Nutrition & Immunity
Meeting evolving consumer needs with science-based solutions
EU Webinar June 30th, 2020
Presenters and moderators

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What we will speak to you about today

What is the state of consumer behavior?
- Insights into consumers needs, priorities, purchasing behavior

How is the market developing?
- What trends are going to pave the way for new opportunities, to differentiate in an already crowded space

How can we approach the immune health space in the ‘new normal’?
- Formulating with ingredients founded in science to meet consumer needs
- Trusted micronutrients and emerging ingredients

What product solutions to meet the specific needs of target consumers?
- Some concepts to help inspire product innovation with the consumer in mind
Building a strong immune system should start early in life
Allergens are a major seasonal challenge for our immune system with an impact on the quality of life.
Living in dense populations exposes us to pathogens and makes it difficult to stay healthy.
Aging people have a natural decline in immune defense & require additional support.
2020 has been an extraordinary year

Bringing lasting changes to our lives
Consumer behavior changes drastically with the pandemic…

1. Eating healthy, doing exercise & the environment are of higher priority for consumers around the globe.

2. Consumers in most countries expect to spend more on healthcare products & in-home food items.

3. Immunity is a key health concern & sales of dietary supplements surges as consumers seek to proactively care for their immune health.
Opportunity 1: Trusted ingredients pave the way for emerging ingredient combinations

- Micronutrients form base of **science** backed immune health solutions

- Within the category of micronutrients and beyond Vitamin C, consider other ingredients which have authorized immunity claims globally, for example: **Vitamins A, B\textsubscript{12}, B\textsubscript{6}, C, D, Zinc, Folate, Copper, Iron, Carotenoids**

- **Rising stars** with no official health claims can benefit in combi with trusted ingredients e.g. prebiotics, probiotics, protein, fibres
Opportunity 2: Functional foods & beverages plays a key role, on top of dietary supplements

- Dramatic increase in global searches for the word ‘food’ and ‘immune system’ in between Feb & March 2020
- Consumers are looking more to ‘real food’ to get their nutrients daily, in line with holistic health trend and consumers taking ownership of their health
- An opportunity pocket exists for immune health in functional nutrition
Opportunity 3: The interface between the gut and immune system

- Consumers are becoming more and more aware of the importance and benefits of a healthy gut and the microbiome

- We see numerous new product launches with digestive and immunity messages on the market

- Prebiotics are on the rise to positively impact the microbiome and the immune system

- Mucous membranes and the gut microbiome play important roles

- Clear positionings can be made for consumers groups such as the elderly and athletes
The immune system:

What is immunocompetence?
The role of nutrition
The immune system functions along three main lines of defense

2 Innate immunity:
- Available at birth
- Reacts quickly in an unspecific manner
- Key defense during first-time exposure to pathogens
- Not adaptable, does not change during lifetime

3 Adaptive immunity:
- Builds up during lifetime
- Reacts quickly with pathogen-specific antibodies
- Antibodies produced after vaccination or first exposure to pathogens; available for lifetime or certain period
- Pathogens are bound by antibodies and destroyed by immune cells before symptoms of disease occur

Source: Muller L et al. 2019
Health ingredients have specific functions & strengthen the immune system

Specific micronutrients work together to reduce the risk, duration and severity of infections.

<table>
<thead>
<tr>
<th>Vitamin A</th>
<th>Vitamin D</th>
<th>Carotenoids</th>
<th>2'-Fucosyllactose</th>
</tr>
</thead>
</table>
| • Strengthens skin, eye, lung, and gut barriers inhibiting pathogen intrusion  
• Precursor of retinoic acid, key regulator in the immune system  
• Improves effectiveness of vaccinations  | • Strengthens skin, eye, lung, and gut barriers inhibiting pathogen intrusion  
• Increases anti-microbial defense proteins  
• Inhibits pro-inflammatory cytokines & cytokine storm  | • Beta-carotene: same effects as vitamin A  
• All carotenoids: antioxidant function, strengthening barriers & tissues  | • Promotes growth of healthy bacteria in the gut  
• Inhibits pathogens in the gut  
• Modulates immune system in the gut & systemically  |

<table>
<thead>
<tr>
<th>Vitamin E</th>
<th>Vitamin B₁₂</th>
<th>DHA/EPA</th>
<th>Overall strengthened immune system. Lower risk of infections, allergies, autoimmune diseases, and chronic inflammation.</th>
</tr>
</thead>
</table>
| • Strengthens skin, eye, lung, and gut barriers inhibiting pathogen intrusion  
• Anti-inflammatory function  
• Stimulates immune cells, particularly in elderly people  | • Strengthens skin, eye, lung, and gut barriers inhibiting pathogen intrusion  
• Required for antibody production  
• Modulates immune cells  | • Anti-inflammatory function  
• Stimulation of immune cells  |
Health claims on immunity are permitted for several micronutrients

EU 28
- Vitamin A contributes to the normal function of the immune system
- Vitamin A contributes to the maintenance of normal mucous membranes
- Beta-carotene: vitamin A contributes to the normal function of the immune system
- Vitamin B₁₂ contributes to the normal function of the immune system
- Vitamin D contributes to the normal function of the immune system
- Riboflavin contributes to the maintenance of normal mucous membranes
- Further health claims on antioxidant function for Vitamin E, Riboflavin, Lutein, Lycopene

Russia & CIS
- Vitamin A contributes to the normal function of the immune system
- Vitamin B₁₂ contributes to the normal function of the immune system
- Vitamin D contributes to the normal function of the immune system
- Vitamin B₂ contributes to the protection of cells from oxidative stress

Turkey
- Vitamin A contributes to the normal function of the immune system
- Vitamin B₁₂ contributes to the normal function of the immune system
- Vitamin D contributes to the normal function of the immune system
- Vitamin B₂ contributes to the protection of cells from oxidative stress

South Africa
- Vitamin E is an antioxidant for the maintenance of good health OR a factor for the maintenance of good health
- Beta-carotene can be converted to vitamin A in the body OR Beta-carotene functions as a tissue antioxidant and so keeps cells healthy
- Vitamin E contributes to the protection of cells from oxidative stress OR a factor in the maintenance of good health

Further information on claims is available at https://myapps.basf.com/CLARA/
**Vitamin D directly modulates nearly all immune cells**

- Vitamin D plays a strong regulatory role in the immune system (*innate & adaptive immunity*).
- Immune cells have Vitamin D receptor and CYP27B1 enzyme (converts Vitamin D to active hormone).
- Multiple effects shown for Vitamin D:
  - Supports production of *antimicrobial peptides*
  - Stimulates function of macrophages and other *immune cells*
  - Negative regulatory factor of the *Renin-Angiotensin-Aldosterone-System* (RAS)
  - Inhibits release of pro-inflammatory cytokines
  - Inhibits antigen-presenting cells increasing tolerance

**Vitamin D impacts key functions required for defense against pathogens**

Benefits of Vitamin D have been suggested based on known functionalities and observations.

Controlled trials from the past showed Vitamin D inhibits acute respiratory infections.

Testing positive for COVID-19 was associated with likely being Vitamin D deficient (Meltzer DO et al, 2020; D’Avolio A et al, 2020).

Clinical studies with COVID-19 patients are underway. In the meantime, Vitamin D supplementation has been suggested to strengthen immune system and lower the risk of severe disease outcomes.

“Vitamin D treatment may decrease the risk of incidence of the COVID-19 infection (…), as well as decrease the mortality and severity of patients with COVID-19.” (Aygun H, 2020)

### Vitamin D and COVID-19

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- Controlled trials from the past showed Vitamin D inhibits acute respiratory infections.
- Testing positive for COVID-19 was associated with likely being Vitamin D deficient (Meltzer DO et al, 2020; D’Avolio A et al, 2020).
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Vitamin B$_{12}$ is needed for production of immune cells & antibodies

- Vitamin B$_{12}$ is required for the **production of immune cells** including B-cells, T-cells and natural killer cells.
- It may **act as an immunomodulator** and enhance the number of cytotoxic T cells, which attack antigen-presenting cells.
- Furthermore, Vitamin B$_{12}$ is **essential for the production of antibodies** from amino acids (in concerted action with Vitamin B$_{6}$ and folic acid).

**Vitamin B$_{12}$ plays a fundamental role in safeguarding production of immune cells and antibodies**

*Source: Gombart AF et al, 2020*
Beta-carotene is a precursor of retinoids, which are key regulators in the immune system

- Beta-carotene is a **precursor of retinoids**
- Retinoids activate & modulate the innate as well as acquired immune functions
  - For example, retinoids regulate cytokine and antibody production, migration and maturation of B- and T-cells
- Moreover, as an **antioxidant**, beta-carotene like other carotenoids helps protect tissues and strengthens barrier function in skin, lungs, eyes, and the gut.

**Beta-carotene supports barrier function and is precursor of key regulator in the immune system**

**Sources:** Miller AP et al, 2020; Toti E et al, 2018
Vitamin E regulates immune functions via antioxidant and anti-inflammatory effects

- Vitamin E has an important impact on immune functions as it modulates both cellular & humoral immune responses.
- In immune cells, Vitamin E is strongly enriched. These cells have a high oxidative stress burden due to rapid metabolic turnover. Vitamin E as an antioxidant helps protect immune cells and impacts their production & function.
- Vitamin E inhibits production of pro-inflammatory prostaglandin E2 in macrophages/monocytes and thereby inhibits inflammatory processes.

Vitamin E helps maintain immune function by inhibiting inflammation & supporting immune cells

Source: Lewis ED et al, 2019; Lee GY et al, 2018; Pae M et al, 2017
Omega-3 fatty acids have major anti-inflammatory function and thereby support healing

- The omega-3 fatty acids EPA and DHA have anti-inflammatory effects. At the site of inflammation, the two omega-3 fatty acids are metabolized into specialized pro-resolving mediators (SPMs) known as resolvins, protectins, and maresins.
- Thereby, resolution of inflammation occurs and healing of tissues is supported.
- Moreover, DHA is a structural fatty acid helping to stabilize membranes of immune cells.

Omega-3 fatty acids support immune cells and resolution of inflammation

Source: Calder PC et al, 2020
**HMO: Prebiotic 2’-FL benefits immune system in the gut & beyond**

**Enteric immune system**
- 2’-fucosyllactose (2’-FL) is the most abundant oligosaccharide in women’s breastmilk
- Important for child development, e.g. building a strong immune system
  - **Stimulates growth of beneficial bacteria** like bifidobacteria and fosters a healthy gut microbiome (prebiotic effect)
  - **Anti-microbial effects** inhibiting pathogen adhesion & colonization (bacteria, viruses)
  - **Strengthens gut barrier** as it supports maturation and helps maintain barrier function, helps restore damages

Beneficial effects observed also in adults

**Systemic immune system**
- 2’-FL likely has positive effects beyond gut health (as shown mostly in experimental studies so far)
  - Decrease in pro-inflammatory cytokines in blood
  - Lower risk of allergies
  - Improved vaccination response

**2’-FL is an important human milk oligosaccharide which supports the enteric immune system**

**Cytokines**
- Messenger molecules of the immune system, which stimulate inflammation. Proper control is needed in a healthy immune response.

Source: Orczyk-Pawilowicz M & Lis-Kuberka J, 2020

02.07.2020 | BASF Nutrition & Immunity Webinar
Learn more about the important role the gut and 2’-FL can play in supporting immune health

Join us at our virtual exhibition “BASF GROWTH DAY 2.0”

Date: Monday July 13, 2020  Time: 11:00 – 15:00 GST

Human Nutrition will showcase relevant products and solutions to meet our customer and your consumer needs. In addition, you will have the opportunity to virtually connect with one of many other BASF segments. There will be excellent networking and information sharing opportunities via live chats and keynote presentations. Visit our booth and don’t miss our webinars where you can directly interact with our experts!

11:15 – 12:00 or 13:15 – 14:00 GST
Food Performance Ingredients: Clean label trend in bakery
Speakers: Kathrin Saur, Global Product Manager Food Performance Ingredients, Jochen Kutscher, Manager Application Labs Food Performance Ingredients and Anna Demnhofer, Head of Product Management & Application Food Performance Ingredients, BASF

12:15 – 13:00 or 14:15 – 15:00 GST
Health Ingredients: Exploring the interface between gut health and immunity
Speakers: Marianne Heer, Scientific Marketing Manager, and Mareike Kampmann, Global Marketing Dietary Supplements, BASF

For more information on the exhibition and registration please CLICK HERE
Consumer Solutions

Providing the right nutrients to the right people at the right time
**Immunity Power Juice**

"I life in a big city and my life is rather stressful. I want to have a strong immune system"

**What is the market need?**
- Beverages for immune support
- Good taste with herbals, fruits & vegetables ("superfoods")

**What is the consumer benefit?**
- Provides (pro)vitamin A, E & C in a modern type of "ACE" beverage
- Beta-carotene is a precursor of retinoic acid, a key regulator in the immune system. Vitamin E and Vitamin C have antioxidant, tissue protective function and stimulate immune cells
- Fruits & vegetables are popular "superfoods"
- Herbals are traditionally used for immune support

**... Better immune function when life is busy**

**Health ingredients**

<table>
<thead>
<tr>
<th>Serving size: 1 glass/day</th>
<th>Dosage per glass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>400 µg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>6 mg</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>40 mg</td>
</tr>
</tbody>
</table>

A market launch is subject to local regulatory requirements.
Immunity Booster Effervescent Tablets

“I want to be as healthy as I was when I was younger. My immune system needs an extra boost.”

What is the market need?
- Easy to consume supplements for elderly people, no big capsules
- Support of immune system as it naturally declines during aging

What is the consumer benefit?
- Provides high-dose beta-carotene, vitamin E and vitamin D₃
- Beta-carotene is a precursor of retinoic acid, a key regulator in the immune system; important for barrier functions as first line of defense against pathogens, and for effectiveness of vaccinations
- Vitamin E has anti-inflammatory properties and stimulates immune cells
- Vitamin D₃ strengthens antimicrobial defence, stimulates immune cells and has anti-inflammatory properties

Health ingredients

<table>
<thead>
<tr>
<th>Health ingredients</th>
<th>Dosage per tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serving size: 1 effervescent tablet/day</td>
<td></td>
</tr>
<tr>
<td>Beta-carotene</td>
<td>20 mg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>200 mg</td>
</tr>
<tr>
<td>Vitamin D₃</td>
<td>15 µg</td>
</tr>
</tbody>
</table>

…Better immune function while aging

A market launch is subject to local regulatory requirements.
Daily Defense Antioxidant Capsules

“What is the market need?”

- Easy to swallow capsules for daily immune support

“What is the consumer benefit?”

- Provides 24 mg of antioxidants per capsule including beta-carotene, lutein, lycopene and vitamin E
- Helps to evenly distribute fat-soluble antioxidants in body tissues
- Antioxidant combination helps replenish the body’s antioxidant defence network and supports barrier immune function
- In addition, beta-carotene is a precursor of retinoids, which are key regulators in the immune system.

... Better protection against environmental stressors

Health ingredients

Serving size: 1 capsule/day

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Dosage per capsule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betatene® Beta-carotene</td>
<td>4 mg</td>
</tr>
<tr>
<td>Xangold® Lutein esters</td>
<td>4 mg</td>
</tr>
<tr>
<td>LycoVit® Lycopene</td>
<td>4 mg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>12 mg</td>
</tr>
</tbody>
</table>

A market launch is subject to local regulatory requirements.

© Registered trademark of BASF in several countries.
Prebilac® 2’-FL plus Vitamin Immune Sachet

“What is the market need?”
- Supplements that can be mixed easily into beverages & foods
- Neutral taste or, alternatively, fruity taste (lemon, orange)

“What is the consumer benefit?”
- 2’-FL fosters a healthy gut by facilitating the growth of beneficial bacteria and supporting intestinal immune functions
- Vitamin D₃ strengthens antimicrobial defence, stimulates immune cells and has anti-inflammatory properties
- Vitamin B₁₂ supports production of antibodies and immune cells
- Vitamin B₂ contributes to the protection of cells from oxidative stress

… Better immune function in the gut

Health ingredients
Serving size: 1 sachet/day

<table>
<thead>
<tr>
<th>Health ingredient</th>
<th>Dosage per sachet</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREBILAC® 2’-FL</td>
<td>3 g</td>
</tr>
<tr>
<td>Vitamin D₃</td>
<td>5 µg</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>2.5 µg</td>
</tr>
<tr>
<td>Vitamin B₂</td>
<td>1.4 mg</td>
</tr>
</tbody>
</table>

“I want to take a supplement that helps boost my gut immune system.”

A market launch is subject to local regulatory requirements.

® Registered trademark of BASF in several countries.
“New Normal” Immunity Smoothie

“My life has changed. I work from home and have virtual meetings all day long. Going out and meeting people is very limited.”

What is the market need?
- Modern nutritional solutions for teenagers & young adults that address changes in lifestyle and the “New Normal”
- Healthy, fortified ready-to-drink beverages

What is the consumer benefit?
- 2′-FL fosters a healthy gut by facilitating the growth of beneficial bacteria and supporting intestinal immune functions
- Vitamin D strengthens the immune system in its antimicrobial defence, stimulates immune cells and has anti-inflammatory properties
- Lutein has anti-oxidant function and helps support eye health, e.g. during prolonged exposure to digital devices

… Better support of immunity and “new normal” lifestyle!

Health ingredients

<table>
<thead>
<tr>
<th>Serving size: 1 smoothie/day</th>
<th>Dosage per 240 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREBILAC® 2′-FL</td>
<td>200 mg</td>
</tr>
<tr>
<td>Vitamin D₃</td>
<td>200 IU</td>
</tr>
<tr>
<td>Xangold® Lutein</td>
<td>2 mg</td>
</tr>
</tbody>
</table>

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We are close to our customers & close to their markets

- Combining expert know-how of health and performance ingredients with state of the art equipment
- Deep understanding of local needs, preferences and habits
- Access to local ingredients from diverse cultures and tastes

Tarrytown
Ballerup
Ludwigshafen Illertissen
Jacarei
Istanbul
Shanghai
Singapore

Solid applications
Liquid applications
Food Performance Systems
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Stay healthy!

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Thorsten.schmeller@basf.com