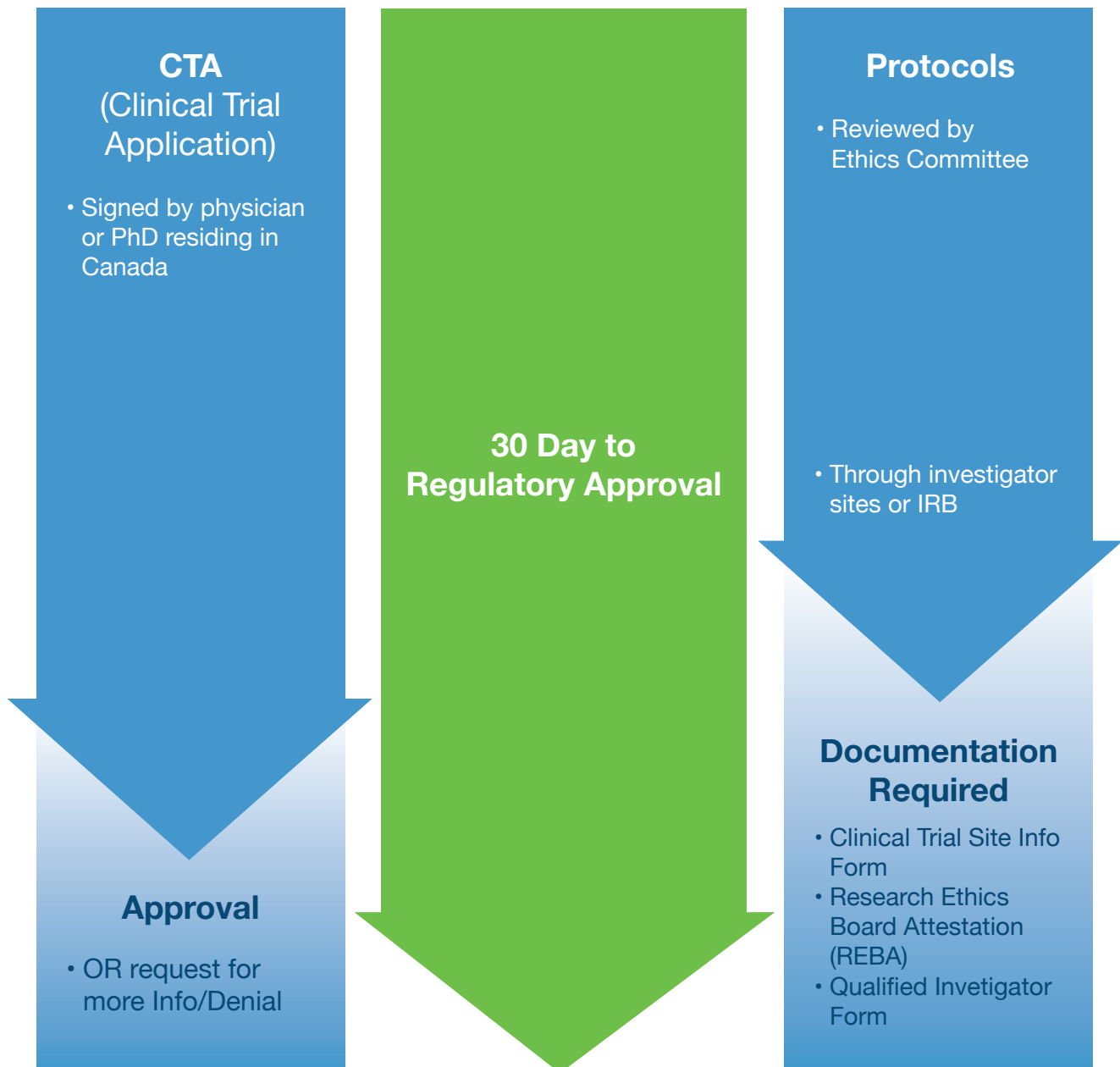
Health Canada, a federal agency, is responsible for:

- Setting and administering the principles embodied in the *Canada Health Act*;
- Supporting provinces/territories in funding healthcare services;
- Delivering health care services to specific groups (e.g. First Nations and Inuit and veterans); and
- Providing public health protection programs and health research.

The agency regulates the sale of drugs and their use in clinical trials, and Canada's Food & Drug Act and Regulations are in keeping with the principles of good clinical practice and the International Conference on Harmonization (ICH). Guidance documents (E6, E8, and E2A) define the parameters for how clinical trials are designed, conducted, monitored, analyzed, and reported. Health Canada reviews clinical trial applications, performs site audits, and tracks reported side effects.

Regulatory Approval

The process for gaining approval to conduct a clinical trial in Canada is efficient and straightforward, resulting in one of the world's fastest trial start-up timelines. If applications are processed without encountering any difficulties, approval can be granted in 30 days.



Drug sponsors seeking approval to conduct Phase I-III trials must submit a Clinical Trial Application (CTA) to Health Canada. (Some sponsors depend upon their clinical trial partners to complete the CTA.) The agency is required to respond within 30 days, either with an approval (in the form of a No Objection Letter (NOL)), a request for more information, or a denial. Sponsors are required to have the CTA signed by a scientific medical advisor who must be a physician or Ph.D and residing in Canada.

The information required on the CTA is very similar to that needed for an Investigational New Drug (IND) application in the U.S., and information prepared for one form can easily be “cut and pasted” into the other. Note that at this writing, CTAs are still submitted in hard copy form, however, Health Canada is piloting an e-submission process with the goal of moving to electronic-only submission.

Sponsors must also get approval on their final protocols from the Ethics Committees at investigator sites or through a central IRB, although this effort can run in parallel with the CTA approval described above to save time.

The documentation required from each site before it can be activated includes:

- A Clinical Trial Site Information Form. This can be sent to Health Canada as part of the CTA, although usually sponsors have not completed their investigator recruitment at the time that they file their CTAs.
- A Research Ethics Board Attestation (REBA) or equivalent
- A Qualified Investigator Form

Investigator Site Contracts

This step often takes longer than gaining Health Canada approval, and, especially if the sites are large institutions, may take three to four months. The process, timing, and cost of contracting with investigator sites are similar to what sponsors experience in the U.S. At the current exchange rates of U.S. and Canadian dollars, U.S. companies will find the costs slightly discounted for sites willing to be paid in Canadian dollars.

Tax Credits

An often-overlooked benefit to conducting clinical trials in Canada is the federal tax incentive available through the Scientific Research and Experimental Development (SR&ED) program. Administered by the Canada Revenue Agency (CRA), it is designed to encourage Canadian businesses to conduct R&D in Canada, and is regarded as one of the most generous such programs in the industrialized world.⁶

Canadian controlled private corporations (CCPCs) can earn a refundable investment tax credit (ITC) at the rate of 35% on qualified expenditures, up to maximum of \$3 million. This ITC is 100 percent refundable on qualified expenditures and 40% refundable on qualified capital expenditures. CCPCs can also earn an ITC at the rate of 15% on amounts over the \$3 million threshold.

Other corporations can earn a non-refundable ITC at the rate of 15% on qualified expenditures. The ITC can be applied to reduce the tax bill. More information can be found at:

www.cra-arc.gc.ca/txcrdt/sred-rsde/clmng/lgblywrkfrsrdnvstmnttxcrdts-eng.html#s2_1_4

Import Licenses for Investigational and Comparator Drugs

Conveniently, the NOL obtained from Health Canada upon approval of a trial doubles as an import license. Additionally in Canada, sites themselves can be listed as the importers of record. When this is the case, sites should be educated as to the responsibilities that come with that designation. For instance, they must have certificates of analysis on file regarding the stability and expiry of all investigational products and medical devices.

Patient Recruitment

Canada's population is concentrated in a narrow swatch of the country along the U.S. border, which is a plus for selecting sites and recruiting patients. Sponsors must take into consideration, though, the vastness of Canada's geography and the distance that its border with the U.S. stretches. Extensive travel is required to visit multiple sites. For instance, Toronto is five hours by air from Vancouver.

Trials may be promoted through any media in Canada, and experience has shown that people are generally receptive to participation. In fact, they may be especially motivated to take part in clinical trials because pharmaceuticals are not covered by the country's universal health plan. They may also consider trials an attractive alternative to waiting for treatment via the publicly funded healthcare system.

Throughout most of Canada—with two exceptions—most patient materials can be prepared only in English. One exception is that the drug label must be also translated into French throughout the country. The other is that all patient materials for trials in the Province of Quebec must be translated into French, as that is the region's official language.

⁶ www.actionplan.gc.ca/en/initiative/scientific-research-and-experimental-development

Conclusion

Canada remains an extremely attractive location for conducting clinical trials, providing many advantages for sponsors. Although the vastness of the country requires extensive travel, the population is primarily located in six major metropolitan areas and along the U.S. border. This means that recruitment efforts can, nonetheless, be quite focused. Canadians are generally receptive to clinical trials, especially when it improves their access to medications that are either not covered by universal healthcare or to treatment that would be delayed through the public system.

With the exception of Quebec, Canada is English speaking. And, the application process for trial approval is exceptionally efficient and sponsor-friendly. Tax incentives for Canadian corporations and a favorable exchange rate for U.S. companies are other inducements.

While the federal government oversees healthcare provision and trial regulations, certain aspects of both may vary from province to province. Sponsors are, therefore, well advised to work with a clinical trial organization having operations in, and experience with, Canada to ensure a smooth study start up and ongoing trial success.

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 Canada, contact info@pharm-olam.com.



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