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Personalized Medicine Special

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Are they worth the time and investment?

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Recruiting at senior level amid the corruption fallout

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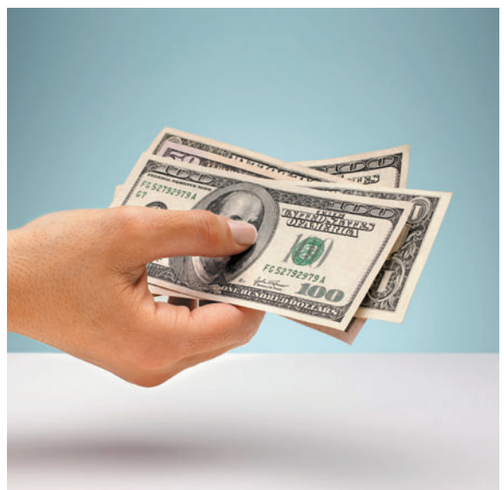

Is Your Anti-Bribery Strategy in Order?

It's not just US pharma that has to shape up to deal with the big uptake in bribery and corruption enforcement actions.

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Upcoming global conferences in the pharma space

Personalized Medicines: Worth the Effort and Investment?

Professor Franz P. Hessel questions whether personalized medicine and companion diagnostics are actually enhancing the drug development process.

Some stakeholders are afraid that the era of blockbusters will be replaced by a new era of 'niche-busters'.

Personalized medicine is sometimes regarded as a potential solution to the problems associated with the worldwide economic pressures on healthcare systems and on pharma companies to achieve drug reimbursement at premium prices for large patient population. But some stakeholders, for example, some European payers and reimbursement decision-making bodies, are afraid that the era of blockbusters will be replaced by a new era of 'niche-busters'. This means lots of additional high-priced drugs for small subpopulations of patients and additional high-priced biomarker tests, with the overall consequence of only slightly improved patient outcomes for a massive budget impact.

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A few years ago, for example, dozens of genetically different subgroups of patients all had the same diagnosis of colorectal or non-small cell lung cancer. But for only a few of those subgroups is a specific therapy available and recommended by clinical guidelines. It is therefore a myth that the pharmaceutical industry will be able to develop a new and efficient specific drug therapy for every individual patient or genetically differentiated patient subgroup.

Two sides to the coin

Looking at the number of new drugs approved by the FDA and EMA, we can say that personalized medicine technologies are on the increase. But the landscape has not changed dramatically. There are two sides of the coin, and the incentives for pharma to develop personalized medicine technologies are ambivalent.

There are a number of success stories of impressive gains of patient outcomes, but the development of genetically stratifying patients' therapy also bears risks and uncertainties. Neither the cost-effectiveness of personalized medicine technologies nor the efficiency of the drug development process is enhanced in every case. But there are promises that both objectives can be achieved.

Personalized medicine technologies are on the increase, but the landscape has not changed dramatically.

The most important factor by far in the drug development process is the extent of patient benefit. The proof of a convincing ratio of clinical benefits and drug safety compared to standard

treatment is necessary for approval by regulatory bodies and guarantees reimbursement for a premium price. Per definition in personalized medicine, a selection of the responders — or even a subgroup of patients with a better response — increase the average clinical efficacy of the drug for the remaining patient population, with equal frequencies of adverse events. Some personalized medicine drugs would therefore not have been approved without a stratifying biomarker test; for others the chances for an accelerated approval are enhanced by the use of a biomarker test.

Consequently, a companion diagnostic test might enable drug companies to achieve the necessary statistical power to demonstrate a medical efficacy in clinical studies, sufficient for approval with smaller patient sample sizes. Studies with a smaller sample size generally bear larger uncertainties about the results, unless the effect of the intervention is extraordinary powerful. With regard to this aspect, biomarkers can make a big difference.

Personalized medicine technologies lead to decreased development times, as well as smaller and possibly fewer clinical trials. Conversely, another inevitable consequence of a biomarker strategy to select the subgroup of patients responding to the drug is a narrowing of the indication.

The biomarker test is more than just a commodity.

Taking just these two aspects into consideration, lower development costs will be offset by lower revenue potential. The extent of the latter is mainly determined by the prevalence of the marker with regard to the number of positive test results. The case of Pfizer's crizitonib perfectly illustrates this, to a certain

extent, unforeseeable problem, especially as the prevalence of the marker (ALK) was much lower in routine care compared to the pre-launch pivotal studies.

The biomarker test, then, is more than just a commodity. The technical quality and performance of the test massively influence when and if a drug is used. The lower the prevalence of the marker, the more relative impact has the technical validity of the test.

From a drug development perspective, an additional challenge is to select the optimal test, test technology and cutpoint and to align the development and regulatory processes for both companions, the drug and the test.

But even assuming a perfect test, the prevalence of the marker determines the size of the target population. In some cases the number of patients remaining for clinical studies might be so small that it becomes difficult to recruit the required number in a reasonable time. A single-digit prevalence of a marker might make further development of a new drug unattractive to the manufacturer, in spite of a promising patient benefit. In addition to the simple calculation "less patients = less revenue", a low prevalence of the marker has further consequences to the drug manufacturer.

The road to reimbursement is still fraught with uncertainty.

Although the cost for the biomarker test usually is much lower than the drug costs, it has a considerable influence on the overall budget impact, as well as on the acceptance of personalized medicine by providers and patients if, for example, more than 30 patients must be tested to detect one patient suitable for the drug.

For new personalized medicine drugs, at least, the increased complexity of the drug–companion diagnostics technology, combined with uncertainties of reimbursement modalities, seems to be a barrier for adequate use. From a drug manufacturer's point of view this requires increased market access and marketing efforts.

In European countries with DRG-based payment systems in-patient care, especially, the reimbursement modalities of biomarker tests are complex, heterogeneous and often not transparent. Only a reimbursement of test and drug in addition to the DRG would help to avoid the problem of the right patients not getting the right drug because of insufficient incentives by reimbursement modalities that are not yet adapted to personalized medicine technologies.

The road to reimbursement

Generally though, personalized medicine drugs are potentially more likely to be successfully evaluated by reimbursement bodies in Europe. The increased potential for reimbursement by healthcare payers is accompanied by a higher chance to realize or keep a premium price. Although there is a history of less than three years, so far all personalized medicine technologies evaluated by the German reimbursement body G-BA were attested to have an additional clinical benefit. In comparison, about 35% of all evaluated new drugs were said to have no patient-relevant additional benefit.

Nevertheless, the road to reimbursement is still fraught with uncertainty for personalized medicines. Most reimbursement institutions base their decisions on strict criteria of evidence-based medicine. There are, for example, ongoing discussions about the required sample size and whether prospective-retrospective studies using biobank samples could

be classified as high-level evidence studies required for reimbursement.

Here to stay

Sequencing the human genome more than a decade ago initiated a new era of science. Genetically stratifying therapy is therefore a logical consequence; it is not a pharma industry invention aimed at solving the problem of blockbuster drugs approaching patent expiry. Pharma cannot ignore personalized medicine. Consequently, all research-orientated drug companies are investing in it, and they will continue to do so.

Co-development of drugs and companion diagnostics offers an opportunity to reduce the risk of drug development.

Recently, regulatory and reimbursement bodies have started to revise their approach to personalized medicine, although there is still much work to be done.

For all stakeholders there are uncertainties to consider, but overall co-development of drugs and companion diagnostics offers a great opportunity to reduce the risk of drug development, to increase return-on-investment for pharmaceutical companies, and to improve patients' healthcare without unreasonable increases of expenses. It can be a classic win-win situation if the right drug for the right patients is developed.

About the Author

Dr Franz P. Hessel (franz.hessel@srh-hochschule-berlin.de) is Professor of Healthcare Management at SRH University, Berlin, Germany.

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Pathology in the Era of Personalized Medicine

With their knowledge of molecular genetics, pathologists are transforming the way healthcare is provided, writes Jordan Sarver.

Pathologists will have an integral role in the new era of personalized medicine.

In its present form, healthcare is largely reactionary. The limited knowledge of the external factors that lead to various diseases has led to a "one-size-fits-all" approach to care. But personalized medicine, the idea of tailoring treatment of a patient based on his or her unique physiological characteristics, is poised to change the practice of medicine. It will allow healthcare providers to detect susceptibility to disease and potentially preempt or prevent disease progression by considering genetic and environmental factors that may increase predisposition.

Pathologists will have an integral role in this new era of care. Personalized medicine relies on new methods of molecular analysis to determine predilection

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toward certain diseases, but also the likelihood of a certain treatment's efficacy. Relying on these types of precision diagnostics makes the pathologist more visible to physician colleagues, says Gene Siegal, MD, Robert W. Mowry endowed professor of pathology and director of the Division of Anatomic Pathology at the University of Alabama at Birmingham (UAB). Siegal is also the executive vice-chair of Pathology in the UAB Health System, and a member of the American Society for Clinical Pathology (ASCP) Board of Directors.

"Pathologists are absolutely critical to companion diagnostics," said Siegal. "Companion diagnostic tests reside in the lab. Pathologists have total familiarity with the tests and they are best able to report test results to the clinician who is providing the therapy to the patient."

Pathology and the future of personalized medicine

James L. Wisecarver, MD, medical director for Clinical Laboratories at The Nebraska Medical Center (TNMC), where he is also the director of both the Histocompatability Laboratory and the Human DNA Identification Laboratory, said pathologists have been making personalized diagnostic interpretations for decades.

"Pathologists follow new therapies. We've been doing that for many years," Wisecarver said. "Pathologists have to stay familiar with new therapies and learn about certain genetic differences in patients to determine who will respond to which drugs."

The full scope of personalized medicine has not yet come to fruition, but it is already influencing cancer care.

Appropriate therapeutic regimens for various cancers are being determined by molecular testing. Tumors might present as a textbook example of a certain type but with molecular techniques like florescence in situ hybridization (FISH) technology, might actually be revealed as a completely different type of lesion.

"This can especially happen with soft-tissue tumors," said Wisecarver. The ability to understand such differences is a critical skill possessed by pathologists, aiding in effective diagnosis.

Personalized medicine in a customer service culture

Patients are now more involved in their own medical choices. They are knowledgeable of many medical conditions and options for care; this change requires physicians to work more closely with patients not only as a healthcare provider, but as a partner in treatment and care.

Customer satisfaction is a common metric by which businesses measure their performance. Pathology services, which are largely unseen, do not normally make patient and client satisfaction a priority.

As personalized medicine spreads, however, pathologists play a more intricate and visible part in patient care. This new transformation requires more attention to the "business" of pathology, and leading with customer service.

> Progress in the field of molecular pathology is poised to move pathology from a referral-driven specialty to one that has direct interactions with patients.

Pathologists no longer solely perform tests and interpret results—they are directly involved in improving the efficiency and quality of care. Improving patient care is done largely through appropriate test utilization, and pathologists and laboratory professionals

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are heavily involved in the development of guidelines for both the appropriate use of laboratory tests and advanced laboratory diagnostics.

In February, my group, ASCP, the world's largest professional membership organization for pathologists and laboratory professionals, released a list of five tests that physicians and patients should question as part of the American Board of Internal Medicine's (ABIM) Choosing Wisely campaign. Our society was one of more than 50 that identified often inappropriate and potentially harmful tests that are frequently used by healthcare professionals. The goal of the campaign is to promote quality and efficiency in healthcare.

Pathology, personalized medicine, and health reform

The new era of personalized medicine can also be attributed to the changing landscape of new payment models. One of many changes to how physicians are paid, due in large part to the Patient Protection and Accountable Care Act (ACA), is value-based purchasing. The primary goal of the many reforms initiated through the ACA is a reduction in cost and an improvement in quality.

As pathologists become more involved in the development, management, and application of patient information and health records, they are well-positioned to deliver care that is personally tailored, highly effective, and cost efficient.

"Pathologists are focused on patient safety and quality," said Siegal. "[Pathologists] bring to the multidisciplinary team of physicians a unique skill set for the better and encourage more interaction between pathologist and physician."

Highlighting the value of the pathologist to patient care requires pathologists to be more visible in their hospitals, but it also requires appropriate compensation, according to Siegal.

The economics of healthcare doesn't just apply solely to the cost of care to patients. Changes to reimbursements and laboratory fee schedules are also affecting pathologists. Molecular tests can be labor-intensive and costly. Third-party payer reimbursements do not reflect the cost of performing these procedures and Medicare reimbursement rates are even lower. While pathologists are up to and able to meet the challenges presented in this new era of healthcare, it is uncertain that the United States will be able to maintain an adequate supply of experts in the field without proper compensation.

Recognition as a vital member of the healthcare team

As the field of pathology has expanded, so have the skill sets, knowledge, and value of its practitioners. The field of informatics, which is growing increasingly important as a diagnostic technique, is becoming an essential area of pathology training. This new knowledge allows pathologists to gather and interpret complex patient data using 21st century technologies.

Progress in the field of molecular pathology is poised to move pathology from a referral-driven specialty to one that has direct interactions with patients. Highly specialized training in the area of molecular genetics makes pathologists invaluable as we transition to the new era of personalized medicine and care. It is important to acknowledge the benefits pathologists bring to the entire healthcare team as personalized medicine promises to transform the way healthcare is provided.

About the Author

Jordan Sarver is Web Writer at the American Society for Clinical Pathology. He can be reached at Jordan.sarver@ascp.org

Clearing the Remaining Emerging Market Hurdles

Despite the long-held promise of the emerging markets, dominance in these territories has eluded leading pharma companies. Hussain Mooraj addresses the key issues and offers a strategy for success.

No more than 10 to 30 percent of the revenues of many of the Top 10 pharma companies come from the emerging markets.

As markets around the world become saturated, the life sciences industry is becoming increasingly aware that sustained growth may become dependent on an effective strategy for emerging markets.

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These markets, particularly the BRIC nations (Brazil, Russia, India and China), are increasing areas of focus for life sciences companies due to the potential revenue streams.

For instance by 2016, at least one projection is that the four BRIC nations will all be in the top 10 global pharmaceutical markets and will constitute 30 per cent of the Top 10 market.

Despite this potential, many pharmaceutical firms have not been able to establish and maintain a major foothold in emerging markets.

A glance at the publicly available financials of the

top nine pharmaceutical companies reveals that for many of them, no more than 10 percent to 30 percent of their revenues come from emerging markets.

There is a need for an effective multifaceted strategy to get established, maintain competitiveness and drive profit.

Research has shown several reasons for this, from complexities in the manufacturing and supply process to fragmentation of markets and shortage of skilled labour.

Thus, although "expansion into emerging markets" is now a popular topic for boards at many life sciences companies, there is a need for an effective multifaceted strategy to get established, maintain competitiveness and drive profit.

Through our research we have analysed current value chain capabilities in the BRIC markets and identified six main challenges and trends that could help break the impasse for leading pharmaceutical companies.

- **Immature logistics and distribution.** The distribution value chain in emerging markets is often immature, inflexible and highly fragmented. Take the example of the typical Chinese distribution system that, by western standards, appears complex and restrictive, with many distribution companies operating at all levels. A lot of these distributors are province-based or city-based, and cover a small area of the country. Five primary distribution centres supply more than 200 provincial-level wholesalers, which, in turn, supply around 3,000 local distributors. This system may have the advantage of simplicity, but it can also be highly inefficient.

- **Inadequate manufacturing infrastructure.** Different emerging economies have very different levels of maturity in terms of their manufacturing ecosystems. A great deal of fragmentation exists among pharmaceuticals manufacturers. In India, for example, no single company has more than seven percent of market share. And in Russia, manufacturing has often not been able to cope with the growing needs of the country's market; currently, local pharmaceuticals companies are able to meet only a small per cent of Russia's requirements — therefore, reliance on imported pharmaceuticals is growing.
- **Diverse regulatory environments.** Successful expansion into emerging markets depends on a comprehensive understanding of the different regulatory environments of these nations. Approval times can range from about 18 months in Russia to more than three years in China — over and above the timelines for registration in the United States and the European Union.

- **Uncertainty in pricing and reimbursement.** Success in emerging markets also requires understanding of how pricing and reimbursement systems work in the different regions. Although each market employs some combination of free-market pricing and price controls, the level of pricing controls can vary significantly across markets and is, in part, a reflection of local economic conditions and the government's role in healthcare provisioning. For example, although both Brazil and India have similar market sizes in terms of

value, drug prices in India are only a fraction of the prices in Brazil.

- **Complex taxation structures.** Recognition of the vital role of R&D and innovation has led to the implementation of specific tax incentives in many of the emerging and developed markets. Many local government bodies are trying to attract investments in their regions by setting up tax-free zones and providing access to better infrastructure and resource pools.

- **Shortage of skilled talent.** As opportunities in emerging markets expand, the competition for skilled talent is likely to be intense, especially in areas such as cold chain management, biologics manufacturing, demand planning and pricing analytics. The support structure to provide a consistent stream of skilled talent is being developed but, at the moment, demand is outpacing supply.

These significant challenges make it vital for life sciences companies to establish and execute a strategy that looks for commonalities across the BRIC markets — commonalities that support cost-effective approaches while also being sensitive to unique market, governmental and consumer attributes within any specific region.

Our research recommends the following four-pronged approach that companies should adopt that in order to gain a competitive edge in these markets.

The importance of submarkets and 'customer clusters'

Any particular emerging market has some diverse segments requiring differentiated treatment. However, our analysis of markets in the BRIC countries suggests that customer clusters or submarkets can be identified within a national or regional market based on an understanding of consumers who have common health needs, such as those suffering from a particular disease such as Type 2 diabetes.

Submarkets can also be identified based on common characteristics related to factors such as demographics, accessibility and technology penetration. For example, an analysis of urbanization trends and per capita income can help identify common customer clusters, which then plays an important role in determining a life science company's market access strategy.

By focusing on customer clusters and submarkets, life sciences companies can develop a more detailed understanding of the specific needs of potentially profitable groupings of customers, leading to more effective and customer-centric R&D, as well as stronger marketing and sales strategies.

Cross-border similarities

When developing an emerging-markets strategy, companies should not be constricted in their planning by national boundaries. An approach, which is too focused on individual nations and regions could mean that customer similarities across markets are not being sufficiently leveraged to create solutions that can move across borders.

By focusing on customer clusters and submarkets, companies can understand the needs of potentially profitable groupings of customers.

For example, a recent Credit Suisse Global Wealth Report revealed that an average Brazilian household spends 10 per cent of its income on healthcare — almost double the level spent in China and India. However, the number

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of households earning more than $2,000 per month is three times more in India and six times more in China than in Brazil. These kinds of analyses can identify cross-border insights that enable companies to serve groups or clusters of customers more effectively and efficiently.

Global reach with local relevance

Whether in an urban or rural market, it can be beneficial for companies to "think globally and act locally" in meeting the needs of consumers in the BRIC markets. Cities that may be similar in economic strength are often quite different in terms of human capital components such as population growth, working-age population, entrepreneurship, risk-taking mind-set and quality of education.

Understanding these different levels of maturity can give a company an overall assessment of a particular function and also help it understand the drivers that can improve the existing maturity of that function. This more granular assessment can help companies develop more customer-centric, localized solutions.

Effective and rapid execution capabilities

The fourth strategy to consider for potential success in emerging markets in the life sciences ties all the other strategies together: execute the solution across the markets in a timely and cost-efficient manner. Such execution can be a difficult task for life sciences firms, given that many of them continue to operate in functional silos. It is important for companies to create a single, coherent strategy instead of trying to coordinate separate supply chain strategies, commercial strategies and so forth.

Two capabilities are especially critical when planning the rapid execution of an emerging-market strategy. The first involves developing the ability to understand and to get very close to the customer—by leveraging networks and chains of influence so that a market strategy can reach consumers quickly. The second involves companies improving their risk management capabilities to the point that they can take well-considered risks as a means to rapidly seize market share.

Cities that may be similar in economic strength are often quite different in terms of human capital components.

Conclusion

It is evident that growth strategies in the life sciences industry are becoming more and more dependent on expansion into emerging markets. A growing middle class in these areas represents an opportunity for life sciences companies to improve the quality of life there, while also improving their own market standing. Companies that are more advanced in areas such as manufacturing infrastructure, logistics, distribution and talent management — and, of course, in understanding consumer needs and behaviors — can gain an edge in achieving high performance.

About the author

Hussain Mooraj is global managing director for the Accenture Life Sciences Supply Chain practice and Accenture Enterprise Services for Life Sciences. He has more than 20 years' experience in manufacturing, supply chain, technology, sales and marketing, strategy and consulting to his role.

China: Recruiting Talent Amid the Corruption Fallout

The fallout from the recent GSK bribery investigations in China has given recruiters pause for thought. Gregory Lovas provides some do's and don'ts for keeping your talent recruitment drive on track in the emerging markets.

The GSK bribery investigations in China are a wake-up call for all Big Pharma companies committed to finding top talent in high-growth emerging country markets.

The recent GlaxoSmithKline bribery investigations in China provides a wake-up call for all Big Pharma companies committed to finding and deploying top talent in high-growth emerging country markets. Following this case, it appears that Chinese investigators have also contacted Bayer, Eli Lilly, Sanofi, Novo Nordisk, H Lundbeck, Astra-Zeneca, and UCB.

GSK reportedly placed a number of compliance officers in China, so how did it land in a quagmire of toxic bribery claims? The company alone clearly had the staff resources that should have made a difference. According to Reuters, GSK conducted "up to 20 internal audits in China a year", including an extensive four-month probe earlier in 2013.

In spite of this, GSK was blindsided by police

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allegations of massive corruption involving travel agencies used to funnel bribes to doctors and officials. The scale of funds signed off by GSK to pay travel agencies for organizing educational medical meetings has triggered heated debate, with some saying such spending looked legitimate while others argued it should have raised alarms inside GSK and at its external auditor, PricewaterhouseCoopers.

Warning signs abound

Pharmaceuticals and healthcare businesses say that corruption and weak laws are top threats in emerging markets, according to the "Business Perspectives on Emerging Markets 2012-2017" survey by Global Intelligence Alliance (GIA). In the study, 94 percent of respondents said they would like to have done something differently in how they planned and executed their emerging markets strategies.

Paying to play in Asia Pacific

It is not difficult to see why corruption is a persistent problem in emerging markets. Unlike mature markets where decisions are made by highly compensated individuals in healthcare institutions, those who order drugs and medical devices in this region can earn one-tenth of what their counterparts earn in the United States.

In fact, the salaries of young physicians in Chinese state-owned hospitals are often compared with the wages of local taxi drivers. This underlying wage factor has led to a culture where Chinese doctors feel a need to supplement their incomes as physicians through other sources.

This opens the way to the development of less-than-ethical practices. As another consequence, highly qualified medical professionals in China are often willing to give up their years of specialist training and work as pharmaceutical sales executives, where their pay scales may be three times higher. Such problems are not limited to China. One just needs to look across the borders into other Asian countries and to see similar problems, albeit manifested in other ways.

It is not difficult to see why corruption is a persistent problem in emerging markets.

The "c suite" reacts

The tremors from the investigations in China have spread far beyond the country. From global boardrooms in America to those in Switzerland, there is a higher state of caution. Some players are adopting a wait-and-see attitude about the market, crossing their fingers that things will "blow over."

After all, emerging markets like China are vital to continued growth. In their study, GIA pointed out that global pharma expect about one quarter of their global revenues to come from emerging markets by 2017. Within the next few years, China is poised to surpass Japan as the world's second-largest pharmaceutical market. For the time being, the market is skittish about China.

Things are awfully quiet. Many Chinese doctors are now less willing to make appointments with sales representatives because of the fear that they too will be targeted for investigation. Local sales organizations have been impacted, as customer meetings are much harder to schedule. Similarly, pharmaceutical companies have toned down their commercial sales and marketing activities in order to maintain a lower profile.

Even more intensive checks. While there has been no major slowdown or increase

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in executive recruitment in China, companies are now demanding even more in-depth background checks.

Who you personally know. Some companies have decided to rely on internal organizations or even personal networks when it comes to hiring. Even when there may be stronger talent available in external markets, some companies are shying away from hiring people they don't personally know—shrinking an already small pool of emerging market talent.

Candidates shy away. China used to be an ideal work destination for ambitious top-tier job candidates who knew that the market was vital to their company's long-term plans. There would be promising prospects for continuing development and major career advancement. Recruiting with such important career commitments could even supplement compensation packages.

It is ironic that the Chinese government has implemented far-reaching human resources policies over the last few years to attract international senior talent, particularly for industries such as new energy, bio-pharmaceuticals and life sciences. Such market scandals are giving candidates pause for thought.

Alternative talent grooming locations. An immediate reaction on the part of multinationals has been the consideration of other locations to transplant their senior managers for international exposure. However, there are companies that are still sending their top talent to places such as Singapore, Hong Kong, and Australia.

Three tips on placing senior executives in emerging markets

Make in-country experience a top priority. It is critical to hire individuals that are knowledgeable and experienced in the region or country that you are placing them.

Look for individuals, local or expatriate, who have worked with your key target customers, managed local teams, negotiated and closed deals locally, and who know local distributors and channel partners relatively well.

Adapt your global recruitment practices in emerging markets. Companies must be nimble on recruitment and retention matters, fine-tuning their strategies to the specifics of each situation rather than seeking to impose a one-sizefits- all approach upon all emerging markets. Flexibility is key, as is sensitivity to cultural as well as business dynamics in each location.

Close the cultural gap. In the "2013 Ethics & Compliance Leadership Survey Report" by LRN, 45 percent of senior ethics, compliance, and legal executives from multiple industries said their operations in emerging markets represent the greatest concern in promoting a strong ethical culture.

Such issues exist across all industries, and it is useful for global companies to provide training in the ethics and compliance issues that are specific to various emerging market cultures for all stakeholders across the organization. In addition, they need to ensure that red flags are identified early and communicated back to the relevant global heads by mitigating the fear to speak up by explicitly rewarding those who apply the proper due diligence.

About the author

Gregory Lovas leads CTPartners' Life Sciences Practice in executive search in the Asia Pacific ceuticals and healthcare players region.

Europe: Doubts over Data Disclosure

The European Medicines Agency (EMA) has admitted that it cannot meet its own time-line on disclosure of clinical trial data. Has it bitten off more than it can chew? Reflector reports.

The European Medicines Agency's ambitions are huge — as befits a body with such huge responsibilities. But its capacities to achieve what it sets out to do are now falling ever shorter. The latest deficiency is revealed by its admission that it cannot meet its own time-line on disclosure of clinical trial data.

On this hugely contentious question, the agency had made clear that it was going to go ahead rapidly to bring in a new era of pro-active release of data. The plan was to get final agreement on a policy at the end of 2013, with a view to wider disclosure as from the beginning of 2014.

But earlier this month (November) it recognized that the timetable was too tight. The delay is a consequence of the massive response to the public consultation on its thinking that it launched earlier this year. This has generated more than 1,000 comments — and "from an unprecedented range of stakeholders", said an EMA statement. It is still reviewing and analysing these comments, and "in order to conduct the appropriate in-depth analysis, the Agency will spend additional time in this reviewing phase, which may delay the finalisation." Instead, all the agency can guarantee now is that it will deliver "an update on timelines" in December.

> This latest challenge comes on top of the difficulties that the EMA has been facing in fulfilling its new role at the centre of European pharmacovigilance.

There is some logic to the Agency's decision to go public on its postponement. That way, it has been able at least to reaffirm its commitment to the principles of access to clinical trial data. Pro-active disclosure will happen later, but it is still going to happen, is the agency's clear message. It needs to make that clear, because the plan has provoked such polarised views — caution and even hostility from many industry quarters, and unbridled enthusiasm from health

campaigners and many academics. In addition, even before the new plan comes into effect, the current agency policy of data-release in response to requests is under attack in the courts — the action by AbbVie and InterMune to prevent the agency from releasing data to rival drug firms is yet to be resolved, but is meanwhile inhibiting the agency in its bid to broaden disclosure. So for the agency it is important that the delay is not seen as backing down or rowing back. This is no chance of stance, its officials insist.

This latest challenge comes on top of the difficulties that the Agency has been facing in fulfilling its new role at the centre of European pharmacovigilance. Last year it had to defer full implementation of these new rules because it simply did not have the time or the resources to match the demands created by EU legislators.

When Guido Rasi took over at the head of the agency two years ago, it was desperately in need of dynamic management. Rasi has been dynamic, but his ability to manage is constantly constrained by lack of resources. The EU is unlikely, in the current economic climate, to increase those resources, so if ambitions are to be matched with action, the additional resources may depend on the agency's other revenue stream — fees from the industry, which currently cover more than three quarters of its costs.

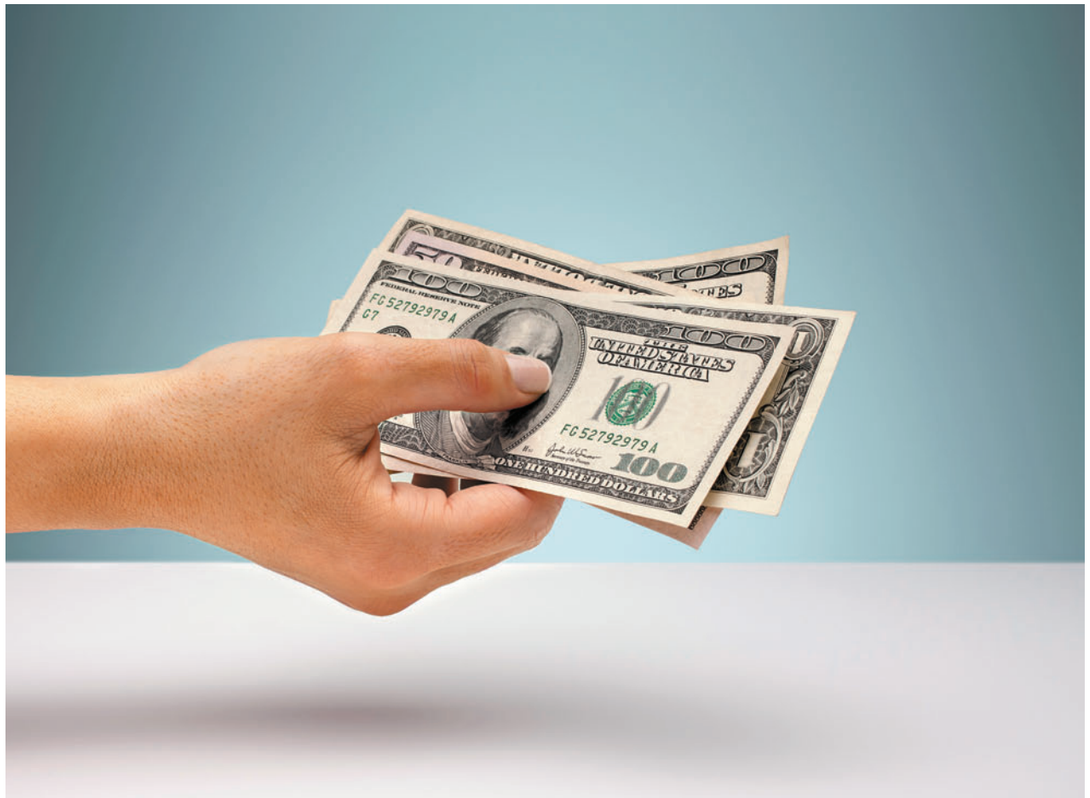
So Rasi could be faced with a choice between biting off more than he can chew, or biting the hand that feeds him.

Is Your Anti-Bribery Strategy Active?

The pharmaceutical sector needs to shape up to deal with the big uptake in bribery and corruption enforcement actions — and not just in the USA, write Toby Duthie and David Lawler.

Pharma must actively re-address anti-bribery policies and ensure that "adequate procedures" are in place.

Most multinationals are already familiar with the Foreign Corrupt Practices Act (FCPA). US regulators have been aggressively prosecuting companies and individuals for bribery with increasing zeal for the past decade, with healthcare companies being specially targeted. Recently, leading manufacturers of orthopedic implants: Zimmer, Depuy, Smith & Nephew, Biomet and Stryker settled with US regulators regarding US public sector contracts under the False Claims Act (paying penalties totaling $310 million) and accepted that they had paid bribes (cash and in-kind) and kickbacks to doctors and consultants who had bought and recommended their products. More recently there have been a number of FCPA settlements in the



Anthony Bradshaw/Getty Images

Table 1: Summary of Selected Key Settlements by Pharmaceutical Companies

Company	Settlement (USD)	Violation(s)	Year
GSK	3 bn	Off-label promotion / Medicaid fraud / Kickback	2012
Pfizer	2.3 bn	Off-label promotion/ Kickbacks	2009
Johnson & Johnson	2.2 bn	Off-label promotion/ Kickbacks	2013
Abbott	1.5 bn	Off-label promotion/ Kickbacks	2012
TAP Pharmaceutical Products	875 million	Medicare fraud/ Kickbacks	2001
Johnson & Johnson	70 million	FCPA violations	2011
Pfizer	60.1 million	FCPA violations	2012
Eli Lilly	29.4 million	FCPA violations	2012
Biomet	22.8 million	FCPA violations	2012
Smith & Nephew	22.2 million	FCPA violations	2012

There have also been settlements from pharma companies that won orders under the Iraqi government's Oil for Food Programme (Novo Nordisk and Akzo Nobel both have settled).

sector which we list out below. However, a couple of companies in this sector received 'declinations' in this sector based FCPA investigation — that is undertakings that the US Government would not prosecute — for reasons we will discuss later. Often these FCPA cases have their ultimate provenance in US Anti-Trust, US Healthcare Fraud or False Claims Act prosecutions and are continuations in kind.

The biggest news by far in 2013 has related to the high profile dawn raids by Chinese authorities...

In the UK, the Serious Fraud Office (SFO) — the body charged with prosecuting bribery and corruption — has had a slow start in prosecuting under the UK's Bribery Act, which came into force in 2010. But the SFO did have some success under prior legislation in its prosecution of Robert Dougall, a former Vice President of Market Development of Johnson & Johnson subsidiary, Depuy International. Dougall was found guilty of conspiring to make corrupt payments and give inducements to medical professionals working in the Greek public healthcare system. Despite Dougall's full co operation with the SFO, the Court sentenced him to a year in jail, although in a welcome show of sanity, this was reduced to a suspended sentence on appeal.

Tigers and flies

However, the biggest news by far in 2013 has related to the high profile dawn raids by Chinese authorities, which have focused on many leading pharma companies. GSK, Astra Zeneca, Sanofi and Novartis have, according to the press, all received such attention from Chinese prosecutors. GSK's vice president of China operations has publicly admitted that the company used third party vendors to help stage legitimate conferences however at inflated prices. The vendors, such as travel agents, then allegedly used the extra money to pay the bribes to doctors presumably to help promote the sale of relevant product. The US Department of Justice and the UK's SFO are apparently also investigating these allegations.

Table 2: Pharma Companies under Bribery Investigations

US authorities	Chinese authorities
Sanofi SA	Sanofi SA
GSK	GSK
AZ	AZ
Eli Lilly	Eli Lilly
Novartis AG	Novartis AG
Teva Pharmaceutical	Bayer
Bristol Myers-Squibb Co.	Novo Nordisk
Baxter International Inc.	UCB
Merck & Co.	Lundbeck

The risks from business partners

Many companies use agents or distributors to interact with government officials; to import and export; arrange permits; market their products; or act as intermediaries or facilitators: this is one of the main areas of risk. This is because in most anti-bribery statute, companies are liable for the actions of not only their subsidiaries, but also these joint venture partners, distributors and agents.

Risk areas for multinational managers

All business managers recognize that passing bundles of cash in brown envelopes to senior governmental officials in return for lucrative contracts is indefensible. Many of the recent prosecutions for bribery, however, have excluded such blatant activity. Instead, they have involved routine, smaller payments, in mundane circumstances, simply to get things done in far flung parts of the world.

Having a very wide ambit, the relevant laws do not define a bribe by the payment of cash, but rather, giving a "financial or other advantage" to the recipient. This can include paying expenses on behalf of someone (paying school fees for the recipient's children is popular) or where entertaining crosses the boundary of acceptability and has no link to legitimate product promotion.

In our experience, many of the business managers who have been investigated for bribery:

* Are unaware that the activity is criminal.
* Believe that the activity is "standard business practice."
* Do not realize the seriousness of the criminal penalties if they are prosecuted.
* Do not realize the damage that can be caused by their corrupt act.
* Do not believe that they will be caught.
* Are required to condone the corrupt activity and are afraid to refuse to do so.

Implications for pharma

This sector cannot be passive. It must actively re-address anti-bribery policies and ensure that "adequate procedures" are in place. Governmental organizations have an increasing ability to fully resource and inform more technical investigations.

Governmental organizations have an increasing ability to fully resource and inform more technical investigations

Back in 2009, Lanny Breuer, whilst a senior prosecutor in the Department of Justice (DoJ), made a keynote address at Pharmaceutical Regulatory and Compliance Congress and Best Practices Forum. His experience is that: "In the pharmaceutical context,

we (the DoJ) have additional expertise that significantly enhances our ability to proactively investigate and prosecute these often complex cases. That additional expertise is located in our healthcare fraud group, where we have prosecutors and analysts with the industry knowledge necessary to quickly identify corrupt practices. These two groups — our FCPA unit and our healthcare fraud unit — are already beginning to work together to investigate FCPA violations in the pharmaceutical and device industries in an effort to maximize our ability to effectively enforce the law in this area."

Clearly other regulators and prosecutors are closely scrutinizing the sector also.

We believe pharma companies need to take these three key steps to start to address their exposure to regulatory prosecution:

Set the tone from the top. Appoint a Bribery Czar, educate management and employees, and agents and suppliers on the likely impacts of the Act, and show people how to avoid falling foul of the law. Implement rigorous controls regarding payments and expenses.

Check high risk areas. Review past practice to identify areas or transactions at risk, and seek independent advice and help to deal with problems and to improve processes.

Pharma has clearly become a sector where the question is not 'if' but 'when', or even 'when again' will regulatory investigations strike.

Business partners must structure their business to ensure there are contracts with all agents and suppliers that require clear, honest practice. They must put contingency arrangements in place wherever risks lie and retain the right to audit a business partner's practices — and actually be prepared to audit in the event of a red flag or whistleblower allegations. Increasingly, many companies are rolling out a specific programs to do just this taking into account the risk based approach referenced above. They need to be able to terminate the contract if found to be noncompliant.

As Mark Pieth, Chair of the Organisation for Economic Co operation Development (OECD) Working Group on Bribery, has stated: "Bribery is indeed still out there. Perhaps part of the problem is that the closer you look, the more you find."

On the positive side, if companies can demonstrate a robust compliance culture and infrastructure, this has led to declinations from prosecutors. Pharma, as has long been the case with Natural Resources industry, has clearly become a sector where the question is not 'if' but 'when', or even 'when again' will regulatory investigations strike.

About the Authors

Toby Duthie is one of co-founders of the Forensic Risk Alliance (FRA) and heads its London office. FRA is an international firm of forensic investigators and accountants, data protection experts and eDiscovery specialists with offices in the US, UK, France and Switzerland.

David Lawler is an expert forensic accountant with over 20 years' experience. He is the author of Frequently Asked Questions in Anti-Bribery and Corruption (John Wiley & Sons, 2012).

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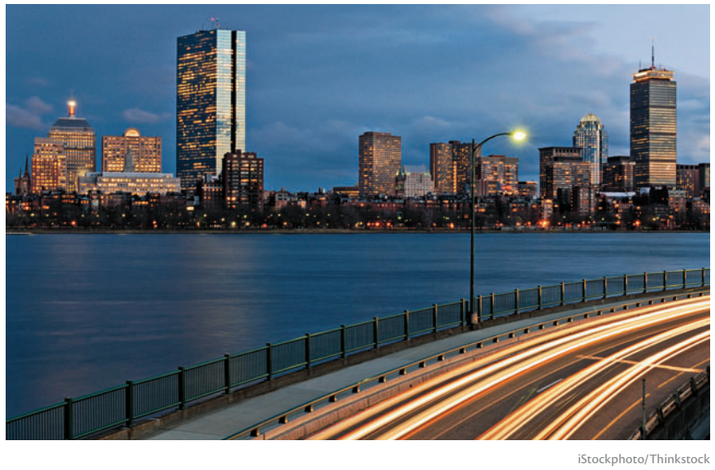

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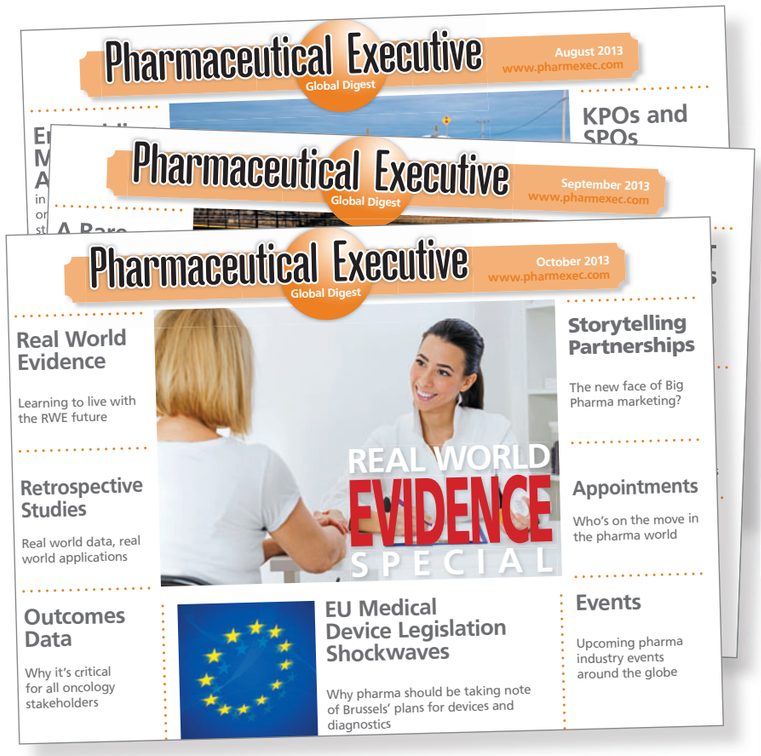

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