

## R&D Directions

### 'Globalization' may have broad strokes, but its effects on drug research in three particular regions is clearly evident

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Nov/Dec 2009

No longer solely the domain of major players in the United States and Europe, the pursuit of new and innovative drugs for burgeoning patient populations has blurred lines around the globe. High on the list of new pharma frontiers are South America, the Middle East, and Africa.

"There are pressures in all geographies from an expanding middle class demanding increased access to healthcare and, by implication, access to new drugs," says Steve Heath, VP, head of EMEA operations, **Medidata Solutions** (mdsol.com), a global provider of clinical development solutions. "As such, all these regions represent market opportunities for pharma."

**IMS Health** endorsed that point in October, predicting a 4% to 6% growth rate for the drug industry as a whole in 2010 – driven by strong near-term growth in the U.S. market – and a 4% to 7% annual growth rate through 2013, taking into account, among other factors, the impact of a global macroeconomy on market demand. Global market value is expected to expand to more than \$975 billion by 2013.

"While our outlook for the global market is more positive than earlier this year, the industry still faces funding pressures, a potential gap between new drugs and expiring patents, potential healthcare law changes, and a weakened global economy," says Murray Aitken, senior VP, healthcare insight, **IMS** (imshealth.com).

#### South of the border

Specifically contributing to the worldwide advance are the major markets that comprise South America – including Brazil, Argentina, and Venezuela – which are expected to represent a market value of \$63 billion by 2012, according to **Espicom Business Intelligence** (espicom.com). The region accounts for 7% to 8% of global pharmaceutical sales, though some forecasts predict the growth rate will approach 20% during the next several years.

Brazil is the region's largest single component and the sixth-largest individual market in the world, with a \$13.6 billion value in 2007 that showed 18% net-dollar growth compared with 2006. Generic drugs are expected to represent 20% of Brazil's pharmaceutical sector by the close of 2009.

Argentina's market was estimated at \$4.7 billion and is largely dominated by the world's top 20 pharmaceutical manufacturers. Venezuela's market worth is estimated at \$4 billion, though the country's future growth will depend heavily on governmentally regulated imports because domestic production has dropped significantly.

The region's overall patient population is particularly suitable for studies in oncology, cardiovascular, infectious diseases, metabolic disorders, pediatrics, and vaccines, because the incidence and prevalence of those conditions is similar or greater than in the United States or Western Europe. The Hispanic population in the United States is now 14% and is expected to rise to 25% during the next decade. Therefore, subjects can contribute to a new drug application patient database by making it more similar to the United States in terms of ethnic origin distribution.

"With more than 500 million people – double the population of the United States – Latin America offers a large population for patient enrollment in clinical trials," says Wendy Buckland, VP, clinical development, **PPD Inc.** (ppdi.com), a contract research organization.

More than 80% of Latin Americans live in highly urbanized areas, meaning patients are easily accessible to participate. "Many investigators were trained in North America or Europe and are eager to participate in clinical trials," Ms. Buckland says. "In addition, the region has reputable health science and academic institutions, which serve as a tremendous resource for conducting clinical trials."

Latin America's adoption of clinical trial management tools such as electronic data capture has followed a pace similar to the United States and Europe. Internet usage in the major metropolitan areas is high, making it easier to implement at the physician site level – which was previously a limiting factor.

Expenses are being reduced by an estimated 10% to 50% by conducting trials in emerging regions such as South America, due to lower clinical and hospital costs outside the United States.

Conversely, regulatory approval times have historically been the greatest challenge for trials, although new and updated regulations in several countries have begun to improve the process.

“In addition to patient access and cost savings, there are a number of advantages in Latin America,” says Alcides Cupido, VP, Latin America clinical operations, **Quintiles** (quintiles.com), the world's largest contract research organization. “We are in similar time zones with the United States, and the reverse seasonality allows for seasonal studies – allergies, vaccines, etc. – when they cannot be conducted in the Northern Hemisphere.

“We also have excellent medical infrastructure and well-trained investigators in countries like Argentina, Chile, and Brazil, with standards and procedures in university hospitals similar to the United States, a tradition of Western medicine, and well-established regulations for clinical trials in most countries.”

Mr. Cupido also points out that Latin America houses a particularly large number of previously untreated patients in countries with no traditional history of clinical research.

Other specific regional challenges include bureaucratic requirements, importing/exporting processes, international shipping costs, language barriers, cultural differences, and lack of experience.

“It is up to the authorities, pharmaceutical and biotechnological companies, and CROs to rise to the challenge and perform high-quality, ethical trials to help speed up the development of new compounds globally, and to do so at more reasonable cost,” says Katie Margules, senior director of project management, Latin America, clinical development services, **Covance** (covance.com). Based in New Jersey, Covance is a publicly traded contract research organization.

### **Middle East management**

The pharmaceutical market in the Middle East is likely to grow by between 10% and 15% annually during the next three years, outpacing more mature markets, according to a report by **URCH Publishing** (urchpublishing.com).

URCH analysts predict massive growth for the pharmaceutical and biotechnology markets of Middle Eastern states, driven by moves to liberalize national economies, the introduction of mass health insurance, and the determination of the region's governments to become self-sufficient in pharmaceuticals production. All these factors are leading to large investments taking place in the private and public health sectors, with major benefits to the pharmaceutical industry.

The population of the Middle East now exceeds 370 million and is expected to reach more than 520 million by 2030. The growing population, dominated mainly by the expatriate community in most of the Gulf Corporation Council countries, has given rise to a rapidly growing market for healthcare and its associated industries – estimated at \$75 billion in the Middle East alone.

The biggest threat to pharma growth in the Middle East is a heavy reliance on the fluctuating price of oil, which dictates the strength of local economies and, in turn, is reflected in healthcare provision and the drug market.

“There is high potential for growth due to rapid economic growth as well as rapid population growth,” says Janos Filakovszky, VP, Eastern Europe and Middle East, Quintiles. “Clinical research potential of the Middle East today is comparable to Central and Eastern Europe 10 to 15 years ago, in terms of sites with very few competing studies, eagerness to participate in clinical research, largely untapped patient population, and willing, if somewhat inexperienced, regulators.”

According to Mr. Filakovszky, doctors in the Middle East are well-trained, have excellent command of English, and have international experience. He says many physicians have already logged significant

time in conducting clinical trials, with large drugmakers having run trials in the Middle East for a number of years.

According to [clinicaltrials.gov](http://clinicaltrials.gov), the number of industry-sponsored clinical trials conducted between 2006 and 2009 in Turkey was 250, followed by 56 in Egypt, 37 in Lebanon, 28 in Saudi Arabia, 10 in Jordan, five in Kuwait, two each in Bahrain, Qatar, and Syria, and one in Oman.

The overall pharmaceutical market in the Middle East is valued at \$12 billion, according to URCH. More than 450 pharmaceutical manufacturers are located in the region. With the exception of Egypt, Middle Eastern countries have high import rates of branded drugs. Egypt, meanwhile, is more than 90% self-sufficient.

Jordan is at the forefront of regulators in the region by establishing procedures at the level of EU countries and actively promoting the benefits of participation in trials to the public. Jordan was the first to develop a comprehensive law on clinical research, with Egypt, the United Arab Emirates, and Syria pursuing similar legislation.

Given the seemingly perpetual state of military flux in the Middle East, safety is a primary concern for outside entities wishing to conduct clinical research – though armed conflicts have had no direct effect on research.

“There are some areas where we only work with locally based staff, who understand any local sensitivities or tensions,” Mr. Filakovszky says. “In our more than 10 years of operation in the Middle East, military conflicts have never had any negative impact on clinical trial conduct.”

## **Into Africa**

On the southernmost tip of the continent, the Republic of South Africa far outpaces its African neighbors in terms of the vastness of its pharmaceutical market. The overall value of the market, which represents one of the world’s most diverse medical environments, is \$1.7 billion.

Although South Africa’s segregated regime ground to a halt more than a decade ago, rich urban areas retain many of the high-end facilities developed for whites during apartheid. In fact, only in recent years have rural areas and predominantly black townships begun developing modernized health services.

The region’s most serious and highest-profile healthcare concern is the HIV/AIDS epidemic. South Africa has one of the highest infection rates in the world but has little money to purchase antiretroviral treatments that are commonly available in the West.

After lengthy debate and many delays, the South African government finally passed its major piece of pharmaceutical legislation in May 2003 – the Medicines and Related Substances Amendment Act. The bill was aimed to bring national procedures more in line with international standards.

**“Dysfunctional health systems, combined with the burden of disease and poor patient education has led to an overwhelming increase in the number of disability-adjusted life years,” says Sohini Gowan, director, clinical operations – Johannesburg, Icon Clinical Research ([iconclinical.com](http://iconclinical.com)), a division of Icon Plc., a contract research organization. “Development of facilities and capabilities in the main cities in South Africa and Botswana mirrors those of developed countries. In sub-Saharan Africa countries where patients are restricted to remote sites, investment by government or industry sponsors is required to develop the necessary infrastructure, facilities, and site personnel capabilities.”**

Basic investments are regularly included in set-up budgets for prospective trial sites. They can include the provision of bicycles to field workers traveling from village to village, satellite phones and dishes for Internet connection, specialized packing materials to maintain temperatures across long distances, surge-protection units, and transportation for patients from remote sites to clinics.

Unique to Africa, the informed consent process is most often put into effect due to multiple local languages and dialects, the need for local community leader support of trials, familial consent, and cultural taboos.

Visual aids such as pictorial demonstration of study procedures are employed when dealing with illiterate patients or in areas where multiple dialects are in use. Additionally, community leaders, village chiefs, and traditional healers are sensitized to the benefits and risks of clinical trials before approaches to potential research participants are attempted.

“Africa is the last frontier in emerging markets, and companies need to start now if they want to be a part of the market in 10 years’ time,” says Gillian Corken, CEO, Quintiles Africa.

Ms. Corken is a native of South Africa. In June, Quintiles opened a new office in Ghana to handle the growing number of clinical studies conducted in western sub-Saharan Africa.

“Pioneering international and South African companies have shown the substantial and unexpected business potential across African markets since many have entered a new phase of growth, relative stability, and openness to business,” Ms. Corken says. “Economic growth is picking up, and Africa will be the fastest-growing region over the next five years.”