Formulation

SENSORY

Let's Talk About Sense Appeal

Taste is an obvious factor when formulating drugs, but the other senses play a role as well | BY **JEFF WORTHINGTON**

Optimizing the sensory experience of products is the top priority for consumer packaged goods companies. Numerous departments are assigned to the task—and significant resources are allocated—to ensure the target sensory profile meets product positioning and business strategies. But in the pharmaceutical industry, it's a different story. Product attributes may be used to support strategic marketing goals, but these attributes relate almost exclusively to medical claims of better efficacy, longer lasting effects, milder side effects, or faster onset of action.

Such claims are undeniably important, but they aren't the only ones available to savvy marketers. The products' aesthetics—appearance, aroma, flavor, texture, skin feel, sound, and more—can build an emotional connection with the product. This can have a dramatic effect on patient compliance and increase brand loyalty.

Unfortunately, drug products' aesthetic characteristics are not fully considered and utilized by many companies. This often leads to the launch of drugs unacceptable to many patients, despite their medical benefits. When medication compliance is compromised, health outcomes suffer and drugs fail to realize their sales potential.

For many therapeutic indications, the patient is able to perceive clearly whether or not the drug is working. Examples include non-steroidal anti-inflammatory drugs for muscle pain; antiemetics for nausea; antibiotics for ear, sinus, and throat infections; cough suppressants; laxatives; and more. Diabetics effectively self-manage insulin levels on an ongoing basis using blood glucose test kits. Today, simple blood tests for cholesterol let patients and their physicians monitor the effectiveness of statin therapies by providing periodic feedback on their cholesterol count (albeit infrequently). Despite the advent of these simple blood tests, however, many patients stop taking cholesterol-reducing drugs. In part, this is because there's no obvious physiological result or improvement in well being, proving the reputation of cardiovascular disease as a "silent killer."

The Drug Sensory Experience

Patients undergo a sensory experience every time they self-administer a drug, whether it's swallowing a tablet or capsule, chewing a tablet, swallowing a liquid, or using a nasal spray, inhaler, or injector. It's a ritual involving perceptions that can powerfully affect a patient's view of treatment effectiveness. An innovative product manager would strive to ensure that all the sensory elements of this therapy regimen work together to create positive perceptions that complement the medical attributes. Yet, surprisingly little attention is paid to the sensory attributes of a vast majority of dosage forms. (Continued on p. 34)

(Continued from p. 32)

In a study published by Brandsense.com, consumers rated sight most important (58%), followed by smell (45%), hearing (41%), taste (31%), and touch (25%).[1] The report also noted that 83% of all commercial communications are visual, which leaves only 17% targeting the other four senses: hearing, touch, taste, and smell. "This is extraordinary given that 75% of our day-to-day emotions are influenced by what we smell and the fact that there's a 65% chance of a mood change when exposed to a positive sound," the report stated. "This is a long way of saying that the importance of our senses has been completely overlooked in the brand-building business."

The central point the author makes is that the greater number of senses a product appeals to, the greater the potential for creating an emotional attachment to the product, which translates to product and brand loyalty and ultimately to sales.

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Taste

Flavor perception is a combination of taste (gustation), smell (olfaction), and trigeminal sensations. Each has its own physiology and biochemical pathways, yet the terms are often used interchangeably.

Taste is perceived through stimulation of receptor cells clustered in the taste buds on the epithelium of the tongue. There are four basic tastes: sweet, sour, salty, and bitter. The vast majority of drug substances with reported taste effects are bitter. Efforts to develop structure/bitter activity databases have met with limited success; the taste effects of the drug substances are discovered by serendipity in the laboratory or in early clinical development. For many drug substances, the challenge is to mask bitterness, both in the initial flavor and throughout the aftertaste, and the pharmaceutical industry devotes considerable resources to developing palatable formulations. These efforts take many forms, from isolating the drug substance from the taste receptors in the oral cavity (encapsulation and complexation) to overwhelming the bitterness with another taste (sweet) to creating a "white taste" by balancing all the basic tastes.

Isolation is often assumed to be the most effective technique; however, attaining complete coverage (encapsulation) or complete binding (complexation) of the drug substance is generally not possible. Because many drug substances are extremely bitter, these approaches often represent partial solutions, meaning further taste optimization will be required to develop a palatable product. While a number of *in vitro* models have recently been developed, none are able to fully replicate the *in vivo* results obtained by human subjects. For many years, tablets were sugarcoated to facilitate swallowing and reduce the perception of the active. Film coating continues to replace sugarcoating and is, in large part, driven by manufacturing economics. Recently, high-intensity artificial sweeteners have been incorporated into the coating material in to replicate the characteristic sweet taste of sugar-coated tablets. It can be a challenge to match the taste of sugar, however, a fact manufacturers and consumers of diet soft drinks can attest to.

The sense of smell plays a key role in taste. Odors are perceived through stimulation of the olfactory epithelium, which contains receptor cells and the free nerve endings of the trigeminal nerve. The olfactory receptor cells lie in the upper reaches of the nasal cavity, called the olfactory epithelium. There are two ways odors are perceived. The first involves what is perceived through the nose as we breathe: Think of the aroma of apple pie baking in the oven or the smell of recently mown grass. The second involves odors perceived during gustation, when volatile odorous molecules reach the olfactory center through the nasopharyngeal passage. Many people complain they cannot taste their food when suffering from nasal congestion. Actually, they can taste the food (i.e., they can perceive the basic tastes), but they can't smell the aromatics; hence,

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(Continued on p. 36)

(Continued from p. 34)

the food is perceived as bland. Flavor (aroma) in pharmaceuticals has historically been used in dosage forms in which the active comes in direct contact with our receptors. Some examples are liquids, chewables, fast-dissolving tablets, and nasal sprays. For instance, McNeil Consumer Healthcare uses this approach in its vanilla-flavored Tylenol caplets and berry-flavored Viactiv multivitamin caplets.

In addition, compounds found in ginger, horseradish, and mint stimulate the endings of the trigeminal nerve, producing sensations of warmth, burning, stinging, cooling, and pungency in the mucosa of the nose and mouth. These trigeminal sensations are anatomically independent of taste and smell but are important characteristics of many products, including drugs and certain excipients. A low level of cooling can help minimize other perceived negative sensory characteristics such as tongue sting or throat burn. Higher levels of cooling can become part of the flavor identity, as in the case of Tylenol Cool Burst Sensation caplets or Zantac Cool Mint tablets.

Finally, a product's physical properties can play an important role in flavor perception and have a dramatic effect on product acceptability. The most common pharmaceutical examples include tablet hardness, grittiness, stickiness (films and soft chews), and ease of swallowing. Marketers have used the perceived mouth feel characteristics of their products to distinguish them from the competition. Some examples include TUMS Smoothies (GlaxoSmithKline); Viactiv Flavor Glides, combining a smooth coating and a berry flavor/aroma; and Citrucel Fiber Shake (GlaxoSmithKline), which leverages the product's thickening properties.

Smell

According to the Brandsense.com study, 75% of all our emotional connections are based on smell. Smells can be alluring (fragrance), alarming (natural gas, spoiled milk), calming (lavender), and refreshing (ozone after a summer thunderstorm). They can affect nearly every human emotion. Consumers have access to a seemingly limitless variety of food and beverage aromas. The same is true for personal care products. Think about the number of fragrance choices for perfumes and colognes, shampoos and conditioners, skin creams and moisturizers, deodorants and antiperspirants—to name a few. Similarly, in the eternal battle for shelf space among consumer healthcare companies, there's a proliferation of flavor-line extensions of popular over-the-counter medications. This is in stark contrast to the market for prescription pharmaceuticals, in which manufacturers promote dosing compliance (rather than product consumption) as they endeavor to develop a single formulation suitable for worldwide marketing.

The distinction between taste and odor has important implications for drug developers. Many drug substances are bitter, yet developers often focus on the addition of flavoring materials (e.g., orange, cherry, mint) to the formulation

to improve its palatability. Given the physiology of taste and smell, one would not expect an aromatic flavoring material to mask a basic taste—bitter or otherwise. But some drug products, including certain antibiotic oral suspensions, have a strong and repugnant odor that may cause an immediate gag reflex in the person opening the bottle or ingesting the product. In these cases, the addition of flavoring materials can have the beneficial effect of masking the odor characteristics of the drug substance.

Touch

The way a substance feels when it comes in contact with the body can have a profound effect on consumers' feelings toward the product and brand. Product marketers in a variety of industries have embraced this fact. Think of slogans such as "See and Feel the Difference" (Crest toothpaste, Procter & Gamble), "Advanced Comfort and Protection for Men" (Gillette Series shaving foam, Procter & Gamble), and "Make Your Life Comfortable" (Cotton Incorporated).

The cosmetics industry focuses an enormous amount of its research and development on creating products with superior skin-feel properties. In contrast, the pharmaceutical industry has historically focused on the efficacy of its topical products, with little regard for how the products feel during application and use. Ingredients that produce warming, cooling, and irritation have been used in pain relieving ointments such as BenGay (McNeil) and Flexall (Chattem Inc.) for decades. They have been used as well as for first-aid tools such as cold packs that reduce inflammation and—more recently—warming patches that relieve muscle pain. Perhaps these same kinds of sensations could be used in traditional topical pharmaceuticals or in transdermal patches to provide an indication of efficacy, even if it is only a placebo effect. The boundary between pharmaceuticals and cosmetics continues to blur, as evidenced by the emergence of "cosmaceuticals" in the popular consciousness. Pharmaceutical marketers would be well served to study and emulate some of the formulation directions and marketing communications used by cosmetics and personal care manufacturers.

Sight

The pharmaceutical industry has long relied on product appearance to differentiate its products from the competition. Many companies have used tablet size, shape, color, and sheen effectively. This is key, because tablet size and geometry are known to affect a patient's ability to swallow a dose.

Color has also been used effectively in advertising. In consumers' minds, the color pink has long been associated with Owens Corning Fiber Glass insulation; in pharma, it's indelible as Pepto-Bismol. For many years, International Business Machines was synonymous with the color blue, as evidenced by its nickname in the business lexicon—Big Blue. In pharma, the best-known blue product is unquestionably Pfizer's little blue pill, Viagra—an icon in today's pop

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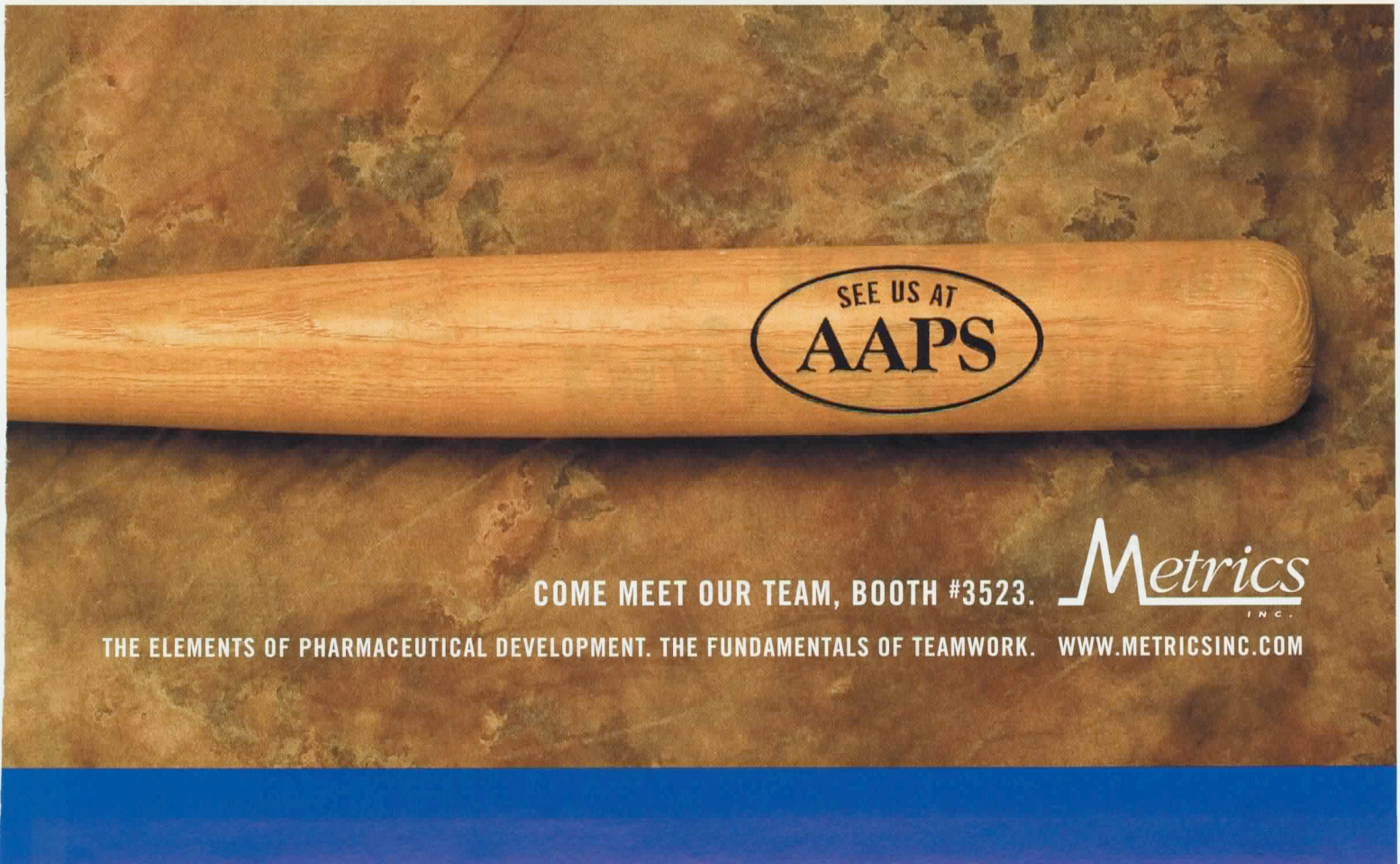

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culture. And who can forget how AstraZeneca successfully got ahead of the patent expiration curve by migrating millions of Prilosec users to Nexium on the backs of the color purple (Prilosec: "The Purple Pill" became Nexium: "Today's Purple Pill"). Pharmaceutical companies need to become more aware of the effect of product appearance.

Hearing

The sounds products make during use can be extremely powerful. This fact is evidenced by sounds as disparate as the signature rumble of a Harley-Davidson motorcycle, the crunching of a breakfast cereal, and the refreshing "pop" when opening a cold can of soda or beer. These sounds are often highlighted in television commercials. Sound has long been used by Bayer to convey its claims of the fast action of Alka-Seltzer tablets in the famous jingle: "Plop, plop, fizz, fizz, oh what a relief it is." Any unique sound a product makes is an opportunity to build an emotional bond with the consumer. Pharma has only begun to explore the possibilities, which are limited more by our imagination than by technology.

In the end, the challenge for developers and marketers of some drug products is overcoming a negative sensory attribute to improve patient acceptability. This represents the minority of all drug products, however. The larger opportunity is to discover the sensory attributes that can be leveraged for the many drug products differentiated solely by price (generics) or that offer little in the way of an emotional connection to the patient.

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Powerful insights come from a true understanding of consumer beliefs, perceptions, and behaviors. Many consumer research techniques, ranging from traditional surveys and focus groups to ethnographic studies, can be used to support this exploration. Descriptive sensory analysis can identify and quantify sensory attributes for in-depth consumer research. New techniques in development combine sensory and consumer research to help sensory responses drive consumers's actions. ■

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REFERENCE

1. Lindstrom M. *Brand Sense: How to Build Powerful Brands through Touch, Taste, Smell, Sight, and Sound.* New York, NY: Free Press, Simon & Schuster; 2005.

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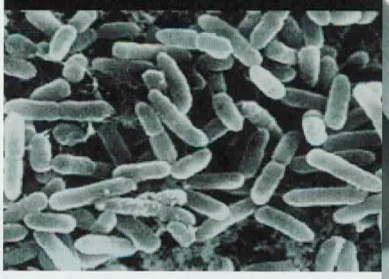

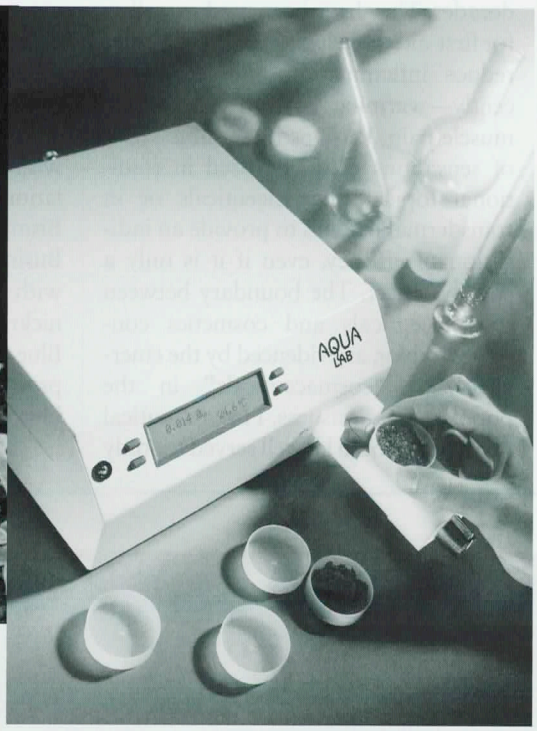

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