



INSIDER[®]



A SPECIAL ALL-DIGITAL ISSUE

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Year-Round IMMUNE HEALTH

Analyzing market trends,
ingredients and regulations

SEPTEMBER

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	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

CONTENTS



4

3 Viewpoint

4 Natural Ingredients for Immune Support

Suffering from colds and flus can cause anyone to feel blue once the winter weather hits. With consumers ranking immune support as the second most desired functional food benefit, now is the time to delve into the realm of natural ingredients for immune system support.



14

14 Taking the Pulse of the Immune Health Market

While cold and flu season may conjure thoughts of immune-boosting supplements and functional wellness products, in reality, consumer interest in products that support immune health is no longer confined to illness or allergy-prone times of year.



20

20 Healthy Marketing: Immune Products Vulnerable to Regulatory Scrutiny

Marketing immune products legally is tricky business, as the immune system's primary job is to identify and eradicate disease-causing pathogens.

A Year-Round Need

Like clockwork, every year in the late fall, I get a nasty cold that lingers unwelcomed for a week or more. Most years, it grabs onto one of my kids too. It's an all-too-familiar prelude to the holidays. Yet, we all joke and shake our heads when a friend gets a cold in July around here. I mean, it is 115 degrees or more, and somebody is sniffing and coughing!



But in reality, attacks on the immune system aren't just seasonal beasts. And as folks are training for that sprint triathlon in April, preparing for a summer vacation or planning to get through flu season without the flu vaccine, they are increasingly thinking ahead and incorporating immune health products.

This **Natural Products INSIDER** Digital Pulse lets manufacturers know which immune health ingredients and trends are most important to their customers right now.

Included in these pages are several articles—first, an overview of the most popular immune support ingredients. There are many ingredient options to consider, and there are always new ingredients trying to break through to grab consumers' attention. Keeping up with the latest trends, research and innovations is critical to your business, and **INSIDER** is working diligently to help you navigate the options.

Second, we address market data as it relates to ingredients, age-related demographics, consumer attitudes and delivery systems. Perhaps what you see here will correspond to sales trends you're seeing in your own business. If not, we would love to hear from you.

Third, the talented **INSIDER** editorial team has outlined the all-important labeling considerations. This content can help guide you in adequately promoting the incredible immune benefits of your products without mistakenly crossing the line into an illegal disease claim.

Our online content archives include more on immune health, particularly valuable if you are looking for a historical perspective in this arena. Most of the top suppliers also leverage the **Natural Products INSIDER** site to share their research via content such as Whitepapers. We intend to continue being your go-to source for the information you need to excel. Please let us know if there is anything else we can research, spotlight or answer!

A handwritten signature in dark ink that reads "Danica Cullins".

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Beat the Blues

New research on natural ingredients for immune support

by Kate Lloyd

Suffering from colds and flus can cause anyone to feel blue once the winter weather hits. With consumers ranking immune support as the second most desired functional food benefit (according to a 2012 Datamonitor survey), now is the time to delve into the realm of natural ingredients for fighting colds, flus and other illnesses that plague the population.

Datamonitor's survey indicated 88 percent of consumers are interested in buying functional foods and beverages that aid immune health, but only 40 percent are actually purchasing the products. According to Richard G. Mueller, chief executive officer, Biothera, this gap likely comes from a lack of availability or recognition of immune health products' benefits.

"The immune space is an untapped market," Mueller said. "The gap between immunity product interest and purchase translates into tremendous opportunity for food, beverage and supplement companies that can deliver real immune health benefits. The winners will be manufacturers who understand consumers and their desire for truly efficacious immune health products backed by strong science and that can be consumed daily."

Beta-Glucans

A well-researched ingredient category includes **beta-glucans**, and new studies illustrate its immune benefits in populations of all ages. Studies on Biothera's Wellmune ingredient, a yeast beta 1, 3/1, 6 glucan derived from the cell wall of a proprietary strain of yeast, show supplementation with

INSIDER's Take

- Nearly nine in 10 consumers show interest in buying functional foods and beverages for immune health.
- Researchers continue to find links between ingredients for gut health—probiotics and dried yeast fermentate—and enhanced immunity.
- Some up-and-coming ingredients for immune health in today's market include green tea, curcumin and boswellia.



Source: Datamonitor Consumer

IN THIS ISSUE

Viewpoint p. 3

Immune Health Market Data p. 14

Table of Contents p. 2

Connecting the dots between your product + immune health

Wellmune® is a proprietary baker's yeast beta 1,3/1,6 glucan that is clinically proven to help strengthen the immune system. Safe for daily consumption, it's ideal for all types of food, beverages and supplements. Learn how easy it is to deliver immune health benefits to your consumers. Connect the dots at **wellmune.com**.

100%
natural

innovative

safe

clinically
proven

versatile

 **wellmune**®

Be Well. Stay Well.

Brought to you by

BIOThera
the immune health company

the ingredient can help everyone from young children to older adults maintain immune support during cold and flu season.^{1, 2}

“While Wellmune cannot prevent or treat disease, building a strong immune system year-round is critical to maintaining the foundation of health and wellness,” Biothera’s Mueller said. “This is particularly true during cold and flu season. Wellmune safely and naturally strengthens innate immune cells that help keep the body healthy, as evidenced by multiple peer-reviewed clinical studies demonstrating its ability to reduce upper respiratory tract infection symptoms and improve overall physical health.”

Because children can easily succumb to diet inadequacies, it’s important that they consume enough nutrients to keep their immune systems from failing. In a 28-week, double blind, placebo-controlled study, 310 children took three servings per day of a Mead Johnson formula with Wellmune or unfortified cow’s milk.¹ Results indicated the Wellmune formula better supported their immune systems and significantly reduced the number and duration (days) of acute respiratory infection (ARI) episodes, resulted in fewer antibiotic treatments and also led to fewer missed days of daycare due to illness.

**It’s important
that children
consume enough
nutrients to
keep their
immune systems
from failing.**

A company-published study on 100 healthy adults ages 50 to 70 years illustrated Wellmune beta-glucans’ benefits in older populations.² During a 90-day study, adults consuming 250 mg/d of Wellmune experienced reduced numbers of upper respiratory tract infections (URTI), as well as statistically significant changes and trends in cytokine levels, which are part of the body’s response to viral encounters and inflammation.

Dried Yeast Fermentate

Another yeast-derived ingredient, EpiCor **dried yeast fermentate** from Embria, plays a role in immune health by supporting a healthy gut.

“Every day, more people are associating immune health with digestive health,” said Larry Robinson, vice president of scientific affairs, Embria. “Products supporting gut health generally have a positive impact on the beneficial bacteria inhabiting the gut. These bacteria, collectively known as the microbiota, play a major role in immune function and health.”

Recent research showed EpiCor can increase levels of butyrate, a short-chain fatty acid (SCFA) beneficial for gut immune health.³ Researchers used a multi-stage simulator of the human digestive system to better understand EpiCor’s effect on intestinal microbiota and the resulting protection against inflammation. In addition to increasing butyrate levels, EpiCor significantly increased levels of beneficial bacteria; it also contains mannan-oligosaccharides (MOS) and beta-glucans, both known to benefit gut immune health.

Probiotics

Probiotics are also critical for a healthy gut and a fine-tuned immune system. Considering 80 percent of the immune system is located in the digestive tract, consumers should focus on maintaining a healthy gut to support overall health and immunity, according to John Deaton, vice president of technology, Deerland Enzymes.

Probiotics play a critical role in developing and operating the mucosal immune system in the digestive tract. In particular, Bifidobacteria provide a barrier for gut protection, and research shows these beneficial bacteria support the immune system by promoting normal lymphocyte and phagocyte activity—cells that are essential for fighting infections.⁴ Many strains of Lactobacilli have also been shown to support immune function, and they tend to promote anti-inflammatory benefits.

In another recent study, elderly volunteers who consumed a probiotic *Bifidobacterium lactis* Bi-07 strain (Bi-07; 10(9) colony-forming units/d) from DuPont Nutrition & Health experienced improved phagocytic activity of the white blood cells known as monocytes and granulocytes.⁵ The study results indicated effects from probiotics and prebiotics may last longer in the elderly compared to adults.

Probiotics may also help prevent common throat infections in children, which are known as streptococcal and viral pharyngotonsillitis.⁶ In a 2014 study using the probiotic strain *Streptococcus salivarius* (BLIS K12 from Stratum Nutrition), 30 children ages three to 13 years old consumed lozenges with BLIS K12 for 90 days, while another 30 children served as a control group. Results showed a 96-percent reduction in streptococcal sore throat incidences in children taking BLIS K12, an 80-percent reduction in episodes of viral infections and a reduction in the number of days antibiotics (amoxicillin) and antipyretics were used.

“Absolutely everyone from a young child to the oldest person should be taking a probiotic everyday—definitely during the cold and flu season—to help support the immune system,” said David Keller, vice president of scientific operations,



Immune health isn't just for the winter months—consumers today want to fight off illnesses year-round. For more information on immune-boosting ingredients, such as vitamin C, zinc and probiotics, visit **INSIDER's Immune Support Content Library**.

DOWNLOAD HERE!

Ganeden Biotech. “While people right now are not necessarily connecting probiotics and immune health, and really understanding the preventative benefits of taking them every day, it just takes consumer education to understand [the advantages] of taking probiotics.”

Glutathione

Consumers should also understand **glutathione** (GSH), known as the body’s master antioxidant, needs replenishment each day due to depletion from a number of lifestyle factors, according to Karen Todd, R.D., director of marketing, Kyowa Hakko USA. Some of these factors include smoking, drinking, eating fatty foods and exercise.

“Those who consume a poor diet or a diet that is mainly processed or prepared foods will have a difficult time getting enough glutathione on a daily basis,” Todd said. “As early as age 40, glutathione levels begin to decrease and should be replenished every day.”

Todd added GSH levels are lowest in the morning, so one should consume foods or supplements rich in glutathione soon after waking up.

A 2014 study on 54 non-smoking adults taking 1000 mg/d of Kyowa Hakko’s Setria glutathione demonstrated the supplement raises GSH levels in the blood and helps support the immune system.⁷ Natural killer (NK) cytotoxicity increased during the six-month study, showing GSH supplementation can help the body target infected cells.

Everyone from a young child to the oldest person should be taking a probiotic everyday to help support the immune system.

— David Keller, vice president of scientific operations, Ganeden Biotech



Immunoglobulins

Immunoglobulins (IgGs) are proteins present in bovine whey protein, which transport antibodies for fighting harmful microorganisms, such as viruses and bacteria. These essential proteins can help consumers maintain healthy immune systems to fight off foreign invaders, as well as prevent conditions such as recurrent pneumonia.⁸ David Eisenberg, vice president of nutraceutical sales, Equitech-Bio, explained that IgGs have been marketed for years, just like vitamin C, and they deserve recognition for their benefits.

A 2013 study illustrated the need for individualized IgG therapy for patients with primary immunodeficiency diseases (PIDDs).⁸ Researchers chose two case studies for scientific review and found patients with PIDDs can receive optimal treatment through individualized IgG therapy to become free of infection or pneumonia. Separate research explored the effect of an oral serum-derived

bovine immunoglobulin (SBI) on eight HIV-positive participants experiencing diarrhea for one month or longer (an effect of HIV on the enteric mucosa).⁹ After eight weeks of SBI administration, patients reported improvements in diarrhea occurrences (cramping, urgency, etc.), but more research is required to support the findings.

Mushrooms

A wide range of research demonstrates the power of **mushrooms** for maintaining immune health. Dan Lifton, president of the proprietary branded ingredients division of Maypro, explained how the company's AHCC (active hexose correlated compound) mushroom mycelia extract can benefit both the sick and the healthy.

"Most previous studies on AHCC focused on immune-compromised patients, specifically cancer patients, those with hepatitis C, non-viral liver disease and those with HPV infections," Lifton said. "While AHCC has been consistently shown to provide a benefit for these conditions, more recent data shows a benefit for healthy adults seeking to maintain peak immunity and stay healthy during the flu season."

One recent study from Michigan State University illustrated that taking AHCC in combination with a flu shot increased anti-body titers to influenza B three weeks post-vaccination, while the vaccine alone failed to produce statistically significant benefits.¹⁰ Another double blind, placebo-controlled study on 21 healthy volunteers showed AHCC supplementation for four weeks increased the number and activity of dendritic cells, which are responsible for detecting, consuming and presenting foreign bodies, as well as activating adaptive immunity.¹¹ Finally, a controlled four-week study published in August 2014 demonstrated healthy participants who took AHCC maintained normal NK cell activity and index-scored immune competence, while subjects taking placebos experienced a significant decline in NK cells and immunological vigor.¹²



Echinacea

Another ingredient proven to aid immune health is **echinacea**. In a 2007 analysis published in *The Lancet Infectious Diseases*, researchers noted echinacea may cut the risk of catching a cold by up to 60 percent.¹³ In addition, echinacea can partner with vitamin C to further enhance the benefits to immunity, explained Steve Siegel, vice president of Ecuadorian Rainforest. In the same analysis, researchers observed a study on a combination of echinacea and vitamin C that reduced the chances of catching a cold by 86 percent, while echinacea alone reduced cold incidences by 65 percent.



French maritime pine bark

Supplementing with **French maritime pine bark** in combination with vitamin C and zinc can shorten the duration and lessen common cold symptoms such as runny nose, nasal obstruction, sore throat, sneezing, high temperature, cough and general discomfort.¹⁴ In a 2013 study, subjects supplementing with Pycnogenol from Horphag Research (100 mg/d) in conjunction with vitamin C (200 mg/d) and zinc (30 mg/d) shortened the duration of cold symptoms to four days, compared to the average of seven days when taking Pycnogenol alone, Pycnogenol plus vitamin C or Pycnogenol plus gluconate zinc.

“By experiencing fewer days of symptoms, consumers were able to get back to their normal routines quicker, which could prevent missed work days and additional cold-related costs,” said Sebastien Bornet, director of global marketing at Horphag Research (worldwide exclusive supplier of Pycnogenol). “This research demonstrated a natural path to managing symptoms without the side effects that can come with some over-the-counter medicines.”

Consumers can look to ancient medicines for immune support during the cold and flu season.



Larch Arabinogalactan

Larch arabinogalactan (LAG), composed of galactose and arabinose, can strengthen both the innate and adaptive arms of the immune system, according to Bryan

Rodriguez, global products manager, Lonza. ResistAid LAG (from Lonza) supports the immune system through a triple-action approach addressing multiple pathways in the body. Research showed the ingredient reduced cold episodes when taken in doses of 4.5 g/d for 12 weeks.¹⁵

“Larch arabinogalactan has the ability to modulate and support the two arms of the immune system in a positive manner,” Rodriguez said. “It accomplishes this through direct and indirect pathways within the gastrointestinal tract, optimizing each arm to appropriately respond when challenged by a foreign substance.”

Tinospora

Consumers can also look to ancient medicines for immune support during the cold and flu season. For example, the botanical ***Tinospora cordifolia*** has a long history of use in traditional Indian Ayurveda to promote optimal immune response, according to Chelsea Thomas, marketing coordinator, Verdure.

In a randomized, double blind, placebo-controlled trial studying participants with hay fever (allergic rhinitis), Verdure’s botanical extract derived from Tinospora (Tinofend®) promoted an immune response by stimulating the activity of white

blood cells and reducing the number of eosinophils (immune cells that release histamine).^{16, 17} Tiofenid improved sneezing, runny and itchy nose in all subjects observed, and nasal obstruction in 95 percent of the subjects.

Emerging Ingredients

A few other up-and-coming ingredients for immune health in today's market include green tea, curcumin and bosweillia. According to Cathy Arnold, formulations regional manager, North America, Fortitech Premixes, these ingredients need more studies behind them to establish their immune health benefits, but they do contain properties known to support the immune system. Vitamins A, C, D and E; B vitamins; and a variety of minerals (such as iron and zinc) also boast immune-enhancing properties.

"Immunity is a concern for all ages, whether it's a baby just starting out its life, a growing child, an active adult or an elderly person," Arnold said.

"Maintaining optimal immune status is important for maintaining health."

This year, consumers can maintain confidence in their immune systems with the ever-growing list of natural ingredients for immune support. ■

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EXPLORE

SupplySide Storefronts are always open. Come on in.

Taking the Pulse of the Immune Health Market

With more consumers adopting holistic attitudes toward health, demand for products targeting immune health support are in demand year-round

by Joanna Cosgrove

While cold and flu season may conjure thoughts of immune-boosting supplements and functional wellness products, in reality, consumer interest in products that support immune health is no longer confined to illness or allergy-prone times of year. According to “Health + Wellness A Culture of Wellness 2013,” a report from The Hartman Group, consumer attitudes have shifted to reflect an desire for total, year-round wellness. Products geared for immune health support are following suit, branching out of pill formats and into more lifestyle-oriented functional foods and beverages.

“Over the past decade, we have observed a shift away from a perfunctory, ascetic, reactive and compliant notion of wellness to one that is more experiential, positive, holistic, proactive and self-assessed,” the report stated. “There has been a cultural shift—now complete for all intents and purposes—from ‘health’ to ‘quality of life,’ from reactive health to proactive wellness.”

Consumers know more about how to maintain their own health, and “this broadened notion of wellness has become a tacit part of culture rather than a lifestyle choice or an alternative movement.”

The Hartman Group also found the notion of maintaining personal wellness is driven by “personal consumer practices of self-assessment and ongoing self-management” supported by “enjoying fresh and delicious food—supported by, and supporting, good digestion” as the “dominant consumer route to health and wellness” along with “being active (as opposed to the more narrowly focused ‘exercise’), staying connected with places (as well as people) and resting well.”

Market research from Frost & Sullivan confirmed that the market for immune health products is vibrant and growing. Reuben Sequeira, chemicals, materials and food research analyst with Frost & Sullivan, said many supplements make up the immune health segment. Those ranking among the most

INSIDER's Take

- Market research confirms the market for immune health products is vibrant and growing.
- The biggest demographic for immune health products are middle-aged adults (age 30 to 45).
- Some of the established immunomodulators include specific vitamins, Echinacea, beta-glucans and lactoferrin.

IN THIS ISSUE

- Immune Health Ingredients p. 4
- Immune Health Marketing p. 20
- Table of Contents p. 2

popular for addressing colds, influenza and immune health conditions include amino acids, cranberry extracts, garlic, melatonin, multivitamins, probiotics, resveratrol, super fruit supplements, B vitamins, vitamins C and D, and zinc supplements. “Together, these represent a big market that is worth around USD \$12 billion and is growing in the range of 5 percent to 7 percent,” he said. “This market encompasses both synthetic and natural/organic-based ingredients, the latter representing a faster growing, but very small percentage of the market in between 10 percent and 20 percent.”

Sequeria said the biggest demographic for immune health products are middle-aged adults (age 30 to 45), followed by young adults, adults age 50 and up, and children.

Assessing Consumer Attitudes

As part of its Global Consumer Survey of 2014, Datamonitor Consumer explored the behaviors and opinions of nearly 25,000 respondents from across 25 countries. The process revealed interesting insights pertaining to how people view immune health and the factors that influence it.

Tom Vierhile, Datamonitor Consumer’s innovation insights director, said consumers were asked a pair of immune health questions. The first was “How concerned do you feel about the following issues—germs/bacteria/viruses in your home environment?”

“The response to this question helps point to the type of consumer most likely to be concerned about health issues like immunity,” he said, noting that consumers were asked to respond with “not at all concerned,” “not very concerned,” “neither concerned nor unconcerned,” “very concerned” and “extremely concerned.”

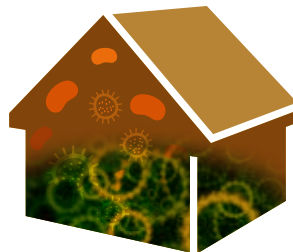
“The age bracket with the highest percentage of consumers that are ‘extremely concerned’ about ‘germs/bacteria/viruses in your home environment’

Germs/Bacteria/Viruses in Your Home Environment

**Very Concerned and
Extremely Concerned**

51%

25 to 34 year old



**Very
Concerned**

36%

18 to 24 year old



“These responses are probably no great surprise because the 25- to 34-year-old age group may be the most likely to have small children in the home, a catalyst for concern given how illnesses can spread based on contact these young children have with their peers.”

The lowest reading, he said, came from respondents in the 18- to 24-year-old bracket. “Just 36 percent saying they were ‘very concerned’ or ‘extremely concerned’ about this,” he said. “These responses are probably no great surprise because the 25- to 34-year-old age group may be the most likely to have small children in the home, a catalyst for concern given how illnesses can spread based on contact these young children have with their peers.”

“Women in the 65 and older age group expressed the least amount of concern, with just 40 percent ‘very concerned’ or ‘extremely concerned,’” Vierhile explained, noting that the response for men was similar, but not identical. “The most concerned group of men was those in the 35-to-44-year-old age group, with 44 percent expressing concern, but this reading tied the 65-plus age group, also with 44 percent expressing concern.”

“extremely concerned” about this. Interest from men was similar, with a high reading of 12 percent of men in the 25- to 34-year-old age group saying they were “extremely concerned” about maintaining hygiene.

|||||

Many products and ingredients have ties to supporting immune health. Some of the established immunomodulators include specific vitamins, Echinacea, beta-glucans and lactoferrin; however, according to Frost & Sullivan's Sequeira, multivitamins rank as the highest revenue-generating products. "This coincides with the assessment that multivitamins address a wide spectrum of health conditions," he said. "The growth of this product segment is maturing around 3 percent,



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while products like probiotics, vitamin D and vitamin B/B complex are also popular, but growing at faster rates in the range of 5 percent to 10 percent.”

Beyond the scope of multivitamins, Datamonitor Consumer’s Product Launch Analytics database identified a number of unconventional ingredients and products targeted toward the immune health segment. “Some include new and novel ingredients for immunity, including superfruits like camu camu, mulberries (a largely unnoticed superfruit that appears to be on the rise), and elderberry as well as fruits and vegetables, vinegar, yerba mate, deer antler and more,” Vierhile said.

The beverage format continues to be a popular vehicle for delivering these immune-enhancing ingredients. For instance, San Diego-based Bona Vita RX



Some “emerging” product groups might seem a little odd to the American palate, such as kombucha and vinegar.

recently debuted a line of Age Defense Waters that are touted to provide “Intense Energy & Immune Support,” and feature “Active Trans-Resveratrol” as the key ingredient. Malibu, California-based Mulberry Love LLC’s eponymous beverage taps into our current penchant for coconut water, paring it with organic mulberry juice and calling attention to its “plethora of health benefits,” including its ability to boost immunity.

Vierhile also said that some “emerging” product groups may also be able to capitalize on growing interest in immunity—even though they might seem a little odd to the American palate. “Drinking vinegar may offer immunity benefits, and kombucha also sometimes references immune health,” he said, pointing to the launch of a new line of “Japanese Drinking Vinegar” beverages from Portland, Oregon-based Genki-Su LLC that blend coconut vinegar with fresh fruit and other natural ingredients, and Master Brew Kombucha beverages from Ventura, California-based KeVita Inc. Both products are targeted to “health-seeking consumers” and specifically reference immune health benefits.

Interestingly, quite a few of the products in the Product Launch Analytics database referenced the inclusion of probiotics as boosting the immune system, with some launches going so far as citing specific strains. To that end, Vierhile noted two important developments regarding the probiotic ingredient

Ganeden BC30 from Ganeden Biotech. “It became the first probiotic strain to be used in a HPP (high pressure pasteurization) juice with the launch of Garden of Flavor’s cold-pressed, organic juices earlier this year,” he said. “And in September, Ganeden Biotech announced a new study found Ganeden BC30 probiotics supported digestive and immune health in HIV subjects, a group with compromised immune systems.” (*AIDS Research and Human Retroviruses*. 2014, Aug; Online. DOI: 10.1089/aid.2014.0181)

Ganeden BC30 is a key ingredient in the recently launched Copper Moon Probiotic Coffee. The packaging even references its ability to “support immune and digestive health.”

Among the most unusual new product launches spotlighted by the Datamonitor Consumer database was Aktiva8vapor, a “full-spectrum deer antler extract” that’s delivered in a cigarette-like e-vaporizer format. The product packaging boldly proclaims the clinically-supported benefits of IGF-1, an immune-enhancing natural growth hormone present in deer antler, but it is not classified as a dietary supplement in the United States.

What Lies Ahead for the Immune Health Segment

When it comes to short-term projections for the immune health market segment, Frost & Sullivan’s Sequeira felt that the interest in the market would remain strong and experience growth, specifically in the absence of vaccines or drugs that address critical illnesses. “The growth spikes tend to be associated with seasonal illnesses and the presence of diseases like enterovirus and ebola,” he said. “Consumers are trending toward buying natural/organic products in situations where there is sufficient preventive health budgets to warrant the benefits of consuming these products.”

Datamonitor Consumer’s Veirhile agreed. “Immunity figures to be an important concern regardless of the legalities pertaining to product label claims because of heightened interest in health issues ranging from the seasonal flu and ebola virus, to the enterovirus D68, which has been found to wreak havoc on the respiratory system,” he said. “These concerns are highly likely to make immunity a hot button concern for at least the next three to six months, and possibly a lot longer than that.” ■

Healthy Marketing: Immune Products Vulnerable to Regulatory Scrutiny

by Steve Myers

Marketing an immune product faces the same challenges other natural products face insofar as none can discuss or imply any effect on a disease. Of course, the immune system's primary function is to defend against disease and illness from harmful viruses, bacteria and other pathogens. Communication tools are available to immune product marketers, but finding the right balance of benefit and non-disease claims can be tricky.

The Federal Food, Drug & Cosmetic Act of 1938 (FD&C) long prohibited foods, including dietary supplements, from claiming to prevent, treat, diagnose or cure a disease, but DSHEA (the Dietary Supplement Health and Education Act of 1994) amended FD&C to give dietary supplements a unique regulatory definition and allow supplements to make certain claims.

Companies believing they have enough scientific substantiation can petition FDA for approval of a health claim, which describes the relationship between a food or supplement and reduced risk of disease or health-related condition. In accordance with the Nutrition Labeling and Education Act of 1990 (NLEA), FDA requires health claim substantiation to meet a significant scientific agreement standard. FDA explained this standard and outlined its "evidence-based review" process for evaluating health claim petitions in a [2009 guidance to industry](#).

When the evidence doesn't meet the health claim significant scientific agreement standard, but shows building evidence of risk-reduction, the agency may consider the petition for a qualified health claim, which is a health claim featuring qualifying language showing the limitation of the evidence. Relative to immune health, a few qualified health claims have been "accepted" by FDA for certain supplement and food ingredients and specific cancers, but these are often required to include a disclaimer that FDA sees little evidence of risk reduction.

A health claim can also be authorized via petition to FDA showing an "authoritative statement" from certain U.S. government scientific entities or the National Academy of Sciences. However, this avenue is only available for conventional foods, not supplements.

INSIDER's Take

- As approved health claims are rare, especially for immune health, most marketers have target allowances for structure-function claims.
- Many marketers and manufacturers often seek out attorneys, consultants and other regulatory specialists to help keep any immune claims within the confines of the law.
- FDA warning letters can show the agency's thinking on specific aspects of immune marketing.

IN THIS ISSUE

Immune Health Market Data p. 14

INSIDER Contacts p. 25

Table of Contents p. 2

Despite the various health claim petition options, most supplement and food marketing, including immune products, aims to stay primarily within the confines of structure/function claims. DSHEA spelled out specific boundaries for structure/function claims, as well as claims for general well-being and nutrient deficiency diseases.

Structure/function claims explain how a nutrient or dietary ingredient can affect the normal structure or function of the human body. General well-being claims are relative to the consumption of a nutrient or dietary ingredient, while claims linking increased intake of a nutrient to a nutrient deficiency disease require additional language noting how widespread the disease is in the United States. While these claims are not required to undergo pre-approval, companies must still maintain adequate substantiation to show the claims are truthful and not misleading, and must notify FDA of the claims within 30 days of marketing the product with the claim. The product must also include the disclaimer that FDA has not evaluated the claim and that the product is not intended to prevent, treat, diagnose or cure any disease.

By definition, a disease is “a disorder of structure or function” of the body, according to the Oxford Dictionary. Also, the immune system is a collection of structures and functions that protect against disease. Given the semantics involved, it is no surprise a gray area exists between a disease claim and a structure/function claim.

This is further complicated by the primary ways consumers take immune products: as a boost during seasons of known immune challenges (e.g., cold and flu season) and as year-round support for general immunity. For the former, structure/function claims are not allowed to address cold or flu illnesses unless they have an approved health claim (there are no such approved claims at this time.) Claiming a benefit related to cold or flu would be a disease claim subject to federal enforcement. FDA is responsible for product labeling and anything considered “labeling,” including inserts and packaging, while FTC is responsible for advertising, including print, broadcast, Internet, catalogs and direct marketing materials.

Marketing language can either expressly claim a benefit or imply a benefit. Thus, a structure/function statement might not expressly claim a disease benefit, but it might imply a disease benefit. For instance, mentioning the words “infection,” “virus” or “bacteria,” even if the language is focused on “supporting” or “boosting” the body’s structure and function, would likely push a statement into implied disease claim status. Simply stating a product or ingredient supports the immune system would be safe, as it does not go far enough to imply a disease claim. However, many supplement and food companies want a more differentiating claim for market advantage.

Given the semantics involved, it is no surprise a gray area exists between a disease claim and a structure/function claim.



Attorney Justin Prochnow, shareholder with Greenberg Traurig, said FDA discusses certain claims that are examples of disease claims and permissible structure/function claims in its [Final Rule on Structure/Function Claims](#). “At page 1,028, FDA indicated that ‘supports the body’s ability to resist infection’ as an example of a disease claim; it cites ‘supports the immune system’ as a permissible claim,” he noted. “FDA looks at the labeling as a whole to determine the ‘intent’ of a company to sell a particular product. Historically, while FDA has identified certain phrases like ‘seasonal support’ or ‘seasonal relief’ in warning letters, such claims have been made in conjunction with express claims that are the focus of FDA attention, like ‘cold & flu defense’ or ‘anti-bacterial.’”

In many cases, companies also have invested significantly in immune-related research on their branded ingredient or product, and want to relay the findings to consumers as much as possible. Care must be taken to avoid implied disease claims, and any structure/function, general well-being or nutrient deficiency claims must be adequately substantiated with “competent and reliable evidence.” When communicating research studies results on specific products and immune function, companies must also be careful if the study included disease endpoints or populations. This can be problematic because many companies, researchers and consumers are most interested in studies on prevention and treatment of disease.

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“As with almost all substantiation, it is really unclear as to what FDA/FTC expects to substantiate immune health claims,” Prochnow said. “Levels of substantiation depend on a variety of factors, including the category of products, the types of claims and how specific the claims are.”

Marketers look to use available claims and to create custom claims for their product, based on a key ingredient, explained Doug Reyes, North American sales and marketing manager for Embria Health Sciences. “To make the substantiation process easier and more efficient for customers, Embria has created tools such as our Substantiation Binder, which is a comprehensive catalogue of science, safety and regulatory information that can be used for formulation guidance and claim substantiation,” Reyes said. “Our Structure/Function Claims Direction sheet provides some claims ideas within diverse categories, depending on the desired product positioning.”

Reyes noted for complex ingredients offering a range of beneficial immune health mechanisms, it is helpful to offer a variety of substantiation options that could contribute to all sorts of creative and effective label claims. “We start with pilot research, build to in-vitro work, continue with animal efficacy and safety trials, and then culminate with large-scale human clinical trials to demonstrate efficacy and varying modes of action to show how EpiCor supports immune strength,” he explained.

The claims situation is so complicated and difficult, many supplement and food companies lean on lawyers, consultants and other industry regulatory and marketing experts to help shape labeling and marketing efforts.

Immune Category's Troubled Past...and Present and Future

Immune products have been singled out by the federal government and various watchdogs as one of the worst claims offenders among supplements and foods. Several of the highest profile claims enforcement cases have involved immune products, and a late 2012 special report from the U.S. Health Department Inspector General's Office focused on structure/function claims made by weight management and immune health dietary supplements—the report concluded many notifications were incomplete, substantiation routinely fell short of requirements, and FDA needs more authority to review substantiation for all structure/function claims.

FDA has sent out many warning letters over the years to supplement and food marketers using express or implied disease claims. There can be debate and argument over the validity of the agency's decisions in some cases, but the biggest black mark on the immune category occurs when waves of warning letters surface in the wake of epidemics, such as ebola or the H1N1 flu virus, as unscrupulous marketers skirt the rules by claiming an express or implied benefit to the epidemic.

Among the high-profile FTC advertising claims cases, the popular Airborne effervescent supplement was charged with inadequate evidence to support its advertising claims indicating the mixture of vitamins, minerals, herbs and amino acids could reduce the risk and severity of colds and other infections. The FTC case was settled in 2008 and included USD \$6.5 million in penalties against both the company and its founder. This monetary judgment added to more than \$20 million in penalties levied in concurrent class action litigation, resulting in around \$30 million in total fines slated to cover attorney fees and consumer refunds.

Nestle was charged with making deceptive claims that its BOOST Kids Essentials probiotic product could prevent upper respiratory infections (URIs) and the cold/flu in children by boosting the immune system. The company entered a consent decree with FTC in 2010, agreeing to stop making those claims unless it could provide the proper scientific substantiation. Around the same time, FTC settled a similar case with Iovate Health Sciences over ads the agency said deceptively claimed several supplements could prevent colds, flus and allergies; the settlement included similar charges for claims made for two weight management products. The total monetary settlement for Iovate was \$5.5 million.

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The FTC orders seem to have established key requirements for substantiation and claims language. The big one was its steadfast requirement for two well-designed clinical trials completed by the time the product with the claim is first marketed. FTC appears to require these studies be double blind, placebo-controlled and focused on finished products, not just ingredients. Further, FTC enforcements suggest a general “supports the immune system” claim can be substantiated by studies on certain immune function biomarkers. However, FTC has maintained consumers interpret the words “boosts,” “strengthens,” or “enhances” the immune system/function to mean the product will defend against illness and disease, so the agency will hold claims using these words to a higher level of substantiation requirement. Yet, somehow the words “supports” and “maintains” are innocuous enough and don’t prompt consumer assumptions of reduced risk of illness.

“Certainly, when you start talking about missing fewer days from work or school or addressing seasonal conditions, there may be room for FDA to treat the claims as implied claims,” Prochnow advised, reiterating how it depends on the overall message that companies are sending. “FDA will review all of the labeling, marketing and advertising of a product to try to make a determination as to what the intent of a company is in selling a product. Thus, the same claim for one product, in the face of all of the other labeling materials, may be a permissible claim while that same claim, coupled with other borderline claims, may be sufficient for the FDA to determine that the real intent of a company is to sell the product to address disease conditions.”

One tool for suppliers is to put protections into trademark licensing agreements, which allow manufacturers and marketers to use the branded mark. “Embria has a mechanism to use with any customer who might make claims that Embria finds objectionable,” Reyes said. “For instance, when swine flu was a top concern, Embria immediately posted a notice that consumers should know that no dietary supplement, including EpiCor, had been tested to show it could treat or prevent swine flu.”

The nature of the immune system and its structure and function can make it challenging to create informative marketing and labeling plans that will be compliant with FDA and FTC requirements, particularly in the area of claims. As much as consumers and marketers desire to share the details of a product’s specific benefits to immune function, especially with seasonal immune products, the safest bet is to stay within the confines of structure/function claims, avoid implying a disease claim anywhere on the label and advertising, including social media activities, and leave disease-related research studies to third-party literature dissemination. ■

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