Jordan's Advancement into the Clinical Market and its Regulatory Framework

The Hashemite Kingdom of Jordan, located in the heart of the Middle East, has been a growing centre of medical culture for many years. Attracting historical tourism as well as medical tourism, Jordan has become one of the biggest medical hubs within the region, ever growing and developing its healthcare systems and technologies. Being the first country in the ME to put a clinical trial law into action in 2001, Jordan has attracted many clinical studies of all phases, constantly developing its laws, sites and investigators.

Having a total area of 89,342 square kilometres and positioned as a gateway to the ME, Jordan is quickly becoming a great attraction for healthcare and medical investment. A large section of this investment is in the fields of clinical and biomedical research. Development of the medical healthcare system began in the 1950s, with the Ministry of Health establishing several institutions that would later on prove to be the pillars of the healthcare infrastructure. In 1953 a nursing college was established, followed by a central laboratory for medical tests in 1955, in addition to the first healthcare insurance system for armed forces, which later became available for civilians (1963 and 1965 respectively).

Throughout the past 50 years, the healthcare system has seen an exponential growth in its many fields; healthcare insurance is provided to citizens with many companies offering the best insurance policies, laboratories are equipped with the latest and most up-to-date equipment, and hospitals have gained worldwide accreditation. All of these factors have played a major role in the advancement of Jordan into the ranks of the most sought-after healthcare provider in the ME.

Hospitals such as the Jordan University Hospital (JUH), the first educational hospital in Jordan located in the heart of the capital Amman, and the King Abdullah University Hospital (KAUH), the largest medical structure in the north (both of which are University-affiliated) are primary healthcare providers as well as teaching institutions. The Jordan Hospital (JH) is an internationally accredited hospital, providing patient care as well as housing outpatient clinics with specialists in many fields. One other key hospital in the capital is the King Hussein Cancer Center (KHCC) which is the only specialist cancer centre within the ME, seeing approximately 3500 new cancer patients per year and providing care for adult and pediatric patients alike. This Center has international affiliations with the University of Texas MD Anderson Cancer Center and St Jude Children's Research Hospital (both ranked among the top specialist hospitals in the world) as well as others.

The technologically advanced and highly certified hospitals and research facilities, all holding international accreditations and certifications, as well as the well-educated and highly experienced workforce, have attracted physicians, patients, investors and clinical study sponsors from around the world. The country has an estimated number of 25,000 physicians, most of whom are board certified in European countries (including the United Kingdom) and the USA.

In addition, the attraction of clinical trials into the region brought about the establishment of clinical research units. Several hospitals now have a functioning research unit as the core operations centre of clinical studies within that hospital; such as the Pharmaceutical Research Center (PRC) at the KAUH and the Office of Scientific Affairs and Research at the KHCC.

Currently 73 clinical trials are registered on ClinicalTrials.gov and the strategic location of the Kingdom, specialised facilities, expert key leaders (as stated above) and fast approval time and competitive costs are only a few of the many factors that set Jordan on the world map for conducting clinical trials.

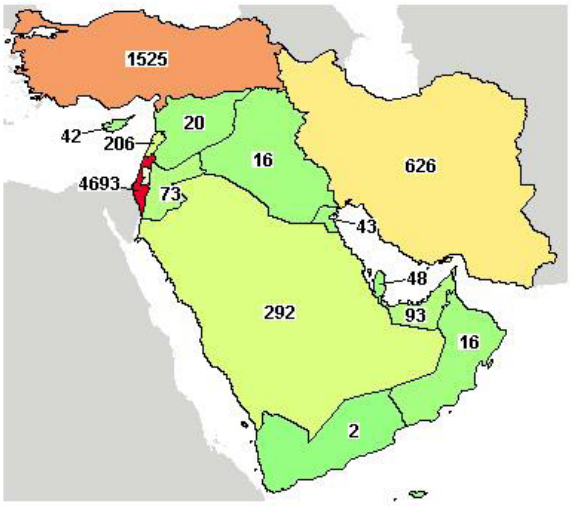


Image 1: Map of Middle East countries indicating the number of clinical trials currently registered at ClinicalTrials.gov

One of the most significant milestones in the advancement of Jordan within the pharmaceutical and clinical fields was the establishment of the clinical trials law in 2001 and the Jordanian Food and Drug Administration (JFDA) in 2003. Since then, a tight network of regulations, laws and guidelines have been woven to set Jordan and its hospitals into the world of clinical research on an international level.

At the moment there is a rather intricate system in place that is alive and adapts to the requirements of clinical trial processes and allows for the advancement of Jordan within the world of clinical research. The JFDA plays a great role through its Clinical Trial Unit (CTU) / Clinical Study Division (CSD) by being involved directly with the hospitals and providing proper accreditation for the hospitals it judges qualified to carry out clinical trials. Accreditation is given to the site where the clinical trial is to be carried out; the laboratories as well as the institutional review board of the hospital. In turn, the hospitals are required to conform to the local JFDA requirements prior to, during, and after the completion of clinical trials.

The Clinical Study Division was established in 2004 with the purpose of monitoring clinical trials in Jordan, and is responsible for the review of applications for site accreditation and IRB accreditation, inspection of sites periodically and the review of proposed protocols.

In 2001 a temporary law was passed: the clinical research law in Jordan was passed in order to provide continuous oversight

over the conduct of clinical studies, and to set a framework of regulations for the increasing number of pharmaceutical companies conducting clinical studies in Jordan; thus making Jordan one of the few countries within the Middle East to have a national regulatory framework governing the conduct of clinical trials and safeguarding and protecting human subjects.

The Law (2001) was based on the Declaration of Helsinki, and thus combines the importance of the formation of an IRB with the requirements conforming to those of ICH-GCP indicated in Article (4), which also specifies which entities are entitled to form IRBs; private hospitals, research institutions and pharmaceutical manufacturing companies, as well as universities and academic institutions.

This Law (2001) also stresses the importance of scientific value, and requests that a protocol be prepared to include a reasonable justification for the conduct of the study, while stating that the protocol requires IRB approval, thus also instituting that scientific validity be maintained.

When addressing the issues of risk minimisation, the clinical trial law (2001) states in several sections that risk to participating subjects should be minimised; Article (5) clearly states that studies must not be performed on patients unless the latter have undergone the required medical tests necessary for maintaining safety of participants.

The above issue is also indirectly stressed in Article (4), which provides the criteria required for the institution to be considered for conducting a trial; public and private hospitals must have the technical capabilities to provide patients and subjects with intensive care and emergency facilities, as well as the capabilities to perform any laboratory or diagnostic testing. In addition, universities and academic institutions, as well as specialised scientific research institutions, can conduct research provided they have the technical capabilities to perform the required activities and provide the necessary patient emergency and intensive care.

The Jordanian Clinical Trial Law (2001) also stresses the roles and qualifications of the principal investigator, stating that the principal investigator is held responsible for the conduct of the study, that he/she be qualified to supervise the trial, and that at all times a qualified physician be available on site to provide the necessary care required for the participating patients.

When protecting the rights and welfare of the patients in Jordan, the Clinical Trial Law (2001) states that the sponsor / party conducting the trial is legally responsible for any injuries to participants that may occur during the study, and the CTU/CSD requires the insurance to be equal to that given to participants in other countries, to ensure equality and a letter stating that the insurance conforms to the Clinical Law Articles (4C) and (5M).

When stressing the importance of informed consent, the clinical trial law (2001) stresses that participation in clinical studies can only take place after obtaining written approval of the patient by signing an informed consent document. One strong aspect of the regulation of clinical trials and compliance to the clinical trial law (2001) is the requirement of the CTU/CSD for adverse event monitoring in coordination with the IRBs.

In addition to the above stated points, the clinical trials law (2001) incorporates a section devoted to highlighting the fines and punishments in the event that the law (2001) is not followed (Article 17). This integrates a sense of retributive justice and allows for strict adherence to the laws and regulations by all parties participating in the clinical trials.

In 2011, following comprehensive consideration by legal and scientific experts, the clinical trial law was revised and was amended and a permanent law was issued in January 2011. The modifications to the law concentrated on the importance of maintaining patient safety, and stressed the rights and wellbeing of the participants in clinical trials; including the importance of written informed consent and of the patients being fully aware of all aspects of the clinical trial and their rights to a medical insurance claim in the event of damage or harm (which was not stressed in the 2001 law).

Another amendment to the law emphasized the roles, responsibilities and functions of all the members of the CTU/CSD, in addition to detailing the penalties on any party participating in a clinical trial in the event of violations or misconduct.

It should be noted however, that despite the recent modifications, the clinical law (2011) has yet to be improved and some aspects require more emphasis, while others need to be mentioned. Even though the law states the importance of maintaining patient safety, there is no specific statement regarding an assessment on the risk-benefit ratio and achieving the proper balance. The CTU/CSD are highly involved in raising awareness of the conduct and the processes of clinical trials, where the JFDA has held several workshops on training interested healthcare professionals on good clinical practice, as well as providing easy access to all necessary information through their website. Sites can find out information on how to become accredited for clinical trial conduct, and sponsors can have access to information on which sites are approved, accredited and registered with the JFDA as well as the entire submission process.

Considering that Jordan began its ascent into the clinical trial market in 2002, within the past 12 years the number of clinical studies has grown, with a current total of 48 non-interventional studies and 25 interventional studies conducted (registered since the year 2002) out of which 45 (60 %) have been completed. The graph below shows the growth and evolution of the clinical trial market in Jordan since 2010.

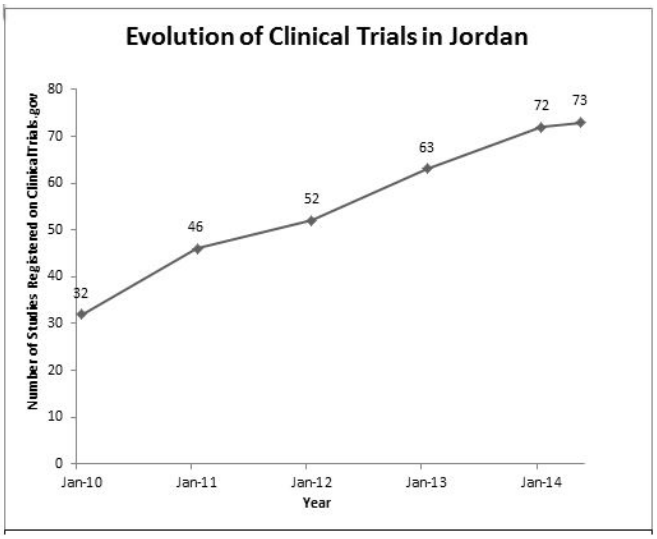
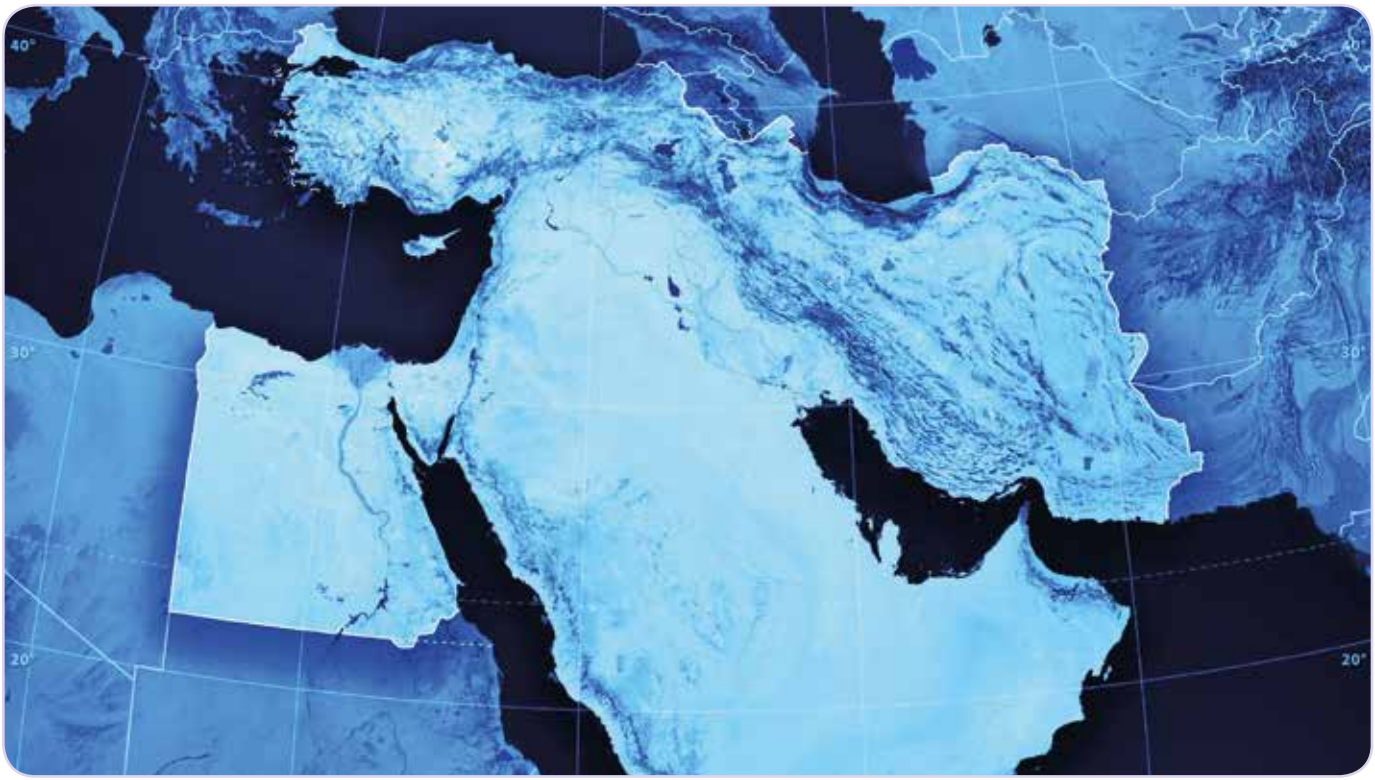


Image 2: Graph showing the evolution of clinical trials in Jordan since 2010 and the evolution of the clinical trial market as per data from clinicaltrials.gov



The regulatory supervision and adaptation of international standards and guidelines has impacted Jordan's position in the clinical research market; yet again, this is only one of the many reasons why Jordan is to be considered the rising star in the Middle East region.

The timelines for submissions are within reasonable limits, and since the sites use local IRBs which hold meetings every two to three weeks, it is reasonable to expect an answer from the IRB within a month from the date of submission. With regard to submissions to the JFDA, these require six to eight weeks to receive approval.

The requirements of the JFDA for submission adhere to the clinical trial law and are readily available for all interested parties and accessible through the JFDA website, along with all the forms which need to be completed and the timelines.

Despite Arabic being the official local language in Jordan, English is used professionally and educationally in parallel. Medicine and scientific studies are taught in English, and the investigators and medical staff are fluent in English. In addition, the documentation that is archived in hospitals and the patient medical notes are in English. During clinical trials, the IRB/IEC and JFDA require that information given to patients be translated into Arabic for ease of communication; however other study-related documents do not require translation, thus keeping the timelines short.

Another major aspect that plays an important role is the recruitment potential within the sites. It should be noted that Jordan holds the potential to be one of the top recruiting countries. Physicians and caregivers tend to participate in clinical trials with enthusiasm, and consider clinical trials to be an approach to provide patients with medication and services that could otherwise be unavailable or could not be afforded by patients. Conducting clinical trials in Jordan could prove a great financial advantage for sponsors, since the total cost of conducting a study in Jordan is less than that of the overall costs of conducting a similar study in Europe or the United States according to the Jordan Investment Board. And major investments in the health and medical sector for both private and public medical sectors have always opened gateways for the advancement of the medical and research technologies within the Kingdom.

In conclusion, it can be said that there are many aspects of clinical trial conduct in Jordan that are yet to be enhanced and developed, but the progression and increase in the mutual interest of both the key opinion leaders in conducting research, and the pharmaceutical and biotechnology companies in considering Jordan, has helped put Jordan on the list of the top countries in the Middle East conducting clinical studies.

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