

# CHALLENGES IN GLOBAL HEALTH CARE

## Access, Outcomes, Litigation

FALL 2013 | Analysis Group Health Care Consulting Services Bulletin

As global pharmaceutical companies continue to expand into emerging markets, they must address a range of issues – varied demographics, the sourcing and quality of data, shifting payer requirements, and increased scrutiny of business practices. In this bulletin, we focus on opportunities, risks, and challenges that companies in international health care are confronting.

## Evaluating International Market Access

Across international pharmaceutical markets, the criteria used to assess the value of new therapies in relation to standards of care vary markedly and are changing rapidly, reflecting the evolving priorities and growing influence of national and regional payers. In the United Kingdom, a value-based pricing scheme will be introduced in 2014 to augment NICE's cost-effectiveness assessment approach. In Germany, pharmaceutical manufacturers face newly stringent criteria for evaluating a new therapy's benefits and for achieving market access and price premiums as a result of "AMNOG" health care policy reform.

Manufacturers must be able to determine a payer's response to the introduction of a new therapy to a new market by studying responses in mature and emerging markets. This includes identifying specific drivers of value and quantifying the trade-offs payers make between access to sub-populations and patients with specific indications or conditions, and the prices allowable to gain marketing authorization. The impact of pricing on access varies significantly by country and under different patient coverage assumptions. Modeling the expected access of a specific product as a function of net price per day, for example, reveals significant disparities between established markets and emerging ones such as China and Brazil.

Innovative market access schemes, including risk-sharing and outcomes-based arrangements, are increasingly common as new therapies seek market access. For example, in Italy such arrangements have been necessary for many therapies to gain market authorization. The process for evaluating options for access arrangements assesses risk exposure and the potential financial benefit to [\(CONTINUED ON PAGE 4\)](#)

## New Beijing Office Opens

Analysis Group-Beijing, opened in 2012, provides health care research and strategic consulting to our multinational



pharmaceutical and life sciences clients in the world's third-largest pharmaceutical market. Led by Managing Principal **Eric Qiong Wu**, the office identifies and develops high-quality data with local partners and collaborates with leading academics, including **Gordon Liu** of Peking University's

Guanghua School of Management and **Jun Liu** of Tsinghua University (and Harvard University), to design and present research for industry, government, and the scientific community.



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ECONOMIC, FINANCIAL and STRATEGY CONSULTANTS

## Using Epidemiology to Identify Unmet Need

When a new renal cell carcinoma treatment faced global reimbursement challenges – because an available on-market drug was considered “standard of care” – Analysis Group undertook an international epidemiological study of patients receiving the existing therapy. Data from this study quantified an unmet need in renal cell carcinoma patients for more tolerable agents and provided our client with empirical evidence of a significant target market for its therapy.

Led by Managing Principal and Chief Epidemiologist **Mei Sheng Duh**, M.P.H., Sc.D., the Analysis Group researchers collaborated with clinical experts in eight countries in North America, Europe, and the Asia-Pacific region to study the use of the competitor’s drug in real-world clinical practice. With medical records data from over 600 patients, the researchers found that more than half of the patients discontinued use of the existing drug, often due to intolerance of drug toxicities and related adverse quality-of-life impact. Patients who discontinued the drug due to adverse events averaged two to three adverse events per discontinuation.

Globally, more than half of patients taking the drug experienced some type of treatment modification – including discontinuation of therapy, dose reduction, treatment interruption, or treatment switching – due to an adverse event.

This finding illustrated that in real-world practice, physicians manage multiple adverse events per patient taking the drug and may discontinue or modify treatment because of intolerability. In turn, these treatment interruptions negatively affect the effectiveness of the drug in achieving tumor response and prolonging progression-free survival. “This epidemiological study provided our client with information that was not available from clinical trials, administrative claims, or electronic medical record databases,” says Dr. Duh. “Rigorous observational studies of this nature are essential to understand real-world treatment patterns and outcomes of existing therapies, and how new therapies may enter the market due to unmet need.” Data from the study supported Health Technology Assessment submissions in several countries. ■

### Extrapolating Results to Other Populations

#### CHALLENGES:

Health outcomes and epidemiology research across multiple databases is costly. Yet limiting research to one source makes it difficult to compare different populations.

#### SOLUTION: POPULATION STANDARDIZATION METHODS

Methods such as indirect standardization or matching-adjusted indirect comparison can weight a study population so that it mimics the demographic and clinical distributions of a specific target population. In addition, these methods can be repurposed to generalize data to a larger population.



“For example,” says Managing Principal and Chief Epidemiologist Mei Sheng Duh, “data can be generalized to a population with different age distributions or social economic status, or to the entire U.S. population.”

Factors used in weighting study data include demographic, social, comorbidity, health resource utilization, and economic information.

## PharmacoEconomics: Special Issue on Health Care in China

Managing Principal **Eric Qiong Wu** and Manager **Jipan Xie**, along with affiliate Professor **Lizheng Shi** of Tulane University, are coediting a special issue of *PharmacoEconomics* devoted to health care in China, to be published in early 2014.

Topics to be addressed by contributing authors include assessment of the impact of policy initiatives such as the National Essential Medicines Policy in rural China and of Urban Resident Basic Medical Insurance; an empirical study of pharmaceutical pricing in hospitals; a 10-year study of trends



**"China's health care system is evolving rapidly – affordable, high-quality care will require rigorous analyses of programs and policies, as well as of clinical treatments."**

— ERIC QIONG WU, MANAGING PRINCIPAL

and determinants of pharmaceutical expenditure; an analysis of economic incentives and the rational use of medicine; new research based on Chinese electronic medical records data; and several disease-specific studies addressing cost and insurance issues

related to acute myocardial infarction, a cost-utility analysis involving adjuvant chemotherapy for resectable gastric cancer, and quality of life related to colorectal cancer. ■

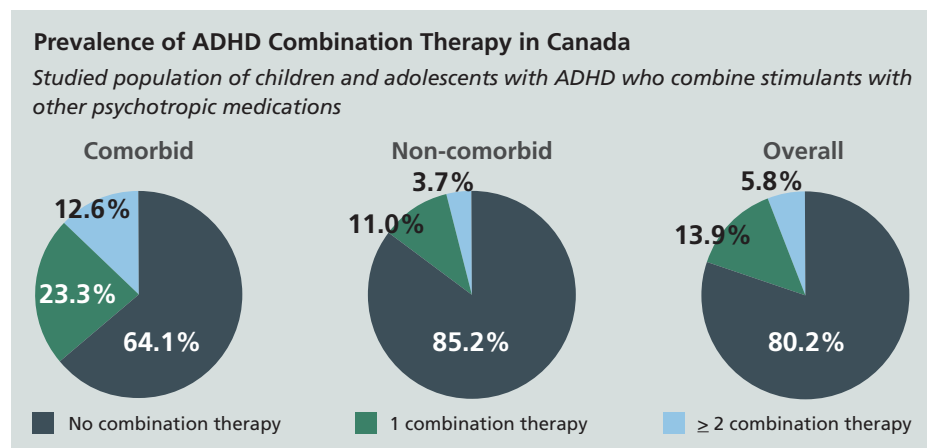
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## International Data Sources: Using Canadian Provincial Health Plan Claims

Medical and pharmacy administrative claims databases provide detailed information on patient eligibility, outpatient medical services, pharmacy dispensings, and hospitalizations. "Researchers use these data to assess utilization and costs, treatment patterns, and drug-specific real-world effectiveness, among other factors," says Vice President **Patrick Lefebvre**.

Research teams from Analysis Group recently used data from Québec's provincial health plan, Régie de l'assurance maladie du Québec (RAMQ), to assess the prevalence of combining or switching therapies for attention deficit hyperactivity disorder (ADHD) in Canada. They found that about one in five children and adolescents combined a stimulant with another

psychotropic medication or switched to a different medication within a one-year study period, and that comorbid patients – those with one or more ADHD-associated mental health or neurological conditions – were more likely to combine or switch therapies (see chart). Despite the relatively high prevalence of combination therapy observed in the current study, the majority of this use was not approved for the treatment of ADHD, suggesting there may be an unmet need in this area.



Analysis Group researchers have also used RAMQ health claims to assess the impact of generic substitution on epilepsy patients. They found that switching patients from branded anti-epileptic drugs to their generic counterparts was associated with increased physician visits and hospitalizations. ■

# Evaluating International Market Access

(CONTINUED FROM PAGE 1) payers; primary research is also useful for testing the impact of different approaches.

In addition, pricing and launch sequencing decisions can benefit from the use of modeling to address the complexities of international reference

pricing, to understand the sometimes disproportionate or unintended impact a pricing change in one country can have on prices in other markets. ■

## Emerging Markets Access: Focus on Pricing

Emerging markets are expected to account for nearly three-quarters of new growth in the pharmaceutical industry in the coming years. Vice President **Christian Frois** discusses how market access and pricing decisions will drive success in these geographies.



Christian Frois

### What access and pricing challenges are unique to emerging markets?

**Dr. Frois:** Low per-capita income and rapid population growth, limited reimbursement options dominated by local governments, and well-established local generic competition – all can exert immense pressure on manufacturers to discount prices at the local level. Many firms also lack the infrastructure, processes, tools, and training needed to help local affiliates and their regional counterparts meet these challenges.

### How do you approach pricing in emerging markets?

**Dr. Frois:** You need a solid understanding of what local payers' needs and priorities are – in a recent BRIC-focused pricing engagement, for example, we captured insights for

the client company on how its drugs are purchased, who the relevant local stakeholders are, and what leverage points would optimize pricing. A key objective should be to help local teams enhance the value proposition of their products, enabling price adjustments only as a last resort, and only through well-established processes.

Many drug companies have tried to minimize price differences between developed and emerging markets. They haven't always focused enough on helping local teams to articulate a product value proposition that will resonate with local payers facing significant affordability challenges to expand drug coverage among their population.

### What advice do you have for companies competing in these markets?

**Dr. Frois:** First, avoid excessive price erosion. Don't expand internationally without first providing adequate support for local teams facing competition from generics or biosimilars.

Second, compete smartly – you can, for example, use tender specifications to differentiate and refine your

offerings, achieve higher prices, and maximize access and use. Recently, in helping a company optimize its tender pricing operations across its entire portfolio and most of its ex-U.S. business, we provided processes and tools for the client's global, regional, and local teams to track, assess, and learn from past and current tender offers.

In emerging markets, cash customers frequently account for most of a brand's performance. Price differentiation and tier pricing will play a key role in maximizing net sales potential for this customer base.

Develop real collaborations with affiliates. Genuine and sustained efforts by global management to provide tools, processes, and insights tailored for local use can really improve the dynamic. ■

# Global Consequences of Local Pricing Decisions

Governments seeking to contain public spending on drugs often set maximum reimbursement based on comparisons with benchmark countries. Drug companies can set their prices above these reference prices in certain markets, but prescribing and sales levels can be negatively affected.

Further, the practice of reference pricing in one market can spark changes across multiple markets – but the impact can be difficult to anti-

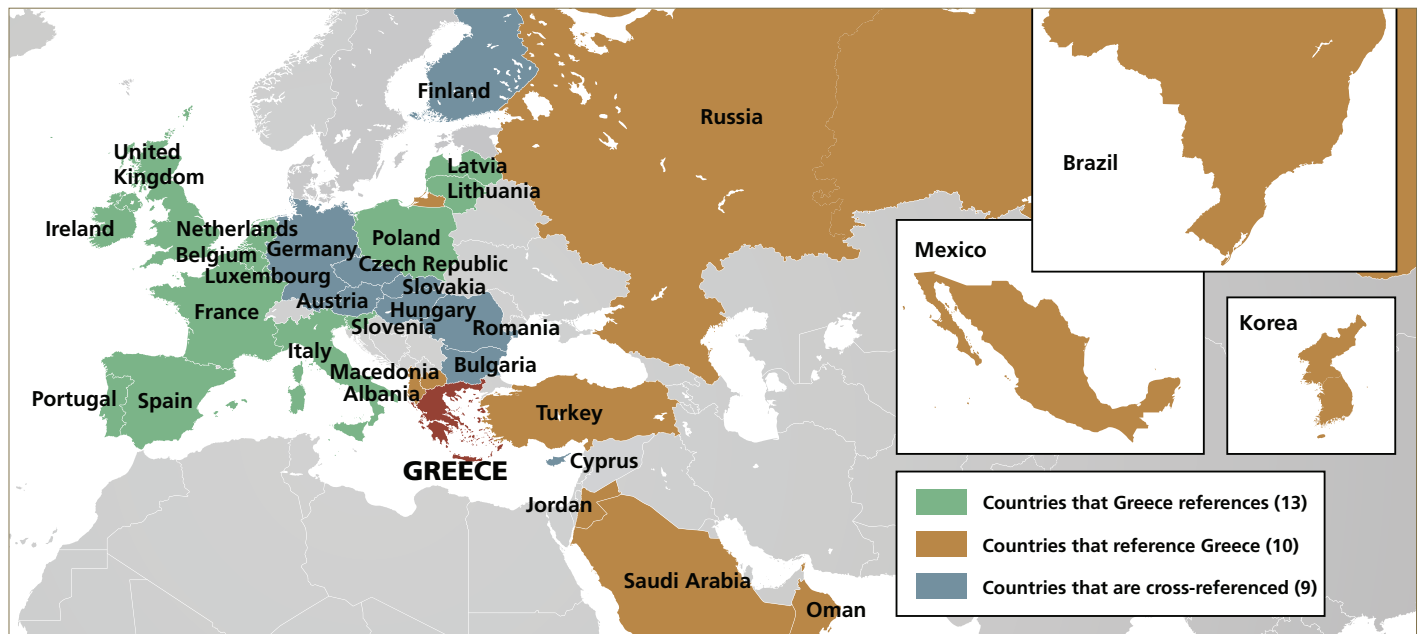
of responses, beginning with countries that reference the price changer directly, followed by second-order referencing changes, and so on.

The result is a complex web of dynamic relationships among prices across global markets, with changes in small markets potentially generating amplified cross-border impacts on prices, revenues, and margins.

The level of complexity involved has far outpaced the ability of even highly

facterer recently looked to create a next-generation international pricing modeling system with linkages to its budget tracking capability. To strengthen the company's strategic pricing decision capabilities, we developed a modeling platform that forecast the revenue impact of price changes in each of the company's thousands of SKUs sold, in any country and over a multi-year forecast horizon, as, over time, price changes pass through reference pricing rules."

## Interrelated Impact of Reference Pricing by Country: Greece Case Example



pate. Countries vary in the number of markets they reference, as well as in the specific countries referenced; the algorithms used to determine reference prices, and how frequently they are applied and updated, can also vary greatly. Further complicating strategic planning, a pricing change in one country can set off a chain

experienced management to fully anticipate the downstream impacts of isolated decisions. Given the level of potential global financial risk, strategic pricing decisions must rely on best-in-class analytical models. "For example," says Analysis Group Senior Advisor **Genia Long**, "a global pharmaceutical manu-

Price modeling systems can also help executives gauge and manage financial risk and assess other important initiatives, such as the optimal strategic response to an anticipated cross-border price impact and policy advocacy efforts in local markets. ■



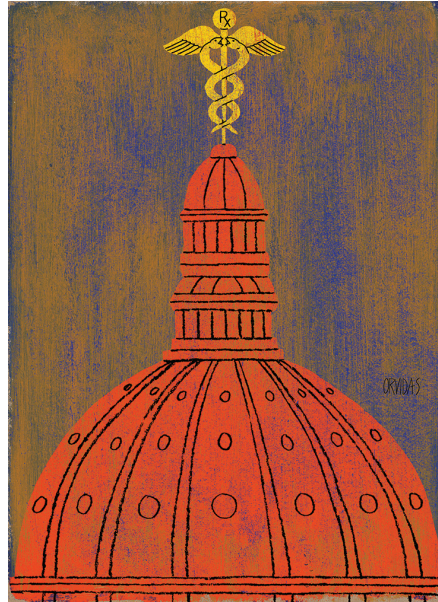
## Behind the Headlines in Pharmaceutical Investigations

Press attention has been trained on government investigations of pharmaceutical firms' marketing practices and of general business practices employed by U.S.-based multinationals in China, India, Eastern Europe, and elsewhere. *The Wall Street Journal*, *The New York Times*, and other publications have also been reporting on notable U.S. corporations, including several drug makers, that have been prosecuted under the Foreign Corrupt Practices Act (FCPA), which forbids the use of cash bribes or kickbacks to foreign government officials. The recent decision in *U.S. v. Caronia*, which granted First Amendment protection to certain off-label marketing statements, has also garnered substantial media attention.

This recent attention has prompted debate in legal circles about the likely future direction of cases against pharmaceutical manufacturers. The decision in *Caronia*, for instance – which states that truthful, non-misleading off-label promotion is protected free speech – could shift investigators to focus on evidence of false or misleading statements, or misbranding. With heightened international scrutiny, investigators are also expected to continue to expand their attention beyond violations of the domestically focused anti-kickback statute to FCPA issues.

In cases featuring any of these allegations, economists can play an important role, particularly in settlement negotiations. In this context, economists strive to develop a platform at the outset that can accommodate a variety of allegations, multiple sources of data, and changing information as

the investigation evolves, says Managing Principal **Paul Greenberg**. “We can draw on health outcomes tools, such as biostatistical analysis of clinical trials data collected both in the United States and internationally, to inform



**Under anti-kickback statutes or FCPA, economists can evaluate the extent to which alleged payments actually led, or would have been expected to lead, to changes in behavior – which speaks to liability as well as damages.**

whether certain promotional messages are false, misleading, or both.” Economics can also figure into determining the magnitude of sales stemming from the conduct at issue, which is a threshold question for damages. This is more than just an accounting exercise, as it involves not only determining the sales base potentially at issue,

which can be complex, but also assessing the causal connection between the conduct at issue and sales.

“In some cases,” Mr. Greenberg notes, “we have assessed the impact of alleged inappropriate messages and improper inducements with benefit of granular data concerning the conduct at issue as well as prescribing at the physician level. For example, we have compared company call note or physician payment data on a doctor-by-doctor basis with third-party prescribing data at the same level of detail – these comparisons can provide insight into the impact of the conduct at issue on prescribing.” To assess the impact of the alleged conduct on sales, economists may also construct benchmarks based on patterns of use of other drugs, as well as the drug in question in other jurisdictions or during alternative time periods.

There is no doubt that international issues will be at the forefront of investigations into pharmaceutical industry business practices, as authorities take an increasing interest in this area. Coupled with several recent U.S. court rulings, this suggests that pharmaceutical companies will continue to be closely watched, although the type of scrutiny may shift over time. ■

**ANALYSIS GROUP HAS WORKED ON MORE THAN 40 FALSE CLAIMS AND IMPROPER INDUCEMENT CASES SPANNING MORE THAN 50 PRODUCTS AND 15 GOVERNMENT OFFICES.**

**MR. GREENBERG HAS PRESENTED ECONOMIC ANALYSES TO GOVERNMENT INVESTIGATORS AND SPOKEN AT INDUSTRY PANELS ON THE ECONOMIC AND STATISTICAL ISSUES THAT ARISE IN GOVERNMENT INVESTIGATIONS OF PHARMACEUTICAL AND MEDICAL DEVICE COMPANIES.**

# Health Care News and Events

## Professor Gordon Liu Joins Analysis Group as Academic Affiliate

Dr. Gordon Liu, a noted figure in Chinese health reform efforts, is a professor of economics and the director of the China Center for Health Economics Research at Peking University's Guanghua School of Management. He serves on the State Council Health Reform Advisory Commission and is president of the Chinese Society for Pharmacoeconomics and Outcomes Research.



President and CEO Martha Samuelson with Dr. Liu in our Beijing office

## Recent Presentations

**ISPOR** Members of Analysis Group's Health Care Consulting Services practice were recognized at the 18<sup>th</sup> annual meeting of the International Society for Pharmacoeconomics and Outcomes Research in New Orleans, Louisiana. Manager **Brad Rice** received a research podium presentation award for "Medical, Drug, and Work-Loss Costs of Diabetic Foot Ulcers." Our researchers received four poster finalist ribbons at the meeting, and Managing Principal **Mei Sheng Duh** moderated a podium session on comparative effectiveness research.

**AAIC** Manager **Noam Kirson** presented research conducted by a team from Analysis Group and Eli Lilly and Company on the economic impact of Alzheimer's disease misdiagnosis at the Alzheimer's Association International Conference in Boston, Massachusetts. Dr. Kirson's research was also featured in a CNN article on the early diagnosis of Alzheimer's disease.

**ICPE** Analysis Group was a sponsor of the 29<sup>th</sup> International Conference on Pharmacoeconomics & Therapeutic Risk Management in Montreal, Canada. Our consultants, including Dr. Duh and Vice Presidents **Francis Vekeman** and **Patrick Lefebvre**, delivered a presentation and exhibited seven posters at the conference.

**PAINweek** Analysis Group researchers, including Principal **Howard Birnbaum**, Dr. Kirson, and Dr. Rice, exhibited two posters at PAINweek, the national pain management conference in Las Vegas, Nevada. The team exhibited "The Impact of an Abuse-Deterrent Formulation of an Extended-Release Opioid on Healthcare Utilization and Costs" and "Hidden Costs to Employers of Opioid Abuse."

**NAMS Annual Meeting** Researchers from Analysis Group, including Dr. Duh, Mr. Lefebvre, and Senior Economist **Marie-Hélène Lafeuille**, contributed to a study on the economic burden of vasomotor symptoms, which was featured at the North American Menopause Society's annual scientific meeting in Dallas, Texas.

## Recent Publishing

### Analysis of Reverse Payment Patent Settlements

Managing Principal **Paul Greenberg** discussed the U.S. Supreme Court's decision in *Federal Trade Commission v. Actavis Inc. et al.* in "Little Guidance For Lower Courts In *FTC v. Actavis*" (*Today's General Counsel*, August/September 2013).

### Review of Brazil's Bolsa Família Program

Associate **Amie Shei** examined innovative social safety-net programs in "Brazil's Conditional Cash Transfer Program Associated with Declines in Infant Mortality Rates" (*Health Affairs*, July 2013).

### Use of Quantitative Analysis for On-Market Pricing

Vice President **Justin Works** and Managing Principal **Andrew Parece** demonstrated potential shortcomings in traditional pricing approaches in "On-Market Pricing Strategies: How to Optimize ROI without Hitting the Cliff" (*Pharmaceutical Executive*, June 2013).

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Analysis Group provides economic, financial, and business strategy consulting to corporations, government agencies, and law firms. The firm integrates analytical expertise in health care economics with knowledge of industry dynamics, disease states, and business strategy honed from more than 30 years of experience in all aspects of pharmacoeconomics, epidemiology, and health outcomes research. The firm has more than 550 professionals, with U.S. offices in Boston, Chicago, Dallas, Denver, Los Angeles, Menlo Park, New York, San Francisco, and Washington, DC, and internationally in Montreal, Canada and Beijing, China. [www.analysisgroup.com](http://www.analysisgroup.com)



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