

MM&M

MEDICAL MARKETING & MEDIA

MARCH 2003

www.cpsnet.com

According to agency president **Lena Chow**, the transformations wrought by advances in genomics will not only affect medicine, but how future drugs will be marketed, and how information about those drugs will be disseminated.

THE NEW CHALLENGES OF PERSONALIZED MEDICINE



With the completion of the first draft of the human genome in 2001, pharmaceutical marketing as we now know it may have changed forever. The intense ensuing efforts to decipher the human genome and proteome are providing a wealth of information about the genetic basis of disease. This understanding extends not only to hereditary factors of diseases, but also to the mechanisms whereby disease-associated genes are brought into action (expressed), leading to disease onset. Just as important, studies of the human genome are uncovering important information about individualized variations in response to therapeutic agents. This ability to assess predisposition to disease as well as response to therapy provides a powerful basis for targeted diagnostic and therapeutic development strate-

gies that will ultimately lead to highly individualized patient management.

In this new era of personalized medicine, physicians — and the empowered patient — are guided not only by phenotypic information such as health status and history, but also by comprehensive information about the patient's genetic makeup or genotype. This change in the practice of medicine has far-reaching ramifications for the stakeholders in healthcare: patients, physicians, payers, the FDA, bio-ethicists, politicians, and manufacturers. These fundamental changes in diagnosis and the therapeutic selection process portend even greater impact upon marketers of diagnostic and therapeutic products. Already, the rapid pace at which disease-associated genes are uncovered, and the number of predictive tests that are becoming available, are forcing changes in regulatory processes and in turn imposing new and different demands on marketing. This article examines current marketing challenges in the dawn of this new era, and offers a view into a future where personalized medicine becomes standard practice.

An introduction to personalized medicine

Personalized medicine is delivery of patient care (preventive, therapeutic, and ongoing monitoring) on an individualized basis, taking into consideration a person's genetic makeup, medical history, and environmental factors. Accurate and specific testing is an integral part of this medicine. In a way, personalized medicine is not a new concept. The advent of convenient, accurate monitoring of serum drug levels in the 1980s made it possible for physicians to increase the efficacious and safe use of drugs with narrow therapeutic windows (for example, digoxin and cyclosporine).

The 1990s saw the introduction of viral load assays, which measure the number of copies of a virus, to monitor disease progression and therapy effectiveness in the treatment of HIV-infected patients.

Still another approach to personalizing therapy was introduced with the launch of Herceptin (Trastuzumab) for the treatment of breast cancer. Herceptin targets the HER2 (human epidermal growth factor receptor 2), which is over-expressed in about 25 percent of breast cancer patients and is associated with more aggressive disease. Herceptin was launched with HercepTest, an immunohistochemical test used to measure the HER2 receptor (a protein) in the tumor sample, which thus facilitated the selection of patients who are most suited to Herceptin therapy. Since then, the FDA has approved a second methodology for determining HER2 status, called FISH (fluorescence *in situ* hybridization), which directly measures the number of HER2 gene copies in the tumor cell. Targeting therapy to patients who can benefit most from the therapy offers significant benefits in reducing the human and monetary costs of unnecessary therapy while achieving a higher level of demonstrable efficacy by identifying and treating only likely responders.

Recent focus has been on the use of genetic testing to identify predisposition to inherited diseases, including cancer, heart disease, neurological disorders, and congenital diseases. Examples are BRCA1 and BRCA2 genes, the presence of which is associated with increased risk of breast cancer and ovarian cancer; factor V Leiden, linked to clotting disorders and in particular deep vein thrombosis; and a constellation of genes linked to cystic fibrosis. Often, identification of these genes provides physicians with solid information based on which prophylactic measures can

THE CHALLENGES OF MARKETING COMPLEX SCIENTIFIC CONCEPTS

Personalized medicine presents marketing challenges unlike any other field of healthcare. The biotechnology market is very complex — representing completely new frontiers in medicine — and formulating marketing strategy for these products involves integrating multiple considerations:

- Regulatory constraints
- The role of the physician in decision making
- Consumer concerns about privacy
- Lack of consumer awareness
- The growing role of payers in drug and test adoption and reimbursement
- Availability of marketers that can interpret complex science

be taken. For example, to improve pregnancy outcomes, thrombophylaxis in the form of aspirin and low-molecular-weight heparin during pregnancy is recommended for women who test positive for factor V Leiden. In other cases, knowledge of genetic risk can lead to more vigilant surveillance, leading to early detection and significantly improved outcomes, as in the case of colon cancer and melanoma. A third use of genetic testing is in genetic counseling and the more controversial prenatal assessment.

Personalized medicine: where it stands today

As marketers, we will probably not see the widespread use of genetic information in drug selection and dosing for a few years, since it will take the incorporation of genetic profiles of patients into clinical trial regimens, completion of those trials and demonstration of the improved efficacy

made possible by tailoring the therapy to genetic profiles.

On the other hand, testing for genetic predispositions is a rapidly growing area. Already, there are a growing number of commercially available and, even more important, reimbursed products such as BRACAnalysis for assessing hereditary risks of breast and ovarian cancer. Once a disease-causing gene (a genetic marker) is identified, designing a test for the presence of that gene in an individual is not difficult. Many sophisticated laboratories, especially those in large teaching hospitals, have developed their own tests, called “home brews,” and are using them in clinical practice.

Recognizing the challenges

Ushering in this new era of personalized medicine means meeting its unique challenges head on. The issues that present themselves to product innovators and biotech marketers are considerable and are highlighted here.

Regulatory factors and constraints

Recognizing the rate at which these tests are being developed and the resources required to put each test through traditional regulatory review, and at the urging of two groups, the College of American Pathologists (CAP) and the American Association of Clinical Chemistry (AACC), the FDA established a new category, called Analyte Specific Reagents (ASRs), for expedited review.

In contrast to *in vitro* diagnostic (IVD) tests, which require extensive clinical trial results and review to demonstrate their relevance to diagnoses, ASR reviews focus on proper documentation and good manufacturing practice (GMP). The review process

is brief, but the trade-off is that what the process yields are simply reagents and not diagnostic tests. This severely limits any marketing claims that can be made regarding what the results of the test tell the clinician; further, no claims can be made about the performance (for example, accuracy and precision) of the test. While this creates an expedited route to market, it leaves biotech marketers with few tools of the past to work with, which in turn, presents novel challenges for marketing and sales.

The challenge of marketing ASRs

Manufacturers sell tests to laboratories that run the tests. Laboratories run the tests on request from physicians. Physicians order tests if they know the tests can help them manage their patients (physicians order only tests that are clinically relevant). So, if marketers cannot discuss the clinical relevance or the accuracy of a particular test, how will they be able to get the word out to practicing physicians about the value of the test? This challenge becomes further compounded when a number of competing diagnostic companies are marketing the same ASRs. Without the ammunition of performance claims, how will 21st century marketers continue to differentiate their products and capture market share?

In many ways, marketing ASRs is not unlike the oblique approach of off-label promotion, and tomorrow’s marketers can certainly look to yesterday’s experience in off-label promotion for ideas for promoting ASRs. For example, medical education is a classical tool in off-label promotion. Here is the parallel: Educate physicians about the genetic markers, not the tests to detect variants in the markers. Provide scientific evidence on how information about a patient’s genetic makeup has guided clinical manage-

ment. Provide information on reimbursement. Then direct the physician to laboratories that provide the test. This process provides the necessary framework whereby physicians can draw conclusions about clinical relevance and take necessary action to include the use of genetic testing (and ultimately the ASRs) in clinical practice.

Getting the word out on the performance of an ASR requires a similar, fact-based approach. Through scientific publications and symposia authored by those in the laboratory — not manufacturers — performance data, including those comparing different testing methodologies, can be disseminated.

While reaching physicians and other decision makers through medical education is a tried and tested marketing tactic, many such programs today fall short in maximizing the opportunity for linking the information to the brand. If brand names are not allowed in these “off-label” promotions, how does one create the association with the brand? The answer lies in the visual cues that are so integral to brand identity. Through colors, graphic treatment, typography, and other visual cues, it is often possible to offer a bridge to the brand and thus “brand” the educational materials.

A second opportunity lies in how a pharmaceutical detail force, trained in presenting therapeutic rationales to physicians, can be leveraged to present new diagnostic tools to physicians and to field questions about the complexities of genetic testing. In a future where personalized medicine means the pairing of a screening test with a therapy, market success will go to the pharmaceutical marketers who are able to bring clarity to complex and potentially confusing issues of genetic predispositions and their role in targeting therapy.

The challenge of securing reimbursement

Another challenge in marketing ASRs is securing reimbursement. This challenge is a particularly difficult one considering that the overall cost of this new personalized approach to treatment is typically many times the cost of traditional medicines, and payers (managed care organizations, Medicare, insurers) who are already feeling the squeeze of rising healthcare costs will bear the brunt of these increases directly. These higher costs mean that more than ever, marketing success will be dependent upon acceptance by payers. With toolkits limited by regulation, marketers will be required to take an even more aggressive role in demonstrating the value of the test to the payer. To achieve the success that one company, Myriad Genetics, recently achieved in obtaining reimbursement by Empire Blue Cross and Blue Shield of New York (approximately \$2,500 for a full sequence BRCA1 analysis for members who have a heightened risk of ovarian and breast cancer) will require planning and persistence.

The challenge of patient privacy

The positive promise of health and healing that genomics and personalized medicine represent is a growing concern among consumers about the negative impact of uncontrolled genetic information. With literally hundreds of genetic-based screening tests now available and hundreds more on the way, consumers are understandably concerned that information from these tests may be improperly used by employers to discriminate against them and that healthcare insurers might also use this information to limit coverage.

Laws in every state currently regulate access to medical records and the disclosure of personal medical information. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) created federal guidelines and extended health data protection to all Americans. Directed primarily at insurers, these regulations will not become fully operational until after 2003, and even then regulations and laws are at best only promises for the future.

The legal debate centers on the adequacy of state and federal laws as they relate to genetic information. What, then, is the role for the healthcare marketer in this debate? Healthcare marketers have an obligation to leverage their knowledge, skills and resources to educate and inform, with the goal of helping stakeholders take positions based on facts and rationale, not hype and hysteria. This obligation begins today, as the accelerated discovery of new mark-

ers and promulgation of genetic testing usher in the new era of personalized medicine.

The challenge of communicating complex science

The single greatest challenge to current marketers can be found in the complexity of the science that has given birth to personalized medicine. The difference between marketing the productized outcomes of personalized medicine and marketing today's pharmaceutical products can be likened to the differences between the layman's understanding of inorganic and organic chemistry. People of reasonable skills in arithmetic can readily grasp inorganic chemistry, but organic chemistry is more complex and difficult to grasp. This comparison essentially rejects the notion that today's product managers and the healthcare advertising agencies that support their current market basket of products will be up to the challenge posed by the advent of personalized medicine. Translating this new, highly complex science into meaningful marketing messages may well require a different breed of 21st century marketer, advancing to the forefront those with intimate understanding of genomics, proteomics and experience in healthcare marketing. We are already starting to see the emergence of highly specialized biotech advertising agencies and a move toward further specialization within them, and it is likely that this trend will continue.

Meeting the challenges in the years ahead

With a veritable explosion of genomic and proteomics research-based products on the horizon, pharmaceutical marketers will soon be facing challenges all but unknown in previous years. Regulatory constraints, changing roles of physicians in decision-making positions, consumer concerns for personal privacy, increasing importance of third-party payers and scarcity of biotech-savvy marketing, public relations and advertising talent will combine to change the face of the pharmaceutical marketing industry as we know it today. ■



LENA CHOW

Lena Chow is founder of Lena Chow Euro RSCG, a Silicon Valley-based healthcare advertising agency that specializes in the branding of transformational products. She can be reached by e-mail at lena@cityofparis.us, or by phone at (650) 380-3827.
