

# FOOD AND NUTRITION UPDATE



**TNO** innovation  
for life

## INTERNATIONALIZATION

While most of TNO's food and nutrition research activity is conducted at our own facilities in the Netherlands, our food and nutrition clients are found in many countries around the world. Internationalization is a key element of TNO's strategy to maintain and strengthen its position as a leading global food and nutrition research and technology organization.

In 1999, TNO established an office in Boston to increase the organization's visibility to companies in one of its key regions: North America. TNO activities in North America have 2 main objectives: (1) valorizing TNO's strengths in applied food and nutrition research, and (2) developing long-term relationships with companies across the USA food production value chain.

### MAJOR PLAYERS

Our North American client base includes many of the major players in agro biotechnology, commodities, food ingredients, food manufacturing and specialized nutrition. Our collaborations with North American companies are very diverse, but can be divided into 2 different categories.

The first category is contract research services. Based on its broad and deep portfolio of *in vitro* and *in vivo* models for various health end points, TNO is widely

used by North American companies for the safety, efficacy and/or regulatory assessment of (bioactive) food compounds and products. Our unique research tools, for example our *in vitro* digestion models and our humanized mouse models for cardiovascular and metabolic health, as well as our expertise in navigating the complex European regulatory environment, are of particular value to its US clients.

The second category focuses on food product and process innovations. Here, TNO serves as a solution provider in areas such as moisture migration, texture control, shelf-life prediction and natural preservation.

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## HILLSHIRE AND TNO: WORKING TOGETHER ON CLEAN-LABEL, TOP-QUALITY MEATS

Recently, TNO and US company Hillshire Brands signed a collaboration agreement to work on clean-label preservation of packaged, processed meat products and to improve the texture of *fresh from the oven* microwaveable sandwiches. “We want to become the most innovative company in the USA in our field”, say Senior Vice President Research & Development Jeff George and Bob Reinhard, Vice President Food Safety and Quality. “The collaboration with TNO is helping us to achieve this goal.”

Hillshire Brands, based in a new HQ in downtown Chicago, is a leader in meat-centric food solutions for the retail and foodservice markets. Its portfolio includes well-known US brands like Jimmy Dean, Ball Park, Hillshire Farm, State Fair, Sara Lee frozen bakery and Chef Pierre pies, as well as artisan brands Aidells and Gallo Salame. Hillshire was formed out of the June 2012 split of the Sara Lee company into two independent companies: D.E. Master Blenders 1753 (based in the Netherlands) and Hillshire Brands.

### PERFECT MOMENT

“That transition offered a perfect moment to sharpen our innovation strategy”, says Jeff George. “During the last six months we searched for global research and technology partners who would add value to our own research and

development activities.” Hillshire is determined to become the most innovative meat-centric products company in the US market. Bob Reinhard, Vice President Food Safety and Quality, “One of our focus areas is natural-ingredient convenience-meats that meet or exceed clean-label specifications.”

TNO stood out from the other candidates. “TNO has a strong track record in both fundamental and applied food-related research and has the tailor-made approach we were looking for”, Reinhard explains. “For example, TNO has developed a microbial genomics tool, for DNA-based analysis, which is already being used in many TNO projects. This approach determines how product-relevant micro-organisms react to changes in their environment such as natural

preservatives. Compared to conventional microbiology, microbial genomics is faster, gives more-detailed information and can detect more micro-organisms, including those that do not grow on media. Of significant value to Hillshire is TNO’s ability to interpret the test results and translate them into practical, value-adding interventions and processes.”

### FRESH FROM THE OVEN EXPERIENCE

“The clean-label research programme will support our efforts to rapidly screen new ingredients and manufacturing processes”, says Reinhard. “This will allow us to meet the consumer desire for clean label foods while ensuring the highest levels of food safety.”

TNO also supports Hillshire Brands in developing technology solutions to deliver a *fresh from the oven* sensory experience for microwaveable sandwiches. The ideal *fresh from the oven* bread is referenced as having a dual texture: crispy exterior and softer interior. “TNO and Hillshire are working together to identify mechanisms and potential ingredient solutions to deliver the desired texture for bread products”, says George.

George and Reinhard have high hopes for the collaboration: “We expect Hillshire and TNO will enjoy a fruitful and lasting relationship.”

## HYDROCHIP: FAST AND RELIABLE ASSESSMENT OF SURFACE-WATER QUALITY

The Hydrochip allows for quick and reliable assessment of the quality of surface water and so facilitates efficient water management. The Hydrochip consortium, coordinated by TNO and part of the EU Life+ program, continues development of the tool.

Good quality surface water is vital for the production of clean water for domestic use, fishery and recreation. Diatom presence and concentration are good indicators of water quality and are a popular metric in analyzing water quality. Microscopic analyses, however, are time-consuming and expensive.

Introduction of the Hydrochip is expected to improve this situation markedly. The tool allows, by detecting algae DNA, quick and reliable assessment of the diatom types present and what this implies for the ecological condition of the water.

The Hydrochip is developed by the Hydrochip consortium: a partnership

between TNO, Hoogheemraadschap Hollands Noorderkwartier, STOWA, Vitens en Waternet. The project is sponsored by the EU Life+ program and started in September 2012.

### WIDE RANGE OF APPLICATIONS

The aim of this project is to optimize the predictive value of the Hydrochip by developing applications for detection of a wide range of diatoms. In addition, applications will be developed for detection of other relevant algae and bacteria, for example blue algae. In future, the Hydrochip could become a standard tool for routine water analysis, in line with the European Water Guideline Framework (*Europese Kaderrichtlijn Water, KRW*) and the Dutch guidelines for bathing water (*Zwemwaterrichtlijn*).

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## USING INSECTS AS A PROTEIN SOURCE: TNO STUDIES ALLERGY RISKS

TNO is investigating the risks of food allergies caused by consumption of mealworm proteins. Insects are receiving considerable attention as a possible sustainable protein source for the future, along with algae and beetroot leaf. The project outcomes will support all parties involved in the application and consumption of foodstuffs containing mealworm protein.

Mealworms, the larval stage of the mealworm beetle, could soon become a sustainable alternative to chicken, beef or pork. However, it is necessary to ascertain if they are safe for consumption. TNO has added this issue to its research portfolio, in line with its goal of investigating ecological and sustainable proteins for human consumption.

The first *in vitro* tests, conducted in collaboration with UMCU, revealed that patients with a house dust mite or shellfish allergy could be at risk when eating products containing mealworm proteins. In January 2013, the two research partners began a follow-up project in order to investigate the clinical relevance of these results. The project, supported by the NVWA (Dutch Food and Consumer Product Safety Authority) focuses on cross-reactivity with known allergens: whether patients with a house dust mite and/or shellfish allergy will develop an allergic reaction after eating mealworm proteins, or whether mealworm allergic patients will become allergic to house dust mites and shellfish.

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## TNO INTRODUCES NEW SENSITIVE MARKER FOR STUDYING INTESTINAL INTEGRITY: [14C]-LPS

TNO has successfully produced pure 14C-LPS from *E. coli*, for use as an efficient and affordable microtracer, in preclinical and clinical studies on intestinal integrity following bacterial infection.

Bacterial lipopolysaccharide (LPS) is an endotoxin that induces a profound disease response after having passed the gut epithelium and entered into the blood circulation. Depending on the dose

and exposure time, the response can vary from mild inflammation to serious acute illness and induction of tissue damage. LPS may enter into the blood stream as a result of a decreased gut

## CHALLENGE TEST PUT THROUGH ITS PACES

TNO has successfully carried out a first pilot study involving a high-fat challenge test. The study indicated that, as expected, the challenge approach is able to measure the subtle effects of nutrition on health.

The challenge approach defines health as the body's ability to adapt to changing circumstances and to show sufficient resilience to social, physical and emotional disturbances. The challenge approach will offer nutrition, food and health professionals tools to assess health more accurately and to predict the *tipping point*, when poor health transforms into disease. This will be of great benefit in the substantiation of health claims and in the development of health interventions, for example in cardiovascular health.

### NEW BIOMARKERS

Together with the food industry and academia, TNO is working to establish a new generation of biomarkers based on the challenge approach. Several experiments and pilot studies have been performed.

In the recent study, 10 healthy men were challenged via a high-fat load – delivered as a milkshake – before and after a four week overfeeding period. Overfeeding was accomplished by means of a daily surplus of calories, presented in a snack-pack. Both the high-fat challenge test as well as the overfeeding period were modeled on a realistic scenario: excessive consumption of fat and calories.



The challenge test discovered that glucose metabolism changed, towards a less favorable condition, after the four week overfeeding period: the challenge response of GIP-, GLP-1 and glucose levels showed similarities with the challenge responses of men with characteristics of *Metabolic Syndrome*, although the change was relatively small. In contrast, the overfeeding period led to a 'healthier' fat metabolism, as shown by a decrease in fasting levels of non-esterified fatty acids (NEFA), fructosamin and resistin and an increase in fasting HDL cholesterol and adiponectin levels. Thus, the fat metabolism of the men adapted to the overfeeding, whereas the response to the challenge test showed that glucose metabolism was unfavorably changed towards a less healthier state.

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barrier function, for example due to stress or unhealthy dieting. Therefore, LPS in plasma is regarded and used as a marker for gut integrity. Assaying for the presence of LPS is, however, difficult and expensive.

The pure 14C-LPS from *E. coli*, manufactured by TNO, offers an efficient and affordable analysis tool. Initial experiments with Caco2 cells, living pig-gut segments and minipigs have shown that 14C-LPS is absorbed by and transported across the gut epithelial wall and enters the minipig's central circulatory system.

The, extremely low, radioactive signal transmitted by the microtracer, is detected using TNO's Accelerated Mass Spectrometry at our location in Zeist, the only facility of its type in Europe. More experiments are ongoing to establish 14C-LPS as an important new tool in gut research.

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## TNO STARTS PROJECT ON FOOD REWARD

The drive to eat in the absence of energy deficit or nutritional need leads to overeating and can contribute to obesity. The reward effects of food – liking and wanting – are considered to be important in this respect. Studies in animals indicate that the endocannabinoid system (based on endogenous fatty-acid-derived signal molecules) plays a major role in food reward and, therefore, in the regulation of appetite and food intake.

The aim of this (PhD) project, carried out in collaboration with Wageningen UR, is to elucidate the role of endocannabinoids in food wanting and liking in humans, focusing on the perception of sweet and fat taste intensity and reward and also on the cephalic phase response. This project is an initial step in the development of strategies to discourage overeating.

The project combines expertise in sensory sciences, eating behavior, pharmacology, analytics and nutrition

interventions including imaging technologies. The project, lead by Dr. Gerry Jager and supported by the Graduate School VLAG, will provide psychophysical and psychohedonic insights into the role of endocannabinoids in food reward and overeating. Duration of the project is from February 2013 – February 2017.

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## SHORT-TERM STUDY CONFIRMS HEALTH EFFECTS OF EATING VEGETABLES

In a short-term study, TNO has demonstrated, for the first time, positive health effects from vegetable consumption on central physiological processes. The outcomes confirm that subtle effects of nutrition can be measured via sensitive assessment techniques.

Demonstrating the health benefits of vegetable and fruit consumption in an intervention study is, for various reasons, a difficult exercise. Particular challenges are the subtlety of the effects, the difficulty of including a placebo treatment and the length of time needed for the benefits to manifest. Not surprisingly,

the healthy image of vegetables and fruits originates more from epidemiological research than from intervention studies.

### SUBTLE EFFECTS

Current nutritional health research is able to demonstrate these subtle effects by a combination of sensitive analytical

platforms, statistical tools and bioinformatics - for the interpretation of results; TNO has a proven track record in applying these tools.

In a recent study TNO used these tools to investigate the health benefits of vegetables. The study design was a randomized cross-over trial in which 15 lean and 17 obese men consumed 50 or 200 grams of vegetables daily over a four week period. At the beginning, the 17 obese men had significantly higher insulin, glucose and triglyceride concentrations than the 15 lean men, indicating that the obese group could be considered less healthy. Analysis of blood markers revealed that, after four weeks of high vegetable consumption, both groups showed lower liver-enzyme activity and reduced signs of oxidative stress. Network analysis of these data, in combination with gene expression changes observed in adipose tissue, revealed a central role for Nuclear Factor Kappa Beta (NFkB) in inhibiting inflammatory processes.

The study has been submitted for publication.

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## NEW SCREENING PLATFORM DETECTS SATIATING NUTRIENTS

Hormones secreted by the gut are important regulators of hunger and satiety feelings. As early signals, these hormones are released by endocrine cells in the epithelium as a response to the presence of dietary components. TNO has developed a new medium-throughput platform, *InTESTine*, that enables screening of components for their hormone-releasing capacity.

The platform uses living pig-gut segments, mounted in small vials and kept alive for a few hours. It allows for the testing of compounds that might become relevant in new approaches to combat overeating. By using freshly-prepared intact pig-gut epithelium, the assay results probably better reflect the *in vivo* response than using murine cell lines. The platform has been described by Voortman et al. (*J.Agric.Food Chem.* (Chem., 2012, 60:9035-904) and is offered as a service to both the ingredient and food industries. Ongoing research at TNO is aimed at extending the application of the platform, for example to study metabolism, adhesion, immune response and more.

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## CLEAN LABEL WITH TNO

TNO invites food suppliers and manufacturers to participate in a joint program to clean-up the ingredient labels of food products. The collaboration will deliver new insights into natural alternatives for chemical additives and shorten the time-to-market of Clean Label products.

There is growing consumer demand for wholesome foods combining health and sustainability. Recent studies by the European Food Information Council (EUFIC) revealed that an increasing number of consumers avoid artificial ingredients and look for natural, fresh or additive-free foods. Moreover, increasing legislation, focusing on safety and sustainability, puts increasing pressure on producers using chemical food additives.

To meet these challenges, the food industry needs new insight into the functionality of natural ingredients as an alternative to chemical food additives. TNO is developing a knowledge platform, focusing on new, natural ingredients with desired functionalities, natural modification strategies and better understanding of the processing conditions that determine product quality.

### JOINT INNOVATION

In order to shorten the time-to-market of clean label products TNO is bringing together ingredient suppliers and food manufacturers in a joint innovation program. Clean labels require ingredient suppliers to understand the application needs of potential end-users. Vice versa, manufacturers need to know how clean-label interventions affect product quality. TNO facilitates knowledge exchange between the different stakeholders across the production chain and supports them in defining effective clean-label strategies. Advanced TNO technologies for product reformulation, high-throughput screening for novel natural preservatives and physical modification have been integrated into the program to provide a technological one-stop solution.

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## TNO SCIENCE FEATURES AT IFT 2013

More than 20,000 of the world's top food science and technology professionals will join us at the IFT Annual Meeting & Food Expo in Chicago this summer. 3 TNO papers have been selected for the Scientific Program lecture series during this major event.

The annual IFT Annual Meeting & Food Expo, to be held this year 13-16 July in Chicago, brings together professionals involved in both the science and the business of food-experts in R&D, product development, and QA/QC, as well as executive management, marketing, new business development, and more - from industry, academia, and government. Attendants learn about the most recent product, ingredient, and technology developments and their potential business impact, and to identify trends that will shape the industry.

3 TNO papers have been selected for the Scientific Program lecture series during the event:

› Reformulation of food into products with healthier ingredient compositions is a hot topic in the food industry. Dr. Anneke Martin and Martijn Noort will present *From Ingredient to Consumer: Multiple Product Reformulation Across the Chain* and will demonstrate an integrated approach, using case studies.

› Obesity is an ever increasing health problem in our society. Controlling satiety is an important target for the regulation of food intake by consumers. *Screening For New Bioactive Compounds in Weight Management* will provide solutions for the food industry to help consumers to eat healthy. Dr. Henk Hendriks and Maurits Burgering will discuss the development of the TNO gastrointestinal model for satiety research - *TIM Satiety* - and how it can be combined with the TNO intestinal segment system - *InTesTine*.

› A major threat for food shelf life is microbial spoilage. Food preservation is aimed at reducing spoilage risk, through the interplay of selected ingredients, processing conditions and hygienic measures. Investigating the effects of this interplay on spoilage organisms is based on culture-based microbiology. Dr. Frank H.J. Schuren will discuss TNO's expertise in the field of *bacterial gene expression read-out as the basis for improving food preservation*.

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MEET TNO @  
THE IFT 2013  
(CHICAGO, USA).  
MAKE AN  
APPOINTMENT  
WITH OUR FOOD  
EXPERTS:**

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## UPCOMING EVENTS:

Apr 15-17	Singapore
PharmaNutrition	
Apr 21-25	The Hague, The Netherlands
ECCE9/ECAB2	
Apr 23-25	Nürnberg, Germany
POWTECH	
May 14-16	Geneva, Switzerland
Vitafoods Europe	
May 28-29	Rotterdam, The Netherlands
6th Protein Summit	
Jun 4-5	Freiburg, Germany
Free from Food	
Jul 13-17	Chicago, USA
IFT	
Aug 19-23	Fiskebäckskil, Sweden
ISOPOW 12	
Sep 5-6	Brussels, Belgium
Global Food Safety Summit (ENG)	

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### TNO HEALTHY LIVING

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