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VYING FOR SCREEN TIME

Pharmaceutical Executive

SEPTEMBER 2013
WHERE BUSINESS MEETS POLICY
VOLUME 33, NUMBER 9
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High Noon *for* Hot Markets

What's Next for Pharma's Cloud-Breaking Bet on

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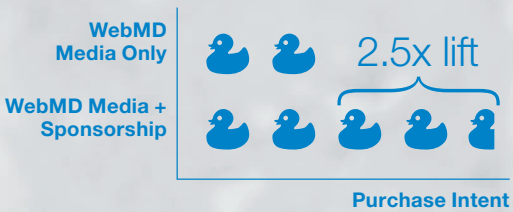

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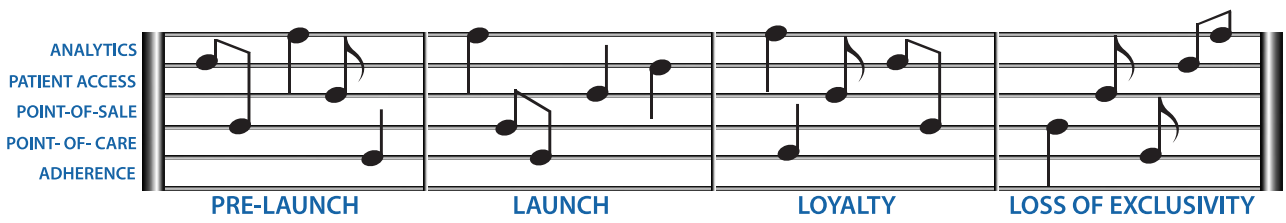

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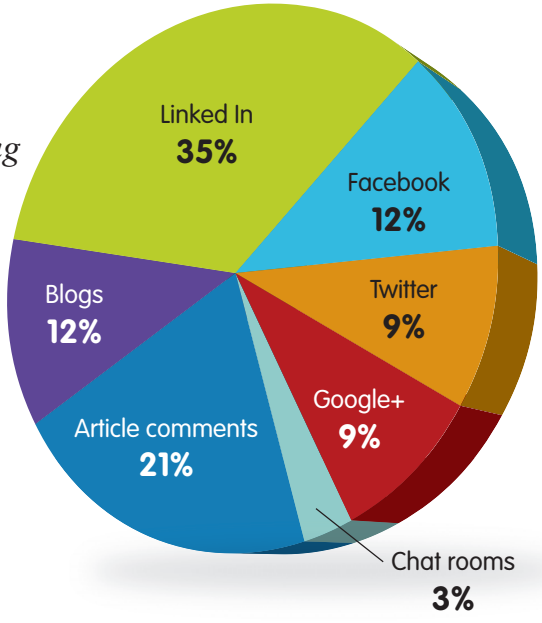
Data Point

Poll data courtesy of online *Pharm Exec* readers between July 29, 2013 and August 15, 2013

Q: What is the primary social media tool you use for drug development research?



Readers Weigh In

It seems that GSK senior management has failed to learn the lesson from last year's case in the USA—most companies would ensure worldwide compliance particularly after a $3 billion fine. They've clearly failed to put their house in order over the last 12 months.

Adrian Jones, 8/6/13
"One Company, One Defining Moment"
http://bit.ly/14yoYtK

Even though companies like Boehringer and Medtronic deserve credit for putting their toes in the water with respect to experimenting with social, I have yet to see a "business" use. Much of the activity could be classified as "community relations" or practitioner and/or patient education. Even those strategies are cloudy.

Richie Bavasso, 8/5/13
"Social Media's Not So Scary. Now for Social Business'"
http://bit.ly/15cxb9v

The song for a decentralized contract strategy has been sung for a generation now without any real answer regarding "best price" regulations.

John Waddell, 8/14/13
"Tackling the Skills Shortfall in Revenue Management"
http://bit.ly/14W9fRM

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Trying to Control Pharma Costs?

William Looney
Editor-in-Chief
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A KEY ISSUE FOR BIOPHARMA MARKETERS TODAY is balancing cost and value factors around specialty biologic drugs, particularly those for cancer and other high profile, life-altering diseases. The financial and reputational stakes for players in this hotly contested commercial space are high, compounded by a startling lack of awareness of the incentives that drive specific actions by payers, providers, health professionals, drug manufacturers—and, ultimately, the patient. Bridging this perception gap was the theme of *Pharm Exec* sister organization CBI's annual conference on Access and Reimbursement, held in Philadelphia earlier this month. Speaker after speaker noted that pharmacy spend is now the fastest growing cost segment for insurers, and specialty drugs are the principal factor.

A highlight of the meeting was the release of a survey by a new community-based practitioner network, The Health Payer Council, examining how US payers are responding to access and financing challenges for specialty medicines. The council conducted interviews over a 10-day period in August with 52 US-based medical and pharmacy directors—whose decisions affect 60 million commercial policy lives. The objective was to identify what payers are doing at present to manage pharmaceutical costs and to assess cost control measures that are likely to be applied over the three years, particularly in the oncology space.

Here are three key findings:

• Current strategies emphasize the application of standard pharmacy benefit techniques to infused medicines and biologics, reflecting their higher visibility in terms of reimbursement exposure. Some 44 percent of the survey group have programs underway or in the pilot stages. Significantly, 39 percent are working on strategies to wean physician practices away from their dependence on revenues from these drugs—a difficult task in light of the fact that most oncology practices would be insolvent without the income from administered drug treatments. Especially relevant here is the offering of performance bonuses to physicians when plan-approved clinical treatment pathways are observed; 36 percent have this in place or under pilot. In lowest order of use are drug capitation/bundling and differential ASP reimbursement, at 31.2 percent and 21 percent, respectively.

First, understand how other people make money.

• Overall, there was no ringing endorsement of the success of these approaches: the majority of plans consider their efforts to be only "somewhat successful." Pharmacy benefit management techniques (86 percent) were rated the highest in terms of success, followed by differential ASP reimbursement (67 percent). In contrast, efforts to wean physicians off of drug revenues received a high 17 percent score for being "somewhat unsuccessful." And no one was particularly enthusiastic about performance bonuses—a full 100 percent of the survey population ranked this tactic as "somewhat successful" rather than "very successful."

• A sea change is expected in management of oncology specialty drug spending over the next three years. More than two thirds—69 percent—believe aggressive cost controls targeting this therapeutic segment will be in place before mid-decade; half think this will happen over the next year. An interpretation of the poll results suggest in turn that capitation/bundling and pay for performance will be the toolkit of choice for cost cutters, since these two have captured the most interest among payers; they are seen as the most effective methods not currently in wide use.

Roger Green, an industry veteran who conceived and administers the Health Payer Council, tells *Pharm Exec* the survey evidences a "disconnect" between what payers are doing now to manage high drug costs in specialty and strategies that are not being applied—despite the perception that these are the ones most likely to be successful. "Payers by and large are still fixated on a philosophy that relies on the incentive of the carrot or the stick. This is not the optimal way to accomplish what is necessary to facilitate change, which is getting the various siloed parts of the system to cooperate, share, and work in partnership. More emphasis must be placed on changing basic behaviors." At root, Green says, is a simple lack of awareness. "No one in the system understands how anyone else makes money."

The council, which now has 107 members drawn from the medical director and pharmacy payer community, has a mandate to do just that. It won't make policy but is to serve as a forum to exchange information and build dialogue, with Big Pharma a principal focus. You might call it a Venn diagram of the payer community, writ real.

AS THE HEALTHCARE SYSTEM EVOLVES, THERE IS ONE CONSTANT—PHYSICIAN EDUCATION

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— Eric J. Topol, MD
Editor in Chief, Medscape

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Biopharma Innovation in Trouble?

Regulators, sponsors seek more productive research strategies.

User fees are going up because it takes more time and resources for the Food and Drug Administration to review applications for more complex products—and because the volume of new drug applications (NDAs) is going down. The dip is slight for submissions expected in 2014, according to an announcement of Prescription Drug User Fee Act (PDUFA) rates published in the Federal Register Aug. 2. FDA expects to see 116 filings in 2014, slightly less than the 122 submissions in 2012. And because the agency has to collect a certain amount of fee revenues each year, which is revised to reflect inflation and a "workload adjuster" for the new drug review program, fewer submissions means that each sponsor pays a little more.

So next year it will cost $2.2 million to submit an NDA or biologics license application (BLA) for agency review, and $1 million for a supplement with clinical data, generally to support new indications or expanded labeling. Review of a new biosimilar application that carries clinical data will be just as costly.

While a $2 million application fee may be relatively inconsequential for a large pharma company, compared to the vast sums it spends on clinical trials and product development, the amount may be considerable for small firms with limited resources. Manufacturers moreover will pay higher establishment fees ($555,000 for each of 455 facilities) and product fees ($104,000 for 2,425 marketed products).

Boosting breakthroughs

The drop in anticipated NDAs may reflect an ever-longer and more costly drug-development process that is squeezing pharma investment in R&D. FDA has a ways to go to approve as many new molecular entities (NMEs) in 2013 as the near-record 39 NMEs in 2012, and maintaining momentum will be harder in the future if initial submissions drop. Of course, if sponsors file more high-quality applications that yield a greater percentage of approvals, the final numbers could continue to rise—an outcome that would bring cheers on all sides.

The drop in anticipated NDAs may reflect an ever-longer and more costly drug-development process that is squeezing pharma investment in R&D.

A more positive view of the approvals-and-innovative issue is to distinguish truly important NMEs—"first-in-class" and "advance-in-class" medicines that account for a growing proportion of new drugs—from "addition-to-class" drugs that are declining, according to FDA analysis (http://bit.ly/197KlG6). A rising number of advanced new therapies are coming to market, according to this assessment, even if total approvals remain static.

FDA's new breakthrough drug program promises to support this shift by speeding the development and authorization of promising, critical therapies. Not only will FDA accelerate the review of applications for therapies that win the "breakthrough" designation, but agency scientists will provide advice and leeway to streamline clinical development. According to Friends of Cancer Research, a lead advocate for the program, FDA received 73 requests for breakthrough status as of late July—much more than the handful initially expected. The designation has been denied for 22 requests and granted for 25 experimental drugs that demonstrate early signs of clinical improvement over existing therapies for serious diseases, such as cancer and cystic fibrosis.

The program's success appears linked to advances in genetic understanding of drug response that enable FDA and sponsors to detect efficacy in early clinical trials, noted

Jill Wechsler is *Pharm Exec*'s Washington correspondent. She can be reached at jwechsler@advanstar.com.

Janet Woodcock, director of the Center for Drug Evaluation and Research (CDER), at a Friends briefing in July. Jay Siegel, head of global regulatory affairs at Johnson & Johnson, described how the breakthrough designation may shave two years off the timeframe for developing ibrutinib, a new oral leukemia medicine.

At the same time, there are clear challenges in bringing these innovative treatments to market. Insurers and health plans may hold off reimbursement until additional clinical data confirms efficacy and added benefits. Manufacturers also face problems in scaling up quickly to commercial production.

FDA advice for implementing this and other expedited review and development programs should help, as seen in a June draft guidance that offers sponsors insight into which factors lead to a breakthrough designation for a drug, plus accelerated testing and review. FDA also plans guidance on accelerating the development of diagnostics that can help sponsors demonstrate which patients respond to therapy. Pharma and biotech firms are happy to announce when an experimental product receives breakthrough or expedited designations, but there's much less information out there on what FDA turns down—and why.

Streamlined studies

Biopharma R&D productivity also could benefit from a more robust clinical trial infrastructure that uses biomedical data more effectively, says Woodcock, who would like to see more ongoing clinical trials utilizing standardized data and methodologies that can rapidly screen candidate compounds for signs of efficacy. "Let's not reinvent the wheel with every trial," she commented at a July conference on biomedical innovation sponsored by the Brookings Institution. Instead, a "network of data sources" linked by common protocols for data standards could greatly compress the clinical testing process.

The National Institutes of Health (NIH) similarly aims to help reduce the high failure rate of clinical trials through a target validation consortium, starting with pilots for Alzheimer's disease, diabetes, rheumatoid arthritis and schizophrenia, added NIH deputy director Kathy Hudson. And the Patient-Centered Outcomes Research Institute (PCORI) has launched the National Patient-Centered Clinical Research Network to improve the conduct of clinical outcomes research. The program will consist of some 25 research networks formed by research organizations and patient groups, each able to tap into health data for over one million individuals, explained PCORI chief science officer Bryan Luce at the Brookings conference. Luce acknowledged challenges, but predicted the program would provide "a dynamically linked clinical research network" that can test hypotheses and do adaptive studies, Bayesian trials and observational studies.

Pharma post-marketing studies stand to benefit from the networks' data from real-world patients in usual care settings. Although the PCORI networks may not be that useful in conducting randomized trials for investigational medical products, the program could help identify and recruit patients for clinical studies, encourage use of patient-reported outcomes, and indicate to sponsors why certain patients don't respond to treatments. Key issues are how PCORI develops the governance and structure of the research networks and who has access to the data. PE

Diverting FDA Resources?

The fast growth in the breakthrough designation program has raised concerns about shifting FDA resources and attention away from the conventional drug approval process. CDER officials acknowledge an "all-hands-on-deck" approach to dealing with breakthrough therapies, and that continued program growth could stress agency resources.

FDA might be able to handle expedited drug development initiatives more effectively if it received the full amount of user fees paid by regulated firms. Unfortunately, the budget sequestration process has created a serious revenue shortfall. The agency has lost approximately $85 million of its $1 billion user fee payments this year under the budget cutting-process, which applies to all FDA revenues, including fees paid by pharmaceutical, generic drug, and medical device companies. Congressional leaders are pushing for legislation to give FDA access to all drug user fee revenue; without such a bill, a portion of user fees will remain stuck in the Treasury Dept.

Engaging the future

HP Applications Transformation

"Engagement" is the coin of the new life sciences realm.

To position themselves in the emerging patient-centric world, pharmaceutical companies are building more informed, personalized relationships with healthcare consumers. Companies are forging closer ties to strategic partners, regulatory agencies, and globalized value chains. Many now seek the innovative power of a more mobile and collaborative workforce.

Most executives now also recognize the need for information technologies that will support a more connected pharmaceutical business. To more fully appreciate this shift, it may help to take a closer look at the rationale for and requirements of this more engaged approach.

Change is a given

Powerful forces are driving the move to a more integrated and patient-centric business model.

Leading companies have worked to adopt consumer-centric strategies designed to improve market share and penetration. Those strategies are increasingly less dependent on blockbuster drugs through traditional sales channels; they are more attuned to the personalized, consumer-driven marketplace of the future.

Accelerating products through the pipeline remains a core objective. Firms are working to optimize their portfolio of existing commercialized products, and to find new indications for current products. Many look to emerging markets to drive new sales and revenue.

At the same time, companies must respond to a more challenging regulatory environment and the need to continually improve patient safety, outcomes, and consumer satisfaction. Not surprisingly, many are refocusing on the core competencies that drive innovation and maintain profit margins.

In pursuit of those objectives, firms across the life sciences spectrum are working to boost R&D output, to spur collaborative efforts, and to maximize the value of their partner ecologies.

Forging closer engagements

To do this, forward-looking pharma companies are leveraging a "new style of IT."

This new model represents an incremental shift away from traditional transaction-oriented systems of record. There is now a clear move toward a new generation of engagement-oriented systems that enable change, encourage innovation, and open the collaborative links needed in the new pharmaceutical marketplace. This engagement-based approach is tuned to give end a seamless and satisfying experience as they seek anywhere, anytime access to information and services. It fully exploits today's most powerful cloud, data, analytic, and mobile capabilities.

This model reshapes how technology is delivered, paid for, and consumed. It gives pharmaceutical companies the insights needed to meet changing consumer and market demands.

Organizations that embrace this new style of IT will have the tools to succeed in tomorrow's changed environment. Those that do not will be the also-rans of the patient-centric marketplace.

Ask the right questions

So how can we best understand this more engaged approach to business? We can start by taking a critical look at how companies engage their most important constituencies.

What will consumers expect and demand in a post-reform environment? Who exactly are your producers and suppliers, distributors, research allies, and provider-side partners? How will more stringent regulations shape your business options? Finally, how can you better understand, connect, and engage with this dynamic environment?

Those are the tough questions, and pharma execs must press for clear answers across their organizations: from supply chain and enterprise resource planning, to research and development, production, IP management, and increasingly important consumer relationships.

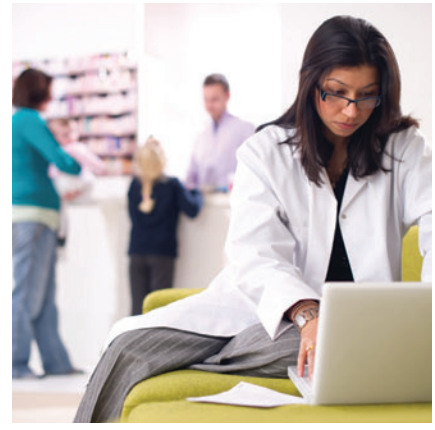
The most critical question, however, may be how to get there. What must happen to move a big pharma company from a legacy records-oriented environment to the coming more nimble and collaborative engagement-driven approach?

Applications are important

For any pharmaceutical company hoping to improve time to market, gain customer insights, and accelerate clinical trial outcomes—that shift will require the modernization and transformation of its enterprise software applications.

That should come as no surprise, because a typical pharmaceutical company currently runs up to 80% of its business on traditional system of record-type applications. Those legacy systems are used to manage R&D pipelines, supply chains, production, customer relationships, and more.

Most applications function behind the scenes and draw executive attention only when they cause problems or need replacing. But enterprise applications increasingly play an absolutely vital role in the success or failure of modern pharmaceutical companies. Unfortunately, many previous-generation IT architectures lack the transparency and flexibility needed in today's unforgiving life sciences marketplace.



In fact, many legacy apps now act as costly barriers: obscuring consumer preferences, stifling partner and supply chain collaboration, preventing change, and slowing time to market. Outdated apps can seriously reduce the ability to deliver innovation, care, and value in a changed pharma environment.

The destination is clear, but life sciences firms must take care as they move toward a more rewarding engagement-based model.

Many will update enterprise systems on a selected or sequential basis, and so will need to manage a complex mixed environment of legacy and modernized applications. It is important to first define realistic requirements, to design appropriate applications, and then to manage the transformation to that future state.

But transformation is the key

It can be a daunting task, but it is one that can be managed with expertise and experience.

Forward-looking organizations now recognize the need for a truly transformative journey—from a current state defined by fragmented stand-alone systems to the more connected and proactive healthcare environment of the future.

HP recommends a holistic approach for pharmaceutical firms that seek a more patient-centric, real-time, integrated healthcare model. It is an approach that can help bridge the gap between existing systems of record and the new engagement-driven landscape.

As we have noted, four key technologies will be absolutely essential: big data, cloud, mobile, and social. Aggressive pharmaceutical companies are already leveraging those advances to optimize alliances and sales activities, to foster collaboration, and to accelerate their product pipelines. Data and analytics, in particular, can yield real insights into R&D, patient safety and efficacy, consumer preferences, physician needs, and market demand.

Assuring these new technologies align with business process is also essential. Technology change often impacts current processes, and these processes must be reviewed and updated to align with the technology roadmap. Acceptance of the updated processes depends on buy-in from those who will benefit from the change; therefore, their input is highly valuable and a critical success factor.

This proven approach leverages enterprise applications to deliver a superior experience for pharmaceutical companies, employees, and customers. It envisions a complete ecosystem that makes full use of cloud integration, modernized applications, and a well-designed user experience.

Making the move

Regardless of the final contours of a post-reform marketplace, pharmaceutical companies will compete in a more transparent, integrated, value-based environment.

Success will be driven by optimized portfolios, Genomics and more personalized medicine, and increasingly collaborative business structures. Winners will pursue both top-line growth and bottom-line savings. They will exploit emerging markets and find personalized ways to serve more informed consumers.

Survival will be measured by speed to value, and speed to value can only be achieved through technology-enabled integration.

Those are the realities and the promise of a more engaged pharmaceutical marketplace.

Matt Bills, Segment Leader, U.S. Life Sciences Industry, HP

For more information, go to **hp.com/enterprise/healthcare**

T-TIPing the Balance in Industry's Favor

By the start of 2014, industry expects to have a clearer idea of how far the US-EU free trade pact is going.

So ceremonial was the launch in July of the EU-US trade talks that one might almost have misinterpreted it as a celebration of a hugely satisfying conclusion. EU leaders trilled excitedly about "a special moment," and "historic negotiations." The White House effused about "significant benefits" in international competitiveness, jobs, and growth. And both sides spoke of "a comprehensive trade and investment deal" and "strong political will." The transatlantic business community also threw its collective hat into the air, rejoicing at the prospect of "greater access to a huge market." And the pharma industry on both sides of the Atlantic has gone public with its own greeting for greater efficiencies through addressing regulatory differences and duplicative requirements, leading to expedited patient access to innovative medicines.

As the process gets underway on an 18-month bid to create T-TIP—the Transatlantic Trade and Investment Partnership—the European Union's chief negotiator Ignacio Garcia Bercero and his US counterpart Dan Mullaney have been more realistic, uttering cautiously optimistic noises, but acknowledging the scale of the challenge. However, after the first round of real talks, in Washington, DC, the mood is still upbeat. Garcia Bercero returned to Brussels still speaking of a deal that could be "transformative for our economies." So as negotiators prepare for the second round of talks, in early October, what is the likelihood of drug firms—and patients—reaping any rewards from the negotiations?

The European Union's chief negotiator Ignacio Garcia Bercero and his US counterpart Dan Mullaney have been realistic, uttering cautiously optimistic noises, but acknowledging the scale of the challenge.

Much of the answer resides in the sheer complexity of T-TIP. Some 150 negotiators in two dozen working groups are focusing on distinct sectoral areas, and pharmaceuticals has to take its place on a long list ranging from agriculture to energy and raw materials. And on the horizontal issues, although pharma stands to be influenced by what comes out of the scheduled discussions on public procurement, trade facilitation, or competition, it is not the only sector bidding for attention.

In this context, there is an acknowledged risk that negotiators might go for an easy regulatory deal for pharma, the low-hanging fruit that would offer only limited gains from among the drug industry's agenda of real regulatory alignment, market access, and greater clarity on intellectual property. This risk is enhanced by the broad range of interests at stake. The pharma industry is not monolithic, and the emphasis differs widely in the distinct positions taken in the run-up to the talks. There is some common ground in seeking greater mutual recognition of audits and inspections, and of foreign data. But the research-based industry is looking not only for regulatory compatibility initiatives, but also intellectual property protections, market access provisions, and customs, tariffs, and public procurement measures. The generic sector has set its sights on a single development program and harmonization of data requirements for approval of generic medicinal products, as well as provisions allowing production of protected products prior to patent expiry, to allow for rapid launch. Non-prescription producers are chiefly interested in greater market exclusivity for products newly classified for over-the–counter access, and active ingredient manufacturers would like to see greater international harmonization of good manufacturing practices, and of pharmacopoeia.

Not all these ambitions overlap neatly. The joint submission by the European Generic Medicines Association and the

Reflector is *Pharm Exec*'s anonymous columnist, a commentator so close to the action in Europe his identity must be kept secret.

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US Generic Pharmaceutical Association is deeply reserved over harmonization of "the different regulatory intellectual property systems between Europe and the United States," while one of the focuses of the European Federation of Pharmaceutical Industries and Associations and the Pharmaceutical Research and Manufacturers of America is closer alignment of intellectual property regimes.

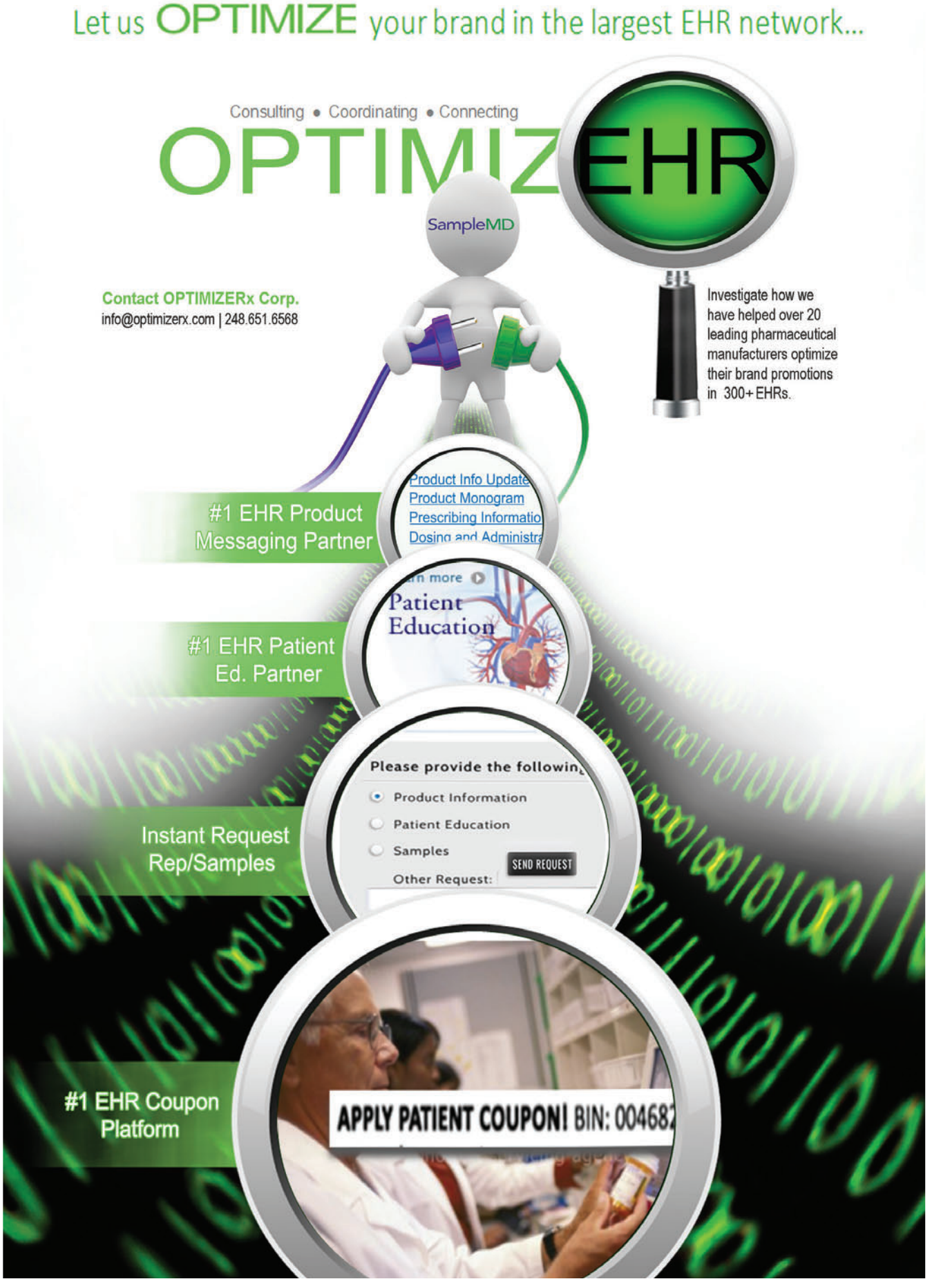
In addition, despite an unprecedented degree of transatlantic collaboration in establishing positions (the alliances forged by EFPIA/PhRMA and by EGA/GPA are mirrored in other healthcare sectors too), there is an inescapable reality in that while much of the industry may be international, the negotiators have a strong territorial affiliation. The United States and the European Union are both looking for advantages in terms of greater trade for firms based in their own territories, to boost their domestic economies. Consequently, any gains for EU exporters to the US market are unlikely to emerge without equivalent gains for US exporters to the European Union. There are also potential winners and losers among regulators, in terms of prestige and influence. Richard Bergström, the head of EFPIA, is conscious that some resistance is to be expected among national regulators. "Will there be sufficient senior-level political pressure to overcome that?" he muses. And some industry players are uncomfortably aware that risk of greater openness of trade in medicines could also lead to greater pressure for harmonization of prices—reinforcing existing downward pressures. The US industry has been vocal in its attacks on Europe's "short-sighted cost-containment measures."

For some of the inveterate critics of the industry, T-TIP is viewed with suspicion. Patients could be left out of the benefits, they fear—and patients in poorer countries might even suffer from reduced flow of drugs to their markets as manufacturers seek to maximize new opportunities in a bigger developed-world market. Consumer advocates, still outraged at what they see as drug industry sabotage of nominal concessions offered to poorer countries in earlier international trade agreements—notably TRIPS—are urging attention not just to the wording of any agreement, but to its implementation. "We should consider also how it could be used or abused by a stronger partner," warns Jim Murray, a leading European healthcare campaigner.

Some industry players are aware that risk of greater openness of trade in medicines could also lead to greater pressure for harmonization of prices—reinforcing existing downward pressures.

The industry's stance on release of trial data—viewed as grudging at best, and fiercely resistant at worst—plays into the climate. There are fears that the US side will use the negotiations to combat moves towards transparency, fuelling anxiety that big business is getting together to push for a raft of deregulation. PhRMA's president, John Castellani, told the House Subcommittee on Commerce, Manufacturing, and Trade in July of concerns over the current European environment because of the European Medicines Agency's "current and proposed data disclosure policy." Some of these concerns are recognized at a senior industry level, although Hugh Pullen of Lilly underlines: "We are not looking for deregulation. What we want is better alignment between EU and US rules."

At present, drug industry trade experts are genuinely impressed by the scope for the much-vaunted stakeholder involvement, promised to all comers for more than a year, and so far providing good access for industry views as the talks evolve. This is "not the old-school trade talks just focusing on tariffs," one closely involved Europe-based industry figure said. "The EU side is seeking real input and involvement." So in the heat of summer, pharma industry expectations—and hopes—remain high. Hugh Pullen of Lilly says it would be "a shame to lose what is a lifetime opportunity." But he recognizes that the industry is very much in the hands of the negotiators: "We have set out clear objectives. Now we rely on them to deliver." The autumn will be crucial. By the end of this year, pharmaceutical executives expect to have a clearer idea of how far T-TIP is going. PE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High Noon For Hot Markets

Fading growth; restless, overstretched governments; and a global governance backlash against pharma business as usual are turning up the heat on the performance of emerging country markets. The message for Big Pharma? Stand steady, but don't forget to duck. By William Looney, Editor-in-Chief

Whatever used to be wrong with the world of Big Pharma could be fixed with a single tag phrase: emerging markets. Had enough of grumpy, cost-conscious, risk-averse payers and regulators? Consider the vast new opportunities in countries with undeveloped health infrastructure, a largely out-of-pocket payment system and no requirement to negotiate access.

Facing loss of exclusivity on multiple blockbuster products? Fill the gap with high-margin branded generics that benefit from a privileged market position and local infant industry protection.

Too many jaded customers skeptical of more "me too" medicines? Tap that billion plus population of aspiring, middle-class healthcare consumers in Asia, Africa, and Latin America, all with untreated chronic diseases.

And you say you don't have much to show for all those costly investments in corporate reputation? Stand out with imported brands that confer automatic respect because of multinational producers' association with quality, safety, and service—still a hit or miss prospect for drug purchasers in much of the world beyond North America, Europe, and Japan.

The idea that countries classified as middle and lower income could spawn new growth for an industry increasingly characterized as mature is now an ingrained part of the strategy of every Big Pharma company. It's that rare instance where geog-

raphy itself qualifies as a disruptive innovation. The biggest players—Pfizer, Novartis, GSK, and Sanofi—tout their stake in emerging markets as a trump card in differentiating themselves against the competition, just as a healthy drug pipeline used to do in years past. "Less than a decade ago, no company had a dedicated strategy for these markets," said IMS Consulting vice-president Waseem Noor, in a roundtable discussion with *Pharm Exec* last month. "It was all opportunistic and short-term, focused on a small elite segment of the local population. Today, you can't be a true pharma multinational if you aren't present in the emerging markets in a big way."

Tattered playbooks

But that first blush of anticipation is yielding to some harsh realities glossed over in all those forward-looking statements to investors. The reality is buttressed by some hard truths:

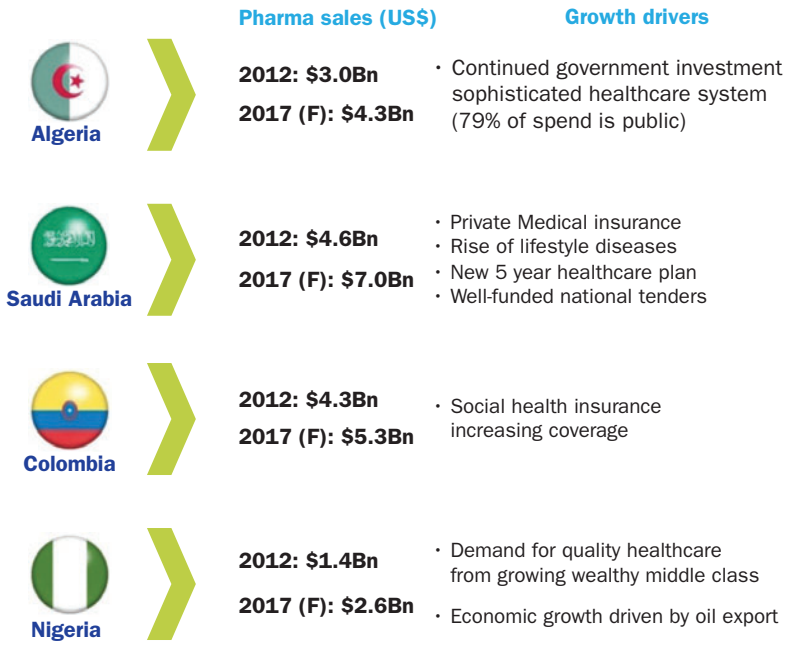
- There is no prototype "emerging" market; each is distinctively complex, with its own rules and culture of business, an intimate, ongoing knowledge of which is necessary for success.
- Most are "emerging" in name only, having capitalized on technologies first developed in rich countries to leapfrog the time span for new business innovation; in some areas of health services and delivery, like biosimilars, these countries are emerging as market leaders, not laggards.
- Growth, while a blessing, can also be a curse, as exemplified by civil unrest and governance problems spawned by rapid fire social and economic changes that in the West took multiple generations to work through.

The pace of change in emerging markets is making it harder for unwieldy Big Pharma organizations to execute on strategy. For many companies, results have failed to keep pace with projections. And there are signs of overall market fatigue, as these economies adjust to lower global commodity prices and pressure on local capital and currency markets due to the more attractive interest rates now offered on money invested in the United States and Europe. China excepted, real GDP growth is trending flat in the BRICs as well as other standout emerging markets like Turkey; even in China, the official real GDP growth forecast of 7.5 percent for 2013 is only two thirds of what it was two years ago.

There are real implications beyond the numbers. The expanding middle classes that Big Pharma is depending on to drive demand for medicines are taking a hit. Consumer discretionary spending is down, an important indicator in geographies where drugs are purchased mostly out-of-pocket. Governments are trimming subsidies and scaling back investments in neglected health infrastructure, with a ripple effect on incomes felt by physicians, pharmacists, distributors and others all the way down the pharma supply chain. Lower rates of growth are also exposing deficiencies in institutional oversight and good governance, manifested in the rise of an activist, take-to-the streets civil society determined to pursue reform on its own—and on the fly. Institutions of law are still in the adolescent phase, to the point that a well-intentioned crackdown on corruption can quickly become a vehicle for settling political scores. This only yields more uncertainty for investors.

As a result, the narrative has changed. "The buzz about emerging markets has been tempered by a message of constraint. Optimism about long-term growth is still there, but management is being more selective about where they intend to find it," says Noor. Sanofi has abandoned

The New Tier 3 Pharmerging Countries Emphasize the Potential of the MEA and Reinforce LatAm Position



*At ex-manufacturer price levels, LC$. Contains audited and unaudited data.
Source: IMS Health Market Prognosis, March 2013

earlier multi-year guidance promising double-digit revenue growth in emerging markets; Pfizer has dropped its revenue projections for 2013 from the high to mid single digits, with "fluctuations due to long-term uncertainties" thereafter; and GSK, while predicting continued solid growth in emerging markets for pharmaceuticals and vaccines, posted turnover increases for the second quarter that put the United States back at top of the league, with a five percent gain compared to only two percent for the Asia (ex-Japan), Africa, Latin America and Mideast regions.

What is now apparent is a stark difference between straight line forward projections of market expansion and the reality of actual historical growth rates in the emerging markets, which are highly volatile. Companies have no choice but to look at the record and be more cautious about raising expectations.

Pfizer also announced last month it was shutting down its business unit devoted to emerging markets, preferring to refocus its businesses there around different therapeutic franchises.

Pfizer also announced last month it was shutting down its business unit devoted to emerging markets, preferring to refocus its businesses there around different therapeutic franchises. It simply confirms the new view that these geographies are far too diverse to be managed as a single segment.

Game changers

Pharm Exec's roundtable exchange with the IMS Health team as well as other experts identified a number of additional factors that are helping to push the reset button on Big Pharma strategies for the emerging markets.

Real institutions—with the power to drive resource decisions on health—are taking root. As their economies expand, emerging markets are increasingly in a position to set their own public health and disease priorities. Brazil is a good example, with its selective government policies that provide 100 percent public reimbursement for medicines for the treatment of HIV and hepatitis C, while most other medicines must be obtained from private insurance or out-of-pocket. There is also the close involvement of Brazil's major public health institutions in industry development of a vaccine for dengue fever, a near-endemic disease in Brazil, a cure for which could generate enormous health savings.

Almost every emerging market country has adopted a comprehensive plan to guide development in the health sector, the common feature of which is promoting eventual universal access to basic health services. The WHO tagline "Health for All" is the unifying theme, but the larger driver is the idea that health creates wealth.

This more overt public engagement, along with the choices being made by a more affluent and informed patient community, will transform investment opportunities in emerging markets, in many therapy areas. As local health infrastructure matures, Big Pharma will need to make tough choices on where to focus its efforts—now, before it is too late. It certainly will not work to continue the previous path of touting a few costly imported medicines that attract negative attention because only a fraction of the local population can afford them. "The advantage is to companies that create a locally appropriate portfolio of products, with an aggressive commitment to be number one in each therapeutic category, against those that simply decide to adapt what's already in their global asset set," said Sydney Clark, IMS Consulting group vice president based in Latin America. "It won't work to build a business by repurposing the global pipeline—that's like trying to put a square peg into a round hole."

Business blunders can go viral very fast. Commercial transactions in emerging markets are not transparent and are poorly understood even by locals with years of experience. Interlocking group dependencies rooted in personal relationships often matter more than official rules or legal safeguards, so keeping a "nose to the ground" is a vital skill for foreign investors wanting to stay out of trouble.

In many cases, however, the sheer density of these relationships makes this task very difficult. In Brazil, for example, the local drug distribution system is larded with so many intermediaries that it is hard for anyone to track exactly what is going out to the marketplace. Earlier this year, Sanofi discovered this fact when its local management responded to an imminent rise in the VAT paid directly by consumers for medicine by forward-selling huge amounts of inventory that, instead of meeting demand, overwhelmed it. The miscalculation resulted in a bill of nearly $300 million for unsold, returned, and expired products. The loss affected the entire company, forcing it to take a charge that cut €0.17 per share off corporate earnings for the second quarter.

CEO Chris Viehbacher attributed the Brazil setback to "bumpiness in

the trade channels" but the big lesson here is how emerging markets can impose stiff penalties on the unwary. As Ansis Helmanis, Principal of RegLinks LLC, told *Pharm Exec:* "The firetraps can come from anywhere, because in these markets no one but you, the investor, is in charge. Is it any wonder that corruption is endemic in China when there is no effective institutional control over the promotional practices of a pharma sales force that is now the second largest in the world?" Another prerequisite is knowing the most about the customer base, which begins with an understanding of each stage of the patient's journey with your medicines.

Local competition shifts global. Emerging market drug companies are taking the blinders off and extending their reach beyond the home market, relying on partnerships, licensing, and M&A activities to acquire technology and know-how from the Big Pharma multinationals. A case in point is Aspen Pharmacare, South Africa's largest generic drug-maker, which has sealed deals with GSK and Merck to acquire underutilized manufacturing capacity in Europe as well as products that appeal to customers beyond its current geographies. Likewise, EMS, Brazil's biggest drug company, is increasing investment in R&D and exploring stakes in research projects conducted by academic institutions in the United States, with a particular focus on new therapies for senile dementia. Due to the increase in life expectancy, this is becoming a leading cause of death and disability in Latin America.

Another milestone occurred in June when a small Indian-based drug firm, Zydus, obtained final regulatory approval in India to market a new combination therapy, Lipaglyn, for high cholesterol and the high blood sugar associated with type 2 diabetes. Zydus management touts the drug as the first original patented medicine intended for the global market to be discovered and developed entirely in India, by an Indian company. At the same time, however, many other Indian companies are abandoning their home base due to unpredictable pricing rules and controls on investment capital; one of the country's largest generics producers, Lupin, now derives nearly half of its global revenues in the United States and is actually repositioning itself as a virtual US company, with a new CEO based in Baltimore, MD.

The implications of these moves for Big Pharma are twofold. First, it reinforces the need for a permanent visible presence, on the ground, in emerging markets. Companies there are poised to grow from a lower—and different—base and thus serve as a window on the future of global competition, most prominently as a source of product and process innovation. Today, few, if any, of these

The IMS Health "Pharmerging" Markets: 21 is a Charm

Making sense of the growth prospects in emerging markets is a bit like the weather—there is a steady cycle of day to night, but beyond that anything goes. IMS Health, which has been tracking industry sales and forecast data in what it calls the "pharmerging markets" for nearly a decade, is optimistic about the segment's overall contribution to industry global performance. The big news is that local variations within this theme are becoming more pronounced. "We see a new and higher level of market opportunity in the emerging market segment, in smaller countries outside the BRIC's," said IMS Consulting Group vice-president Waseem Noor at a recent dialogue organized by the *Pharm Exec* editorial team.

In its latest iteration of the "pharmerging" countries, IMS Health has expanded the list from 17 to 21, the four new additions being Algeria, Saudi Arabia, Colombia, and Nigeria. In March, IMS created a new designation of 15 "frontier" countries, drawn from outside the 21, that are poised to grow pharma sales anywhere from $250 million to $1 billion over the next five years. The "frontier" list includes: from Asia, the Philippines, Malaysia, and Bangladesh; from Latin America, Chile, Peru, and Ecuador; from Eastern Europe, Kazakhstan; from the Middle East, Iran, UAE, and Lebanon; and from Africa, Morocco, Tunisia, Ghana, Kenya, and Ethiopia.

Noor says there is a "notable sense of energy" around countries like Algeria and Kazakhstan, with their relatively large populations, resource wealth, and less up-front competition—"there is on the ground opportunity for companies willing to take an early bet on the future." IMS Health expects growth in these smaller markets to take up some of the slack now being experienced in the BRIC countries. Overall, the consulting group remains very bullish on the emerging market segment, with the CAGR for the 21 pharmerging bloc expanding by a multiple of 13 percent between 2012 and 2017, compared to only two percent in the eight major industrialized countries, over the same period.

IMS Health data show that Big Pharma does face a growth challenge due to its weakness in the generics business, which in many countries is dominated by entrenched local players. This explains why the multinationals are paying top dollar to acquire stakes in the generics space to diversify their strength in originator brands. The key danger point here is over-regulation, as this predominance in patented compounds makes Big Pharma particularly vulnerable to the current vogue among some governments for the compulsory licensing of IP assets, as an industrial policy tool. This is why a creative reliance on JV partners is so important.

local companies can carry an identifiable pharma brand beyond their own borders, but that is likely to change over time. Also, many have a common feature in being family-owned, which avoids all that shareholder baggage and makes them faster than Big Pharma in seizing opportunities.

Second, the greatest benefit will accrue to companies that find the right way to partner with local market leaders. "Smart companies are using joint ventures with domestic players as part of a new business model, using them to create go-to-market strategies with a lower cost structure. With a strong local partner, you can manage the economics of going broader into the marketplace," says Matt Guagenty, IMS Consulting group vice president for APAC and China. A good example is Pfizer's new joint venture with a leading Chinese generics company, Hisun, which will help expand the product portfolio in therapy areas where Pfizer is weak while lending sales and distribution muscle to penetrate those second- and third-tier urban centers—China has some 160 cities with more than one million people—that represent the next phase of market growth.

Two of the biggest emerging markets, India and China, are moving to end their historic protection of the profitable branded generics segment, a special focus for Big Pharma as it looks to extend the geographic range of its large inventory of off-patent medicines.

Industry price and access regulation is morphing—at warp speed. Early on in the emerging market gold rush, it was assumed that these governments would take many years to build the capabilities found in mature markets on controlling access and rewards in the medicines trade. But technology and communications improvements are such that regulators in emerging markets are closing the gap. This is particularly evident in pricing and reimbursement, where pharmaceuticals are easy to target, as a highly visible element in the health distribution chain. The issue is also politically sensitive because in most emerging countries pharmaceuticals comprise an uncomfortably high percentage of health spending—upwards of 40 percent or more of the total, compared to less than 20 percent in the industrialized countries. The rationale for action is simple: if countries want to build and finance a modern, integrated health system, then the share of spending on drugs has to fall.

The bump up in regulation is evident in a number of areas, including the application of domestic competition law to limit pricing freedom in South Africa; adoption of reference pricing in Vietnam; preferential access treatment based on local production commitments in Russia; discriminatory misuse of WTO GMP certification standards to delay foreign drug registration in Turkey; and a requirement for proof of cost-effectiveness for public drug reimbursement in Brazil.

Emerging governments are also obtaining support from their mature market counterparts eager to share best practices in regulation. Cross-border chatter is increasing. One example is the MOU signed in June between India's Department of Health Research and the UK National Institute for Health and Care Excellence (NICE) to help India establish a national health technology assessment (HTA) board to review the cost-effectiveness of new drugs. The transfer of expertise through this kind of de facto consulting contract is actually becoming a source of income for NICE and several other Western regulators. "Everyone is sharing this economic evidence. Cost effectiveness studies right now are simply nice to have as part of the reimbursement process, but in three years time we think it's going to become a requirement to obtain access in most emerging markets," Cem Baydar, IMS Consulting's senior principal based in Turkey told *Pharm Exec*.

In addition, two of the biggest emerging markets, India and China, are moving to end their historic protection of the profitable branded generics segment, a special focus for Big Pharma as it looks to extend the geographic range of its large inventory of off-patent medicines. India is adopting a plan to require licensing of generics only by their WHO INN name rather than by company brand. China is phasing out price preferences for products that date back to the time when the country did not offer patent protection for drugs, and are

The IMS Health "Pharmerging" 21

Algeria (new)	Poland
Argentina	Romania
Brazil	Russia
China	Saudi Arabia (new)
Colombia (new)	South Africa
Egypt	Thailand
India	Turkey
Indonesia	Ukraine
Mexico	Venezuela
Nigeria (new)	Vietnam
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now off patent. It is also expanding price controls on a list of more than 300 drugs deemed essential to public health that includes patented and branded off patent products.

As the pace of price regulation continues, the danger is a global convergence—in the form of a pricing race to the bottom. China's National Development and Reform Commission (NDRC) is conducting an investigation of production costs and drug pricing at 60 domestic and foreign-based manufacturers to determine whether China, with its relatively low GDP per capita, might be paying too much for its medicines compared to other countries. The inquiry includes a comparison of local prices against those in nine other countries. Adoption of a system of international reference pricing seems a logical consequence once the commission's findings are made public, along with plans to overhaul the drug registration process, later this year.

Overall, finding the "right" price for a product and then securing access to patients is destined to become a bigger headache for Big Pharma in emerging markets. The task is made more complicated by another, little-noticed trend: the majority of the world's poor now reside in a few of the biggest emerging countries—China, India, and Nigeria—that are also becoming richer. Politically sensitive "tiered" pricing schemes vulnerable to price leakage among consumers with vastly different buying power within countries appear to be the only way out of this conundrum.

This makes it more important to maintain a balance in the P&R process overall, by limiting global exposure to price points that reflect the lower level of purchasing power in emerging markets; if you tilt too far toward the latter, it could have a disastrous impact on prices in the rich countries where Big Pharma still derives most of its profits. Industry market access managers must operate in a world where no country wants to pay more: everyone wants to be "average." The risk is that a mishandled pricing strategy in individual emerging markets can drive that average way down. From a strictly organizational view, P&R is one function that has to be managed globally, even if your local management might prefer it otherwise.

Just a few years ago, emerging markets were lionized for introducing basic patent protection for biopharmaceuticals, accomplished largely through their ratification of the 1994 WTO Agreement on Trade-Related Intellectual Property Rights (TRIPS). Today, much of that optimism has faded.

Testing the boundaries on patent rights. Just a few years ago, emerging markets were lionized for introducing basic patent protection for biopharmaceuticals, accomplished largely through their ratification of the 1994 WTO Agreement on Trade-Related Intellectual Property Rights (TRIPS). Today, much of that optimism has faded. Industry encountered an early setback in November 2001, when WTO members unanimously adopted a ministerial declaration, on TRIPS and public health, allowing developing country governments to defer certain IP protections (including restrictions on compulsory licensing) in the event of a vaguely defined "public health emergency."

Use of this public health exemption has exploded in the last 18 months, mainly in the form of compulsory licenses that neutralize enforcement of a drug patent and/or compel the transfer of production rights from the originator to a generic competitor. While India remains the chief culprit—local patents have been revoked on products owned by Roche, Merck, Novartis, Pfizer, Bayer, Allergan, and GSK—the practice is now occurring in other countries, including Indonesia, Thailand, and the Philippines. China, which has a compulsory licensing provision in its new IP law but as recently as March said it had no plans to use it, imposed a license in July against the Gilead ARV drug, Viread. The decision has been interpreted as a means to promote local generic alternatives and drive down prices for a treatment that is critical to containing the growing incidence of HIV and Hepatitis B in China.

Due to the uncertainty it creates, this backsliding on IP has a cascading negative impact on the basic "back office" infrastructure required for any country that wants to compete globally on innovation. Foreign patent holders will hesitate to make important seed investments in local clinical trials, also limiting growth prospects for key innovator support functions like CROs. It complicates due diligence in negotiating research partnerships with the local private sector and academic institutions that rely on such links to facilitate basic science and entrepreneurship. Finally, concerns that exclusivity will be violated tends to knock the country down the list in any Big Pharma "go to market" launch strategy, which means that patients wait much longer to get access to the latest treatments.

Pfizer agrees. "The only way to shift the balance in our favor is by

showing that patent protection will increase the range of options—from medicines to service platforms and new delivery technologies—required to treat and cure neglected diseases. It's not the entire solution; its just part of the fabric of confidence that clothes the response," Roy F. Waldron, Pfizer's senior vice president and chief IP counsel told *Pharm Exec*.

China is a good example. A sketchy record of enforcement against patent violators means that, despite an investment in local R&D that now surpasses $1 billion, most foreign drug companies have erected internal "firewalls" that prevent the more promising breakthrough compounds from being tested in the country. The result is that China may be punching below its weight on drug innovation. Most experts believe it unlikely the government will achieve its goal of introducing a new "made in China" biologic to the world market before 2020.

Urge to mature

Taken together, these trends suggest that the emerging countries are actually entering a "maturing" phase—some are even beginning to exhibit structural characteristics of the industrialized country markets. Despite a slowdown in economic growth, the ascent of the middle-class consumer interested in obtaining more Western medicines will continue; many of these consumers are also aging, meaning that disease patterns between the West and the pharmerging countries are converging. This in turn will force governments in these countries to seek the same kind of policy solutions to healthcare financing and supply found in the United States and Europe—solutions that by definition will require more overt involvement from drug makers in expanding access to care, and not just for pharmaceuticals.

A key question for Big Pharma in emerging markets is how far it is willing to go in stretching for sales beyond the top tier, to the vaster set of opportunities found in the "middle of the pyramid." Success here requires abandonment of an operating principle that industry used to regard as sacrosanct: that is, we do nothing beyond developing and selling the pill. Instead, expanding sales is going to depend on offering something extra to the customer, the most important element of which is making that product affordable—and hence accessible—to a population base that is still more aspirational than affluent.

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Key to access: alternative funding

Despite having an advanced biologics portfolio that carries a stiff price premium in Western markets, Roche has made significant sales inroads in poorer countries like China, Brazil, and India by following this approach to business development. Struck by the fact that many cancer patients in China had to pay directly out of pocket for medicines they could not really afford, especially for a full course of treatment, Roche recently negotiated a new service model with the global reinsurer giant Swiss Re. With health data, testing and screening tools supplied by Roche, Swiss Re has set up insurance contracts with five Chinese insurers to provide private, reasonably priced individual drug coverage as a supplement to the government subsidized hospital treatment for certain types of cancer. The goal is to have 12 million enrollees in China by the end of this year, a small but still measurable dent in the access challenge that fosters goodwill from the government and other stakeholders while serving as a precedent for something larger in the future.

Roche has also been successful in offering its personalized diagnostics capabilities to narrow the range of patients eligible for its oncology medicines. This has resulted in government-backed funding for its breast cancer treatments in countries ranging from Brazil to India to the Philippines. "What Roche has proved is that there is a viable business in emerging markets for high-end products—the catch is finding innovative purchasing solutions that align with governments and deliver a market where there was not one before," says Guagenty.

You don't think the business of Big Pharma should play any role in healthcare reform? The message from emerging markets is, well, think again. In the end, what is going to make the most difference here is the same as anywhere else Big Pharma chooses to play: reducing that lengthy time to market. You've got to engage to get paid.

And the best way to do that is by adding others to the dance card. "Launching new products jointly with a reputable domestic partner is here to stay as the big differentiator against the prevailing paradigm of offering only your off-patent, late in life-cycle drugs," concludes Les Funtleyder of Poliwogg Investment Advisers.

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Front & Center

Operational Approaches for Oncology Clinical Trials with Targeted Patient Populations

The growth of personalized medicine is dramatically changing the ways oncology clinical trials are envisioned, designed, operationalized and managed. These new trial paradigms offer the promise of more effective oncology treatments for targeted groups of patients, but the transitions from traditional approaches to newer, more dynamic modalities also bring new challenges.

Research organizations and sites, among other things, need to devise new solutions that accelerate clinical trial enrollment for these targeted populations, and control costs if the benefits of personalized medicine are to be realized.

"As the volume of cancer research progresses, clinical trials are becoming more complex with the inclusion of biomarkers, rare tumors and a focus on small patient populations," said Cheryl Sampson, Senior Director, Clinical Trial Operations, US Oncology Research, McKesson Specialty Health, at the outset of her presentation at CBI's conference —Clinical Trial Budgeting & Project Management on July 17-18.

"What then, is the impact of personalized medicine on the development of targeted medicines?" asked Sampson. "In addition, what are the operational implications for clinical trials, and what are the approaches to optimize enrollment and execution of those trials?"

What is personalized medicine?

It is a promise to better tailor medical treatment to the individual characteristics of each patient. The blockbuster model of medical treatment offers the promise of some degree of efficacy for large populations. Personalized medicine offers the promise of superior efficacy for smaller, more targeted populations.

In oncology, four decades of scientific breakthroughs have moved treatment away from broad cytotoxic approaches toward more targeted tumor-toxic approaches that are potentially more effective against specific types of tumors.

This new paradigm has transformed cancer from a single disease to an array of diseases with multiple targets. Patients are no longer treated for cancer; they are treated for a specific type of tumor that has been identified with genetic or molecular testing.

Clinicians are increasingly looking to the pathology of a specific tumor when selecting treatments. It is crucial, for example, to know whether a particular breast cancer tumor is ER-positive or ER-negative in order to tailor treatment. The advent of KRAS testing is bringing a transformation to the treatment of colon cancer by identifying tumors likely to be susceptible to KRAS inhibitors. These more targeted, more personalized therapies are among the early results of a transformation in oncology research and development. Targeted therapies associated with a diagnostic agent currently account for more than half of the oncology pipeline. According to an article published in the Journal of Personalized Medicine in 2012 [R. Fleck and D. Bach, *J. Pers. Med*. 2012, *2*, 15-34], only a quarter of the molecules in clinical development could be considered targeted in 2000; that ratio had increased to two-thirds by 2010.

Targeted therapies and immunotherapies are projected to account for over 60% of global sales by 2017 (Datamonitor). And while therapeutic options that target biomarkers specific to small patient populations are expensive, they are also more effective than traditional therapeutic agents and can result in rapid market uptake.

The move to develop more targeted oncology agents requires the screening of a high number of patients to identify a small number of eligible patients. The influx of data has the potential and the power to change the trial and error methods that oncologists are forced to use in the absence of evidence-based data, which, in turn, will change drug selection, according to Sampson.

"The three specific areas of increased complexity that we think will impact research programs is the focus on more targeted patient populations, the need for accelerated development, and stricter criteria for investigational agents."

US Oncology Research

US Oncology Research, supported by McKesson Specialty Health, has enrolled more than 56,000 patients in clinical trials over the past 12 years, according to Sampson. "The network of researchers has approximately 900 investigators enrolling patients at

more than 225 locations," she said. "The number of trials US Oncology Research participates in has grown by about 18% in each of the past three years, but the average enrollment per trial has dropped by half. We now have to manage more trials of smaller size. We had to re-think our model and develop new solutions adapted to today's research paradigm."

An all-comers trial in lung cancer might enroll 400 patients. A trial for ALK-positive lung cancer, which represents about 6% of all lung cancers, is more challenging.

While accelerated development is important, biopharmaceutical companies must execute high quality trials that are operationally efficient and support high quality data output in a cost-efficient manner.

Operational Excellence

Good research practice is just beginning to adapt to the era of personalized medicine. Sponsors, CROs and other stakeholders must balance two opposing forces. On one side, clinical trials are becoming more complex and enrollment is becoming more restrictive. Operational and financial efficiencies are more difficult to achieve. On the other side, business imperatives call for accelerated trial completion, faster regulatory approval and ever-stronger data to support product differentiation and value propositions.

The majority of oncology treatments in early clinical development rely on biomarker data. That can leave sponsors and CROs in an operational quandary. Within the industry, there is no firm consensus on when to test. There is inconsistent testing and inconsistent data capture standards across organizations and even within the same organization. Payers are increasingly skeptical of molecular testing and diagnostics until and unless clinical value has been demonstrated in specific patient populations. Identifying and enrolling patients becomes more difficult as the target population becomes more closely defined.

New Solutions

"US Oncology Research, supported by McKesson Specialty Health, has redesigned its approach to clinical trials to create new solutions that evolve with the clinical trial process and treatment needs," said Sampson.

Solutions include the selection of two preferred lab vendors for molecular testing and corresponding physician guidelines on molecular test ordering. IT connectivity with lab vendors ensures structured lab results. These structured data can drive accruals for clinical trials as well as clinical decision support, prior authorization and payer utilization reviews.

To respond to the increased complexity of oncology clinical research and the need to maintain a high quality of research, US Oncology Research has created a model that includes three layers of oversight. In addition to the Principal Investigator (PI) required for all FDA-sanctioned studies, the US Oncology Research model adds two new roles.

A Study Investigator (SI) oversees the trial across the entire research network, championing the trial by driving provider awareness and education. The SI is also the primary contact for institutional review boards.

A Site Research Leader (SRL) leads the research at an individual site and acts as the local program champion. The SRL is responsible for adherence to study protocol and conducts oversight meetings.

The PI, the one role required by FDA regulation, oversees trial conduct, education and enrollment at the local site level and signs form FDA 1572, Statement of Investigator.

Central site management drives efficient study design, start up and site management. The central model is based on integrated technology solutions that are designed to support central budgeting and contracting on behalf of all study sites, a recommended site list supported by comprehensive feasibility study results, a central institutional review board (IRB), central preparation and collection of all site regulatory documents and a central investigational product center that controls delivery and management of all investigational products. This central model supports study start up in 45 days for Phase I and 90 days for Phase II-IV.

Two distinct technology platforms, iKnowMed and Care 2.0, interact to provide unmatched operational efficiency. iKnowMed is the top-ranked electronic health record in oncology and hematology according to the 2012 Black Book Rankings, and iKnowMed data currently represents more than 1,300 physicians. CARE 2.0 mines the EHR for specific patient data that matches open study protocols. Patients can be screened for trial qualification, and appropriate trials automatically appear in a list of disease-specific regimens at the patient's next visit.

The STAR (Selected Trial for Accelerated Rollout) system can generate needed regulatory documents as well as budgets and contracts within 14 days. Unlike traditional trial design in which sites are opened and patients recruited, STAR first locates eligible patients and then opens the site and begins data capture.

"This new model," said Sampson, "integrates clinical trial components that have never before been able to communicate and feed data to maximize trial speed, agility and data quality to drive the personalization, the precision and the effectiveness of cancer treatment."

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Promotional Review Committees: How to Achieve High Performing Teams

What it takes for promotional review teams to function at their best and avoid costly mistakes. By Arthur Lazarus

Most pharmaceutical companies have interdisciplinary committees with regular team meetings to discuss and review promotional material. Promotional review committees (PRCs) provide this essential function for pharmaceutical companies. They review all forms of advertising and promotion for medical accuracy, completeness, and realism, as well as for legal and regulatory compliance with the FDA and other authorities. PRCs also ensure compliance with company policies, voluntary industry codes, and anything that might create liability risk for the company, including patient privacy, and related content issues.

In addition to advertising and promotion, PRCs may also review unbranded, disease-state information and internal communications that describe marketing strategies or provide direction to the sales force. PRCs touch many parts of the organization, not only sales and marketing, but also R&D and health economics and outcomes research. Integrating data from clinical trials and other sources into advertising and promotion is one of the primary functions of PRCs.

PRCs must perform flawlessly, otherwise companies run the risk of receiving an enforcement letter from the FDA's Office of Prescription Drug Promotion. Enforcement actions undertaken by the FDA may spark investigations by the Department of Justice, sometimes resulting in significant fines, reputational harm to pharmaceutical companies and the in-

dustry, and corporate integrity agreements that impose additional processes and restrictions on companies.

I have served on many PRCs in different therapeutic areas across several companies. Here are some best practices issues critical to achieving high-performing teams.

Find a common voice. Given the diverse training and background of individuals who typically comprise the PRC—doctors, pharmacists, lawyers, and others—it is nearly impossible to obtain one writing voice among team members. Yet, word-smithing advertising copy or writing copy during team meetings takes up valuable time. PRC meetings should be spent optimizing claims and the promotional value of marketing material rather than wasting time on rewrites. PRCs should employ an editor to handle the "King's English," and any changes in advertising copy should be made only when absolutely necessary, as opposed to discretionary. No two people have the same writing style, so teams should not deliberate on minor differences in wording that say essentially the same thing. Be brief, be brilliant, and be gone.

Respect everyone's opinion. Differences of opinion among members of the PRC are inevitable. Although it is necessary to discuss these differences in team meetings, ultimately the PRC as a team is accountable for resolving any disagreements. Medical, legal, and regulatory team members must learn to trust each other and rely on the expertise of the individual in whose discipline the controversy lies. Occasionally, highly contentious or risk-management issues may be escalated to an "executive" PRC to overcome an impasse, but no one should ever be insulted or attacked for his or her opinion. Collegiality must prevail in all instances.

Create dedicated roles. Team cohesiveness develops over time, especially when dedicated positions are created on PRCs for each team member. A rule of thumb is that every hour spent in team meetings requires approximately two hours of individual review time before the team meets. Thus, for a team that meets six hours per week, each team member should plan to devote 12 hours of review time outside team meetings. This would be approximately the equivalent of a half-time position, assuming a 37.5 hour work week.

Maintain consistency. Continuity of team members from meeting to meeting is important. If there is a different representative from any discipline on Tuesday versus Thursday, additional work and revisiting of position will occur. Product managers, who are vital to PRCs, should be held accountable for carefully reviewing all material before it is submitted to the PRC to ensure consistency with prior decisions. Rules that guide the decision-making process in PRCs should be applied consistently within and between teams.

Manage team turnover. PRCs should be aware that a change in team composition due to turnover may create friction or change the chemistry of the team. PRCs should approach such a change with patience, helping to on-board new members while remaining receptive to their suggestions. PRCs should refrain from responding negatively to new members. "That's not the way we do it"—and other dismissive messages—are hurtful and unwelcoming. It is easier for teams to disregard feedback they don't agree with than hold themselves accountable for change. By the same token, new team members should keep in mind that their entry may cause apprehension or alarm in existing members. New team members should bring skills and experience from previous positions, but they should not boast how a previous employer allegedly did things better.

Balance autonomy and teamwork. To be effective, PRCs must work diligently with a relatively high degree of autonomy. Otherwise, team meetings may become suboptimal, bogged down by inefficient operations, potentially creating tension among team members and possibly compromising the integrity of the promotional review process. PRCs walk a fine line, because the workload is divided among team members from various disciplines who work independently, yet they must function as a unified team. A purely "divide

and conquer" approach, wherein individual team members work in a silo and seldom meet face-to-face, cannot be sustained.

Lead and influence. Even though PRC members are trained to be autonomous, promotional review is like a team sport, requiring the ability to be both a team leader and a team player. Conflicts and "turf" battles often arise as to who has the final say in team meetings. The truth is, although PRCs commonly fall under the leadership of regulatory affairs departments, a case can be made for medical and legal departments to govern PRCs. Unless team members accept their roles as both a team captain and a team member, and know when to exert their authority and when to acquiesce, dissention will ensue. Team members must also learn to appreciate the differences between authority and leadership and how to influence others to change from the status quo. Leadership should be viewed as a personal quality that enables an individual to influence others, independent of positional authority or the ability to reward or punish others.

Adhere to timelines and deadlines. PRC meetings should start and end on time. The meeting agenda should estimate the time required for each job and avoid squeezing too many jobs into the allotted meeting time. Jobs should be prioritized by a marketing operations committee well in advance of team meetings. Generally, all material should be submitted a full week before it is expected to be discussed in a team meeting. In this way, PRC members will have ample opportunity to review the material before the team meets. "Rush" jobs and jobs that require expedited reviews are to be expected from time to time—for example, press releases and updates to the prescribing information. Thus, the agenda should allow some flexibility, but it should not become a moving target in which jobs are constantly rearranged or changed at the last minute.

Conduct all relevant business in team meetings. The goal of the PRC is to make clear and responsible decisions by having all the necessary medical, legal, and regulatory personnel and resources in place during the team meeting. Working excessively offline, between team meetings and on weekends, may signal a dysfunctional team. Responding to excessive e-mails and "copying all" can become fatiguing and disrupt the flow of material into an otherwise healthy PRC. Team morale can become deflated by incessant job changes and requests for job approvals outside team meetings.

Strive for economies of scale. In the traditional business model, PRCs are constituted around marketed products. In this model, the PRC reviews jobs that are designed for both healthcare professionals and consumers, but there is usually only one dedicated team per product. An alternative model is to segment PRCs into "healthcare professional" and "consumer" teams. In this model, each team is responsible for reviewing two or more products, potentially achieving greater economies of scale (fewer overall PRCs). A third team—the "disease state" team—could be tasked to review information promoted to increase awareness of diseases for which the company has marketed products.

Innovate. Every member of the PRC is expected to review his or her job individually, before the scheduled interdisciplinary PRC meeting. However, a different method may be better suited for some jobs, for example, jobs that are heavily weighted toward one discipline—medical, legal, or regulatory—and jobs that were previously reviewed at a "live" meeting and require a "second look" by only one or two team members for final approval. Likewise, new marketing concepts are probably best discussed in a forum other than the PRC, because only one or two PRC members may be necessary to provide specific feedback requested by the project originator. Select individuals may know potentially viable ideas in compliant terms from the outset, reducing the number of "non-starter" concepts. The project can be reviewed by the full team once the concept is fully "baked" and the job has been submitted to the PRC.

Include additional personnel in team meetings as necessary. PRC meetings are often slowed down by lengthy discussions in the absence of important stakeholders who can shed light on the nature of the job. These stakeholders, often from marketing, sales, or sales training, usually have the answers to questions such as: "How will this article reprint be distributed to healthcare professionals?" "Will this brochure be too complex for consumers to understand?" And, "Who is the intended audience for this visual aid—healthcare professionals, managed care organizations, consumers, or others?" PRCs must make decisions not only about the medical, legal, and regulatory ramifications of marketing material, but also about the "taste and tone" of advertising and whether approved marketing items can be responsibly executed in the field. Input from non-core team members may be helpful in this regard.

Take the guesswork out of work. In addition to marketing and sales personnel, the attendance of marketing agencies may be required at PRCs. Their presence may be especially helpful when understanding marketing projects in the digital realm or when fulfilling multicultural marketing initiatives. Because the latter often require translation (and accurate back-translation) of content from English to another language, it may be desirable to have a certified translator attend the PRC meeting. There is no reason a PRC should have to make assumptions about questions other people can readily answer.

Delegate with authority. It should be incumbent upon all team members, including project originators, to find qualified and knowledgeable substitutes to attend team meetings in their absence. Alternatively, absent members could attend the PRC "virtually," using any number of web-based applications to collaborate with the team. In any case, whoever is participating in the PRC should be able to represent their discipline and should be empowered to make final decisions on all but the most difficult issues.

Embrace the digital domain. Finally, PRCs must learn to adjust to the digital promotional age in order to evaluate proposed tactics and strategies in this realm. They must champion new technology designed to enrich traditional marketing channels and relationships with customers. However, because it is unlikely that regulatory authorities will carve out the digital domain from the regulations that apply currently to print and broadcast material, PRC members will need to sharpen their digital skills, and teams may need to add specialized members or partner with niche companies specially equipped to work with PRCs in areas critical to the future of e-promotion—namely, the use of social media and Internet-connected devices such as computers, tablets, smartphones, and game consoles to engage consumers and providers with online advertising. PRCs must have mechanisms in place to track changes in the various social media platforms that alter their programs regularly, often without much notice to the advertisers, and sometimes without a strong understanding of the regulatory implications.

In my experience, by following these basic principles, PRCs should be able to produce a quality product while working in an atmosphere of trust and respect. Equally important, the output of the PRC, whether a sales aid, journal ad, website, television commercial, or advertising through any other format, should be medically and legally sound, capable of meeting the requirements of regulatory authorities in the host country. The ultimate goal of such a team should be the creation of a finished product which provides accurate and complete information to guide the prescribing physician or the patient in utilizing the advertised product to achieve the desired health outcomes. PE

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Making Sense of the Sunshine Act:
A New Era for Drug Promotion

Now that the Sunshine Act's Open Payments spending disclosure program is live, the federal government's lead officer for compliance explains how the new web-based system will work—and how US industry, providers, and patients will be better off by making their relationships fully transparent. By Shantanu Agrawal

For decades now, financial relationships have existed between pharmaceutical companies and physicians and hospitals, some of which have come under scrutiny and caused considerable public controversy. One example of a common financial relationship are payments made by pharmaceutical companies to physicians for consulting services on experimental products under investigation or development. These transactions have involved research activities, gifts, speaking fees, meals, or travel, and often occur privately so that no one except for the parties directly involved knows the details of the transactions.

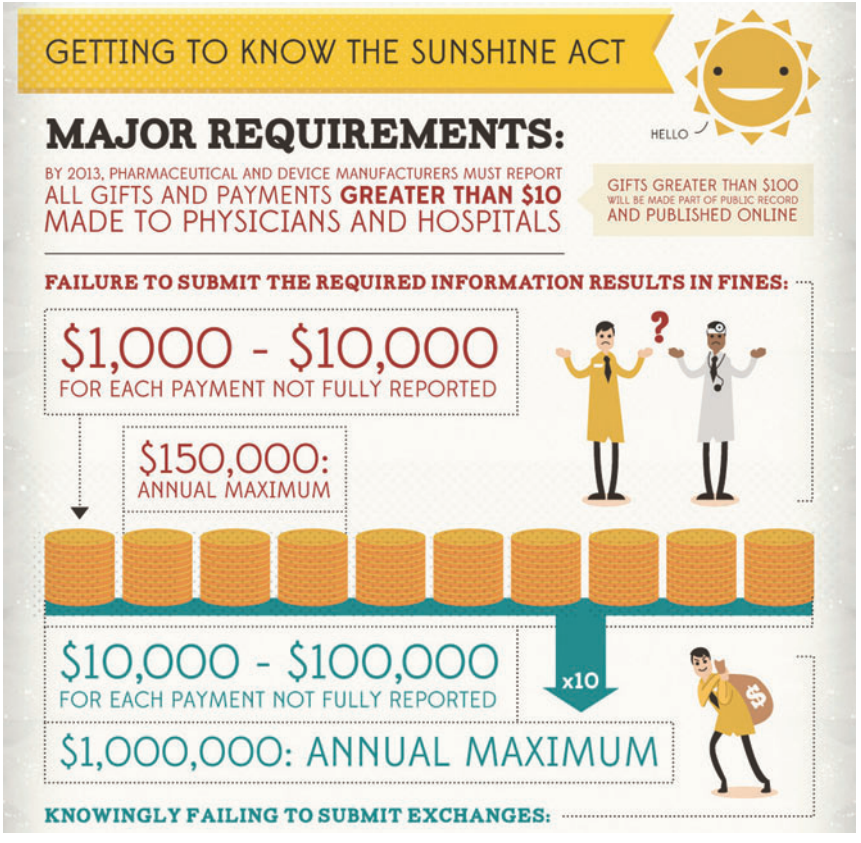
The typically private nature of these relationships has recently changed, as the Centers for Medicare & Medicaid Services (CMS) now requires public transparency about these transactions occurring on or after August 1, 2013. A newly enacted law, the Physician Payments Sunshine Act (also known as the Open Payments program) is intended to make information about these payments between pharmaceutical companies, physicians, and hospitals transparent. Open Payments requires that manufacturers of drugs, devices, biologicals, and medical supplies annually report to CMS most payments and "other transfers of value" that they make to covered recipient physicians and teaching hospitals. Manufacturers and group purchasing organizations (GPOs) will also report ownership and investment interests held by physicians or their immediate family members during the preceding calendar year and payments made to those physicians.

As a result of the Affordable Care Act (ACA), such financial relationships will be publically disclosed on a CMS Open Payments website so that healthcare consumers, clinicians, and stakeholders can be better informed about the nature and magnitude of these relationships. Industry data collection tracking these transactions began on August 1. Industry will register with the program and submit 2013 data by March 31, 2014. In the fall of 2014—a little more than a year from now—CMS will post the 2013 data on the Open Payments website, which will be accessible to the public. This public posting will occur annually.

You may be considering what this new law means for your organization and have serious questions. Is my organization ready for this new law? Do I know what we have to do to comply or how to go about doing it? How much will compliance cost? And, by the way, what will public transparency of this information mean—will it be helpful or will it distort public opinion and hamper beneficial relationships between our company and physicians?

Open Payments is designed to do what laws are supposed to do: address widespread public concerns, and in this case, create a window into an area of healthcare previously unavailable to the public. In 2009, the Institute of Medicine published a report, "Conflicts of Interest in Medical Research, Education and Practice" that described such concerns. The influential report also recommended implementing a national disclosure program for payments to healthcare providers and prescribers. The Open Payments program was created to address this and other calls for transparency of these financial relationships between the industry and physicians and teaching hospitals.

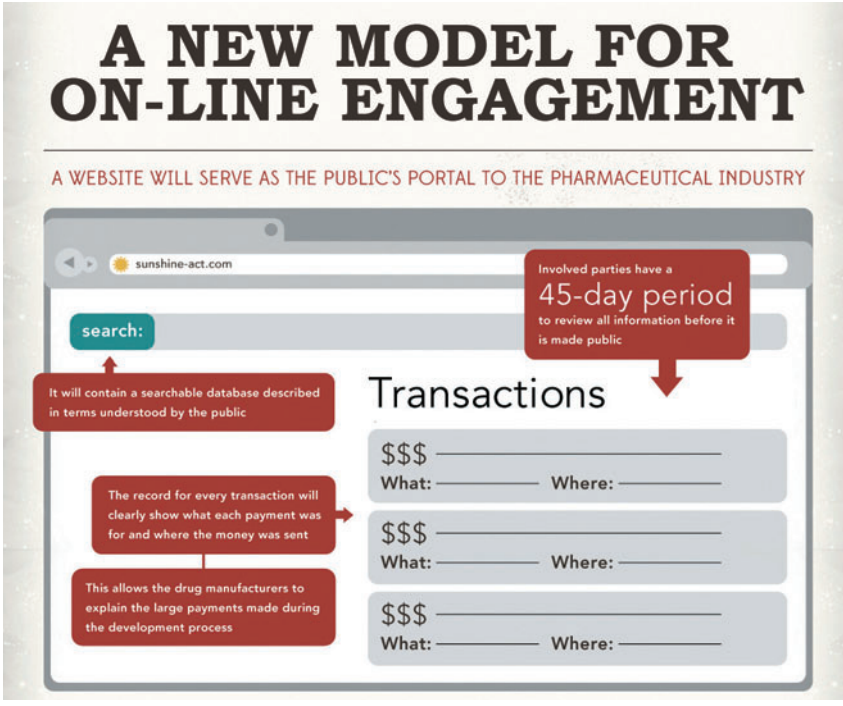
Like industry, CMS fully appreciates the benefits that accrue from ongoing collaborations among pharmaceutical manufacturers, physicians, and teaching hospitals. Those joint efforts have long contributed to the discovery, design, and development of life-saving drugs, and delivered better health to patients worldwide.



Source: Center for Business Intelligence

However, certain financial relationships may not be beneficial, and may in fact create conflicts of interest that negatively affect patients. Under Open Payments, the industry will disclose the nature and extent of such financial relationships. The data will help patients make decisions about the delivery of their healthcare. In the process, disclosure may also help to discourage improper influences exerted over research activities, education, and clinical decision-making that can potentially compromise clinical integrity and the quality of patient care—or potentially lead to higher healthcare costs.

Open Payments will serve as a valuable national resource, addressing a long-standing information void and providing more transparency about the healthcare market. It is in the spirit of transparency that CMS is striving to implement this law, with open engagement and input from the stakeholders.. We have worked closely with stakeholders to better understand the current scope of the interactions between manufacturers and physicians and teaching hospitals. Last December, for example, when finalizing the policy and rule for this program, CMS weighed feedback from nearly 400 interested parties, including pharmaceutical manufacturers. The final regulation was preceded by no fewer than 251 pages of commentary and



Source: Center for Business Intelligence

explanations, an example of the deliberate approach to consider and integrate the comments received and make the rationale for final decisions clear and transparent.

Still, CMS understands these disclosure requirements will be a major undertaking for many companies. CMS is taking great care to simplify the procedures involved and provide support as industry undertakes this effort. Starting with the regulation, CMS has provided accommodations, such as a longer period of time than was required in the law—six months—for industry to prepare for the start of data collection.

Already, the CMS website offers considerable information, often in the form of fact sheets, in straightforward language to help make this program understandable. It has provided manufacturers with three customized file specifications to help implement their data collection. An electronic system is being developed to facilitate the registration and reporting process via a portal on a secure website. All participants will then have a voluntary opportunity—45 days—to review, dispute, and correct any information believed to be inaccurate prior to its publication. This review is very important to help ensure that the information made public is accurate and complete.

Open payments will serve as a valuable national resource, addressing a long-standing information void and providing more transparency about the healthcare market.

CMS has developed new free mobile apps, one for industry and the other for physicians, that can assist in Open Payments implementation. You can download the mobile apps directly from your app store (iOS Apple or GooglePlay) and search for Open Payments. It should be noted that the apps are used for tracking purposes only and do not directly transmit information to CMS

The benefits of compliance are extremely worthwhile. Several advantages are anticipated. Disclosure will enable patients to make informed decisions when choosing healthcare professionals and treatments. Payers will be better equipped to identify conflicts of interest and make better decisions regarding ordering or prescribing physicians. And providers will have more knowledge about those physicians publishing important data and establish guidelines and standards of care.

Compliance with this program is being taken extremely seriously, and the companies involved should understand the consequences for non-compliance. Violations carry consequences: civil monetary penalties are capped annually at $150,000 for failure to report and at $1,000,000 for knowing failure to report.

As implemention of this program in collaboration with the industry begins, CMS encourages you to ensure that your organization is prepared and ready to be in full compliance with the reporting requirements. Start early and integrate the processes into your business operations, and use the CMS website and its resources to help educate your employees about the program. The public deserves to be fully informed about financial relationships among healthcare providers, and industry should welcome the opportunity to be more transparent than previously required. We are all in the healthcare business. Healthcare means taking care of patients, and the new law will better enable all of us to keep putting patients first. PE

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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.

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 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."

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. —Gene Siegal, MD

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

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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.

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 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."

Pathologists are well-positioned to deliver care that is personally tailored, highly effective, and cost efficient.

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. PE

Editor's note: Founded in 1922 in Chicago, the American Society for Clinical Pathology is a medical professional society with more than 100,000 member board-certified anatomic and clinical pathologists, pathology residents and fellows, laboratory professionals, and students. ASCP provides excellence in education, certification, and advocacy on behalf of patients, pathologists, and laboratory professionals. For more information, visit www.ascp.org.

The Drug Combination Competition

Companies are leveraging combinations of drugs and other products to gain competitive advantage and market share.

The development, commercialization, and utilization of drug combinations have skyrocketed in the United States. According to PharmaCircle research, the number of fixed dose combinations (FDC) approvals has more than tripled over the last decade compared to the early 1990s. Currently, there are numerous marketed FDCs and other combination regimens spanning multiple therapeutic areas, including infectious disease (HIV/AIDS, Hepatitis C, bacterial infections); oncology; endocrine disorders (diabetes, lipids); cardiovascular disease (hypertension, heart failure); women's health (contraception, menopause, osteoporosis); and respiratory diseases (asthma, COPD). According to an Oliver Wyman analysis, there were over 25 notable novel combination development programs underway in oncology alone in 2011.

Several factors have driven the dramatic escalation of combination products over the last decade:

Greater scientific understanding. Recent scientific advances have enhanced our understanding of the pathophysiology of HIV, cancer, and other complex diseases. Highly active antiretroviral therapy (HAART)—the use of at least three HIV drugs acting on different viral targets—reduces HIV replication, viral resistance, patient mortality, and morbidity rates while improving quality of life. Similarly, increasing recognition that most cancers use multiple pathways to grow and proliferate has spurned development of entirely new classes of oncology agents, such as immunotherapies and targeted therapies, which are being combined to inhibit distinct pathway targets in order to improve treatment response while minimizing tumor resistance and side effects.

Supportive regulatory and clinical environment. Historically, the FDA and the US medical community were skeptical about drug combinations. However, regulatory policies and clinical thinking have dramatically changed over the last decade. The FDA established the "Office of Combination Products" in 2002 to evaluate combinations of drugs with other medicine products, such as devices and biologics. In 2004, the US government announced an expedited pathway for the FDA to review low-fixed dose combinations, co-packaged therapies, and single-ingredient HIV therapies for use by grant recipients of the US President's Emergency Plan for AIDS Relief. This past June, the FDA issued guidance for the "co-development of two or more new investigational drugs for use in combination" to address the rising number of novel combinations.

Addressing public health threats. FDCs are critically important for managing global infectious disease threats such as HIV/AIDS, malaria, and tuberculosis. The World Health Organization and other public health entities have encouraged the development of fixed-dose combinations which may improve adherence, reduce costs, and facilitate distribution in developing countries.

Product differentiation opportunities. With increasing brand competition, companies are eager to demonstrate better efficacy, safety, and convenience using a combination which is synergistic or additive. Companies competing in HIV, asthma/COPD, and diabetes have demonstrated higher efficacy rates with combinations versus single agents.

Increased utilization. Companies are pairing second- and third-line drugs with first-line products to enhance market access, earlier use, or preferred utilization. For example, many companies have combined their diabetes type 2 agents with first-line metformin, including Merck's combination of its best-selling brand Januvia with metformin to create Janumet.

Leveraging the portfolio. Companies increasingly are adopting a "multi-level competition" approach where they seek to win not only with a single brand but also across their product franchises and portfolios. Gilead Sciences wants to maximize sales of multiple HIV products to enhance its HIV franchise as well as with its new Hepatitis C (HCV) products to win with its overall anti-viral portfolio. Similarly, Roche bolsters sales of individual brands and its overall oncology portfolio by

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encouraging the use of combination regimens of its cancer agents.

Extending the patent life. Industry critics note that companies combine drugs nearing patent expiry with newer drugs with longer patents to extend the proprietary rights and marketability of the older agent. Some believe that Pfizer was using this "evergreening" strategy in its failed attempt to develop its powerful HDL-raising developmental agent torcetrapib only in combination with its best-selling, near patent-expiration agent Lipitor, instead of as developing it as monotherapy.

Combination drugs can be classified into two general categories: "combination drugs," consisting of drug-drug combinations; and "combination products," consisting of drug/non-drug combinations. A *combination drug* most commonly refers to a fixed-dose combination, a formulation including two or more active pharmaceutical ingredients combined in a single dosage form. However, companies may promote drug combination regimens which are not necessarily fixed dosed, such as co-packaged products or "free combinations," two or more medicines with separate formulations and specific labeling for simultaneous use. Initially, fixed-dose combination drug products were developed primarily to target a single disease, such as Gilead's anti-HIV FDCs. However, some FDCs target multiple diseases or conditions. For example, Pfizer's Caduet is a FDC containing Lipitor to treat hypercholesterolemia and Norvasc to treat hypertension.

The FDA defines *combination products* as those which "combine different types of medical products, such as drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity." Examples of combination products include a monoclonal antibody combined with a therapeutic drug; a device coated or impregnated with a drug or biologic such as a drug-eluting stent; an orthopedic implant with growth factors; or insulin injector pens and metered dose inhalers.

Competitive combination strategies

Pharmaceutical companies have leveraged combination products in a variety of ways to gain competitive advantages and enhance product sales:

Roche/Her2+ combination products. Roche has been masterful in designing and executing winning drug combination strategies as exemplified by its fixed-dosed, free, and drug-conjugate combinations targeting patients with HER2+ breast cancer. For over a decade, Roche's monoclonal antibody Herceptin combined with chemotherapy has been the mainstay of treatment for HER2+ metastatic breast cancer (mBC). Last year, the company launched Perjeta, a first-in-class HER dimerization inhibitor to be used in combination with Herceptin for mBC. Early this year, Roche launched Kadcyla, the first antibody-drug conjugate (ADC) for the treatment of HER2+ mBC. Roche is positioning Kadcyla—which contains Herceptin—to eventually replace Herceptin as a first-line mBC agent in combination with Perjeta and become the monotherapy of choice for second-line treatment of mBC. "Kadcyla is an antibody-drug conjugate representing a completely new way to treat HER2-positive metastatic breast cancer, and it helped people in the EMILIA study live nearly six months longer," said Hal Barron, MD, Roche's chief medical officer and head, global product development. "We currently have more than 25 antibody-drug conjugates in our pipeline and hope this promising approach will help us deliver more medicines to fight other cancers in the future."

Gilead Sciences/HCV combinations. Gilead is using a similar drug combination strategy to win in the HCV infection space as it did in HIV. Data presented in March demonstrated that a triple regimen of the HCV sofosbuvir, ledipasvir, and ribavirin produced a 100 percent response rate after 12 treatment weeks for HCV genotype 1 patients. In June, the FDA granted priority review for Gilead Sciences new drug application for sofosbuvir, a once-daily oral nucleotide analogue inhibitor for the treatment of HCV infection in combination with ribavirin (RBV) as an all-oral therapy for HCV-infected patients with genotypes 2 and 3 and in combination with ribovarin and pegylated interferon for treatment-naïve patients with genotypes 1, 4, 5, and 6. Gilead is developing a sofosbuvir-ledipasvir coformulation that is being tested with and without ribavirin. FactSet Research Systems estimates that annual sales of sofosbuvir and its combinations will exceed $6 billion and become the company's biggest selling product by 2017.

Teva/combination strategy. Teva Pharmaceuticals, the world's largest generic manufacturer, has announced that combination drugs and products represent an integral part of its new competitive strategy. Teva is pursuing "new therapeutic entities," new formulations or combinations of older drugs, which would leverage Teva's competitive advantages in generics, innovative specialty CNS drugs, and product formulation. For instance, Teva recently acquired Alexza Pharmaceuticals and its Staccato aerosol delivery system to serve as the platform for many new product combinations using already-approved drugs. In January, the FDA approved Alexza's first product Adasuve, which combines the nearly 40-year-old anti-psychotic drug loxapine with the company's new inhalation delivery device.

Scientific, clinical, regulatory, and commercial factors will continue to stimulate the development and utilization of drug combinations and shape the competitive landscape. Progressive companies will seek to preempt rivals by evaluating and developing their in-house drug candidates, identifying external drug and product combinations and partners, and by preparing insightful competitive strategies to win the drug combination competition. PE

Source: Artisans of Bali, http://artisansofbali.com

UNIVERSAL COVERAGE: Weaving Indonesia together

Ask Indonesians about a bad experience in medical care and each will have a story to tell. The poor state of Indonesia's health care system has turned 'improving quality' into the top priority of the government of Indonesia. Better quality of care has become especially important as the fourth most populated country in the world moves into full traction with its plans to achieve universal health care coverage.

According to the Ministry of Health, 72 percent of the population, just over 176 million Indonesians, were already part of some type of health financing scheme. Now Indonesia's policymakers are committed to covering every citizen by 2019. The implementation of universal health care coverage will start in January 2014 and is widely seen as a significant step forward for Indonesia's 238 million people.

Badan Penyelenggara Jaminan Sosial, BPJS as the system is locally referred to, aims to drastically increase the quality and access to medicines and medical treatment to the entire Indonesian population. From policymakers to health care providers, drug manufacturers to distributors, all stakeholders in Indonesia's health care and pharmaceutical sector are now facing the critical task of defining their role within this changing environment.

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Most multinational companies (MNCs) do not expect to play a major role within BPJS but, despite the vast volume, serving BPJS will not be easy or cheap for local manufacturers either. Not only are they required to ramp up manufacturing capacity to serve a growing market, permits to manufacture –due to Indonesia's Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S) adherence– have become stricter than ever.

Increasingly important within Indonesia's changing pharmaceutical landscape is the role of the distributor. Not only will distributors play a key role in making universal healthcare coverage a reality by physically making medical devices and medicines available across Indonesia's complex geography, they will also play an essential role in identifying where and how the market will benefit from BPJS by providing the manufacturer with the latest data from the field.

Promising macro-economic data, exponential growth rates, demographic potential, and a growing middle class have drawn Indonesia into the international spotlight, earning a place among the world's 'pharmerging' countries. Executives should not stare themselves blind on the double digit growth rate however. Indonesia remains a market where both MNCs and local pharmaceutical companies can enjoy steep growth curves-- provided they are willing to invest in the long run. These long term investments can take on various formats, including manufacturing, partnering, and brand building. All will be central to function as an agent of change while Indonesia heads towards universal health care coverage.

POOR CARE NO MORE

BPJS implementation ends an era of uncertainty around the government's commitment to launch universal coverage. Assigned as the chairman for the implementation of universal health care coverage in Indonesia is the country's Vice Minister of Health, Mukti Ali Ghufron MSc, PhD. Ghufron and his team define

TOTAL MARKET
(Prescription medicines and OTC/Non-prescription)

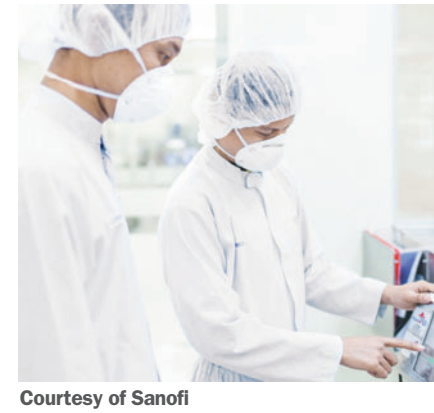
RANK	COMPANY
1	KALBE FARMA
2	SANBE FARMA
3	SOHO
4	PHAROS INDONESIA
5	DEXA MEDICA
6	BIOFARMA
7	TEMPO SCAN PACIFIC
8	DANKOS
9	FAHRENHEIT
10	SANOFI
11	INTERBAT
12	KONIMEX
13	DARYA VARIA
14	BAYER INDONESIA
15	PFIZER
16	KIMIA FARMA
17	NOVARTIS
18	LAPI
19	HEXPHARM JAYA
20	NOVELL PHARM

Source: IMS Health

KEY INDICATORS INDONESIA

Population	247 million (4th largest)
Gross national income per capita (PPP international $)	USD 4,500
GDP growth	6.20%
Total expenditure on health as % of GDP (2011)	2.70%
Total pharma market	USD 7.6 BN
CAGR	12%

Source: 2012 data, IMS, WHO & World Bank



Courtesy of Sanofi



From left: Dr. Nafsiah Mboi, Minister of Health; Eric NG, President Director - Sanofi; Parulian Simanjuntak, Executive Director - IPMG

government commitment as a key success factor to a successful implementation. "From a legal point of view, a law has already been formulated and launched. We have created a roadmap, together with all stakeholders, including the unions and the Chamber of Commerce, for the successful implementation of the plan. From a financial point of view, a budget has already been agreed upon: for 2014, an amount of IDR 1.75 trillion (USD 1.7 billion) will be provided to cover the poor and the 'near poor'," he said.

In parallel, increasing the quality of care is seen as equally important to the Ministry. "My main concern is the quality of our health care services. It would not make sense to provide health care to everyone in the country if its quality is poor," said Minister of Health, Nafsiah Mboi, Phd. "So far, we have been preparing rigorously to improve the quality of care. For health care facilities, our vision is a very strong primary care network combined with a good quality referral system." According to the Ministry, Indonesia now has roughly 9,500 primary care centers or one for every 30,000 people. "Although these numbers match the required standards, we need to work on improving the quality at primary care level," she said. "In terms of hospital care we now have 2,138 hospitals, 829 which are government owned, across the country. These hospitals have standards and accreditation which guarantee the quality of care that we need."

FROM ROSE-COLORED GLASSES TO REALITY CHECK

MNCs are ramping up their sales force, a scarce resource, to serve a growing medical community at Indonesia's private hospitals, but they remain puzzled about public procurement opportunities to serve public hospitals and BPJS. "These companies are trying to understand what their place will be within the system," said Parulian Simanjuntak, executive director of the International Pharmaceutical Manufacturers Association (IPMG). "In order to contain cost, the government has already proclaimed that generics will be mainly used under the new plan. Therefore, the question arises whether the MNCs are allowed to participate in the generics business. "We would like more clarity on what exactly will happen with regards to the social insurance

system. There should be no limitation as to who can participate in the universal health care plan." And even though Indonesia is the fourth most populated country in the world, big pharma still only touches a fraction of that market. Universal health care coverage, however, is expected to enlarge the patient base that can afford innovative medicines.

From left: Dorodjatun Sanusi, Executive Director-GP Farmasi; Johannes Setijono, Chairman-Kalbe Farma

"Today, just about half of the Indonesian population has some sort of access to health care insurance," said Eric Ng, president director of Sanofi Indonesia. "When you zoom into the situation however, you immediately see that the most advanced coverage is only provided for the civil servants through the Asuransi Kesehatan Indonesia (ASKES) program. Most of the MNCs primarily operate in this segment of the market, which at present only amounts to an estimated 20 to 30 million people. Universal health care coverage sometimes sounds exciting, but it may not be an opportunity for everyone. The plan targets a very basic package of health care based on low cost generics. However, we believe that the growing base of the population, which the government aims to cover in full by 2019, will serve as a driving force to increase the overall access to medicines. We believe that the base of the aforementioned 20 to 30 million people, which most of the MNCs target today, will theoretically increase to roughly 120 million people in 2014 alone. While we should not assume that our business will increase proportionally because of the price-volume effect, which implies that greater volumes will gradually push down the price of medicines, we do believe that Sanofi will have a much greater role to play in this country when such a large number of population requires access to medicines."

Filling the voids

With only 2,7% of GDP spent on health care, Indonesia offers room for growth. Prodia, a local health care services company created in 1973, was sparked by the ideas of 'better diagnosis' and 'quality as a way of life'. The lack of health care infrastructure and clinical laboratories due to years of underinvestment pushed Andi Widjaja and three other founders to pioneer the market for clinical laboratory services. "We were the first International Organization for Standardization (ISO) certified laboratory, the first local independent contract research organization (CRO), the first occupational health institute, the first in diagnostics, and the first in stem cell research," said president director Endang Hoyaranda. "We are not active in areas where other companies are already active." In an emerging market like Indonesia, the private industry has a key role to play in shaping, if not creating, the market. For the clinical trials side, for instance, the Badan Pengawas Obat dan Makanan Republik Indonesia (National Agency of Drug and Food of the Republic of Indonesia) assigned a team of industrialists and academics to develop Good Clinical Practice (GCP) guidelines, which became an adapted and adopted version of the International Conference on Harmonisation Good Clinical Practice (ICH GCP). As the first CRO in the country, Prodia had a strong presence on this team. Today, the company partners with the leading CRO Quintiles to include Indonesia in global clinical trials.

Andi Wijaya, Founder, Prodia Group

Endang Hoyaranda, President Director-Prodia Group

PIC/S & PENNIES

When it comes to serving the generics-focused BPJS niche, Indonesia's local pharmaceutical companies are in a prime position. "These pharma companies will need to look at ways to increase their current capacity and ensure the readiness of their products," said Darodjatun Sanusi, executive director of GP Farmasi Indonesia, the association of generic drugs manufacturers. "At the same time, they have to find and sustain the competitive advantage of their products, particularly as the markets will open up more and barriers to trade will decrease,"

If Indonesia's local manufacturers supply BPJS, they will also be the ones feeling the much expected price-volume effect. "It will change the whole landscape and turn Indonesia from a self-payers market into a government and private insurance-driven market," said Johannes Setijono, chairman of Kalbe Farma, the largest listed pharmaceutical company in the ASEAN region. "The private insurance companies, which are still small today, are therefore expected to see their bargaining power increase significantly. The plan is expected to not only drive up market volume but also create severe price pressures."

Two decades ago, one could already see several manufacturers moving out of the big cities and into industry-friendlier outskirts, moves that coincided with a government push to force GMP standards upon the industry. "Meprofarm was founded by my father in 1973. Two decades later, in 1995, we moved premises," said Eric Darius Mardiwidyo, president director of Meprofarm,a local generics manufacturer. Now, the company is based on the outskirts of Bandung, the second largest metropolitan area in Indonesia 87 miles southeast of the capital, Jakarta. "The move was the direct result of the company's rapid growth, as well as new government regulations to comply with GMP standards," Mardiwidyo said. "GMP compliance was achieved by December 1995, boosting the growth of the company further. In 2006 we acquired additional land next to our existing facilities in order to build our new facility 'Meprofarm 2'. This second facility was completed in 2010 and added a number of new lines to the company: injectables, liquid syrup and creams. It also includes storage space that now makes up our central warehouse. Most of the growth will sit in generic tablets and capsules. Specialty products like hormones, oncology and vaccines, for instance, are going to be attractive areas to invest in."

A FOR ACCESS IN THE ARCHIPELAGO

Partnering with a top notch distributor may be desirable in any pharma market; it is a must in Indonesia. With over

Indonesia Report

6,000 inhabited islands scattered across both sides of the equator, the Indonesian archipelago is the world's 16th largest country in terms of area. "As a distributor, you easily have to deal with forty-plus companies for transportation alone," said Santiago Garcia, CEO of APL Care, the country's leading distribution company for the pharmaceutical and health care sector. "Moving goods and people is very difficult because the links between some of Indonesia's key cities are missing. We also notice that truck loads are often incomplete while the discipline among logistics companies is often lacking. Electricity cuts are another big issue, especially when we start talking about cold supply chains. However, the situation is improving and changes are happening in this respect, and these challenges are an integral part of doing business in Indonesia. Every time companies are under pressure, goods are being sold to wholesalers at severe discounts. We, however, target the proper channels consisting of hospitals, doctors, clinics and pharmacies. We want them to work with us and work on demand generation, rather than flooding our channels at discount prices." While Indonesia's leading independent distributors APL Care, Dos Ni Roha and Pentavalent have a significant presence in the market, they compete head-on with in-house distribution companies that belong to local pharmaceutical manufacturers such as Kalbe Farma and Dexa Medica.

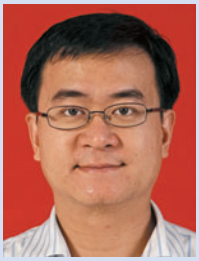
From left: Erik Darius, President, Meprofarm; Santiago Garcia, President Director - APL Care

2013 is an exciting year for the industry, a year of preparation for implementation of universal health care coverage in 2014. The industry will see itself forced to reshape business strategies to supply the system with quality medicines, be it branded originals or their generic counterparts. MNCs with the ability to play in the generics space will stand a good chance in excelling in the Indonesian market, while those without generic capabilities are likely to continue along a growth path nurtured by optimistic macro figures. Local companies must professionalize their operations and invest in more capacity and better quality standards. The expectation is for Indonesia to continue its double digit growth path, which makes it an exciting pharmaceutical market with many opportunities. But growth will require more than finding the right portfolio. It will come down to becoming a true partner to Indonesia's healthcare system and its many stakeholders.

HR War

Luthfi Mardiansyah, President Director of Novartis Indonesia

"When I interview people, I ask them why they want to change for the same position in another company. In general, it always comes down to incremental salary increases," said Luthfi Mardiansyah, president director of Novartis Indonesia. "We see similar HR scenarios in markets like China. In the past, there were no MNCs and the market was not growing. But today, the situation is very different. At Novartis, we have grown from 230 medical representatives in 2011 to almost 500 today. If another company wants to build similar capabilities, they will naturally look at Novartis to source new talent. There is a talent war at the moment. This is quite a normal phenomenon indeed, but the only thing we need to look at is how we can retain the best people. We have to do more than create remuneration-based incentives alone. Instead, we need to look at other elements such as career development, international opportunities, and so forth."



Steve Yang, Chief Executive Officer - Metiska

Family grip on local pharma

According to Family Business Network, the largest global association for family-owned businesses,, more than 90 percent of businesses in Indonesia are family-owned and controlled corporations. Mostly created in the 1960s or 70s, these companies have now reached a crucial moment: the handover to the second generation. Doing so, they are taking aggressive measures to adopt good corporate governance. Metiska Farma, a generics company headquartered in Jakarta, recently went through a change in control when its owner was temporarily immobilized by stroke. "My father is still involved in the running of the company, but I took over full-time in 2009," said his son Steve Yang, now chief executive officer. Yang, a PhD in biotechnology from the Massachusetts Institute of Technology with experience at global consultancy McKinsey & Company, gave his perspective on change management. "In 2009, the company was still very much being run as a family company, which was reflected in Metiska's management structure. Standard Operating Procedures (SOPs) were either not in place or not being followed. The first step I took was to restructure the top management of the company. Both the restructuring and the sales force have driven our growth in recent years, but it has still not reached the level I would like: we are looking ideally for 40 percent growth year-on-year. There is still a lot of organic growth that we can pursue for the next few years, but after around 2020, we will have to look outside to grow the company further. This is most likely to take the form of an IPO, to then use the funds generated for mergers or acquisitions on a regional level."

The Art and Science of Creating Discomfort

What does a challenger brand need to do?

Discomfort drives change. But by the same token, change creates discomfort.

The tension between these two paradoxical concepts lies at the core of healthcare marketing planning and communication. And as healthcare marketers, our ability to leverage the comfort/discomfort paradox appropriately defines our ultimate success in the marketplace. This is especially true of challenger brands, who need to make their competitive value instantly clear by making direct hits on an emotional level.

Allure of comfort

We human beings are hardwired to find and sustain comfort: comfort food, comfort zones, and old favorites. We are loyal to the tried and true. We move to and try to stay in our place of comfort.

Yet our job as marketers is to change customers' perceptions, preferences, and behaviors towards our products or services. Our job is to make people uncomfortable enough to change their current behavior. Their comfort is not in our best interest. Left to their own devices, our target customers would choose to stay in their comfort zones, which means they wouldn't use or even try the product or service we're offering.

Discomfort, unmet needs, and challenger brands

Obviously, not all product categories are populated by fiercely loyal patrons who cling to their comfort zones like intrepid Chicago Cubs fans. Many categories of consumer products have users loyal only to the next coupon or sample. In our industry, the challenge of changing customer preferences is made more intense by the seriousness of the healthcare professional's responsibilities. Changing preferences for toothpaste carries a significantly lower risk than changing preferences for chemotherapy alternatives, diagnostic techniques, or surgical protocols. There's got to be a very compelling reason to consider changing.

If we want to convince a physician to change prescribing behavior, we must first convince him or her that there is something lacking with the way things are currently done. We must stir the pot a bit to create discomfort with the current brand, brands, or processes that can only be rectified by changing to our brand. We must move them to the point of discomfort that creates urgency to change, where not changing is simply unacceptable.

This process is especially true when developing plans for challenger brands that don't have the big budgets. Challenger brands need to think differently from market leaders. They need to offer new criteria for choice. For challenger brands, a clear path to leveraging your target customer's discomfort is critical to success.

Enter Maslow's hierarchy of needs. You remember: it's that pyramid-shaped chart (like the government's original food chart that told us we couldn't eat Frito's and cheesecake with every meal). The idea is that our most basic of needs (like

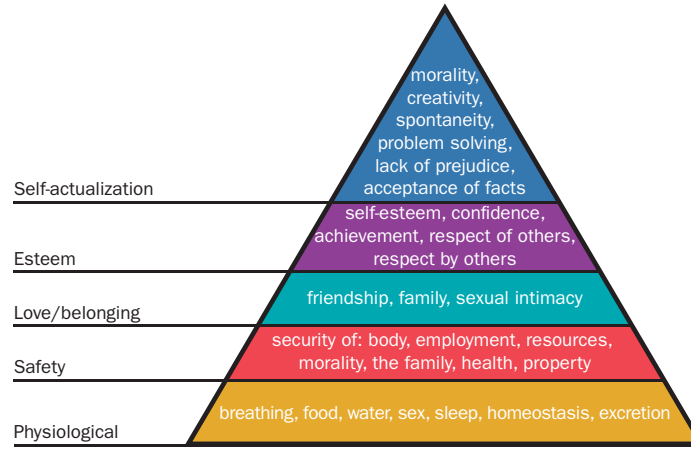


Figure 1: Maslow's hierarchy of needs.

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breathing, eating, and drinking) must be satisfied before we can attain higher levels of needs (like self-esteem, respect by others, morality, or creativity). Applied correctly, it defines the key areas of comfort and discomfort for our species (Figure 1).

Our job is to engage an HCP in a conversation about a product or service and point out issues that may: diminish confidence in the status quo; limit problem-solving; or make patients less satisfied with the outcomes achieved. If we can demonstrate how our product or service can help the HCP perform better, find a clinical issue that might make them doubt their current preferences, or isolate a patient type that might better benefit from a different product, we can use this discomfort to drive change.

The process

Let's see how this thinking plays out in terms of a process. We often characterize marketing as a process that moves prospects from awareness, to interest, to desire, and finally to action (AIDA). With challenger brands viewing the process (and our job as marketers) as moving customers from their comfort zone to a point of discomfort, then into a new comfort zone that includes our product or service, this multiplies the impact of the marketing plan (Figure 2).

Some call it disruption. Some call it creating a tipping point in the customer's beliefs. But it's all based on creating discomfort, then moving the customer to a new comfort level. This creates a more productive framework to evaluate challenges, develop strategies, and formulate the marketing mix. The process consists of five stages:

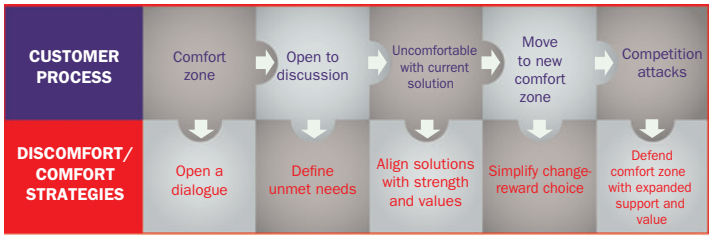

Figure 2: Deconstructing the discomfort/comfort process.

Stage 1. The customer is in his or her comfort zone with the product currently used.

Create discomfort—open a dialogue to make the status quo less secure.

Stage 2. The customer becomes engaged and neutral/mildly open to discussion or consideration.

Create discomfort—clearly define unmet needs with current product.

Stage 3. The customer becomes uncomfortable with the current practice and is open to considering new solutions.

Create a new comfort zone—align your product's strengths and values with your customer's needs.

Stage 4. The customer moves to a new comfort zone with your product.

Strengthen the comfort zone—make the change as easy as possible and reward the new choice.

Stage 5. The customer settles into the new comfort zone as competition begins to attack.

Strengthen the new comfort zone—defend the comfort zone with expanded support and value.

Finding unmet needs

Behind the process is an assessment of the underlying comfort and discomfort drivers, somewhat akin to an ATU study. This begins with key questions about the physician and his or her practice.

How comfortable are your target customers?

- How long have they been using the product or service?
- What's the risk involved in the use or treatment?
- How well do they understand the disease or drug category? (For example, a PCP may be the initial treater for a specialty disease and would not have in-depth experience.)
- How difficult is it to administer or use the product?

How and when do they use the product(s) you plan to displace?

- At what stage of the disease?
- On which type or profile of patients?
- Which treatments do they use and when?

Do they recognize specific unmet needs?

Is their attitude open or closed?

- Age of physician
- Department or individual formulary?
- Do they practice at a teaching or community hospital?
- Are they the decision maker?

Armed with the details of your customers' basic attitudes, trial, and use drivers and a well-structured process, moving them from their comfort zone to yours can help convert a challenger brand into a significant contender. PE

Share of Screen

Are electronic health records a viable channel for engagement?

When asked why he robbed banks, Willie Sutton supposedly responded: "Because that's where the money is." Anyone who has seen a doctor in the last couple of years knows that the computer screen gets more face time than the patient, so it follows that pharma ought to be prioritizing the EHR channel as a way to deliver timely messages to that critical customer, the one holding the Rx pad. Right?

Maybe. Discussions about EHRs can get complicated quickly, due to the sheer technological heterogeneity among EHR providers, not to mention their differing business models; free and ad-supported, or expensive and ad-free, for example. That's in addition to other important considerations such as, what stage of Meaningful Use has the physician's practice or hospital obtained? Or, how does the EHR fit into a given physician's workflow, and what tasks are delegated to administrative staff?

Don't be bedeviled by the details, says Ed Fotsch, CEO at PDR Networks, a provider of drug label information and product support that now partners with EHR providers to deliver services to physicians and patients. Between 60 and 70 percent of physicians have now adopted some form or EHR, and as a result, their workflow has altered dramatically, says Fotsch. Now, "it's all about information flow into and out of the EHR." For those early-adopting physicians and hospitals that have already been using EHRs, Stage 2 of Meaningful Use is just six months away, and that requires physicians to send "customized patient education" to at least 10 percent of their patients, or sacrifice the Meaningful Use incentive payment. Where will docs get the patient education and resources they'll be required to distribute?

Pharma, if the industry plays its cards correctly. Drug companies have spent untold millions on developing patient education materials, a lot of it never seen by actual patients. These materials—in addition to financial assistance programs and copay cards—can be repurposed to meet the needs of physicians who want to qualify for Stage 2, says Fotsch. The key is to support the doctor's decision to prescribe a given product by providing services that help patients afford a medication, remain adherent on therapy, and understand the risks and benefits of a product.

Despite a lot of talk (and conferences) about the need to transform industry from product peddler to service provider, you don't hear that many CEOs regaling analysts on earnings calls with stories about what's happening above and below the pill. Some brand managers still don't understand why services like customized patient education matter after a physician has already chosen what to prescribe. Fotsch says he asks these brand managers why they return to the same restaurants, or buy a certain kind of car. "It's because of a good experience" with that restaurant or car, and it's the same for medicine, he says. "If you can help a doctor and a patient at the time of prescribing—with an adherence program, or financial assistance, et cetera—that's a better drug," says Fotsch.

But patient materials don't appear in EHRs by magic; there's a lot of work that goes into it. Fotsch says Bristol-Myers Squibb and AstraZeneca are two examples of "forward-looking clients that are thinking like service companies" with respect to EHR. Fotsch says biopharma EHR initiatives should consider a physician's full range of prescribing habits, and not try to push single-drug materials into EHRs. It's also important to understand the level of EHR adoption in a given specialty, and to identify opportunities that engage physicians in context-appropriate ways. Finally, it's a good idea to understand the Stage 2 requirements in order to meet the needs of physicians, says Fotsch.

As more and more physicians spend more and more time looking at a screen, it makes sense to support their prescription decisions through the EHR channel. Newly covered lives coming into the system next year will need to be educated about their diseases and treatment. At the point of care though, patients might find it harder than ever to make eye contact with a doctor. PE

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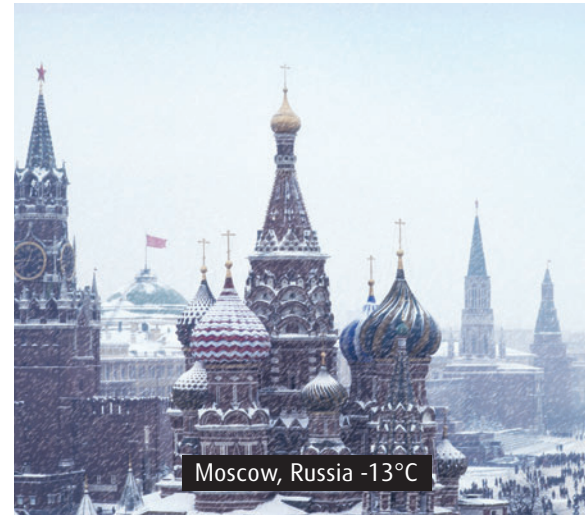

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