



Drug Delivery's **RISE** **CHALLENGES** Big Pharma's Dominance

Set to soar from just \$2.4 billion to about \$12 billion in just five years, the value of drug-delivery technologies and the market clout of developers are making established pharmaceutical giants sit up and take notice, according to a study released today by Kalorama Information, a division of Market-Research.com.

According to the study, delivery technologies themselves currently account for 16% of total revenue in the oral delivery market, with the rest attributable to sales of the pharmaceutical being delivered. But by 2005, the technology component will soar to more than 40% of the total, in a market valued at almost \$30 billion. This growing importance means more money for the delivery industry, but it also means that drug delivery companies will exert more influence over product design and development.

The oral drug-delivery market is twofold, encompassing drug delivery technology and the revenue earned from licensing that technology and the sales of pharmaceuticals themselves. Because drug delivery technology is an integral part of the pharmaceutical product and the drug delivery technology cannot exist without pharmaceuticals, revenue has traditionally been reported as total sales. This is inclusive of the entire market for oral drug delivery. Kalorama believes inclusion of the pharmaceutical portion gives a distorted picture of the value of drug delivery technologies themselves. Therefore, the report, provides market data for the pharmaceutical and drug delivery revenue in total and provides the percentage of revenue attributable solely to drug delivery sales. Data are presented for the entire forecast period from 1996 to 2006.

Recent technical advances and market events have significantly raised the profile of drug delivery technologies. A spate of big-market patent expirations is giving delivery innovators a chance to challenge big pharma for market share with new formulations. In addition, splashy new products on the horizon (such as inhaled insulin) have given the sector high visibility.

"It is no longer possible to turn a blind eye to the importance of delivery technology to the overall pharmaceutical industry," says Steven Heffner, acquisitions editor for Kalorama. "Patent extension, product differentiation, and the promise of the drug discovery revolution all depend on innovative delivery technology."

According to the study, this growing importance will cause some changes in the industry's landscape; namely, large pharmaceutical companies may voraciously begin acquiring drug delivery companies to expand presence, deepen product lines, extend product lifecycles, and forestall further incursions into their market share.

The report released today is the first volume of a large, ongoing market study of drug delivery technologies from Kalorama. Volume one, *The Market for Oral Drug Delivery Systems*, examines the market for modified-release, fast-dissolving, and taste-masked products and technologies, and is priced at \$1,995.

Pharma Sales Reps:

LEARNING FROM THE LEADER

Pharmaceutical salesforces have grown 85% in the past five years. As salesforces grow, revenue per sales rep tends to decrease. Due to this recent trend, leading pharmaceutical companies need to improve the effectiveness and efficiency of their sales reps.

Pharmaceutical sales representatives operate in a highly competitive world where the most successful excel at weaving brief interactions with doctors into valuable long-term relationships. According to research from Best Practices LLC, sales managers can ensure that their sales representatives win favor among physicians by incorporating proven relationship management techniques as part of their training.

"Pharmaceutical sales is very much a relationship-building process," says Chris Bogan, president and CEO of Best Practices. "Consequently, the practices used by leading sales reps to build those associations are the companies' most valuable sales collateral."

TIPS FOR DEVELOPING WINNING RELATIONSHIPS

- ▶ Read clues that help discern the unique cultural and operating differences of each office
- ▶ Tailor detailing and sales messages in ways that achieve maximum impact
- ▶ Build rapport with physicians by openly discussing goals, office service needs, and personal needs

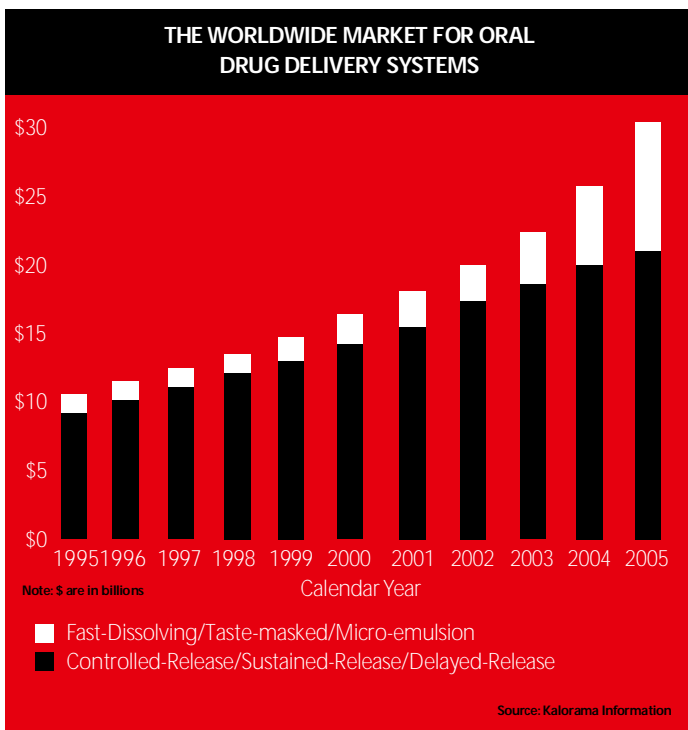
Consumers Want **SEARCH ENGINES** that Lead to Quality Health Websites

In addition to significant consumer concerns about the quality and reliability of information on health-related Websites, survey results released by the Washington, D.C.-based health organization, URAC, also known as the American Accreditation

HEALTH WEBSITE ACCREDITATION STANDARDS ADDRESS:

URAC STANDARDS HAVE BEEN DESIGNED FOR THE ACCREDITATION OF CONSUMER ONLINE HEALTH RESOURCES

- ▶ Health content editorial process
- ▶ Disclosure of financial relationships
- ▶ Links to other Websites
- ▶ Privacy and security
- ▶ Consumer complaint mechanisms



HealthCare/Commission, found that consumers want search engines that will help them locate high quality health information on the Web. More than 75 millions consumers use search engines to find health information.

The URAC study reports that more than 90% of consumers would prefer a search engine that indicates whether health Websites are accredited according to rigorous standards. URAC suggests that such a system would help consumers find Websites more likely to provide the high quality, reliable information they desire.

A recent RAND Health study sponsored by the California HealthCare Foundation underscored the importance of this issue. The study found that search engines are usually inefficient and searches lead to irrelevant health information. Also, the study found that search engines are inconsistent and often provide very different results for similar searches.

"As things now stand, search engines are sometimes an unreliable way to obtain health-related information," says Garry Carneal, president and CEO of URAC. "Consumers are unable to determine from search engines which sites and information are relevant and accurate. They want assurance that the search engines they use will lead them to sites that adhere to quality standards."

Health-related Website traffic is critically dependent on search engines — only one-quarter of the estimated 100 million people who seek health information online go directly to a particular Website.

"The challenge with online health information and search engines is one of quality and trust," Mr. Carneal says. "Not only did we find that the majority of consumers want a quality 'seal of approval' on health Websites, but they also want to know there is a way to find those Websites through search engines."

E-HEALTH PARADOX: It's Harder to Reach Patients Online Than to Have an Effect on Them

Although the Internet is increasing its influence on how patients approach their healthcare, strategies borrowed from consumer sites fail to reach them, according to Harris Interactive and The Boston Consulting Group. A recent study found that shifts in how people search for healthcare information present industry players with new opportunities to engage and capture patients online.

Deborah Lovich, a Boston Consulting Group VP and co-leader of the BCG's e-health initiative notes

Genetics in Drug R&D: **HUGE REWARDS, HIGH RISK**

The application of genetics to biopharmaceutical R&D holds enormous potential, but is a high-stakes game. An original research report issued by The Boston Consulting Group (BCG) details the potential: savings, in the best case, of more than \$500 million and up to two years in developing each new drug. In effect, that would more than halve the current cost of bringing a drug to market, and would transform pharmaceutical R&D and perhaps even the delivery of healthcare in general. But the report indicates that the application of genetics lags that of genomics technologies, and that there are many hurdles over which the approaches could stumble.

"The potential rewards from applying genetics tools to R&D are enormous," says Peter Tollman, a BCG vice president in the Boston office and leader of the firm's biopharmaceutical R&D practice. "It's possible that companies could, under certain plausible assumptions, cut the costs of drug development by more than half. This promise should be tempered by the many associated uncertainties however, significant scientific and technical problems that have yet to be solved, along with questions about market and regulatory acceptance."

Mr. Tollman continues, "If companies ignore genetics, they could falter in the face of a truly transforming technology. On the other hand, to embrace genetics involves placing high-risk bets. The future of many firms may well depend on how successfully they navigate between these currents."

The report concentrates on two genetics approaches that are applicable

to pharmaceutical R&D: Disease genetics, the search for disease-susceptibility genes as potential drug targets, and pharmacogenetics, predicting patients' drug responses by analyzing the genetic variations in their DNA.

The two genetic approaches are applied at opposite ends of the pharmaceutical R&D continuum. Disease genetics is invoked early in the drug discovery process to help identify and validate key target genes for therapeutic intervention. By contrast, pharmacogenetics is used mainly to streamline the later stages of drug development by selecting for clinical trials those patients likely to respond favorably to the candidate drug.

"Disease genetics holds the potential to change fundamentally the way drugs are discovered, whereas pharmacogenetics could radically change the way they are developed," says Philippe Guy, senior VP, and leader of BCG's worldwide healthcare practice.

A targeted approach to drug development would make clinical trials more efficient and safer, but pharmacogenetics will not apply to all drugs. Pharmacogenetics will work only where the drug's response and/or side-effect profile is clearly linked with genetics, and where that relationship can be identified at the appropriate stage of development.

Market implications will need to be considered as well: using Pharmacogenetics to exclude certain patients from clinical trials will shrink the potential market for the drug. Once again, pharmaceutical executives will confront the question of risk versus reward.

DISCOVERY AND DEVELOPMENT

The Impact of Disease Genetics

Disease genetics should yield the larger share of cost savings, with the bulk being realized by improvements in the success rate of drug candidates. But, these savings might be limited by the following:

- Although culprit genes have been identified for numerous rare, single-gene disorders, very few of the underlying genes have been pinpointed for common multigenic disorders. So it remains unclear whether a genetics-based approach to drug discovery will really work, and if it does, for which diseases it will be relevant.
- The cost of a comprehensive survey of disease-related genes is exorbitant. However, this cost is expected to shrink in the next few years.
- Original disease genetics studies are expected to identify only a small number of genes, and thus a small number of drug candidates, which then must struggle to progress all the way through clinical trials.

The Potential of Pharmacogenetics

Pharmacogenetics could fundamentally change the clinical development of drugs in two ways:

- Streamlining clinical trials — Clinical trials could be greatly reduced in size and cost by identifying and excluding in advance those patients unlikely to respond to the candidate drug. With a preselected patient population, the trials could assess a drug's positive therapeutic effects far more effectively.
- Salvaging compounds that would have otherwise failed — Genetic analyses could identify and exclude in advance those patients unlikely to respond to the drug, or who are likely to suffer from negative side effects. That might enable companies to continue developing drug compounds that would fail to secure regulatory approval for broad patient populations.

PATIENT'S INTERNET BEHAVIOR MAKES THEM DIFFICULT TO REACH ONLINE

PRIMARY WAY PATIENTS SEARCH FOR HEALTH-RELATED INFORMATION ON THE WEB

% of patients accessing health information

- 65% Use search engines (includes banner ads)
- 24% Use general health portals
- 11% Use disease specific Websites

Source: Harris Interactive and BCG Analysis

Note: Results for 14,278 respondents using the Internet for health-related information; weighted to reflect the demographics of the entire online patient population.

that two contradictory findings have surfaced. "Patients who use the Internet to explore health issues report that the information they find online has a real impact on how they manage their overall care and comply with prescribed treatments," she says. "This makes the Web an important lever for companies seeking to get patients more involved in care decisions. Yet, typical online traffic-building strategies don't seem to work, since usage patterns in e-health bear little resemblance to those in e-commerce."

Research shows that the more patients use the Web for health, the stronger their response to the call to action issued by healthcare companies.

Indeed, those who use the Internet frequently are two to three times more likely than infrequent users to take action that affects their diagnosis and treatment.

For example, the data patients find online result

in their asking physicians more questions and in greater detail. But more importantly, when patients who frequently use the Internet for health consult with their doctors, about 36% suggest the specific illnesses that they are suffering from and 45% request specific treatments. In comparison, among those who hardly ever venture online to find health information, only 16% and 19% of patients respectively exhibit the same active involvement.

Harnessing the power of the Internet will be daunting for healthcare companies, since reaching patients online is difficult. Recent research from Harris and Boston Consulting Group reveals two key dissimilarities between the searching behaviors of patients and consumers:

First, unlike consumers seeking other information online, patients don't explore health topics on the Web at their leisure or for entertainment. The vast majority, 77%, use the Internet for health issues only when they have specific questions.

Second, the same Internet users who might visit an automobile site to find information about cars or visit and return to Amazon to purchase books typically don't turn to health sites directly when searching for health information. To answer their health queries on the Web, 65% of patients usually start with general search engines such as Yahoo, Ask Jeeves, and Alta Vista. Only 24% make health portals such as WebMD and IntelliHealth their first stop; 11% start with disease-specific Web sites such as Oncology.com or MSWatch. And even those who favor specific health-related sites report that they initially found them through general search engines.

These findings hold promise for all healthcare companies that benefit from influencing patient behavior, such as pharmaceutical companies pro-

THE IMPACT OF E-HEALTH INFORMATION ON PATIENTS AND PHYSICIANS

BCG SEGMENTED PATIENTS INTO FOUR PATIENT POPULATIONS BASED ON THE SEVERITY OF THEIR CONDITION AND THEIR ATTITUDE TOWARD PHYSICIANS

55% Informed — Rely on doctors to make health decisions but typically go online after an office visit to learn more about a diagnosis or prescribed treatment without, in their view, wasting the doctor's time with questions

28% Involved — View themselves as partners with their physicians in making care decisions and seek information online both before and after visits to discuss with their doctor; however, still rely on their clinician to make the ultimate decision regarding care

9% In control — Feel best suited to determine their care; use online information to diagnose themselves before visits to determine which treatments they want and to convince their doctor to treat them accordingly

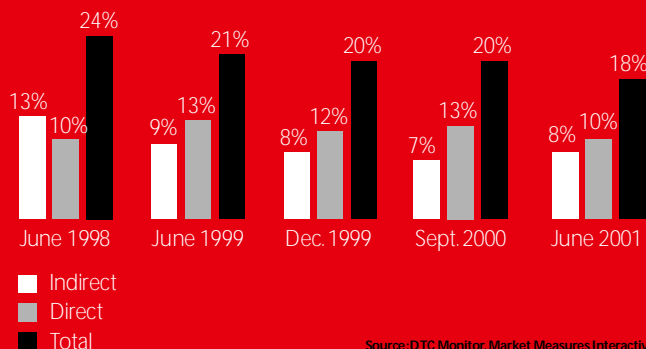
8% Accepting — Rely entirely on doctors for health information and decisions

Source: Harris Interactive and BCG Analysis

A DTC UPDATE

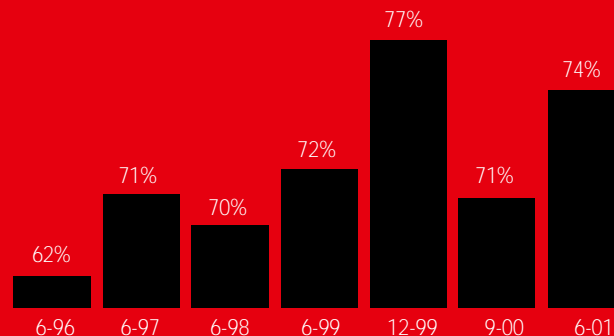
PERCENTAGE OF RESPONDENTS CONTACTING A DOCTOR AS A DIRECT RESULT OF VIEWING A DTC AD

In 2001, DTC ads are not generating the direct doctor contact rates of nine months ago. However, more casual (indirect doctor contact) discussions with physicians have held steady for the last 2 years. This finding supports other consumer data from the 2001 DTC Monitor, which shows that consumers' discussions with physicians about DTC have become integrated into their ongoing healthcare behavior



ADVERTISING AWARENESS OF DTC: ALL CONDITIONS JUNE 1996 TO JUNE 2001

While overall doctor contact rates have fallen off somewhat, general consumer awareness of DTC advertising has increased 3% points in the nine months. In fact consumer awareness of DTC has been trending up since 1996 — the first year of the DTC Monitor.



moting new therapies and managed-care players promoting patient compliance with disease-management initiatives. The struggle will be figuring out how to reach them. Tracking patients through search engines when logging on for answers to healthcare questions remains highly unpredictable. Emerging shifts in patient behavior, however, suggest that healthcare companies can home in effectively on the patient segments that they wish to target online.

Research shows that while 46% of in-control patients and 30% of involved patients often use the Web for health, only 14% of the informed and 3% of the accepting segments use the Internet in the same way.

Because different segments of patients use e-health differently and for different reasons, some patients are easier to find, and therefore easier to influence-online. Two important behaviors of these groups have emerged:

- Patients already have begun to migrate to more active segments in the past year. This suggests that greater patient access to online information is leading to greater patient involvement. Ultimately, if these shifts continue, the more active patients could well become the largest portion of the healthcare market.
- Patients who take a more active role in their care are beginning to "stick" to sites. These patients are more likely than patients in other segments to visit health sites and disease-specific sites in particular. Only 28% of patients in the accepting segment visit health-related portals and disease-specific Web sites, compared with 42% of the in-control group. With roughly the same percentage — 23% to 27% of each segment visiting healthcare portals, the differences in behavior are fueled by visits to disease-specific sites. This suggests that disease-specific sites are an attractive pull for return visits among the most active and valuable segments in healthcare.

"If, as the data suggest, patients continue to become more active and therefore more likely to visit disease-specific sites, we can expect a shift to deep, narrow health sites," Ms. Lovich says. "Consequently, understanding the disease-specific and segment-specific offerings that attract and retain patients will be an essential element for healthcare companies to build a future presence online. For the time being, however, search engines remain the most dominant vehicle for reaching patients online."

Empowered Patients Are **TAKING CHARGE** and Getting Involved

Healthcare is continuing to undergo fundamental changes as a result of new business models, developments in science and technology, and a growing emphasis on alternative or complementary therapies, according Euro RSCG Worldwide.



"New technologies and genetic breakthroughs are further personalizing the healthcare process, whether by allowing patients to monitor their medical conditions at home, providing broader access to information, or enabling doctors to tailor treatment via genetic testing," says Mark Goldstone, director of development for Euro RSCG Healthcare.

Among the key trends uncovered by Euro RSCG's S.T.A.R.: Strategic Trendspotting and Research, in-home monitoring is on the rise. A new generation of monitoring technology is allowing patients to take routine medical care out of the doctor's office and into their own homes. The ability to monitor one's own condition at home becomes important not just in terms of cost savings, but also because of the greater sense of independence it affords.

"Patients who play an active role in monitoring their chronic conditions are likely to feel greater 'ownership' of the problem — and, hence, may be more proactive in the pursuit of a solution," Mr. Goldstone says. "Empowered consumers are, by definition, more involved in their own healthcare. The downside is that they will be expected to make difficult decisions and will need to have enough information to make those decisions. The benefit is that they will be able to help shape more-individual treatments with more-precise and specific courses of action."

Web access has brought into consumers' homes not only the kind of sophisticated health information once available only in medical-school textbooks, but also increased access to information on physicians and medical facilities. Together, the thousands of health-related sites available enable people to approach their personal healthcare from a position of knowledge and increased power.

"The passive healthcare consumer is becoming a relic of the past," says Ann O'Reilly, author of the report and director of Euro RSCG's S.T.A.R. "Technology, particularly the Internet, is an enabler, but this shift is centered more on the overall attitudinal trend toward prosumerism. To an increasing degree, individual consumers are becoming more demanding, more savvy, and less willing to accept mass-market solutions that don't fit their individual needs. This applies regardless of whether the 'product' in question is a pair of running shoes, kitchen cabinets, or a cancer treatment."

The trend toward patient empowerment, combined with new technologies and scientific breakthroughs that permit such things as in-home monitoring and genetics-based prescriptions, ensures that traditional modes of patient care will be increasingly vulnerable to change. After a shift to sterile doctors' offices and regimented hospitals, healthcare is once again becoming an integral part of everyday life. Treatments are taking place in the home, doctors are treating the "whole" patient rather than the disease, and patients are playing a larger role in determining how and where their conditions will be managed.

CONSUMER PHARMACY Purchasing Patterns

The second AmeriSource Index, a nationwide, quarterly survey released by AmeriSource Health Corp., polled 1,022 consumers about a range of topics including the types of special services they would like to see in their local pharmacies, Internet buying, prescription purchasing patterns, and where they received the best service.

WHERE SHOULD THE DRUG STORE OF THE FUTURE BE LOCATED?

- 56% Adjacent to doctor's offices
- 19% Shopping malls
- 5% Internet
- 3% Office buildings
- 2% Health clubs and gyms
- 1% Restaurants

Source: AmeriSource Health Corp.

WHICH TYPE OF PHARMACY OFFERS THE BEST SERVICE?

- 39% Locally owned neighborhood drugs stores
- 36% Chain drug stores
- 15% Supermarkets
- 4% Mass merchandisers

Source: AmeriSource Health Corp.

ELECTRONIC DATA CAPTURE Market Cited for Growth

There's no mistaking the growth and the future potential of the electronic data capture (EDC) market, according to Frost & Sullivan. For CB Technologies Inc. — a premier provider of technology tools and services, including MetaTrial EDC software to the life-sciences industry — the results of the U.S. Electronic Clinical Trials Market report, emphasize the strength of its market position. According to the report:

- Hybrid EDC technology will be favored by the life-sciences industry
- Alliances with electronic patient diary players are strongly encouraged to create integrated data capture solutions, enabling the collection of patient data directly into case report forms (CRFs)

- Consulting firms and other major technology players, such as Computer Sciences Corp. and Siebel Systems, are closely watching the EDC vendors for potential partnerships and affiliations with the top players

The Frost & Sullivan report states industry experts agree that regardless of technology, the type that will become most favored will be the hybrid model, because it offers the convenience of Internet uploading while maintaining 'on call' clean data at the investigator site. Hybrid EDC also allows for batch edits of patient records, a disadvantage of a pure Web system. CB Technologies pioneered hybrid EDC to offer pharmaceutical, biotechnology, medical device companies and contract research organizations a consistently reliable, secure means to capture electronically the critical data collected during the clinical trials process.

"We see this report as further affirmation that our innovative technology has become the industry gold standard," says James L. Coyne, CEO of CB Technologies. "We knew when we built our MetaTrial Hybrid EDC that Internet performance and speed were major concerns in adopting EDC technology. We worked to eliminate that as a barrier through MetaTrials design."

Primary-care Physicians Will Initially Remain LOYAL TO PROZAC

The U.S. patent expiry of Eli Lilly & Co.'s Prozac (fluoxetine) on Aug. 2, 2001, and the subsequent approval of several generic competitors are expected to dramatically alter the competitive landscape for selective serotonin reuptake inhibitors (SSRIs). In response to the question of whether and to what extent sales of other SSRIs will be adversely impacted by the release of generic fluoxetine, Decision Resources Inc., announced the results of a June 2001 survey of 72 U.S.-based primary care physicians (PCPs) who are high-volume prescribers of antidepressants.

The survey results indicate that 20% to 25% of the physicians in this influential group will initially retain their loyalty to branded Prozac rather than turning to the newly available generic fluoxetine for newly diagnosed depression patients. Preference for the branded product drops dramatically for existing patients, for whom weekly Prozac is another option. Prescribing patterns will be heavily influenced by potential formulary restrictions, as shown by physician responses when considering various managed-care-mandated treatment scenarios.

The extent to which sales of other SSRIs — Pfizer Inc.'s Zoloft, GlaxoSmithKline's Paxil, Solvay Pharmaceuticals' Luvox, and Forest Laboratories' Celexa — will be adversely impacted by the availability of generic fluoxetine is highly dependent on the patient diagnosis and brand of SSRI. The survey finds that the remaining branded SSRIs will not be on a level playing field in terms of generic erosion. Survey results show the specific patient subgroups and individual brands that will be the most vulnerable.

Formulary restrictions will influence significantly physicians' generic fluoxetine prescribing patterns, particularly when physicians are considering switching patients' medications. Results of interviews with seven pharmacy directors of national HMOs showed them to be surprisingly consistent in their opinions of the future positioning of generic fluoxetine in their formularies and potential treatment directives that would be forthcoming.

COX-2 Inhibitors to Propel Pain Market to \$30 BILLION BY 2007

The worldwide market for pain-management therapeutics is expected to reach \$30 billion by 2007 from \$22 billion in 2000, according to a report from

Front Line Strategic Management Consulting Inc. The strong market growth that began in 1998, stemming from the introduction of Celebrex, marketed by Pharmacia Corp. and Pfizer Inc., and Vioxx, marketed by Merck & Co., will stabilize at 4.4% during the next six years. This growth rate will be sustained by yearly world population increases and pain management needs of a large population of seniors.

Leading the pain category will be NSAIDs, including top brands such as Celebrex and Vioxx. Analysts expect however that these brands' sales will be effected by the imminent launch of the second-generation COX-2 inhibitors that are in development.

Analysts estimate that about 85 million people worldwide suffer from chronic pain and an additional 193 million suffer from acute pain. Unlike chronic pain, acute pain is well-controlled through the use of NSAIDs and narcotics. Even so, a large portion of episodes of acute musculoskeletal, visceral, and intermittent pain are not treated by a physician.

Follow up

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