

# Conducting Clinical Studies in Lebanon



Since the 1990s, Lebanon, a pioneer in the region in the field of clinical research, has been selected for participation in multiple international multicentre clinical studies sponsored by top-ranked pharmaceutical, biotechnology and medical device companies. According to [www.clinicaltrials.gov](http://www.clinicaltrials.gov), the number of Phase I, II, III and IV trials with an “open” status in Lebanon as of February 4th, 2014, is 53, exceeding by far other Middle Eastern countries such as Jordan, UAE, Qatar and Kuwait. These figures do not take into account the non-interventional studies that are also very widely spread in Lebanon.

Located at the crossroads of the Mediterranean Basin and the Arabian hinterland, Lebanon has a long history of exchanges with Western countries. In the health field, almost all key opinion leaders were educated in the US and Western European countries. In addition, huge investment is being made in Lebanon in the healthcare infrastructure. Most hospitals in Lebanon have a proper and modern set-up and equipment, as per international standards. Lebanon is therefore characterised by a quality of care that is comparable to the one provided in the West. There are 22 university hospitals in Lebanon. Some university hospitals are affiliated to major European and American hospitals such as Clemenceau Medical Center, Beirut, Lebanon, affiliated to Johns Hopkins Medical Center, Baltimore, USA. American University of Beirut – Medical Center was founded 147 years ago. It has a Federal-wide Assurance (FWA) with the Office of Human Research Protection (OHRP), in the Department of Health and Human Services (DHHS), as a domestic institution. Hotel-Dieu de France, also located in Beirut, was established in 1888. Saint George University Hospital started its activities in 1878. Other university hospitals such as Hammoud Hospital in Saida and Ain Wazein Hospital in the Chouf region have flourished during the past 50 years. In line with Lebanese law, it is acceptable to conduct a clinical study at a non-university hospital provided that a special approval is granted by the Ministry of Health. Practice has shown that such approval is usually easy to obtain. Despite the fact that Lebanese hospitals offer a quality of care that is similar to that available in the US and Western European countries, institution and investigator grants remain lower than in the West, which makes Lebanon a country of choice for the conduct of cost-effective and quality-driven clinical studies. Most hospitals in Lebanon have clinical research units, hence adequate monitoring space and staff solely dedicated to the conduct of clinical studies.

With a surface area of 10,452 square kilometres and a coastline of 225 kilometres, where most investigational sites are concentrated, the whole Lebanese territory can be covered by a single clinical research associate based anywhere in the country. Lebanon has a Mediterranean mild climate that does not cause interruptions in professional or clinical activities.

Even though Arabic is Lebanon’s official language, most investigators and site staff are fluent in English. Patient

files are usually not maintained in Arabic. Medical notes and laboratory results are either produced in English or in French. The Ministry of Health and the ethics committees do not require translation into Arabic of the clinical study protocol, protocol synopsis, investigator’s brochure and case report form. However, in compliance with good clinical practice, it is required to translate into Arabic documents provided to the patients (informed consent forms, dosing diary cards, etc.). In case other Arabic-speaking countries participate in the same study, a single translation can be performed and customised to local specifications accordingly.

A significant advantage of conducting clinical studies in Lebanon is the shortness of the overall approval timelines, that do not exceed four months. Moreover, these timelines are very much predictable which is well appreciated by sponsors. Short approval timelines and predictability allow sponsors to consider Lebanon more and more as a rescue country for their ongoing clinical studies. The submission process is sequential and starts with the local ethics committee submission. Once the local ethics committee approval is received (review timelines estimated to two months), and if the study involves an investigational medicinal product, an application for an import licence is submitted to the Ministry of Health. The approximate time for the import licence to be granted is also two months. The Ministry of Health does not review the clinical trial protocol and the related trial essential documents. The focus is put on the importation of the investigational medicinal product. Since Lebanon is not an EU member state, an IMPD is not required. It is necessary to note that clinical trials on narcotics are not allowed in Lebanon. Local ethics committees’ requirements vary but usually remain similar to the ones outlined in good clinical practice. All university hospitals and the majority of hospitals in general have their own ethics committees who meet on a regular basis and comply with good clinical practice. There are no central ethics committees in Lebanon, and hence no need to select and appoint a national coordinating investigator.

In terms of patient recruitment, it is not rare for Lebanon to be the highest recruiting country worldwide in a clinical study. Also, in many cases, the first patient in was enrolled in Lebanon. Indeed, Lebanese investigators are usually motivated to take part in clinical studies. In some institutions in Lebanon, acting as principal investigator is even a condition for a physician to evolve in his/her career. The key opinion leaders treat approximately 90% of the patients. Collaboration with medical societies can easily be established in order to boost patient recruitment. If needed, referral networks have also been shown to be a quick and effective way of boosting patient recruitment. In 2012, WHO estimated Lebanon’s population to be 4,228,000. With the adoption of Western lifestyle habits, the diseases that dominate the industrialised world have become significantly present in Lebanon. On the other hand, life expectancy has increased. For example, cancer rates in Lebanon are similar

to the ones found in the West. Local smoking habits and low public awareness of cancer risk contribute to the high cancer rates. Neurodegenerative diseases such as multiple sclerosis and Parkinson's disease, auto-immune diseases such as systemic lupus erythematosus and rheumatoid arthritis, endocrinology diseases such as Type II diabetes mellitus and osteoporosis, cardiovascular diseases such as familial hypercholesterolemia and coronary artery diseases are also very much prevalent in Lebanon. Indeed, Lebanon has one of the highest worldwide rates of familial hypercholesterolemia. Also, coronary artery disease is the leading cause of death in the Middle East. Moreover, the high consanguinity rate in Lebanon offers a relatively wide patient population for rare genetic disorders such as Gauchers disease Type II, sickle cell anemia, beta thalassemia, glucose-6-phosphate dehydrogenase deficiency, cystic fibrosis, phenylalanine hydroxylase deficiency and fragile X syndrome. Last but not least, the Middle East region could have the highest incidence of pulmonary infections in the world. It is thought that water-pipe smoking is partially responsible for the high rate of pulmonary diseases and infections in this region.

Since the beginning of its civil war in 1975, Lebanon has suffered tremendously from the image broadcast by the media. But in reality, since the end of the war in the 1990s, Lebanon has offered a safe and pleasant environment. Unfortunately, unrest can still be expected in Lebanon at short notice. However, it is usually restricted to a specific area and for a limited time. Local contract research organisations and clinical research professionals are used to working in such circumstances, and unrest risk mitigation plans are already in place. Storing a paper study master file in offices does not constitute any risk as long as adequate fireproof/waterproof measures are followed. Since protocols usually allow a time window for the patient visits to take place, deviations usually do not occur. If a site monitoring visit exceptionally needs to be postponed, the clinical research associate simply performs as many remote checks as possible in the meantime. Communication with sites through email, phone and fax channels is never affected by unrest. As soon as the risk of airport closure becomes probable, site study teams order additional central laboratory and investigational medicinal product kits in order to ensure that a sufficient stock is available at site. The use of a local depot for the storage of large amounts





of investigational medicinal product is encouraged in Lebanon as it allows decreasing the number of import licences necessary for the whole duration of the study. Local depots in Lebanon receive a licence from the Ministry of Health in order to act as a local depot for pharmaceutical products. However, there is no special authorisation requested in Lebanon for the storage, distribution or transportation of investigational medicinal products. A certificate of good practice is not required by local law. In case of unrest, exportation of frozen lab samples does not constitute any risk as the latter can be stored at site for a longer period of time. Ambient lab samples (hematology, biochemistry and urinalysis) can be analysed locally. In Lebanon, local labs are accredited by the Ministry of Health. In the exceptional situation where clinical research professionals' access to the contract research organisation offices is jeopardised by unrest, portable modems are commonly used in Lebanon; staff can thus work from home until the situation is back to normal. In summary, the risk of unrest in Lebanon is indeed higher than it is these days in the West. It is, however, worth mentioning that Lebanon was not affected at all by the current wave of protests in the Arab world. With a solid and exhaustive risk mitigation plan and the ability to activate it at any moment, the impact of potential unrest on clinical studies is, objectively speaking, very low.

In Lebanon, relationships between patients and physicians are usually built on trust. Therefore, out-patients are usually very compliant with the administration of their treatment and other study-related procedures. Many patients don't have social security coverage and high quality medical care is not always available for them. Therefore, being part of a clinical trial is viewed very positively by those patients. The young generation is quite motivated to participate in clinical trials. With a literacy rate of 90% (UN data, 2012), Lebanon offers a large pool of patients who are perfectly able to read, understand and sign the

content of an informed consent form, and fill in health-related questionnaires and other patient documents. Sponsors should, however, take into consideration the local cultural specificity when conducting a study in Lebanon. For example, during the month of Ramadan, a large part of the Muslim population fast from dawn to sunset. This may have an impact on the administration of the investigational medicinal product or on the related study procedures.

Audits at sites in Lebanon usually result in no critical findings. Generally speaking, patient safety is followed up by the investigators in a very timely and rigorous manner. It is common, however, to notice a lack of availability of source documentation corresponding to medical history conditions and to the history of treatments. Electronic patient files have indeed only recently been introduced in Lebanon and are not yet implemented by all hospitals.

As per MCT estimates, and as of December 2013, there were seven contract research organisations based in Lebanon, around 40 clinical research associates with at least one year of monitoring experience and five pharmaceutical companies based in Lebanon who have their own local clinical teams. These numbers do not take into account the contract research organisations based in the region whose staff visit Lebanon on a regular basis for monitoring purposes. As far as the evolution of the number of clinical trials conducted in Lebanon is concerned, and based on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) data, 40 trials were attributed to Lebanon in 2007 ("open" and "closed" status). This number increased to 54 the year after. Between 2009 and 2010, it jumped from 68 to 103. The progression has never stopped since then, with 123 trials in 2011, 153 in 2012 and 187 in 2013. The growing number of contract research organisations with activities in Lebanon and the increase in the number of clinical trials conducted in Lebanon testify to the promising future of clinical research in the country and the region. Indeed, sites in Jordan and the Gulf countries can be easily monitored from Lebanon (no language or cultural barrier, short and direct flights, etc.). A few years ago, local regulation was still lacking basic aspects in Lebanon. But in the recent years several laws, decisions, memos and guidelines on the use of investigational medicinal product by university hospitals, exportation of biological specimens and importation of sterile medical equipment were issued. All Lebanese clinical research professionals are now looking forward to the next milestone, which is planned for the end of 2014: the capacity to destroy locally used and unused investigational medicinal product at the end of a clinical trial.



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