MENA: The Dawn of a New Era

The Middle East and North Africa region has seen a recent increase in clinical trials research.

Clinical trials have had such a great impact on the global scientific community that interest in clinical research has transcended into regions that are relatively naive to conducting trials. Over the past few years the Middle East and North Africa (MENA) region has witnessed the dawn of a new era in clinical research. Though these changes have, by and large, not reached the entire scientific community, they have made a significant impact. Investigators are now beginning to appreciate the significance of conducting local trials.

The MENA region is considered one of the fastest growing economies in the world, with the key drivers being oil, gas, and petrochemicals. As a result, there has been significant investment in healthcare and modern hospitals incorporating state-of-the-art equipment—now available for the conduct of clinical trials. However, this economic growth has also brought about marked changes in lifestyles of the local population. Sedentary lifestyle, low physical activity, smoking, and an increasingly unhealthy diet have become a part of this society. Consequently, the MENA region is thought to be on the edge of a cardiovascular disease epidemic. Turkey, Saudi Arabia, and Egypt are considered the biggest recipients of Foreign Direct Investment (FDI) with investments ranging from $2 billion to $2.7 billion in order to address this issue. The governments of various countries in the MENA region are currently focusing on boosting foreign investment.

In order to boost FDI, hundreds of "free zones" have been introduced in the MENA region, which allow full foreign ownership of businesses. The incentives of free zones, besides allowing complete foreign ownership, are greatly simplified administrative and registration procedures for registration of new businesses. Some countries in the MENA region also offer complete exemption from private and corporate income taxes.

Many countries in the MENA region are also seeking to strengthen their trade partnerships with Europe through the Euro-Med trade agreements. Trade is also being promoted through the Pan-Arab Free Trade Area and the Gulf Cooperation Council (GCC)—these entities are in the process of seeking membership in the World Trade Organization (WTO). In May 2003, the Middle East Free Trade Area (MEFTA) initiative was proposed by the United States with the purpose of creating a United States/Middle East free trade area by 2013. The changes to business and trade processes in MENA countries are expected to facilitate the growth of clinical research conducted in the region.
Therapeutic areas of interest
Cardiovascular disease, diabetes, cancer, and chronic respiratory illness are widely prevalent in the MENA region. Obesity is also extremely prevalent in the region due to significant changes in lifestyle. Indeed, the World Health Organization (WHO) states that “increased consumption of more energy-dense, nutrient-poor foods with high levels of sugar and saturated fats, combined with reduced physical activity, have led to obesity rates that have risen three-fold or more since 1980 in some areas of North America, the United Kingdom, Eastern Europe, the Middle East, the Pacific Islands, Australasia, and China.”

Cardiovascular disease. There has been a considerable rise in the prevalence of hypertension, hypercholesterolaemia, and cardiac disease in the MENA region. Some pharmaceutical companies have undertaken a great commitment to help patients suffering with cardiovascular disease and have conducted clinical trials and epidemiological surveys to increase knowledge and progress the treatment of these diseases in the MENA region.

Diabetes. Diabetes is currently the fastest growing debilitating disease worldwide. Moreover, in the United Arab Emirates (UAE), diabetes is the second most prevalent in the world, affecting approximately 20% of people aged 20 to 79, with a similar proportion of the population at risk of developing the disease. Diabetes treatment currently consumes an estimated 40% of the national health care budget. In addition, heart disease related to diabetes was responsible for 31% of deaths in 2008.

A further five countries—Bahrain, Egypt, Kuwait, Oman, and Saudi Arabia—are among the 10 highest for diabetes prevalence worldwide. Over 26 million people in the MENA region have diabetes, which is the expected cause of approximately 200,000 deaths; as such, satisfactory epidemiological diabetes studies are warranted.

The impact of diabetes in the MENA region is of great interest to pharmaceutical companies, many of whom are currently investigating the effect of antidiabetic drugs in patients during Ramadan fasting. Fasting during Ramadan is an obligatory duty for all healthy adult Muslims and, although the sick are exempt, most Muslims insist on fasting. It is important for diabetics who wish to fast during Ramadan to undergo prior medical assessment and educational counseling. Clinical trials conducted in these patients will provide valuable data on dose requirements of antidiabetic drugs and the use of sustained release formulations. Since these patients are required to eat their main meal after sunset and before dawn, dosing has to be considered accordingly in order to maintain adequate glycemic control. It is also important to understand that for the person undergoing the fasting during Ramadan, any oral or intravenous medications taken during the fasting period is considered as breaking the fast, regardless if it is in response to a medical condition.

Diabetes in the MENA region is of interest to companies investigating the effect of antidiabetic drugs in patients during Ramadan fasting.

Obesity. The increased prevalence of obesity in the MENA region has become a major problem and is an established risk factor for other diseases.

Profound changes in society due to rapid modernization and changes in behavioral patterns are the major causes of this epidemic. Obesity has increased across all ethnic groups residing in the UAE, which is the fifth most obese nation worldwide, closely following Egypt, which is considered the fourth most obese nation globally. Sedentary lifestyle and unhealthy eating habits have also increased the prevalence of childhood obesity. In Qatar, 43% of children are overweight—a statistic that has prompted the Supreme Education Council of Qatar to initiate health awareness programs in schools to address the problem.

Cancer. The overall burden of cancer in the MENA region is rising. Current research is seeking to identify cancer trends which can provide an evidence base for governments to initiate health policy planning. Moreover, several collaborative cancer research programs are currently ongoing in the MENA region to enable the development of cancer control strategies. In addition, palliative care programs are planned or have already been implemented in some countries.

Metabolic disorders. Metabolic disorders such as hemoglobinopathies, glucose-6-phosphate dehydrogenase deficiency, and congenital malformations caused by recessive genetic diseases are common in the MENA region. The Catalogue for Transmission Genetics in Arabs (CTGA) lists the genetic disorders occurring in the Arab world. The orphan-designated Gaucher’s disease—(glucocerebrosidase deficiency) which results in fatty substance accumulation in the spleen, liver, bone marrow, and central nervous system—has been reported in the MENA region. Research is ongoing in patients with Gaucher’s disease to promote medical research and enable the patients to have access to investigational medications. In the UAE alone, as of October 2006, the CTGA database indicates the presence of 228 disease entries. Prevalence of this disorder and other genetic diseases in the MENA region is associated with consanguineous marriages. The tradition of consanguinity is mainly due to socio-cultural factors. In countries such as the UAE, Yemen, and Qatar there has been a rise in consanguinity leading to an increase in recessive genetic disorders, congenital malformations, and postnatal mortality.

Thalassaemia. There is a high prevalence of thalassaemia, a hereditary form of anaemia, in the MENA region due to the high prevalence of consanguinity. Initiatives have been
undertaken by several government bodies to keep a check on thalassaemia by offering premarital screening and services to those already affected.

Many people with thalassaemia require frequent blood transfusions to restore red blood cell levels, which can lead to an iron accumulation requiring chelation to eliminate the excess from the body. Patients with thalassaemia have no inherent mechanism to remove the excess iron, which, if untreated, can lead to significant morbidity and mortality. Advances in the management of thalassaemia and the introduction of patient-friendly medications have increased treatment compliance of thalassaemia sufferers. Ongoing thalassaemia clinical trials in the MENA region are seeking to improve patient satisfaction and compliance with iron chelation therapy.

**Sickle cell disease.** Sickle cell disease (SCD) is widely prevalent in Bahrain and the Eastern province of Saudi Arabia. Several studies have been published that evaluate the hematological findings and ascertain the nature of SCD in Bahraini patients. Within these regions, SCD is present with special features being hematological and clinically mild, with low mortality rate in adults and children.

The high prevalence of SCD in Bahrain and the eastern province of Bahrain is due to the malaria endemic which lasted until 1970. During this time hemoglobin in the local population underwent mutation to impair growth and development of malaria within the body. People, particularly children, are more likely to survive malaria infection if they have the sickle cell trait. The responsible mutated gene is inherited by the next generation, thus conferring a survival advantage.

**Date palm pollen and sandstorm dust.** Dates are commercial crops widely cultivated in the Middle East. The pollen production of the date palm is highly prolific and is widely dispersed into the atmosphere; this is a common cause for asthma and seasonal allergic rhinitis, which are common conditions in these regions. In addition, sandstorms regularly occur in summer and sandstorm dust is a known trigger for allergic and non-allergic respiratory ailments.

**Clinical trial approvals in the MENA region**

There has been an increase in clinical trials conducted in the MENA region in recent years, largely due to the prevalence of the conditions described above. Consequently, there is a growing need for support and training in order to conduct studies in these countries. Clinical trial approvals in MENA region countries can be complex and time consuming. Sound local knowledge is of paramount importance and can expedite approval timelines. Therefore it is imperative that pharma companies and clinical research organizations (CROs) have a clear understanding of the regulatory requirements in the MENA region in order to obtain timely approvals and fast study start-up. Due to the complex requirements of the ethics committees (EC) and regulatory authorities (RA) in the different MENA regions it is recommended that the advice of local regulatory experts be sought to minimize delays during the start up activities.

Clinical trial applications in the MENA region are reviewed by the relevant country's EC(s) who provide a written notification of their approval or rejection. Some countries operate with a central EC which issue a single opinion; however a majority of countries in this region have local ECs. Most of the countries in the MENA region have a regulatory body that provides clinical trial oversight. Recently established regulatory bodies include the Saudi FDA in the Kingdom of Saudi Arabia and the Jordan FDA in Jordan. In other countries the Ministry of Health (MoH) acts as the regulatory body. The ECs and RAs operate in accordance with ICH-GCP guidelines and local regulations. The RAs of most MENA countries have websites in English which lists the procedure and documents to be submitted for clinical trial applications. Although parallel submission of clinical trial applications can be made to the ECs and RAs in a few countries, most countries allow only sequential submission (i.e., the clinical trial application can be sent for RA review only after EC approval has been obtained). There is also a need for adaptation of clinical trial documentation, including the informed consent form, to local requirements. All countries in the Middle East require patient-facing documents to be translated into Arabic, whereas North African countries may also require French translations. Investigational Medical Product (IMP) import procedures vary between MENA countries. In addition, some countries require approval from other authorities for the export of biological samples and IMP back to the originator (if necessary).

Lebanon is a country of interest as it requires only the ethics committee approval and does not require regulatory authority authorization. Therefore the time required to start a clinical trial in Lebanon is typically shorter than that in the other MENA countries.

Egypt is another attractive market for clinical trials due to relatively smaller costs and a large treatment-naive population. As such, there has been a steady influx of foreign companies into the country. Egypt has a particularly high hepatitis C prevalence, thought to be linked to the mass treatment campaigns for schistosomiasis, which used inadequately sterilized needles resulting in widespread transmission of the disease. Hepatitis C is a primary cause of liver cancer and incidence rates in Egyptians are five to seven times as high compared to the general population.

Saudi Arabia is currently leading amongst the GCC countries for clinical trials. Hospitals in Saudi Arabia generally have a good infrastructure with well-qualified inves-
tigators experienced in global clinical trial participation. The Saudi Arabian pharmaceutical market is one of the largest in the Middle East and represents 65%, or $1.7 billion, of the pharmaceutical market in GCC countries, which is currently valued at $2.7 billion per year. In December 2005, Saudi Arabia became a member of the WTO and currently its trade-related aspects of intellectual property rights are compliant with liberalized foreign investment in all economic sectors. There is however a list of excluded activities that is not open for foreign investment that is held by the Supreme Economic Council.

Of late, the UAE has also opened up to clinical research and has hospitals with state-of-the-art infrastructure and Joint Commission International Accreditation. A considerable number of clinical trials are currently ongoing in the UAE and it is expected that this will increase.

Since the MENA countries are still in the emerging phase as far as clinical research is concerned, the costs for conducting clinical trials are not as high as in the United States and Europe. This is an advantage as most global companies are currently seeking to curtail costs and ensure economical conduct of clinical trials. Previously the MENA region was not very open to conducting clinical trials and hence very few trials have been conducted. However, in recent years there has been a remarkable difference—as noted on clinicaltrials.gov—there has been a steady increase in the number of clinical trials in the MENA region. Expediting regulatory reforms, improvements in training, and growing experience are the main reasons for this increase in clinical research conducted in the region. There are 31,309 clinical trials worldwide, of which the United States accounts for 52% of them, whereas the MENA region accounts for 5.5%. The increase in the number of clinical trials reported on clinicaltrials.gov and the increase in the number of FDA inspections in these regions indicates that there is a substantial growth in the region as far as clinical trials are concerned.

Need for clinical research training

The increasing number of clinical trials conducted in the MENA region mandates that all involved personnel undergo the necessary training to work on increasingly complex studies. The importance of training is to ensure adequate quality in clinical trials and adherence to international guidelines. Clinical research trainers can educate and mentor those new to clinical research to meet the challenges of conducting trials in such emerging markets. Education on quality assurance, regulatory affairs, and monitoring provides new clinical research staff with the basic training required to work on trials. For experienced clinical research personnel, this training provides an opportunity to refresh current understanding and keep abreast of regulatory changes that can severely impact the running of clinical trials. Some CROs operating in the MENA region have embarked on a mission to highlight the importance of education and training, many of whom are now providing comprehensive training courses covering all facets of clinical research to address this need.

Conclusion

The MENA region is of great importance in clinical research and has yet to reach its full potential; the number of trials conducted there continues to increase. The rise in clinical research in the MENA region is the result of a cooperative, multidisciplinary effort of the regulatory authorities, ethics committees, investigators, pharma companies, and CROs. Continuing this cooperation is key to the further development and establishment of the MENA region in the global marketplace for clinical research.

References


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