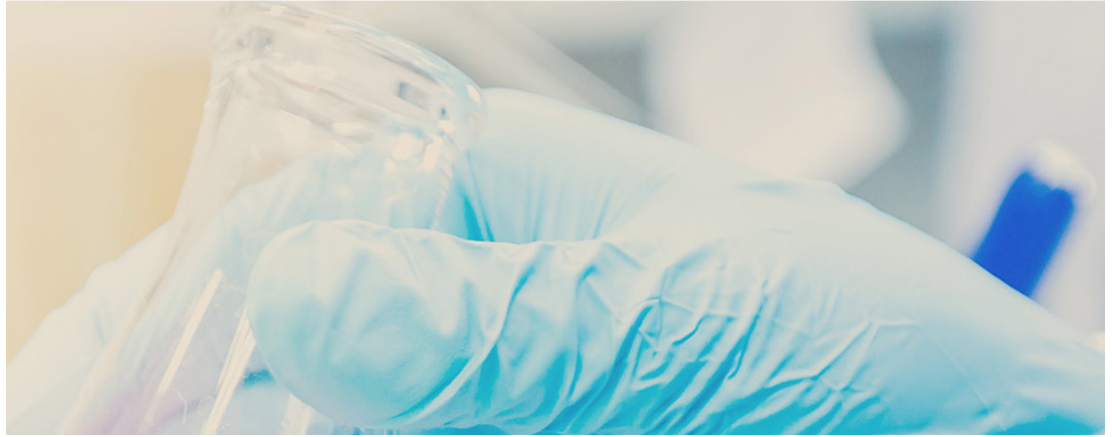


# Quarterly Review

# Chemicals & Materials Q2 2020



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# Nutrition – Dietary Supplements and Probiotics

by Dr. Thomas Schneider, Director, Global Chemicals Group

Due to the increasing global interest in companies in the field of nutrition or rather dietary ingredients, we would like to use this Chemicals DealReader to give an introduction to this strong growing segment of the Chemical Industry.

*“The doctors of the future will no longer treat the human frame with drugs, but rather will cure and prevent disease with nutrition.”* – Thomas Edison's contemplation may come to fruition if the nutritional revolution continues in its current course.

## Malnutrition and Inappropriate Nutrition

Food and nutrition or rather its components like proteins, vitamins and minerals are vital keys to the conditions and the length of life as well as controlling mortality from many (chronic) diseases affecting humankind. For thousands of years the direct correlation between malnutrition and subsequent death due to disease has been known and extensively described in scientific literature. Of course, food and well-balanced nutrition are the key preventative agents for such dietary insufficiency induced diseases, respectively.

Malnutrition is one of the greatest public health problems facing the world today because of the number of children affected and the resulting long-term consequences, whereby enormous progress has been made in last decades. Malnutrition was reduced from 37% to 27% between 1980 and 1999, the percentage of those in rural areas with access to safe water has increased from 13% to 71% and in some countries, such as in China, income-poverty is reduced from 33% in 1978 to 7% in 1994. Despite promising developments, poverty malnutrition, healthcare and education are still hinge-topics in the international system because of global levels of inequality that are extremely high. Global disparities in health, education and other human rights are getting larger day by day, and even if the global level of malnutrition is decreasing, there are still countries whose children are under- or malnourished with scarce possibilities of improving without a specific commitment from international authorities. But the very factor underlying the actual status of widespread malnutrition is not indeed poverty or complete scarcity of resources: war, injustice, bad management, by far are the most decisive responsibilities for children's malnutrition. Recent estimates published indicate that maternal and child undernutrition is the underlying cause of 3.5 million deaths and 35% of the disease burden in children younger than 5 years. The World Health Organization estimates that malnutrition contributes to 53% of child mortality worldwide.

In addition to malnutrition in many countries around the world, inappropriate nutrition is a cause of increasing concern in many industrialized countries because of the increased risk of a range of health problems and diseases, including obesity, diabetes type 2, cardiovascular diseases and several forms of cancer. For example, during the last 40–50 years, the occurrence of obesity has increased considerably. Among the reasons for this increase is “cheap / low value” food, an increasing consumption of convenience food and prepared fast-food meals, a change in the composition of the diet in the direction away from vegetables toward more saturated fats and

sugar, as well as a change toward less physical activity, which has not been accompanied by a corresponding reduction in the energy intake. The U.S. National Cancer Institute expects that only 18% of adults have the recommended intake of vegetables. Consequently, substantial research efforts are devoted to solving these problems, with nutritional, medical and pharmaceutical sciences as some of the most significant contributors. Social sciences are also involved, primarily in understanding consumers' attitudes, dietary and physical activity habits, etc. in an effort to improve behavior in these areas of life.

One of the causes of undernutrition can be attributed to one or more micronutrient deficiencies, principally iron, iodine, vitamin A, folic acid, or zinc. More than two billion people in the world – in all population groups across all regions are affected; however, more frequently in developing countries – suffer from micronutrient deficiencies caused largely by a dietary deficiency of vitamins and minerals. Also known as “hidden hunger,” the micronutrient deficiencies lead to long ranging effects on health, learning ability and productivity. There are high public and social costs associated with reduced work performance and higher healthcare expenditures due to high rates of disability and illness.

The solutions to address these deficiencies include ingestion of oral supplements (tablets, capsules, and syrups), food fortification and other food-based approaches. As national governments recognize and implement a combination of health and nutrition interventions, there has been a steadily growing level of interest in the costs and benefits of micronutrient interventions. A good example for this is the mandatory fortification of all cereal grains (cereal, bread, rice, pasta) with folic acid in the USA in 1998 to prevent spina bifida, a birth defect in which there is incomplete closing of the spine and the membranes around the spinal cord during early development in pregnancy. Almost 80 countries have now instituted similar programs, and countries that fortify have experienced dramatic falls in rates of neural tube defects. Of course, there is less malnutrition in wealthy regions of the world; but in this context it is remarkable that there is no harmonized approach in the EU to the fortification of food: *“The (European) Commission does not envisage the harmonization of the mandatory addition of nutrients, such as folic acid, across the EU. It is up to the Member States to decide whether or not they wish to introduce alternative measures such as mandatory food fortification with folic acid.”*

Source: *Nutrients, Dietary Supplements and Nutraceuticals* (Humana Press, 2011); *Encyclopedia of Dietary Supplements* (informa, 2010); World Health Organization; European Commission; The Council for Responsible Nutrition; Recent Market Reports; Scientific Publications; The Copenhagen Consensus.

The Copenhagen Consensus, a group of world-renowned economists, constantly rank the reduction of malnutrition by supplements and fortification of commonly eaten foods with vitamins and minerals, among the top three international development priorities. Food fortification is a medium- to long-term solution to alleviate specific nutrient deficiencies in a population. It involves the addition of measured amounts of a nutrient-rich “premix,” which contains the required dietary supplements, to commonly eaten foods during processing. Within an integrated approach, micronutrient fortification of foods and condiments allows for an inexpensive and highly cost-effective strategy to improve and protect the health and nutritional status of populations. The start-up cost for food fortification is relatively inexpensive for the food industry, and recurrent costs are rapidly passed on to the consumer. The benefits of fortification can extend over the entire life cycle of humans. It can thus be one of the most cost-effective means of overcoming micronutrient malnutrition. Although it is a fact that the first reason for fortifying foods with essential vitamins and minerals is this approach is safe and effective, the

economics of food fortification has played an important role in its implementation in public policy. In industrialized countries the cost to treat one person with a chronic disease like AIDS would pay for nutritional supplements preventing growth and development problems in thousands of children. Both are worthwhile but not always economically possible.

Besides the treatment of acute deficits, dietary supplements should not be understood as a substitute but as a value-added complementary to a balanced and complete diet. On the other side, we are a steadily growing population on just one earth. In order to meet the demands of the future global population, we will need to produce more with less resources. To feed nine billion people in 2050 and prevent malnutrition synthetically produced dietary ingredients and micronutrients can be regarded as key “enabler” of this challenge. Furthermore, dietary ingredients play a crucial role in the context of functional food, personalized nutrition & wellness and sport nutrition, which are currently “hot topics” and rapidly expanding market segments in the global food industry.

## Dietary Supplements & Ingredients

A dietary supplement is a manufactured product – containing one or more dietary ingredients – intended to supplement the diet when taken by mouth as a tablet, capsule, or liquid. It can provide nutrients either synthesized or extracted from natural sources, individually or in combination, in order to increase the effect of their consumption. It should be noted that dietary supplements can contain not only micronutrients – which are required for the normal growth and development of living

organisms – but also substances that have not been confirmed as being essential to life, but are marketed as having beneficial effect such as polyphenols from plants like flavonoids. Dietary ingredients can be segmented in vitamins, minerals, fatty acids, amino acids, probiotics, prebiotics, enzymes botanicals, herbs extracts and others. Thereby the first four groups are defined as essential, which means in a broader way crucial for life; not only for humans but also for animals.

Class of Dietary Ingredients	Common Examples			Selected Key Producer	
Vitamins	- Vitamin A - Vitamin B	- Vitamin C - Vitamin D	- Vitamin E - Vitamin K	<ul style="list-style-type: none"> <li>■ ADM</li> <li>■ BASF</li> <li>■ DSM</li> </ul>	<ul style="list-style-type: none"> <li>■ Lonza</li> <li>■ Pfizer</li> </ul>
Minerals	- Calcium (Ca) - Magnesium (Mg) - Zinc (Zn) - Iron (Fe)	- Selenium (Se) - Potassium (K) - Phosphorus (P) - Iodine (I)	- Cobalt (Co) - Fluorine (F) - Manganese (Mn)	<ul style="list-style-type: none"> <li>■ Atrium (Nestle)</li> <li>■ Dr. Paul Lohmann</li> </ul>	<ul style="list-style-type: none"> <li>■ NBTY</li> <li>■ Pharmavite (Otsuka)</li> </ul>
Fatty Acids	- Alpha-linolenic acid (ALA)	- Eicosapentaenoic acid (EPA)	- Docosahexaenoic acid (DHA)	<ul style="list-style-type: none"> <li>■ BASF</li> <li>■ Cargill</li> <li>■ Croda</li> </ul>	<ul style="list-style-type: none"> <li>■ DSM</li> <li>■ KD Pharma</li> <li>■ Lonza</li> </ul>
Amino Acids	- Methionine (Met) - Leucine (Leu) - Lysine (Lys)	- Tryptophan (Trp) - Isoleucine (Ile) - Histidine (His)	- Phenylalanine (Phe) - Valine (Val) - Threonine (Thr)	<ul style="list-style-type: none"> <li>■ ADM</li> <li>■ Ajinomoto</li> <li>■ Evonik</li> </ul>	<ul style="list-style-type: none"> <li>■ Kyowa Hakko</li> <li>■ Sumitomo Chemicals</li> <li>■ Wacker</li> </ul>
Probiotics	- Lactobacillus - Bifidobacterium	- Saccharomyces boulardii	- Enterococcus faecium	<ul style="list-style-type: none"> <li>■ Chr. Hansen</li> <li>■ Danisco (DuPont)/IFF</li> <li>■ Danone</li> </ul>	<ul style="list-style-type: none"> <li>■ Deerland</li> <li>■ Kerry</li> </ul>
Prebiotics	- Fructo-oligosaccharides - Galacto-oligosaccharides	- Inulin - Lactulose	- IMethylcellulose	<ul style="list-style-type: none"> <li>■ Cargill</li> <li>■ Friedland Campina</li> </ul>	<ul style="list-style-type: none"> <li>■ Kerry</li> <li>■ Roquette</li> </ul>
Enzymes	- Protease / peptidase	- Lipase	- Amylase	<ul style="list-style-type: none"> <li>■ Chr. Hansen</li> <li>■ Danisco (DuPont)/IFF</li> <li>■ Deerland</li> </ul>	<ul style="list-style-type: none"> <li>■ DSM</li> <li>■ Novozymes</li> </ul>

### Botanicals, Herbs Extracts and Others

Phenolics	Polyphenols like Flavonoids, Tannins, Stilbenoids like Resveratrol
Isoprenoids/terpenes	Carotenoids, Citral, Menthol, Camphor, Limonene, Pinene
Cannabinoids	Cannabidiol
Other lipids	Sphingolipids
Proteins	Collagen
Amino sugars	Glucosamine

Source: *Nutrients, Dietary Supplements and Nutraceuticals (Humana Press, 2011); Encyclopedia of Dietary Supplements (informa, 2010); World Health Organization; European Commission; The Council for Responsible Nutrition; Recent Market Reports; Scientific Publications; The Copenhagen Consensus.*

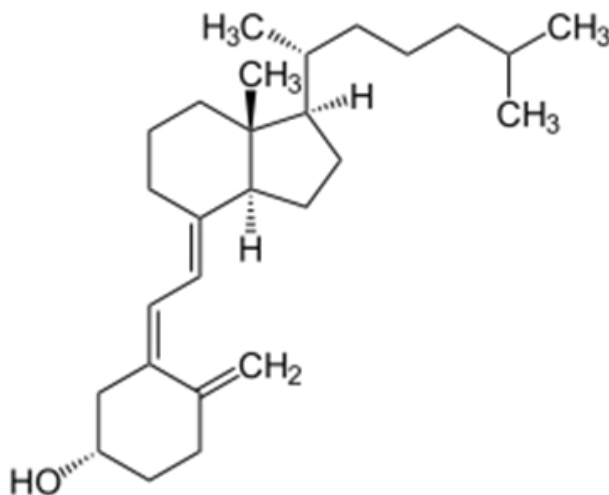
The market for dietary supplements is currently estimated at USD \$110–\$130 billion, with an expected average CAGR 6.6% over the next years. Thus, for example BASF – a key player in the dietary ingredients market – could realize in its Nutrition & Care business in Q1 2020 a sales growth of 6% (8% by volume) in comparison to the same period one year before. These promising industry projections are reflected in a high M&A activity and valuation levels well over 15.0x EBITDA. Major M&A deals in this sector include for example the acquisition of Cognis by BASF (December 2010), the acquisition of Atrium by Nestle in 2018 for USD \$2.3 billion, reflecting an EV/Revenue multiple of 3.30x, the merger of IFF and DuPont's Nutrition & Biosciences business in 2019 with a deal value of the combined company at USD \$45.4 billion on an EV basis (EV DuPont's N&B business USD \$26.2 billion, EV/EBITDA = 16.1x, EV/Revenue = 3.90x). The latter transaction is expected to create significant shareholder value through cost synergies of USD \$300 million and revenue synergies of about USD \$400 million by end of year three post-close. The combined company will have a strong financial profile, including pro forma revenues of more than USD \$11 billion based on fiscal year 2019 estimated results and an adjusted EBITDA margin of 23% pre-synergies and 26% with run-rate cost synergies based on fiscal 2019 pro forma estimated results. In the following we will have a closer look at vitamins, minerals, fatty acids and probiotics.

### Vitamins

Vitamins are essential, organic compounds which are either not synthesized in the human organism or formed only in insufficient amounts. Therefore, vitamins must be regularly consumed with the diet either as such or as a provitamin (precursor of a vitamin) that can be converted to the vitamin in the body. The metabolic functions of vitamins are mainly catalytic or regulatory. Vitamins are classified not by their chemical constitution but by their activity. Vitamins are produced on an industrial scale by chemical synthesis (dominant method) or partial synthesis, by fermentation or by extraction from natural material. Many vitamins have become large-scale products for chemical companies like BASF, DSM, or Lonza due to constantly increasing demand. Thus, for example, BASF announced the expansion of its vitamin A production by 25% or rather 1,500 metric tons in Ludwigshafen in 2018. The worldwide market value for vitamins is around USD \$30 billion per year, whereby the feed industry accounts for 50%, the pharmaceutical industry for 30% and the food industry for 20%.

Vitamin D (calciferols) for example are compounds which play a central role in the maintenance of calcium and phosphorus concentration in the body fluids of humans. Chemically they belong to the steroids in which the B-ring of the steroid nucleus is cleaved between carbon atom 9 and 10. The natural source of vitamin D3 – the most potent form of vitamin D – in warm-blood animals and humans is the transformation of provitamin D3 in the skin when exposed to the ultraviolet component of sunlight. On an industrial scale, the vitamin is manufactured by chemical synthesis only. It should be noted that for Vitamin D3, a strong case for upcoming increasing mandatory nutrition interventions – food fortification – can be made by national governments. There is convincing evidence that the vitamin is of significant value in the prevention of osteoporosis. Furthermore, strong evidence has emerged in recent years that the risk of cancer is significantly reduced when vitamin D levels

are optimal. This applies especially to people at risk of sub-par vitamin D status, notably inhabitants of northern latitudes, such as the northern states of the United States, northern Europe like Finland and Canada.



**Molecule structure of Vitamin D3**

### Minerals

In the context of nutrition, a mineral is a chemical element required as an essential nutrient by organisms like humans to perform functions for life. In the table above, selected crucial elements are listed. However, the four major structural and essential elements in the human body by weight – nitrogen, oxygen, hydrogen and carbon, which compose > 95% of the weight of the human body – are not included in the list, as they are ubiquitous in daily dairy and not considered as nutrients. The essential nutrient minerals for humans listed in order by weight that are needed for an adequate daily intake are potassium, chlorine, sodium, calcium, phosphorous, magnesium, iron, copper, iodine, chromium, molybdenum, selenium and cobalt. Nutrient minerals – as elements – cannot be synthesized biochemically by living organisms. Calcium, phosphorous, potassium, sodium and magnesium are the “major” minerals in the human body. The remaining elements in the human body are called “trace elements”.

Phosphorus for example, primarily in the form of phosphates, is present in all food, whereby food high in protein like milk, eggs, meat and fish are typically also high in phosphorous. Fruits and vegetables have relatively less amounts. Generally, every gram of protein consumed is accompanied by 15 mg of phosphorus. The rate of intestinal phosphorus absorption, 50% to 70% on average, is high in relation to the absorption rates of other minerals. The widespread biological use of phosphate groups makes these anions essential for both organic and inorganic components within cells and in extracellular structural tissues such as bones and teeth. About 600 g of phosphorus is present in the adult human body: 85% in the skeleton, 14% in the soft tissues and 1% in the extracellular fluids, intracellular structures and cell membranes. Phosphate anions participate in numerous cellular reactions and physiological processes and they are key components of essential molecules such as the phospholipids, adenosine triphosphate (ATP) and nucleic acids.

Source: *Nutrients, Dietary Supplements and Nutraceuticals* (Humana Press, 2011); *Encyclopedia of Dietary Supplements* (informa, 2010); World Health Organization; European Commission; The Council for Responsible Nutrition; Recent Market Reports Scientific Publications; The Copenhagen Consensus.

## Dietary Ingredients vs. Food Additive

It is remarkable that phosphate-based food additives, the most rapidly growing source of phosphorus in the diet of U.S. citizens, may contribute to as much as 30% of overall phosphorus intake. This source of the mineral remains largely unnoticed by consumers because the phosphate content of a food product is not required on the label. Many phosphorus containing additives are used by the food industry, for example in soft drinks (e.g. phosphoric acid in cola), processed cheese, luncheon meat and fast food items to preserve moisture and color, as emulsifiers and sequestrants, or to enhance and stabilize frozen foods. Such processing of foods, now commonplace in many often highly developed countries, adds significant amounts of phosphate to daily intakes — an estimated minimum of 200 to 300 mg/day; whereby the recommended intake is around 700mg / day. Approximately 125 phosphate additives are generally recognized as safe (GRAS) for food applications in the United States.

*The right balance:* High phosphate intakes contribute to acid generation and to an acidic urine. Such an increase in dietary acid load may require buffering by bone, which may result in the loss of bone mass and density. Sure, phosphate ions are essential to life for both their cellular roles and their extracellular uses such as the mineralization of bones and teeth. On the other side, excessive amounts of dietary phosphorus combined with a low calcium intake may have adverse effects on skeletal retention of minerals and therefore strength. Again, a well balanced healthy intake of fresh food is crucial. In general, phosphate supplements are not needed because the diet provides sufficient amounts of phosphate anions.

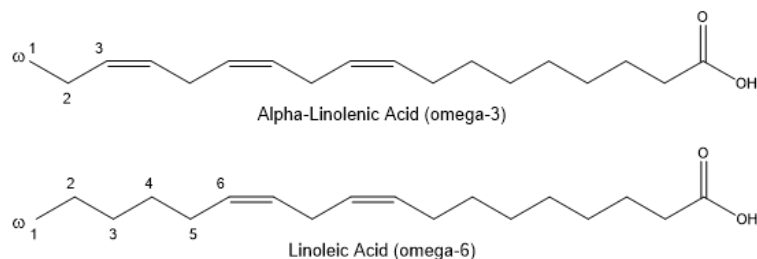
One of the most widespread nutrient deficiencies is that of iron, which is estimated to affect a third of the world's population. Iron is a key nutrient and required for many proteins and enzymes, notably hemoglobin to prevent anemia. The deficiency of iron can induce anemia among pregnant women, which is associated with increased risks in childbirth, causing more than 20% of maternal mortality in Asia and sub-Saharan Africa, with more than 20% of the deaths happening in the first week of life. There are two broad areas in which iron deficiency is considered to have an important functional impact on humans, where economic consequences can be estimated: cognitive ability of children and work capacity of adults. Iron deficiency has adverse effects on work productivity of adults, leading to losses in economic output. It also interferes with normal brain development and learning among children. Studies confirm that children with adequate iron status interact better with others and have better cognitive abilities, as well as perform better in school, hence have potential for higher lifetime income. Women of reproductive age have a higher need for dietary iron to reverse the loss of nutrient body stores by the monthly menstrual cycles. Meat, seafood, nuts, beans and dark chocolate are rich in iron. The common food vehicles for iron fortification are cereal flours, however, other options that are successfully tested or being tested include soy/fish sauce, double fortified salt and rice. On average, adult humans have 2–4 g of iron with premenopausal women having lower values than men. The typical Western diet contains 15–20 mg of iron, of which 1–2 mg/day is absorbed. A number of different forms of iron salts like ferrous sulfate, ferrous gluconate and ferric sulfate are used as fortifications or supplements and vary greatly in their solubility and availability for absorption by enterocytes. The choices that manufacturers of dietary supplements and fortified food face related to form iron to use in their preparations are not only cost-driven, but also take into consideration the chemical properties of each form of iron and what other chemicals or food components are present in the

preparation. The highly soluble sources of iron generally have a high bioavailability, but they are also more likely to participate in oxidation reactions with fats to form color reaction products and have a metallic taste.

A dedicated manufacturer and developer of mineral salts is the medium-sized owner managed German company Dr. Paul Lohmann. Founded in 1886, today the company boasts a range of 400 different mineral salts in a total of 7,000 different specifications for food, dietary supplements pharmaceuticals, cosmetics, animal nutrition and technology applications. For 2018 Dr. Paul Lohmann reported sales of Euro 124.3 million, and an EBITDA margin of 13.5%

### Fatty Acids

Omega-n-fatty acids are unsaturated fatty acids, where the number (n) indicates the position of the first double bond of the fatty acid; this is counted from the "omega end", the end of the molecule opposite the carboxy group. The most important representatives of omega-3-fatty acids includes alpha-linolenic acid (ALA), which is a component of many vegetable oils, and the longer-chain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are present in larger amounts in algae, plankton and the cold-water fish that feed on them, such as herring, mackerel, salmon and tuna. The best-known representative of omega-6 fatty acids is linoleic acid (LA), which is found in almost all fats and oils. Biologically, both ALA and LA are essential food components for the human being. From these short-chain fatty acids, the human organism can synthesize the more important longer-chain polyunsaturated omega-3 and omega-6 fatty acids by introducing further double bonds and a subsequent chain extension.



### Molecule structure of ALA and LA

In contrast to plant organisms, the human body is not capable of converting omega-6 fatty acids into the nutritionally more important omega-3 fatty acids. Therefore, the change in eating habits in western industrial nations over the last 200 years and the resulting high intake of LA or rather an omega-6 fatty

Source: *Nutrients, Dietary Supplements and Nutraceuticals* (Humana Press, 2011); *Encyclopedia of Dietary Supplements* (informa, 2010); World Health Organization; European Commission; The Council for Responsible Nutrition; Recent Market Reports; Scientific Publications; The Copenhagen Consensus.

acid compared to omega-3 fatty acids, leads to a competitive reduction in the synthesis of the longer-chain derivatives of ALA due to the competition for the same enzyme system. Consequently, these nations have an imbalance in the human body, i.e. an excess of long-chain omega-6 fatty acids and only a very small proportion of the omega-3 fatty acids DHA and EPA.

A study shows the extent of the health consequences of this change in diet. A ratio of omega-6 to omega-3 fatty acids in dietary fat of 1:1 was determined for Greenland, 12:1 for Japan and 50:1 for the USA and Europe. The more favorable ratios in Japan and Greenland are due to the increased consumption of fish in these countries. A comparison of heart attack rates in the death statistics shows an enormous difference from seven percent in Greenland to twelve percent in Japan and 40% in the USA and Europe.

EPA is a component of cell membranes and influences numerous physiological functions, such as inflammatory reactions, blood clotting, blood pressure and the immune response. DHA mainly functions in nerve and brain cells and the retina. It plays an important role particularly in fetal growth and early childhood development. Influenced are primarily the brain development, the training of vision and the development of the central nervous system. The need for DHA is particularly high in both pregnant women and infants. From a medical point of view, the preventive effect of omega-3 fatty acids in adults is also of interest. The best known of these is the prevention of cardiovascular diseases such as thromboses caused by arteriosclerosis, heart attacks, and strokes. Furthermore, omega-3 fatty acids seem to improve insulin sensitivity of the body and thus prevent diabetes, improve articular function and positively influence the brain function.

Due to the positive correlations mentioned above, an increase in the omega-3- fatty acid content in the food is useful. Official nutritional organizations therefore give recommendations for the proportion of total energy supplied daily in the form of omega-3-fatty acids. The BNF (British Nutrition Foundation) recommends that adults consume 0.5% of energy intake by DHA and EPA, which corresponds to 1.25 grams per day. The actual intake is on average 0.25 grams, so there is a gap of about one gram of DHA and EPA per day. Ways to close this gap – besides a more balanced nutrition – are the intake of dietary supplements and the consumption of functional food enriched with omega-3 fatty acids.

Traditional source of omega-3-fatty acids is derived from cold-water fish oils. However, mass-scale fisheries are not much longer sustainable if the demand is continuing to grow for these fish-based products. Reliance on the fish oil as the source of omega-3 fatty acids is also complicated by the significant taste, odor and stability problems associated with this type of oil. Furthermore, product quality derived from fish oil is generally dependent on the season and location, and it can be affected by the oceans' pollution. All these complications limit the use of fish oil as a food additive or supplement. Alternatively, novel sources of omega-3 fatty acids can be sustainably manufactured from marine algal or algae-like microbial oils, which eliminates many of the taste and odor problems associated with fish and discard the shortcomings of fish oil-based processes. In this context, DSM and Evonik just recently celebrated the opening of their Veramaris 50:50 JV's commercial-scale USD \$200 million facility in the U.S. for the production of omega-3 fatty acids rich in EPA and DHA

from natural marine algae for animal feed or rather sustainable salmon farming. The initial production capacity of omega-3 fatty acids equivalent to that derived from 1.2 million tons of wild-caught fish. This will meet around 15% of the global salmon farming industry's annual demand for omega-3 fatty acid – a significant contribution to conserving the biodiversity in our oceans.

Major vendors of the fatty acids for food fortification and dietary supplements are for example BASF and DSM. Financial investors are also active in this area: KD Pharma Group – owned by the financial investor Capiton – is a leading omega-3 ingredients producer focused on highly purified omega-3 fatty acids for pharmaceutical and nutraceutical products.

## Probiotics

The use of microorganisms to promote health is very ancient and can even be traced back to classical Roman literature where food fermented with microorganisms was used as a therapeutic agent. Fermented foods have been an important food component during human's history, and still pose a key component of the diet in many cultures. Today's idea of probiotics, prebiotics and synbiotics is to produce food or food supplements which, after ingestion, augment healthy intestinal microbiota, by either adding probiotic microorganisms, indigestible but fermentable prebiotic carbohydrates, or both constituents combined in synbiotics.

The human body is colonized by various microorganisms, and the human gastrointestinal tract is considered the most densely populated ecosystem on Earth. The average human gastrointestinal tract with a length of approximately 6.5 meter and a surface area of 200–300 m<sup>2</sup> offers a home for approx. 10<sup>12</sup> bacteria cells – mostly unculturable microbes – of 800–1,000 distinct bacterial species and subspecies. The gut microbiota is now virtually recognized as a complex whole organ consisting of an incredible amount of bacteria of different species. The collective genome of the entire gut microbiota, designated as "microbiome", exceeds the human nuclear genome by at least 100 times. Acquisition and development of gut microbiota can be influenced primarily by mode of delivery, maternal microbiota as well as genetic factors of the host and later by breastfeeding and other environmental factors. In the course of life, the microbial composition increases in both diversity and richness. The idea of suppressing and displacing harmful bacteria in the intestine by orally administering "beneficial" ones and thus improving microbial balance, health and longevity, was born a century ago. The term "probiotic" derives from the Greek/Latin word "pro" and "bios," meaning "for life". It was created in the 1950s to describe various components of food, essential for healthy development of life, also considered to be the opposite of antibiotics. Today, the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations defines probiotics as "live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host."

An intact and functional gut mucosal surface is essential to the maintenance of intestinal health, and the intestinal microbiota plays an important role. Over the last decades an intense research effort – reflected in a strong increase in scientific publications – has been made to understand the crucial role of gut microbiota in health and disease, whereby many mechanisms have been proposed to explain the effects of probiotics on human health. Probiotics may promote and/

Source: *Nutrients, Dietary Supplements and Nutraceuticals* (Humana Press, 2011); *Encyclopedia of Dietary Supplements* (informa, 2010); World Health Organization; European Commission; The Council for Responsible Nutrition; Recent Market Reports; Scientific Publications; The Copenhagen Consensus.

or maintain the gut defense barrier through both immunologic and metabolic pathways. When pathogenic microorganisms, antibiotics, chemicals, radiation therapy, or even dietary substances perturb either the intestinal epithelium or the normal microbiota, the host's gut defense can be compromised and predispose to disease. Selected other positive effects of probiotics can be summarized as follows:

- Synthesis and excretion of vitamins (vitamin K, vitamin B12) in excess of their own needs
- Competing for attachment sites or essential nutrients prevents colonization of pathogens
- Stimulation of the production of antibodies / boost and "educate" immune system
- Production of a variety of substances, ranging from relatively non-specific fatty acids and peroxides to highly specific bacteriocins that inhibit or kill other bacteria

Due to the increasing awareness of the intestinal microbiota's role in nutrition, health, and disease, the global human focused probiotics market has grown strongly over the last few years and is forecasted to expand from USD \$32 billion in 2015 to nearly USD \$50 billion by 2024. Increasing popularity and shifting consumer preferences have helped fund industry-wide R&D activities focused on the development of novel strains and the discovery of new probiotic applications, including: food ingredients, agricultural (e.g. animal and plant health) and care & beauty (e.g. cosmetics).

Furthermore, probiotics enjoy a growing attention as "medicaments" in scientific research; indicated by an increasing number of clinical trials and a rapidly rising number of clinical publications. Yet, although the current and proposed uses of probiotics in healthcare cover a wide range of diseases and conditions, only a few have significant research to back up the claims. Proven benefits of probiotics include the treatment of acute diarrhea and attention-deficit/hyperactivity disorder. Applications with substantial evidence include prevention of atopic eczema, prevention of traveller's diarrhoea, increased eradication of helicobacter pylori, alleviating

chronic constipation in adults and prevention of necrotizing enterocolitis. Promising applications include maintenance of remission in ulcerative colitis and pouchitis. Furthermore, probiotics are considered as a mucosal delivery system or a vaccine vector.

Lactobacillus and Bifidobacterium – both rod-shaped bacteria – represent the most commonly known probiotic strains. Both are found naturally in the human and animal gastrointestinal tracts and other body sites.



Coloured scanning electron microscope images of *Lactobacillus paracasei*

An ever-increasing number of Lactobacillus and Bifidobacterium strains are currently marketed in food products and as dietary supplements. The mechanisms of action of Lactobacillus and Bifidobacterium are incompletely understood and the evidence available suggests key mechanistic pathways that may be redundant or vary from organism to organism. General effects are postulated to include improvement of intestinal barrier function, immunomodulation and suppression of growth, epithelial binding, or invasion by pathogenic bacteria, such as Salmonella or Shigella species, enterotoxigenic Escherichia coli, and Vibrio cholerae. Suggested mechanisms include direct effects, such as reduction in intestinal pH values, production of organic acids and gut protective metabolites, as well as binding and metabolism of toxic metabolites.

## Related Lincoln International Transactions:

  
**LAKEVIEW EQUITY**  
PARTNERS LLC  
 has sold  
  
**UAS Labs**  
The Probiotic Company  
 to  
  
**CHR HANSEN**  
 Sell-Side  


  
**Doppel**  
Pharma CDMO  
 a portfolio company of  
**TRILANTIC | EUROPE**  
 has acquired  
  
**Dietopack**  
 Acquisition Financing  


In the context of probiotics, we would like to highlight two cross-border transactions. The recent acquisition of UAS Labs, a vertically integrated U.S.-based manufacturer of probiotic solutions, by Chr. Hansen, a leading global bioscience company that develops natural ingredient solutions for the food, nutritional, pharmaceutical and agricultural industries. Additionally, the acquisition of Doppel Farmaceutici, an Italy-based portfolio company of Trilantic Europe, by Dietopack, which focuses on nutraceutical products, pet nutritionals, producing probiotics, vitamins, minerals and high protein dietary supplements.

Source: Nutrients, Dietary Supplements and Nutraceuticals (Humana Press, 2011); Encyclopedia of Dietary Supplements (informa, 2010); World Health Organization; European Commission; The Council for Responsible Nutrition; Recent Market Reports; Scientific Publications; The Copenhagen Consensus.

## Market Intelligence

During Q2 2020, the Lincoln International chemicals & materials indexes and S&P 500 showed a bounce back when compared to the prior quarter. The recovery largely reflects more optimism in the market after the United States and the rest of the world shut down due to the COVID-19 pandemic during end of Q1 and beginning of Q2 2020. April appeared to be the bottom, with months after feeling the tailwinds of countries opening back up and rising confidence in finding a vaccine, which puts the chemical & material indexes back to levels we experienced at the end of 2019.

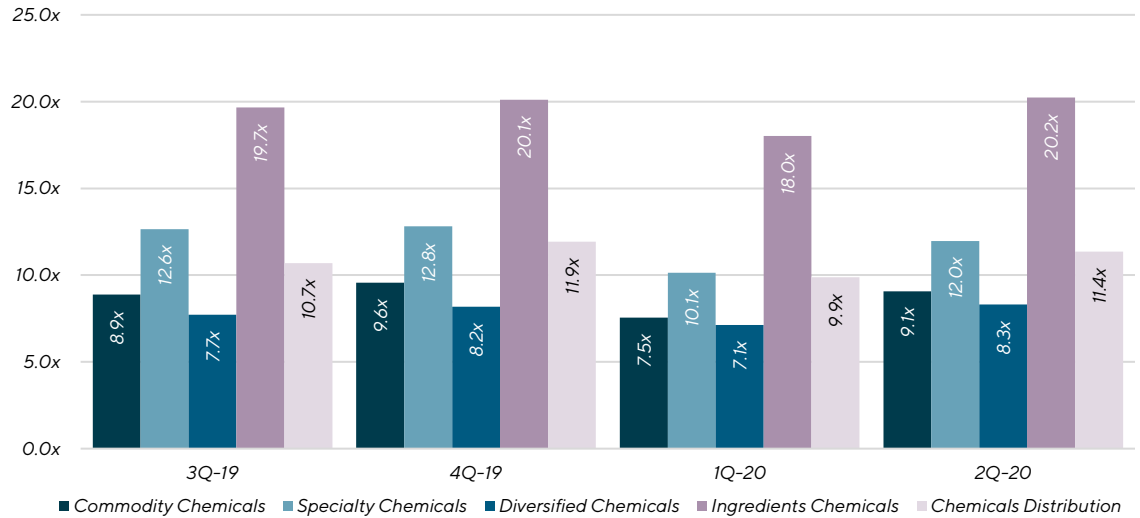
In June, production started to show positive signs related to plastic resins (used in packaging and consumer applications). Production in May was weak globally, besides China experiencing growth. Production for the month of May was down 0.5%, which was an improvement vs. 1.3% decline experienced in April. Three-month moving average for production in May was down 6.6% year-over-year and down 7.7% compared to the end of 2019.

Outlook in 2020 chemical production volumes, spending and shipping will compare less favorably to 2019. Although uncertain, a rebound in 2021 is expected when global GDP, global industrial production and consumer spending likely bounce back.

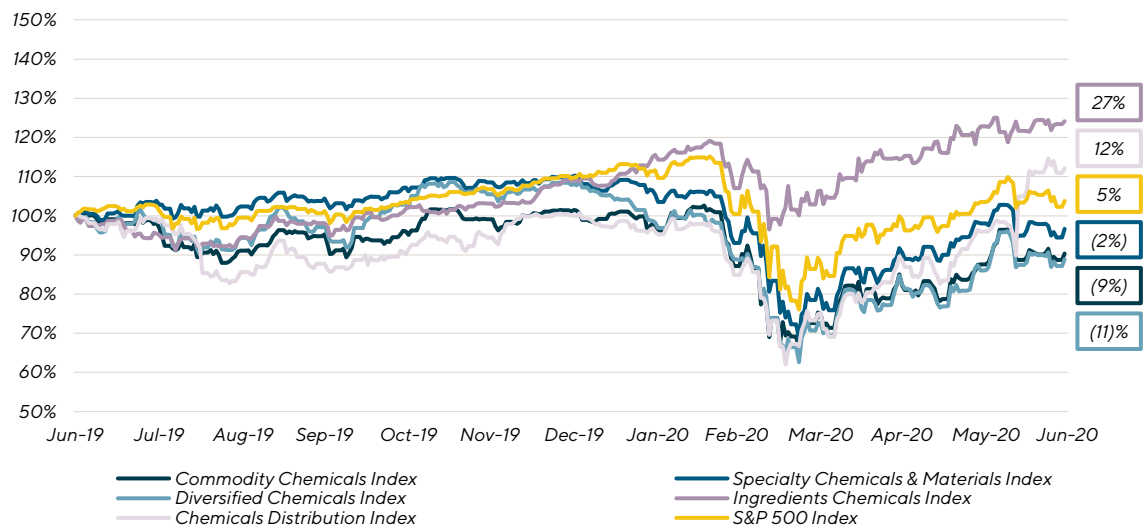
Sources: American Chemistry Council, CapitalIQ, Lincoln International

## Chemicals & Materials Market Update

### Enterprise Value / LTM EBITDA



### Stock Market Performance



### Public Company Valuation Statistics (6/30/20)

Sector	Number of Companies	Quarterly Stock Performance	% of 52 Week High	EV / CY20E		P / E Multiple	Net Debt / CY20E EBITDA	CY20E Growth		CY20E Margin	
				Revenue	EBITDA			Revenue	EBITDA	Gross	EBITDA
Commodity Chemicals	16	22.7%	66.3%	1.99x	15.0x	24.6x	3.1x	8.9%	26.5%	21.4%	14.4%
Specialty Chemicals	32	26.9%	78.4%	2.74x	15.1x	23.8x	2.6x	(10.5%)	(4.0%)	34.4%	16.1%
Diversified Chemicals	13	24.5%	72.2%	1.56x	12.4x	15.5x	2.6x	(8.7%)	(11.1%)	24.7%	13.1%
Ingredients Chemicals	5	19.9%	83.3%	4.75x	21.8x	29.2x	2.6x	5.3%	2.7%	36.2%	20.4%
Chemicals Distribution	5	26.0%	83.4%	1.04x	13.2x	22.0x	3.0x	(0.7%)	10.2%	24.2%	6.3%
<b>Median</b>				<b>1.99x</b>	<b>15.0x</b>	<b>23.8x</b>	<b>2.6x</b>	<b>(0.7%)</b>	<b>2.7%</b>	<b>24.7%</b>	<b>14.4%</b>

Sources: Capital IQ, ThomsonONE, Wall Street research and company data



## Select Q2 2020 M&A Transactions

(\$ in millions)

Closed	Target Company	Acquiring Company	Enterprise Value	EV / LTM	
				Revenue	EBITDA
Announced	Chengdu TALY Technology Co.,Ltd	Chengdu Guibao Science & Technology Co.,Ltd.	\$36	-	-
Announced	Zibo Nalcohol Chemical Co., Ltd.	Shandong Sunway Petrochemical Engineering Co.,Ltd	128	0.67x	-
Announced	TiZir Titanium & Iron AS	Tronox Holdings plc	300	1.74x	7.0x
Announced	Nanjing Zhongchao New Materials Co., Ltd.	Jiangsu Zhongxin Electric Materials Group Co., Ltd.	26	0.58x	-
Announced	Handuk Chemical Co., Ltd.	Lotte Chemical Corporation	113	-	-
Announced	Green Air Co., Ltd.	Hyundai Steel Company	129	-	-
Announced	Petrochemicals Business of BP p.l.c.	INEOS Styrolution Group GmbH	5,000	-	-
Announced	Assets of Sensient Technologies	Frulact - Sociedade Gestora de Participações Sociais S.A.	-	-	-
Announced	Beetlebung Pharma Ltd/Chilmark Labs	Open Book Extracts	-	-	-
Announced	3D Printing Materials Business of Clariant AG	Koninklijke DSM N.V.	-	-	-
Announced	KMCO LLC	ALTIVIA Chemicals, LLC	-	-	-
Announced	Merchant Triethyl Aluminum Business of Sasol Limited	Nouryon Holding B.V.	-	-	-
Jun-20	UAS Laboratories, Inc.	Chr. Hansen Holding A/S	530	-	-
Jul-20	Sensient Imaging Technologies S.A.	Sun Chemical Corporation	-	-	-
Jun-20	Modern Waterproofing Company S.A.E.	Sika Egypt For Construction Chemicals S.A.E.	33	1.06x	6.1x
Jun-20	Cangzhou Lingang Yanuo Chemical Co., Ltd.	Hainan Yatai Industrial Development Co., Ltd.	85	3.18x	-
May-20	Schülke & Mayr GmbH	EQT Partners AB	1,098	-	-
May-20	Functional Polyolefins Business of Arkema France SA	SK Global Chemical Co., Ltd.	369	1.34x	-
May-20	Exsa S.A.	Orica Mining Services Peru S.A.	352	1.76x	16.0x
May-20	CVC Theroset Specialties, Inc.	Huntsman Corporation	306	2.66x	10.0x
May-20	L'Air Liquide S.A. Entities in Czech Republic and Slovakia	Messer Group GmbH	-	-	-
May-20	Les Derives Resiniques Et Terpeniques SAS	Firmenich Productions Participations SAS	1,859	3.12x	17.2x
Apr-20	Hitachi Chemical Company, Ltd.	Showa Denko K.K.	8,994	1.51x	12.5x
Apr-20	Ellison Surface Technologies, Inc	Bodycote plc	200	-	-
Apr-20	Innovativehealth GROUP,S.L.	Evonik Industries AG	-	-	-
Apr-20	Glycom A/S	Koninklijke DSM N.V.	831	10.34x	20.7x
Apr-20	Syntor Fine Chemicals Limited (nka:Syntor by Aceto)	Aceto Corporation	-	-	-
Apr-20	Adhesives division of John P. Kummer	Meridian Adhesives	-	-	-
Apr-20	OMNOVA Solutions Inc.	Synthomer USA LLC	752	0.99x	10.6x
Apr-20	Alderys SAS	Givaudan SA	28	-	-

Source: Capital IQ, Mergermarket, Pitchbook and company data

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