



Expected Growth of Industry-Sponsored Clinical Trials in the Middle East Benchmarked on other Global Regions

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Executive Summary

The evolving business model in the biopharmaceutical industry depends on increased productivity in clinical trials. This demands lower-cost, faster and more effective clinical trial processes. These needs encourage biopharmaceutical companies to expand clinical trial programs into emerging regions. In the Middle East, Turkey and North Africa (MENA), the combination of a high population, a low number of current clinical trials and a growing market for biopharmaceuticals makes an appealing region for expanded clinical-research opportunities. Given that MENA's market for biopharmaceuticals currently outstrips the volume of clinical trials conducted in the region, increasing expectations from regulatory agencies, as well as governments, demand a better balance between these metrics. Based on these drivers and a quantitative analysis of the global market for clinical trials, MENA's percentage of global clinical trial patient-related R&D spend could increase by a factor of 8-10 in the next decade. To fulfill the technical and staffing needs of such growth, the biopharmaceutical industry will probably rely heavily on contract research organizations (CROs). As a result, the annual CRO share of the clinical trial market in MENA could reach hundreds of millions of dollars in the next 10 years.

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Introduction

The Middle East currently fails to attract a significant volume of clinical trials, but that will change over the next decade. In MENA, the population equals about 600 million, which is about 9 percent of the world's total. Nonetheless, MENA, excluding Israel, hosts only approximately 0.4 percent of clinical trial sites and patients (for the purpose of this article Israel is not included under MENA because, although geographically part of the region, in terms of clinical trials development ranking Israel is deemed a developed market and does not share the emerging market characteristics of the Arabic Middle East and Turkey). Despite the imbalance between the region's population and the volume of clinical research, MENA already accounts for about three percent of the global revenue for biopharma, and projections predict strong growth for this metric. Consequently, MENA's clinical trial revenues should increase almost 10-fold over the next decade, which will build an annual market of about \$1 billion.

Given the projected flat growth of biopharma R&D expenditures in the coming years, to increase the proportion of the clinical trial market in MENA, it must decrease in other locations. Several lines of evidence already indicate decreases in certain geographies are already taking place. For instance, Seth Glickman of the Duke University School of Medicine and his colleagues reported that about 94 percent of the clinical trials conducted in 1995 took place in North America and Western Europe, but this fell to about 79 percent by 2005.¹ That's a 15 percent drop in just a decade. Other sources of evidence indicate that the global migration of clinical trials continues. For example, the European Medicines Agency (EMA) reported that nearly 80 percent of the patients in pivotal clinical trials in 2005 came from the European Union (EU) and North America, but that figure dropped to 66 percent by 2008.² Nonetheless, the percentage of trials being hosted in the EU and North America did climb back to about 76 percent for 2009, even though the percentage of North American patients declined from nearly 43 percent in 2005 to 34.5 percent in 2009.

Other studies also indicate ongoing changes in the global distribution of clinical trials. For instance, Johan P. E. Karlberg, director of the Clinical Trials Centre at the University of Hong Kong, reported that North America and Western Europe lost 4.3 percent of their clinical trial sites—about 6,500 sites—to the rest of the world from October 2007 through December 2008.³ Moreover, data published by Karlberg indicate that this trend continues.⁴

What is causing these global shifts in clinical trial locations? In short, the biopharmaceutical industry moves the location of clinical trials in hopes of boosting productivity by shortening the duration of the trials and reducing the cost per clinical trial patient.

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According to the EMA, a collection of factors contributes to the industry's interest in conducting clinical trials in a wider range of countries.⁵ These factors include:

- > *the higher availability of emerging-region patients with the relevant disease profile who are willing to participate in clinical trials*
- > *fewer potential patients are available in developed countries*
- > *the availability of qualified investigators in emerging countries*
- > *emerging regions providing cost-reduction opportunities*
- > *potentially faster clinical trials in emerging countries*

Conducting clinical research in new countries also provides an opportunity to get started on regulatory and marketing approval in those locations.

Although new regions can offer powerful incentives for expanding clinical trials, some challenges also exist. For example, some apprehension remains about the quality of clinical trials conducted in emerging countries. As an EMA paper states: "There is growing concern both among regulators and in public debate about how well these trials are conducted from an ethical and scientific/organisational standpoint (including GCP compliance) and about the available framework for the supervision of these trials."⁶ Likewise, scientific investigators pose questions about these trials. In terms of the results from clinical trials run in emerging regions, for instance, Glickman and his colleagues asked: "Are trial results accurate and valid, and can they be extrapolated to other settings?"⁷ In general, the answer appears to be: Yes. In fact, one quantitative analysis of the existing data provides a positive impression; when Karlberg examined all U.S. Food and Drug Administration (FDA) site-inspection findings for 1997–2008, he found that the highest percentage of inspection deficiencies came from sites in Western Europe, followed by North America, and no site inspection for a location in the rest of the world indicated false data that were reported to the FDA.⁸

The ongoing trends in the pharmaceutical industry of expanding the locations for clinical trials plus MENA's demographics serve as the fuel that will set off an explosion of clinical research activity in this region in the near future.

MENA's Current Market

Before exploring where MENA is heading—in terms of being a desirable site for conducting clinical research—its current status must be described. My analysis of the global geographic distribution of industry-sponsored clinical trial reveals that developed countries keep 78 percent of the sites and 65 percent of the patients.⁹ In contrast, the emerging regions currently capture 22 percent of the clinical trial sites and 35 percent of the patients, but MENA grabs only 1 percent of that emerging-market share.

For now, Central and Eastern Europe (CEE) and the Commonwealth of Independent States (CIS: includes Russia, Ukraine, as well as some other countries of the former USSR [Belarus, Kazakhstan, Kyrgyzstan, Tajikistan, Uzbekistan, Azerbaijan, Georgia, Moldova, Armenia and Turkmenistan]) rank as the top emerging regions for clinical trials. In combination, these regions accounted for 41 percent of the clinical trial patients from emerging regions, even ahead of Asia's 16 percent. CEE and CIS also attracted a total of almost \$5 billion in patient recruitment–related spending on clinical trials. MENA, on the other hand, attracted just over \$100 million. In addition, MENA's clinical trial–patient density—the number of clinical-trial patients per 1 million people in the population—is less than 1 percent of U.S. levels, when excluding Israel. These statistics indicate that MENA's potential for providing clinical-trial sites and patients is not being reached, nor even approached.

Beyond the mere potential to host more clinical trials and produce more patients, data from this region denote another benefit: productivity. In particular, data collected on patient recruitment–related site productivity—defined as the average number of patients recruited per site in a country—indicated that MENA, in terms of patients recruited per site, is more productive than the U.S. In fact, some parts of MENA proved incredibly productive: for example, the combination of Egypt, Jordan, Lebanon and Syria produced a patient recruitment–related site productivity of 475 percent of U.S. levels. So MENA is ripe for more clinical trials and evidence already shows that this region can produce exceptional results.

MENA's Allure

So far, the biopharmaceutical industry usually overlooks MENA when searching for emerging markets where clinical trials might supply higher productivity at lower costs. In large part, the industry has sidestepped MENA because of its negative reputation, especially in the United States, generated by international media coverage, which publishes images of terrorism and war. Much like images of violence in the United States do not depict the country in general, the same can be said for MENA.

Even though the drug-research industry might not see MENA as a key clinical trial region today, it will be. The expected growth of biopharmaceutical sales alone in MENA will be a driving force moving more clinical trials to the region. One 2009 report predicted 10–15 percent annual growth of pharmaceutical sales for the region.¹⁰ This puts MENA in the top three—maybe even the top two (behind Asia)—emerging market–growth opportunities. Moreover, discussions with regional biopharma directors indicate that they now demand a fair share of R&D projects for the MENA region, to help them leverage their companies' R&D muscle when discussing facilitated marketing authorization approvals for new products, and/or negotiating pricing and reimbursement of products with local governments. In addition to expected market growth, two other factors will drive clinical trials to MENA. One factor comes from the region's special patient populations and high prevalence of disease. For example, people in MENA exhibit the world's second highest prevalence of diabetes, as well as high prevalence of more than 700 genetic disorders caused in part by high percentage of consanguineous marriages.¹¹ Many of these diseases—including Gaucher's disease, Fabry disease, Behcet's disease, thalassemia and sickle cell anemia—have orphan status. The region also faces a high prevalence of hepatitis and growing levels of asthma, cancer, cardiovascular disease and obesity.¹²

The third growth factor comes from the search for sites that produce higher site productivity in clinical trials, which has long been the key reason to look beyond traditional markets. The high density of clinical trials in North America, Western Europe and more recently even CEE, spurs the biopharmaceutical industry to explore new regions, and this adds to the appeal of MENA, which currently offers a much lower density of clinical trials. Furthermore, MENA possesses several other desirable features:

- > *highly centralized healthcare systems*
- > *many world-class healthcare facilities*
- > *hospitals and physicians interested in participating in clinical trials*
- > *governments and institutions focused on attracting clinical research*
- > *Western-trained investigators with excellent command of English*
- > *hospital source documents in English or French (except Turkey and Syria)*

Regulatory agencies supply the final factor that makes a region desirable, or not, for clinical research. Documents from the EMA state that well-conducted trials depend on the quality of the data, not where the data were collected, and the data will only be rejected if they fail to comply with GCP and/or ethical requirements.¹³ In addition, the same EMA document notes that countries must participate in clinical trials to develop frameworks for clinical research and healthcare systems in general, and that clinical trials bring benefits to the local professionals, as well as patients. Consequently, EMA guidelines do not discourage MENA-based clinical trials in any way.

Potential Growth in MENA's Market

To forecast MENA's growth potential, we gathered data for three categories: the percentage of global clinical trial patient-related R&D spend; the pharma market-significance indicator; and clinical trial-patient density (see Table 1). Please refer to our published work for details of methodology of global patient recruitment-related R&D spend analysis as well as clinical trial-patient density.⁹

For the purpose of the analysis in this paper, national/regional GDP (expressed as a percentage of global GDP, as measured by the World Bank for 2009) has been used as a surrogate for "country/region pharma market significance" due to the following reasons:

1. While pharma market size data exists (e.g. IMS) for the established markets, and some of the leading emerging markets, such data cannot be found for many of the smaller emerging markets.
2. Percentage of global GDP is a better indicator of future sales potential of emerging countries/regions since sales of global pharma tend to be underperforming in majority of the emerging markets, but now pharma are putting a lot of efforts in capturing growth in the emerging markets to replace vanishing growth in developed markets. Such emerging markets focus, combined with healthcare spend growth ahead of overall GDP growth, projected in many of the emerging markets, will tend to bring emerging regions' pharma market size as a percentage of global market closer to the percentage of their respective contributions to the global GDP. Other sources support this approach.¹⁴

For developed countries, the cumulative percentage of global clinical trial patient-related R&D spend and the pharma market-significance indicator are 65.3 and 64.2 percent, respectively. Given that the bulk—more than 70 percent—of the R&D spend in those countries does not relate directly to patient recruitment, even reducing the patient-related spend by as much as 50 percent would decrease the overall R&D spend in developed countries by only about 10 percent. Still, moving trials to other locations, including MENA, makes sense, especially when considering the cost reduction in combination with the reduced clinical trial-patient density. For example, in MENA—excluding Israel—the clinical trial-patient density is only 0.7 percent of U.S. levels, whereas the developed countries as a group hit 70 percent of U.S. levels.

When considering the CIS and Latin America, the data in Table 1 show good matches between the cumulative percentage of global clinical trial patient-related R&D spend and the pharma market-significance indicator. Consequently, only the low clinical trial-patient densities are expected to attract more trials to these regions.

In CEE, future growth of clinical trials seems unlikely. For one thing, the cumulative percentage of global clinical trial patient-related R&D spend exceeds the pharma market-significance indicator by a factor of 3.8. That is, proportionally more of the biopharma spend is being invested in that region than it gives back in terms of sales. Moreover, the clinical trial-patient density in CEE is 85 percent of the U.S. level and almost 20 percent higher than Western Europe's. Consequently, CEE is likely to lose clinical trials to other emerging regions.

For Africa, the cumulative percentage of global clinical trial patient-related R&D spend exceeds the pharma market-significance indicator by a factor of 2.5. After removing South Africa, however, that metric reverses, such that the pharma market-significance indicator exceeds the cumulative percentage of global clinical trial patient-related R&D spend by a factor of 1.3. Still, the continent's low pharma market-significance indicator does not make a promising case for attracting more clinical trials, despite the very low clinical trial-patient density. In sub-Saharan Africa, for instance, the low pharma market-significance indicator of 0.78 percent does not encourage an increase in clinical trials overall, but the region might attract more clinical trials for treatments of regional diseases, such as AIDS, malaria and tuberculosis.

The numbers for Asia and MENA, however, do forecast the attraction of an increased number of clinical trials. In Asia, the pharma market-significance indicator exceeds the cumulative percentage of global clinical trial patient-related R&D spend by a factor of almost 3, and its clinical trial-patient density is only 2 percent of U.S. levels. In MENA, the pharma market-significance indicator exceeds the cumulative percentage of global clinical trial patient-related R&D spend by a factor of more than 9, and its clinical trial-patient density is only 0.7 percent of U.S. levels. In both of these broad regions, these metrics suggest a strong growth in their clinical trial markets over the next decade. That growth, however, will likely come at the expense of clinical trials lost in CEE, the United States and Western Europe.

In this context it is important to mention that the projected geographic movement of clinical trials driven by factors outlined in this paper may be substantially accelerated or mitigated by actions of local governments: these include R&D incentives, regulatory requirements for proof of conduct of in-country clinical trials as part of marketing authorizations, ease of clinical trial submission of approval process, as well as simplification of administrative hurdles for movement of clinical trial materials in and out of the country. Thus governments will play a significant role in shaping future geographic distribution of clinical trials.

In addition to the economical factors described above, there is a strong ethical factor which will support movement of clinical trials to Asia and MENA: this stems from the ethical dilemma which biopharma companies, governments and national regulatory agencies in Asia and MENA will need to address: in case of these two regions there appears to be violation of one of the key ethical principles of clinical research, the principle of Justice, requiring fair distribution of the burdens and benefits of research: aiming to achieve 16% and 4% of global sales in Asia and MENA respectively while only contributing 5.6% and 0.4% of global clinical trials respectively, appears to be globally unfair and not sustainable. Consequently, both economic and ethical concerns will drive more clinical trials to Asia and MENA.

Table 1

Directional analysis of future-growth potential of the pharmaceutical market based on the current percentage of global clinical trial patient-related R&D spend, pharma market-significance indicator, and clinical trial-patient density, which indicates the level of untapped recruitment potential. See the text for details on the basis behind each category. The data depict a country or region's future-growth potential as strong (green), negative (purple), or based on access to patients (blue).

Region	Percentage of Global Clinical Trial Patient-Related R&D Spend (%)	Pharma Market-Significance Indicator (%)	Clinical Trial-Patient Density (%)
DEVELOPED COUNTRIES			
North America	35.5	26.6	101.0
Western Europe	27.8	27.3	65.0
Australia/New Zealand	1.6	2.0	58.0
Japan	0.4	8.4	3.0
Sub-total developed countries	65.3	64.2	70.0
EMERGING COUNTRIES			
CEE (excluding Russia and CIS)	11.0	2.9	85.0
CIS (including Russia)	3.6	3.6	13.0
Asia (excluding Japan)	5.6	16.6	2.0
Latin America	9.9	7.4	17.0
MENA (excluding Israel)	0.4	3.7	0.7
<i>Israel</i>	1.3	0.3	173.0
<i>Turkey</i>	0.2	0.2	2.9
<i>MENA (excluding Israel and Turkey)</i>	0.2	3.6	0.4
<i>Arabic ME</i>	0.13	2.6	0.5
<i>Levant (Lebanon, Jordan, Syria) + Egypt</i>	0.07	0.5	0.6
<i>North Africa (excluding Egypt)</i>	0.05	0.7	0.6
<i>Gulf (Saudi, UAE, Oman, Qatar, Bahrain, Kuwait)</i>	0.004	1.5	0.1
Africa (excluding North Africa)	3.0	1.2	3.5
Sub-total emerging countries	34.7	36.4	6.0
ALL REGIONS	100.0	100.00	15.0

MENA's Future Pharma Metrics

The prediction of more clinical trials being conducted in MENA also raises this crucial question: How much will MENA's clinical trial market grow? MENA's current percentage of global clinical trial patient-related R&D spend of 0.4 percent equates to about \$130 million. If its clinical trial-patient density of 0.7 percent increases over the next decade to 10 percent of current U.S. levels—a very conservative estimate, well below the levels of CEE, CIS and Latin America—MENA's percentage of global clinical trial patient-related R&D spend would climb to 2.6 percent, which equals a value of \$850 million. If the clinical trial-patient density increases to 20 percent of U.S. levels—still a reasonable estimate, because it would be far less than CEE and just a bit more than Latin America—MENA's percentage of global clinical trial patient-related R&D spend would grow to 3.8 percent, which would generate an investment of \$1.2 billion for the region.

The conservative scenario—increasing the percentage of global clinical trial patient-related R&D spend from \$130 to \$850 million—requires only a 20 percent compound annual growth rate (CAGR). Such a CAGR seems quite modest given the very low clinical trial-patient density in MENA compared with its pharma market-significance indicator (significantly higher annual clinical market growth rates have been recorded in CEE during 1995-2005).

The most likely countries for this growth in MENA will be Egypt, Saudi Arabia and Turkey. The next tier of MENA's clinical trial-growth centers will be Algeria, Jordan, Lebanon, Morocco, Tunisia, and the Gulf cluster, composed of Kuwait, Qatar and the United Arab Emirates.

To reach this clinical trial-growth potential, more clinical trial personnel and services must be available in MENA. Given that most biopharmaceutical companies already show reluctance to increase their internal staff for clinical research in other regions, these companies will probably not develop in-house departments across MENA. Consequently, biopharmaceutical companies may fill some key positions in-house, such as clinical research-management positions, and outsource the conduct of clinical trials to CROs. As a result, CROs might capture 60–80 percent—possibly more in some countries—of the addressable market, which could generate \$300–500 million in annual CRO revenue in 10 years.

In summary, the globalization of clinical trials that started more than 15 years ago should expand even more in the next 10 years. Driven by the biopharmaceutical industry's requirements of increasing the productivity of clinical-development programs, emerging regions could attract a significant increase in their share of the clinical trial market. In addition, in support of their marketing interests, biopharmaceutical companies must improve the balance between the locations of pharmaceutical markets and clinical trial sites and realign R&D investment in countries/regions with expected returns from sales. This combination of a search for improved productivity from clinical trials and realigning the sites to better match the sales markets promises will fuel a significant increase in the number of clinical trials conducted in MENA within the coming decade.

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