2017–2019 Science Trend Report

Insights and Implications for the Future

ILSI North America

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To Our Readers

This *2017–2019 Science Trend Report: Insights and Implications* builds on content presented in our previous two reports: the *2015 Science Trend Report: Insights & Implications for the Future* and the *2016 Signals Watch*. These reports provide insights and early signals of emerging developments in areas of scientific and technology innovation, in addition to emerging trends in regulatory science, research funding, consumer science, and public policy and organization movements. We hope this information provides a window into the future and is useful as background knowledge to impact your decision making.

To compile these reports, data were surveyed from multiple cross-disciplinary sources that have significantly contributed to advancements in food, nutrition, and life sciences research. One clear observation this year is the rapid ascent of the convergence science approach applied to advance breakthroughs in the life sciences, particularly in biomedical research, intelligent sensors in manufacturing, and bioinspired technology innovations.

Report Structure

This *2017–2019 Science Trend Report* adds notable trends emerging in the food science and safety areas, and we expand the consumer environment section to include some insights into the future of the food market environment.

The report now includes seven sections that provide emerging developments in the following: (1) Global Health Trends, (2) Emerging Research, (3) Emerging Technology Innovations and Discoveries, (4) Forecast and Predictions, (5) Emerging Food Safety Trends, (6) Regulatory Science, Science Policy, and Movements, and (7) Consumer, Food, and Marketplace Trends.

Methodology and Limitations

Methodology: Information on emerging trends is constantly changing and being updated. Thus, it was not possible to identify or include all emerging insights in this report. To ensure that relevant (although not all) trends were identified and captured, an informal filtering process was applied using several criteria that included, but were not limited to, governmental science, research, and funding priorities; public and private research areas; strategic priorities of regulatory agencies; future research needs and interests identified by scientific societies; field experts; and consumer and market research experts. Details of methods used by the sources surveyed can be obtained from the source references provided. To enhance the scoping and filtering steps, we interviewed several experts in select areas to provide a richer and "on-the-ground" insight experience into some of the fast-growing areas related to food safety, taste, marketplace changes, systems biology, bioinspired technology innovations, and federal research and regulatory science priorities. Additionally, case examples are provided from an institution that has shown rapid progress and success in innovating technology.

Limitations: The intent of this report is for use as a directional guide only for identifying emerging areas. It is not meant to be either the primary source of reference or the definitive conclusion. It should serve as a stimulus for further discussion and confirmation. The data are derived from multiple publicly available sources that include, but are not limited to, the Internet, publications, journals, books, government brochures, customized searches on grants, and conversations and discussions with private-sector scientists and experts from government, academia, trade associations, and nonprofit organizations. In view of data sourcing limitations and applied filtering criteria, only megatrends are reported.

We hope that you find this *2017–2019 Science Trend Report* useful for your applications, whether for updating your knowledge, strategic planning, or research scoping.

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January 2017

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Summary of Highlights

This *Science Trend Report* highlights several active trend areas to watch in 2017 that have implications for food and nutrition research and initiatives on several fronts.

Global Health Trends

- **Maternal-Child Malnutrition.** Maternal-child malnutrition is an increasing global phenomenon and presents an opportunity for testing new dietary intervention approaches. Specific attention is focused on maternal-child undernutrition, which now exists in over 30 developing countries. Global maternal undernutrition accounts for 800,000 neonatal deaths per year from multiple causes, including small for gestational age births, stunting, wasting, and nutrient deficiencies. Worldwide, over 165 million children are stunted as a result of malnutrition.
- **Fortification Technology.** Advances in fortification technology have opened new opportunities for improved nutrient delivery and stability for use in deficiency intervention. Micronutrient deficiencies are estimated to underlie nearly 3.1 million child deaths annually. To date, no single intervention strategy has been successful in eradicating undernutrition; however, the use of a multinutrient fortification intervention approach presents potential success in reducing risks of multiple nutrient deficiencies (e.g., iron, zinc, and vitamins A and D). Future research must focus on long-term fortification intervention outcomes, maternal zinc supplementation, omega-3 fatty acid supplementation in pregnancy, antenatal psychosocial assessment, and cognitive behavioral therapy for depression.
- **Redefining Measures for Healthy and Successful Aging.** Rapid and progressive growth of the 65-and-older population globally necessitates the need to reevaluate current definitions of and measures for healthy aging. A new study calls for healthy aging determinants to be not just absence of diseases but also inclusion of broader measures. The study investigators found that specific medical diagnoses (cancer and hypertension) and health behaviors (smoking) are less critical than mental health (loneliness), sensory function (hearing), mobility, and bone fractures in defining vulnerable health classes. Determinants of successful aging may need to consider additional factors such as vision correction, proficiency in use of digital technology and devices for eHealth among older individuals, and how older populations define happiness.
- **Obesity Prevalence.** In the United States and Canada, the prevalence of obesity continues to grow in disparate populations.
- **Merging Healthy Dietary and Sustainability Guidelines**. Some countries are developing food-based dietary guidelines with low environmental impact.
- **Restricting Free Sugars in Foods.** The World Health Organization (WHO) has called for restriction of free sugars in foods to reduce noncommunicable disease–related deaths.

Emerging Research

- **Nutrition Research Roadmap.** The release of the first National Nutrition Research Roadmap for 2016–2021 by the Interagency Committee on Human Nutrition Research (ICHNR) has significant opportunities for the nutrition and food communities to consider. The ICHNR identified eating pattern research as its focal research topic directed at three key questions, with the objective to change current population eating patterns to a healthier pattern: (1) How can we better understand and define eating patterns to improve and sustain health? (2) What can be done to help people choose healthy eating patterns? (3) How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?
- **NIH Nutrition Research Task Force Initiative.** The National Institutes of Health (NIH) announced the formation of the Nutrition Research Task Force Initiative, which will develop a 10-year nutrition strategy for the NIH. Areas of potential interest include advancing new tools for dietary and physical activity assessments, biomarkers for specific disease endpoints, effects of circadian rhythm on food intake and metabolism, and the gut microbiome and diseases.
- **DRI Values for Chronic Disease Endpoints.** The Food and Nutrition Board is reviewing a dietary reference intake (DRI) working group report on the evidence-related and intake-response relation challenges that have hampered the inclusion of chronic disease endpoints in the derivation of DRIs with the use of a traditional framework and approach. The report presents several potential options to address those challenges.

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- **Microbiome and Brain Function**. The gut microbiome and its impact on brain neuroactivity and diseases continue to be a research focus.
- **Sodium Intake.** Research shows a relationship between dietary sodium intake and cardiovascular disease and mortality, including the efficacy of sodium reduction in reducing blood pressure regardless of the starting blood pressure level.
- **Delaying Aging.** Delaying aging is a new strategy now used to delay disease onset. Several intervention approaches have been studied that could delay aging progression, including caloric restriction, exercise, metformin, mammalian target of rapamycin (mTOR) inhibitors, modifiers of senescence and telomer delay, mitochondrial targeted therapies, hormonal and circulating factors, and sirtuin activators.
- **Circadian Rhythm and Eating Behavior**. Researchers are investigating circadian rhythm and how it impacts eating patterns, food and cellular metabolism, sleep, and disease pathogenesis and progression.

Technology Innovations and Discoveries

- **Convergence Science Approach**. This approach is becoming the norm and is a leading contributor to current technology innovations, breakthroughs, and biomedical research.
- **Bioinspired and Combination Technologies.** Bioinspired and combination technologies are breaking ground for breakthroughs in tissue and organ biology, brain circuitry and behavior, disease onset, and aging. Examples include optogenetics, CLARITY, 3D and 4D bioprinting with potential for food product development, organs-on-chips for chemical and drug screening and disease modeling, and new nanomaterials and nano things (tiny probes) for use in trapping pathogens.
- **Organs-on-Chips.** The use of this new technology is generating much interest in terms of how it might better reflect the physiological response to an external perturbation/intervention. The NIH is funding several research initiatives that involve using one or multiple organs-on-chips for drugs and chemical screening, and investigators are exploring the use of this technology in future disease modeling.
- **CRISPR.** CRISPR technology was recognized as a “Technology of 2015” and has potential for application in food safety and nutrigenomic research. Investigators are developing next-generation CRISPR technology that enables more "precise" editing using specific base pairs.
- **Advances in Packaging Material.** Researchers have developed a new soft packaging material using nature’s skins, such as chitosan and even shrimp shells. For example, shrimp shells and protein (“Shrilk”) were used to create a bioplastic that is flexible and environmentally friendly.

Forecast and Predictions

- **The Increasingly Digital World.** Advances such as the “data mesh,” artificial intelligence (AI), smart sensors, Big Data analytics, and data visualization are increasing in importance and are advancing avenues for precision medicine, manufacturing, and consumer daily digital experiences.
- **The Future Workforce.** The Institute for the Future has identified 10 skills that it deems critical for the workforce of 2020.

Emerging Food Safety Trends

- **Whole-Genome Sequencing.** Whole-genome sequencing technology will change how federal agencies detect, characterize, report, and regulate food contamination and how the food industry needs to respond to product and ingredient contaminants.
- **Imported Products.** Imported fresh produce and aquaculture products pose potential concern for increasing contamination or use of antibiotics.
- **National Strategy for Combating Antibiotic-Resistant Bacteria.** Multiple programs related to this work are in place at the NIH, US Department of Agriculture Food Safety and Inspection Service (USDA FSIS), and US Centers for Disease Control and Prevention (CDC). The National Science Foundation (NSF) and NIH are funding research for novel antibacteriosides, including exploration of soil and dirt (blue clay) for such use.
- **Adulterated Foods.** The adulteration of foods with fraudulent and even unsafe additives by some exporting countries continue to be an area of concern.
- **Unintended Consumer Uses.** Unintended consumer uses of foods will continue to increase with growing consumer interest in raw or undercooked, natural (preservative-free) foods that can be prepared quickly or are not cooked sufficiently.

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Regulatory Science, Science Policy, and Movements

- **Changing Consumer Food Expectations and Food Environments**. Regulatory science in Canada and the United States will face changing consumer food expectations and purchasing environments.
- **Deliverology.** The use of deliverology in Canada will change how programs funded through tax dollars will change program reporting and accountability, including relevance and benefits.
- **DRIs for Disease End Points.** Release of recommendations for dietary reference intakes (DRIs) for disease end points will be one of the most significant events influencing food and nutrition research and development/messaging in the future. Final recommendations are not expected likely until 2018 but could signal potential inroads into nutrigenomic and precision diets for disease interventions.
- **Food GRAS Rule and Health Claims.** The US Food and Drug Administration (FDA) issued a GRAS final rule in 2016, as well as guidance on use of the claim "healthy" on food labels. In 2016, the European Union also approved health claims on calcium and bone health.
- **Healthy People 2030.** The Healthy People 2030 committee was formed in 2016 and members are developing targets in progress under the directions of the US Department of Health and Human Services.

Consumer, Food, and Marketplace Trends

- **Natural, Green, and "-Free."** Consumers are gravitating to food products that are natural, "greener," and chemical free. They desire better clarity regarding food labels, including added sugars, country of origin, and front-of-pack information. Consumers are avoiding foods that have high sugars, high fructose corn syrup, salt, and preservatives.
- **Sustainable Foods.** Four out of 10 consumers believe that conserving nature and reducing use of preservatives in food is an important approach to producing sustainable foods.
- **Food Waste.** Consumers are concerned about climate change and desire to reduce "food waste." Six out of 10 consumers take food home from restaurants and many feel that the top contributor to food waste is buying too much fresh produce, forgetting about perishables.
- **Convergence in Food and Health**. Food and health are converging, and interest in antiaging foods and time-saving convenience options continues to grow.
- **Taste.** Taste remains at the forefront of consumer decisions when food shopping, surpassing price, healthfulness, convenience, and sustainability.
- **Trusted Sources of Nutrition Information.** Consumers view dieticians, health professionals, and government institutions as the most trusted sources of nutrition information.
- **Confidence in the Food Supply.** US consumers have confidence in the safety of the US food supply (66%); however, they are more likely to trust food that is grown locally or served in local restaurants.
- **Healthy Eating.** Heathy eating practices include eating in moderation, portion control, and variety, with inclusion of healthy foods as building blocks.
- **Healthy People 2020 Targets.** Dietary improvements are made through small gradual changes by including more fruits and vegetables; however, a recent analysis indicated the 2020 Healthy People targets on increasing vegetable intake have not been met (current intake is 0.77 cups compared with the target of 1.13 cups).

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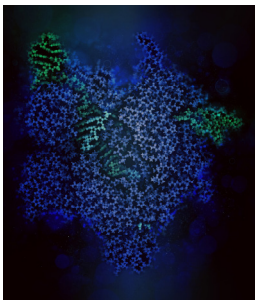
1 Global Health Trends

A. Global Recognition of CRISPR Technology Importance



1. Canada's Prestigious Gairdner Prize Awards Researchers in Three Seminal Biomedical Areas of Global Importance (CRISPR, AIDS, and SARS)

As we described in previous *Emerging Science Trend* reports, *Science* named CRISPR its "breakthrough of the year" in 2015[1] and interest in and application of CRISPR and related research continues to grow. Recipients of 2016 Canada's Gairdner Wightman Award[2] were recognized for their discoveries or contributions to seminal biomedical areas, including CRISPR, AIDS, and SARS, as follows:

- "For development of CRISPR-CAS as a genome editing tool for eukaryotic cells," to Feng Zhang, PhD (Broad Institute of MIT and Harvard and McGovern Institute for Brain Research, Massachusetts Institute of Technology); Jennifer Doudna, PhD (University of California, Berkeley); and Emmanuelle Charpentier, PhD (Max Planck Institute for Infection Biology and Umeå University).
- "For establishing and characterizing CRISPR-Cas bacterial immune defense system," to Philippe Horvath, PhD (DuPont); and Rodolphe Barrangou, PhD (Department of Food, Bioprocessing, and Nutrition Sciences, North Carolina State University).

Implications: CRISPR was chosen as *Science*'s breakthrough of the year in 2015 and has since been applied in many disciplines, notably in agricultural product research and, more recently, in food safety.

Sources: (1) Gairdner (2016) 2016 Canada Gairdner Awards honour CRISPR-CAS researchers and HIV/AIDS leaders [Press Release]. (2) Travis J (2015) And *Science's* 2015 Breakthrough of the Year is… [Blog]. *Science.*

B. Global Aging

At a time of unpredictable challenges for health, whether from a changing climate, emerging infectious diseases, or the next microbe that develops drug resistance, one trend is certain: the ageing of populations is rapidly accelerating worldwide. For the first time in history, most people can expect to live into their 60s and beyond. The consequences for health, health systems, their workforce and budgets are profound.

—Dr. Margaret Chan, Director-General, World Health Organization (2015)[1]

1. The Elderly Population Is Growing Worldwide

The global population aged >60 years reached 912 million in 2014, representing 12.6% of the global population. This segment is forecasted to increase to 1.5 billion or 18% in 2030. This accounts for a growth forecast of 39% between 2014 and 2030. The Asia Pacific (China, Japan, India, and Taiwan) region has the highest rate of population aging.[1] According to Euromonitor, China also has the highest number of individuals aged >60 years forecasted to increase by >46% between 2014 and 2030.[2,3]

Growth of the global older population presents several challenges, as countries see the number of nonworkers increase while the number of workers supporting them decreases. This is particularly apparent in China and India and is more gradual in the United States and European countries. Although China has the largest population of older adults, Japan and Taiwan are emerging with the fastest rate of older population growth and have the oldest populations. Western Europe is seeing an increase in population aging, with Germany surpassing Italy in the rate of population aging in 2014. Compared to other developed countries, growth of the rate of aging among the US population remains low due to high levels of immigration.[2]

Sources: (1) WHO (2015) *World Report on Ageing and Health.* Geneva, Switzerland: WHO. (2) Euromonitor (2015). (3) Maurice J (2016) WHO puts healthy ageing on the front burner. *Lancet.* 387:109–110.

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2. Healthy Aging Is No Longer Just the Absence of Diseases

Psychophysical, social, cultural, and economic determinants are equally important for successful aging. Euromonitor conducted a survey of older adults (aged ≥65 years) titled the "Determinants of Happiness: A 2015 Global Survey." The researchers found several determinants that older adults cited as critical for their happiness, including health, financial security, children and family support and relationships, satisfying work, strong social networks, and long-term goals. Spiritual beliefs ranked the lowest.[1]

Source: (1) Euromonitor (2015).

3. Seniors Are Slow Adoptors of Digital Technology

With respect to the use of technology such as smart and mobile devices for potential eHealth monitoring, seniors are slow adopters of technologies and late adopters of digital technologies.[1,2]

Results of a survey by Euromonitor among older adults showed low usage of digital technology for everyday purposes. Reasons contributing to this include physical conditions or health problems, visual impairment, poor coordination and memory issues, affordability, and wariness of Internet access. These limitations mean seniors will need technical assistance to get them comfortable with and proficient in using these devices.[1]

Implications: The growing elderly population presents several challenges as well as opportunities on how to target subsets of the population for health and nutrition interventions. Absence of disease may be too restrictive in defining healthy aging and may need to take into account other factors such as social, cultural, economic, and family support. Use of mobile and digital technologies to collect information for eHealth (e.g., food intake, physical activity, medication usage, etc.) in elderly individuals may prove challenging due to slow adoption and learning. The "Happiness" survey[1] may provide some insights into more positive ways to target the elderly population.

Sources: (1) Euromonitor (2015). (2) University of Chicago (2016).

4. Poor Vision Is Associated With an Increased Number of Falls in Elderly Individuals

The US Centers for Disease Control and Prevention (CDC) Vision Health Initiative[1] examined the state-specific annual prevalence of falls among persons aged ≥65 years with and without self-reported severe vision impairment. Among the national sample, there was an increased prevalence of falls among older adults with severe vision impairment as well as a variation in that prevalence among states.[1]

The CDC reported that in the 2.8 million persons aged ≥65 years with severe vision impairment in 2014,[2] an estimated 1.3 million likely experienced a fall in the previous year. These findings underscore the importance of state implementation initiatives to improve vision health and reduce falls, especially among elderly individuals with severe vision impairment.

Many common eye diseases are asymptomatic; thus, early detection and timely treatment are important. The National Eye Institute (NEI) has issued the following guidance to maintain healthy vision[3]:

- Maintaining a healthy weight. Overweight and obesity increase the risk of developing diabetes and other systemic conditions, which can lead to vision loss, such as diabetic eye disease or glaucoma.
- Eating a diet rich in fruits and vegetables, particularly dark leafy greens such as spinach, kale, or collard greens. Research has also shown there are eye health benefits from eating fish high in omega-3 fatty acids, such as salmon, tuna, and halibut.
- Research has linked smoking to an increased risk of developing age-related macular degeneration, cataracts, and optic nerve damage, all of which can lead to blindness.
- Diabetes, hypertension, and multiple sclerosis can greatly impact vision, resulting in inflammation of the optic nerve, diabetic retinopathy, glaucoma, and even blindness.

Sources: (1) Crews JE, et al. (2016) Falls among persons aged ≥65 years with and without severe vision impairment — United States, 2014. *MMWR Morb Mortal Wkly Rep.* 65:433–437. (2) US Census Bureau (2016) *Disability Characteristics*. Suitland, MD: US Department of Commerce, Census Bureau. (3) NEI (2016).

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5. Redefining Heathy Aging: New Study Addresses a Long-Standing Measure of Health and Well-Being in Older Adults

The World Health Organization (WHO) has defined healthy aging as complete physical, mental, and social well-being and not just the absence of diseases or infirmity.[1,2] Although this concept has been widely accepted, it is not generally practiced in the health communities.[1] Instead, the current dominant model of health has been a disease-centered medical model (MM).

In a recent study, McClintock et al.[1] approached this issue using a comprehensive model (CM) of health consistent with the WHO definition, giving statistical weights to multiple health domains, including medical, physical, psychological, functional, and sensory measures.[1]

The investigators applied a "data-driven latent class analysis (LCA)" to model 54 specific health variables from the National Social Life, Health, and Aging Project (NSHAP), a nationally representative sample of US community-dwelling older adults. This analysis uncovered five major health categories that were distinct by the presence of diabetes and hypertension, as well as six distinct health classes, including two that were previously obscured by the MM.

The authors found that specific medical diagnoses (cancer and hypertension) and health behaviors (smoking) are less critical than mental health (loneliness), sensory function (hearing), mobility, and bone fractures in defining vulnerable health classes.[1] Furthermore, although the MM places two-thirds of the US population into "robust health" classes, the CM reveals that one-half belong to less healthy classes, independently associated with higher mortality.[1]

In conclusion, this study of a representative US older adult population living in their homes evaluated multiple determinants of health, including "comprehensive medical, psychological, and social data in addition to measures of sensory functions and mobility, all key determinants for independent living and a gratifying life. The CM showed six distinctive health classes that predict mortality/incapacity. The study surprisingly showed that the healthiest aging tended to be the group that were 'robust' and with 'obesity'; two new classes, with twice the mortality/incapacity, were people with healed broken bones or poor mental health. This approach provides an empirical method for inclusion of broader determinant measures for health. Inclusion of these broader measures will be beneficial for health policy planning in future."[1]

- ***Implications:*** This reconceptualization has important implications for food and nutrition development, medical care delivery, health prevention practices, and resource allocation. This study clearly indicates that the current definition of health and well-being in older adults as merely the absence of disease is inadequate. Although the study only examined the CM in diabetes and hypertension, it might be important for future studies to include a more in-depth look at the contribution of obesity, vision impairment, and malnutrition as additional criteria for assessment of healthy aging. This new framework for defining healthy aging and well-being in older adults can be used to assess the contribution of diet and nutritional interventions.

Sources: (1) McClintock MK, et al. (2016) Empirical redefinition of comprehensive health and well-being in the older adults of the United States. *Proc Natl Acad Sci USA*. 113(22):E3071–E3080. (2) WHO (2015). *World Report on Ageing and Health*. Geneva, Switzerland, WHO.

C. Global Nutrition

1. Merging Healthy Dietary and Sustainability Guidelines: Developing Food-Based Dietary Guidelines With Low Environmental Impact

The United Nations General Assembly pronounced the period 2016–2025 as the Decade of Action on Nutrition against a backdrop of multiple challenges.[1] The following issues were identified:

- Malnutrition remains a global issue. Worldwide, over 800 million people are chronically undernourished.
- 159 million children under 5 years of age are stunted.
- Micronutrient deficiencies affect about 2 billion people globally.
- The incidence of overweight and obesity is increasing in all regions. About 1.9 billion adults are overweight, of which 600 million are obese. Childhood obesity is a growing concern.
- Poor dietary habits and unhealthy diets underlie the current nutrition issue.

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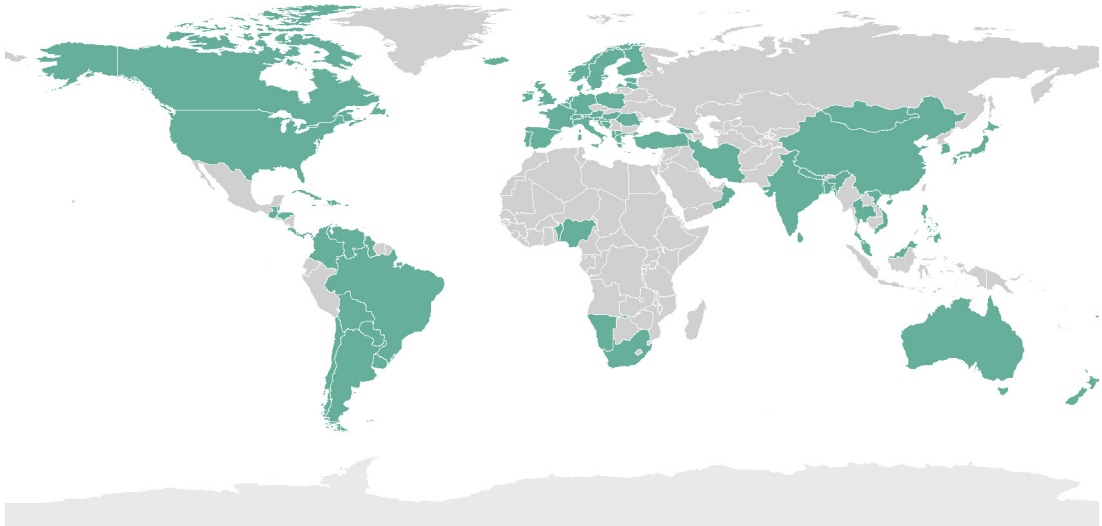
Figure 1. Map Showing (in Green) the 83 Countries With Dietary Guidelines Included in the Synthesis



Source: Gonzalez Fisher et al.[2]

- Recent confirmation that the global climate is changing has added burden to food security, sustainability, and nutrition security.

The Food and Agriculture Organization of the United Nations (FAO) believes that dietary patterns that are healthy also have low impact on the environment.[1] FAO sustainability goals are not just tied to preservation of natural resources, but they could also be tied to food-based dietary guidelines (FBDGs).

There is increasing evidence to suggest that dietary patterns that have low environmental impacts can also be consistent with good health. Both areas have several common features[1]:

- A wide variety of diverse foods
- Balance of energy intake and energy needs
- Minimally processed, focusing on field grown and less prone to spoilage, requiring less of rapid more energy-intensive transport modes
- Rich in whole grains, fruits, vegetables, legumes, and tubers
- Moderate quantity of meat, and all animal parts are consumed
- Dairy products or alternatives (e.g., fortified milk substitutes and other foods rich in calcium and micronutrients) in moderation
- Unsalted seeds and nuts
- More fish and aquatic products
- Limited consumption of foods high in fat, sugar, or salt and low in micronutrients (e.g., crisps, confectionery, sugary drinks)
- Tap water in preference to soft drinks.

Results of a web-based review by FAO of national dietary guidelines worldwide, using publicly available information including food guidelines, press releases, publications, expert opinions, observers, and expert interviews,[1] found that:

- Most dietary guidelines provide a clear, context-appropriate guidance for how people should be eating to maintain good nutritional health, and they provide the basis for the development of policies intended to shift consumption patterns in healthier directions.
- Not all countries have official FBDGs that include sustainability-oriented information.
- Of 215 countries, 83 had FBDGs (Figure 1). The absence of FBDGs is more apparent in low-income nations. In countries where FBDGs exist, the content link to policy is not clear or widely communicated and the target audience is unclear.

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Table 1. Summary of the Most Common National Guideline Messages by Country

	Germany	Brazil	Sweden	Qatar
Fruits and vegetables	Choose mainly plant-based foods. Enjoy 5 portions of fruit and vegetables daily.	Eat foods mainly of plant origin. Choose seasonal and locally grown produce.	Eat lots of fruit and vegetables (at least 500 g per day). Choose high-fiber vegetables.	Eat vegetables with most meals, including snacks. Aim for 3–5 servings of vegetables and 2–4 of fruits every day.
Meat	Eat meat in moderation. White meat is healthier than red meat.	Try to restrict the amount of red meat.	Eat less red and processed meat (no more than 500 g of cooked meat a week). Only a small amount of this should be processed.	Choose lean cuts of meat. Limit red meat (500 g per week). Avoid processed meats.
Dairy	Consume milk and dairy products daily. Choose low fat.	Milk drinks and yogurts that have been sweetened, colored, and flavored are ultra-processed foods, and as such should be avoided.	Choose low-fat, unsweetened products enriched with vitamin D.	Consume milk and dairy products daily. Choose low fat. If you do not drink milk or eat dairy products, choose other calcium- and vitamin D-rich foods (e.g., fortified soy drinks, almonds, chickpeas).
Fish	Once to twice a week.	—	Eat fish and shellfish 2 to 3 times a week. Vary your intake of fatty and low-fat varieties and choose eco-labeled seafood.	At least twice a week.
Fat and oil	Fat and fatty foods in moderation. Choose fats and oils from vegetable origins.	In moderation.	Choose healthy oils when cooking, such as rapeseed oil or liquid fats made from rapeseed oil, and healthy sandwich spreads.	Avoid saturated fat and hydrogenated or *trans*-fat. Use healthy vegetable oils such as olive, corn, and sunflower in moderation.
Processed food	—	Limit the consumption of processed foods and avoid ultraprocessed foods.	—	Eat less fast foods and processed foods.
Behavioural advice	Preferably cook foods on low heat, for a short time, using a small amount of water and fat. Use fresh ingredients whenever possible (this helps to reduce unnecessary packaging waste). Take your time and enjoy eating.	Eat regularly and carefully in appropriate environments and, whenever possible, in company. Develop, exercise, and share cooking skills. Plan your time to make food and eating important in your life. Be wary of food advertising and marketing.	Try to maintain energy balance by eating just the right amount.	Build and model healthy patterns for your family: (1) Keep regular hours for meals. (2) Eat at least one meal together daily with family. (3) Be a role model for your children when it comes to healthy eating and physical activity.

Source: Gonzalez Fisher et al.[2]

- Only four countries have included objectives focused on health and sustainability in their FBDGs. These include Brazil, Sweden, Qatar, and Germany.
- Two countries (the United States and Australia) have experienced attempts to incorporate environmental considerations. Each has reached an advanced stage but not achieved government endorsement.
- France, The Netherlands, and Estonia have "quasi-official" guidelines that incorporate sustainability and may have a role in influencing official processes.
- In countries where sustainability is not mentioned in the FBDGs, many of the main recommendations are consistent with sustainability features such as increasing consumption of fruits, vegetables, and whole grains; limiting red and processed meat; and maintaining energy balance (Figure 1; Table 1).

Countries that provide guidance on sustainability emphasize broadly similar things, and differences may lie in the emphasis and level of detail provided (Table 1). All highlight benefits of plant-based diets for health and for the environment and the negative impact of meat-based diets on the environment. Sweden is notable for more detailed advice on plant-based foods, emphasizing more root vegetables over salad greens. The Brazilian

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guidelines went further, noting the social and economic importance of sustainability, providing advice not to substitute traditional foods for ultra-processed foods, and cautioning against advertising.

The study identified four possible paths for developing dietary guidelines that incorporate sustainability goals.

1. Ownership and target audiences must be clearly defined. Guidelines must be linked to food policies that are practical, implementable, and well promoted.
2. The process for integrating sustainability and dietary guidelines must have clear government champions and participation of diverse scientific groups.
3. The process must involve two distinct and independent components: (a) development based on the advice of scientists and professionals from both health and environmental fields, and (b) a consultation process with civil society and industry.
4. To be impactful on the environmental influence of diets, dietary guidelines need to include strong educational programs to multiple targets linking food, health, and environmental importance.

Some future research needs were also identified:

- Long-term benefits of integrating healthy dietary patterns and food sustainability practices to gain low environment impact.
- Environmental impact of consuming more sustainable aquaculture and plant sources of omega 3s and other options weighing the trade-off between the health benefits of fish consumption and the negative environmental impacts.
- Determining a sustainable level of meat and dairy product consumption consistent with environmental costs and benefits.
- Better understanding of the environmental impacts of high-sugar, high-fat, and high-salt processed foods.
- Implications of sustainability and diets on social and economic impacts in developing countries.

Implications: Unintended consequences of changes in dietary patterns to meet sustainability goals need to be assessed, not just economically but also from nutritional and social/cultural perspectives in any countries adopting the integration. In addition, changes to food, agricultural, and manufacturing systems need to be considered.

Sources: (1) Adapted from Garnett T (2014). *Changing What We Eat: A Call for Research and Action on Widespread Adoption of Sustainable Healthy Eating.* Rome, Italy: FAO/Food Climate Research Network. (2) Gonzalez Fisher C, et al. (2016) *Plates, Pyramids, Planet.* Rome, Italy: FAO/Food Climate Research Network.

2. Sustaining Healthy Food Accessibility in Small Retail Grocery Stores

In 2015, the Robert Wood Johnson Foundation convened a panel of experts in food retail, nutrition, and obesity prevention to review and identify basic stocking, marketing, and sales strategies to help small retail stores in food desert areas be more productive in providing healthy foods and beverages to their customers.[1] In a report titled *Minimum Stocking Levels and Marketing Strategies of Healthful Foods for Small Retail Food Stores*, an expert panel sponsored by the foundation's Healthy Eating Research Program provided recommendations as part of its efforts in "building evidence to prevent childhood obesity."[1]

Healthy food accessibility and availability varies across stores in the United States, both by location of the store and store type. According to the report:

> Communities with predominantly white residents have two to four times more supermarkets and large-chain grocery stores than communities of color.[2,3] In contrast, lower-income and communities of color have more small food outlets, such as small food stores ("corner stores") and convenience stores.[1,3] Products offered in these corner stores tend to sell more convenient and pre-packaged foods and beverages that are lower in nutrition and higher calories. These small retail stores are likely to sell less perishable foods such as fresh produce and healthy staple foods such as fruits, vegetables, whole grain-rich foods, and low-fat dairy products.[2,3] These limitations in perishable food offerings may contribute, in part, to disparities in diet and health.[2–4]

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For stores already meeting these basic levels, the report identifies preferred levels of stocking that provide access to a wider range and larger supply of healthful foods and beverages. According to the panel,

> The report is expected to help local, state, and federal efforts to improve the healthfulness of foods and beverages sold in a variety of small retail food stores. It could be used in setting standards for financing of new retail food stores in underserved communities, designing 'healthy retailer' certification programs, and other local policies and initiatives. The recommendations in this report may also be used to inform policies for stores participating in ongoing federal programs, like the United States Department of Agriculture's (USDA) Supplemental Nutrition Assistance Program (SNAP).[1]

The method used by the panel included extensive review and analysis of evidence from multiple sources, including peer-reviewed research and publications, recommendations and guidelines from the federal government, scientific groups, national organizations, and public health organizations, as well as existing requirements for retailers participating in nutrition- and/or health-related policies and programs at the local, state, and national levels.[1] The panel developed guidance for evidence- and practice-based strategies to incentivize healthy food and beverage sales using in-store marketing strategies. The recommendations provided stocking strategies, qualifying food standards and placement, pricing, and promotion strategies.

- ***Implications:*** This study provides helpful basic inventory and marketing and sales information to corner stores in food desert areas that often do not stock sufficient fresh produce and healthy product options, attributed in part to product perishability and cost.

Sources: (1) Laska MN, et al. (2016) *Minimum Stocking Levels and Marketing Strategies of Healthful Foods for Small Retail Food Stores*. Durham, NC: Healthy Eating Research. (2) Powell LM, et al. (2007) Food store availability and neighborhood characteristics in the United States. *Prev Med*. 44:189–195. (3) Cannuscio CC, et al. (2013) Urban food environments and residents' shopping behaviors. *Am J Prev Med*. 45:606–614. (4) Morland K, et al. (2002) Neighborhood characteristics associated with the location of food stores and food service places. *Am J Prev Med*. 22:23–29.

3. Maternal-Child Malnutrition: An Urgent Need and an Opportunity?

In 2008, Richard Horton[1] warned of the lack of attention paid to the nutritional importance of maternal, newborn, and child health. In contrast, more attention was focused on vaccinations, oral rehydration therapy, and treatment of infection and hemorrhage.

In 2016, the *Lancet* launched a five-part series on maternal and child undernutrition that aims to fill this gap in global public health and policy action. The key messages of the series, led by a team of independent public health scientists, raised the important concerns of maternal and child health worldwide.

Global maternal undernutrition accounts for 800,000 neonatal deaths per year as a result of small for gestational age births; stunting, wasting, and micronutrient deficiencies are estimated to underlie nearly 3.1 million child deaths annually.[2] Ninety percent of global malnutrition is found in 34 countries, including in India and countries in Africa and South Asia (Figure 2).[2]

Worldwide, 165 million children are stunted. Stunting, severe wasting, and intrauterine growth restriction are among the most common problems. There is a critical period from pregnancy to 2 years of age where intervention is effective. After age 2 years, undernutrition will have caused irreversible damage for future development. It is estimated that 80% of undernourished children live in 20 countries across regions in Africa and Asia.

There are proven successful interventions to reduce childhood stunting and micronutrient deficiencies. These include breastfeeding counseling, vitamin A, and zinc supplementation. For optimal maternal health, adequate dietary intake in pregnancy and supplementation with iron, folic acid, and calcium are approaches of value.[3]

To date, there is no known single approach or technology that can solve the problem of global malnutrition. Social, economic, and political changes are critically important to improving maternal-child malnutrition. Long-term investments in the role of women as full and equal citizens worldwide—through education, economic, social, and political empowerment—will be critical to achieve substantive and sustainable improvements in maternal and child nutrition and health.

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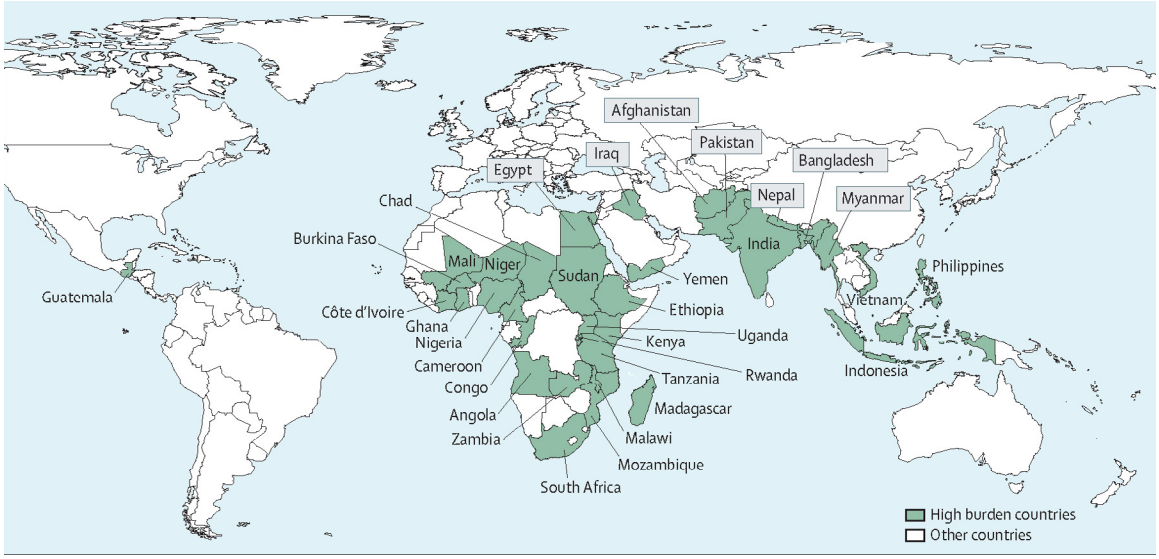
Figure 2. Countries With the Highest Burden of Malnutrition



Source: Reprinted from *The Lancet*, Volume 382, Edition 9890, Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, Webb P, Lartey A, Black RE; Lancet Nutrition Interventions Review Group; Maternal and Child Nutrition Study Group, Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost, Pages 452–477, Copyright 2013, with permission from Elsevier.

Implications: National nutrition intervention programs to successfully eradicate undernutrition in maternal-child health will require governmental support to ensure scale-up nutrition interventions, systems to monitor and evaluate those plans, and laws and policies to enhance the rights and status of women and children. There is concern that the international nutrition system may need better global leadership, more resources, and harmonious systems in order to be successful.

Sources: (1) Horton R (2008) Maternal and child undernutrition: an urgent opportunity. *Lancet.* 371:179. (2) Lopez AD, et al. (2006) Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet.* 367:1747–1757. (3) Bhutta ZA, et al. (2013) Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet.* 382:452–477.

4. Fortification: Assessment of Success as an Approach to Reduce Global Maternal and Child Undernutrition

Food fortification technology is reemerging as a technology of interest to reduce global malnutrition.[1] Because of its long history of use, safety, and cost-effectiveness, fortification is a preferred method to deliver nutrient-dense foods. With advances in material stability, absorption (nutrients, ingredients), delivery systems (nanotechnology), and sources (chemical or crops), fortification is the usual preferred approach to address the widespread problem of undernutrition. Globally, fortification is usually applied at several delivery levels—the mass population, the targeted population at risk, and households. More recently, biofortification has gained popularity as another way to introduce nutrient-rich ingredients. It involves enhancing nutrient content of the food crops at the source. This method is gaining popularity as an alternate to chemical fortification stated previously. Biofortification as an intervention method is gaining interest as a potential approach to enhance iron, provitamin A, zinc, and folate contents in staple foods; however, progress is slow, as widespread acceptance by the target population is low, making this a rate-limiting step. More research is needed to determine how to get these foods to be accepted for widespread usage.

In 2013, Bhutta et al.[1] conducted a meta-analysis to evaluate the effectiveness of multinutrient fortification to reduce malnutrition in children. The study found:

- A meta-analysis of 60 trials of iron fortification of foods showed a 41% reduction in the risks of anemia (relative risk [RR], 0.59; 95% confidence interval [95% CI], 0.48–0.71; $P < 0.001$) and a 52% reduction in iron deficiency (RR, 0.48; 95% CI, 0.38–0.62; $P < 0.05$). Children showed significant improvement in serum micronutrient levels.

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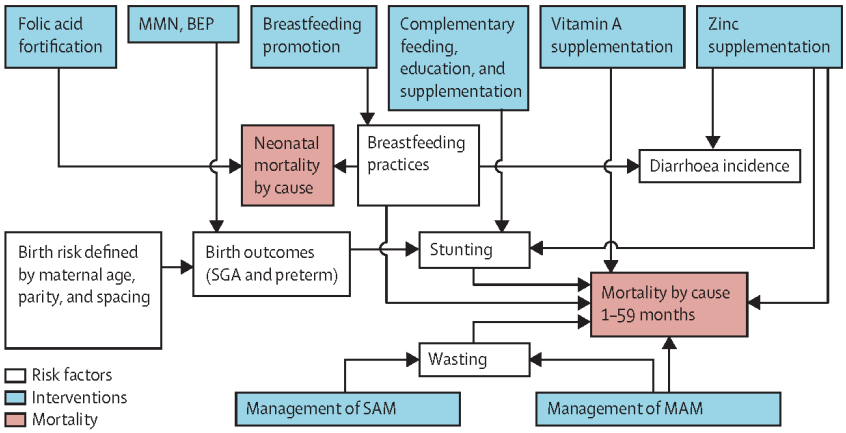
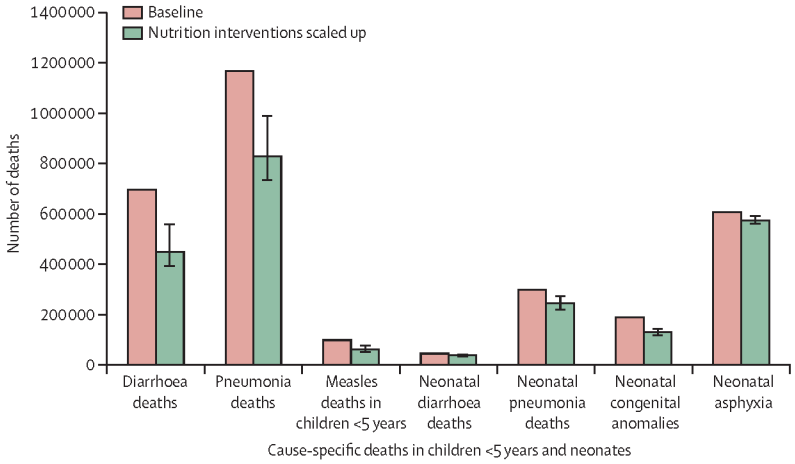
Figure 3. Linkages Between Risk Factors, Interventions, and Mortality in the LiST Trial



Source: Reprinted from *The Lancet*, Volume 382, Edition 9890, Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, Webb P, Lartey A, Black RE; Lancet Nutrition Interventions Review Group; Maternal and Child Nutrition Study Group, Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost, Pages 452–477, Copyright 2013, with permission from Elsevier.

Figure 4. Effect of Scale Up of Interventions on Cause-Specific Deaths



Source: Reprinted from *The Lancet*, Volume 382, Edition 9890, Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, Webb P, Lartey A, Black RE; Lancet Nutrition Interventions Review Group; Maternal and Child Nutrition Study Group, Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost, Pages 452–477, Copyright 2013, with permission from Elsevier.

- A meta-analysis of multiple micronutrient fortification in children indicated an increase in hemoglobin concentrations by 0.87 g/dL (95% CI, 0.57–1.16) and a reduced risk of anemia by 57% (RR, 0.43; 95% CI, 0.26–0.71). The mean ferritin increase with fortification was 11.3 µg/L (95% CI, 3.3–19.2) compared with the control groups.
- Fortification also increased vitamin A serum concentrations compared with control groups (four studies, mean retinol increase 3.7 µg/dL; 95% CI, 1.3–6.1).
- Vitamin D–fortified bread increased serum 25-hydroxyvitamin D concentration as effectively as the cholecalciferol supplement in women.
- Zinc fortification enhanced significantly higher zinc concentrations in serum and erythrocytes and lower serum copper concentrations compared with a placebo group in preterm infants.

In assessing the benefits of fortification on different outcomes with various nutrient fortificants, Bhutta et al.[1] proposed a framework that shows the complexity in the interconnection between risk factors, interventions, and mortality in the LIST Trial (Lives Saved Tools) (Figure 3). In a scale-up model, the investigators also demonstrated the beneficial effect of fortification interventions in reducing the number of deaths in studies that compared before and after outcomes (Figure 4).

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Future research needs include the following:

- Child and maternal vitamin D supplementation over long duration
- Maternal zinc supplementation, and omega-3 fatty acid supplementation in pregnancy
- Antenatal psychosocial assessment and cognitive behavior therapy for depression
- Emollient and massage therapy for preterm infants
- Zinc therapy for pneumonia in young children with malnutrition
- Lipid-based nutrient supplementations

Implications: In the United States and Canada, fortification is an approach that has improved nutritional status in many subpopulations. Future fortification approaches can incorporate advances made in genomics, systems biology, and nanotechnology to provide customized fortification of multinutrients (or bioactives) as part of precision nutrition and precision medicine.

Source: (1) Bhutta ZA, et al. (2013) Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet.* 382:452–477.

5. WHO Calls for Restricting Free Sugars From Foods to Reduce Noncommunicable Disease–Related Deaths

The WHO has issued new guidelines with the aim to reduce intakes of free sugars from foods to reduce deaths related to noncommunicable diseases (NCDs). NCDs are the leading causes of death, accounting for 68% (38 million) of the world's 56 million deaths in 2012.[1] At least 16 million of these deaths were among individuals younger than age 70 years, and 28 million NCD deaths occurred in low- and middle-income countries. Modifiable risk factors for common causes of NCDs include poor diet, physical inactivity, and obesity. Obesity has become a global pandemic.[2]

The WHO report indicated that a high level of intake of free sugars* was linked to poor dietary quality, obesity, and increased risk of NCDs.[3,4] Free sugars increase dietary energy density and promote positive energy balance.[5–7] Maintaining energy balance is critical for healthy weight maintenance and ensuring optimal nutrient intake.[8] There is concern that increased intake of dietary free sugars from sugar-sweetened beverages may contribute to poor food choices and diet quality, leading to an unhealthy diet, weight gain, and increased risk of NCDs.[9–13] Another concern is the link between dental caries and intakes of free sugars.[3,4,14–16] Dental diseases are the most prevalent NCDs globally.[17,18] Dental caries treatments account for 5%–10% of the health care budget in industrialized nations, which would exceed the entire financial resources available for the health care of children in most lower-income countries.[16,17] Debilitating effects of dental caries include persistent pain, anxiety, functional limitations, poor school and job performance, and social handicap through tooth loss.

In 2015, the WHO Nutrition Guidance Expert Advisory Group (NUGAG) completed an extensive systematic review and meta-analysis of available evidence and published guidelines for sugar intakes for children and adults.[1]

- WHO recommends a reduced intake of free sugars throughout the life course (*strong recommendation*).
- In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake (*strong recommendation*).

Residents in countries with low free sugars intake are advised not to further increase intake. Higher intakes of free sugars decrease nutrient quality of diets by providing significant energy without specific nutrients.[3] These recommendations were based on the totality of evidence reviewed regarding the relationship between free sugars intake and body weight (low and moderate quality evidence) and dental caries (very low and moderate quality evidence). Increasing or decreasing free sugars is associated with parallel changes in body weight, and the relationship is present regardless of the level of intake of free sugars. The excess body weight associated with free sugars intake results from excess energy intake. The recommendation to limit free sugars intake to less than 10% of total energy intake is based on moderate quality evidence from observational studies of dental caries.

- WHO suggests a further reduction of the intake of free sugars to below 5% of total energy intake (*conditional recommendation*).

The recommendation to further limit free sugars intake to less than 5% of total energy intake is based on very low quality evidence from ecological studies in which a positive dose-response relationship between free sugars intake and dental caries was observed at free sugars intake of less than 5% of total energy intake.[1]

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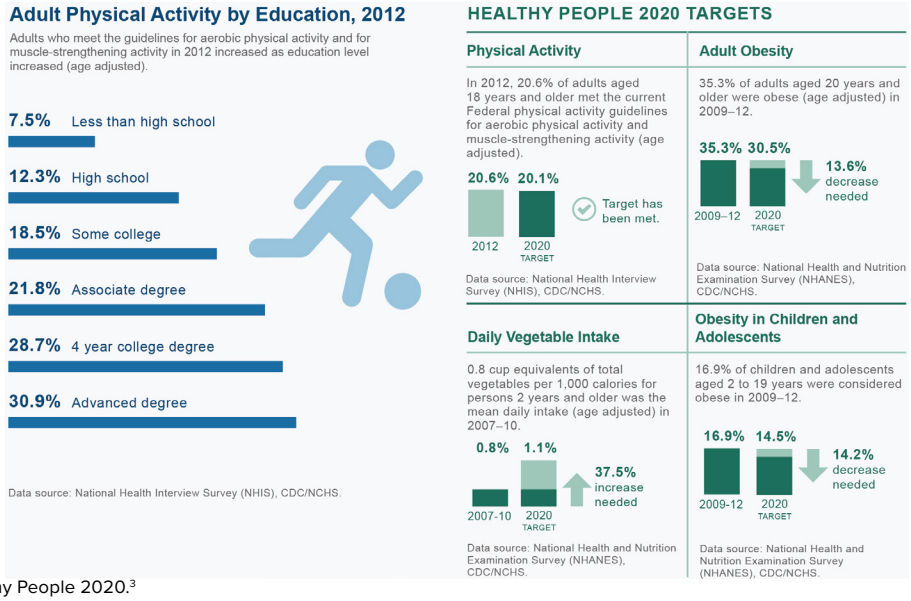
*The term "free sugars" refers to the definition by the 2002 Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases.[3,4] These include "all monosaccharides and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrups and fruit juices."[3] The 2015 WHO NUGAG Subgroup on Diet and Health further elaborated the term as follows: "Free sugars include monosaccharides and disaccharides added to foods and beverages by the manufacturer, cook or consumer, and sugars naturally present in honey, syrups, fruit juices and fruit juice concentrates."

Sources: (1) WHO (2015) *Guidelines Sugar Intakes for Adults and Children*. Geneva, Switzerland: WHO. (2) WHO (2014) *Global Status Report on Noncommunicable Diseases*. (3) WHO (2009) *Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks*. (4) WHO (2003) *Diet, Nutrition and the Prevention of Chronic Diseases: Report of a Joint WHO/FAO Expert Consultation*. WHO Technical Report Series, No. 916. (5) WHO (1990) *Diet, Nutrition and the Prevention of Chronic Diseases: Report of a WHO Study Group*. WHO Technical Report Series 797. (6) Johnson RK, et al. (2009) Dietary sugars intake and cardiovascular health: a scientific statement from the American Heart Association. *Circulation*. 120:1011–1020. (7) World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) (2007) *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*. Washington, DC: AICR. (8) Elia M, et al. (2007) Physiological aspects of energy metabolism and gastrointestinal effects of carbohydrates. *Eur J Clin Nutr*. 61(Suppl 1):S40–S74. (9) FAO (2010) *Fats and Fatty Acids in Human Nutrition: Report of an Expert Consultation*. FAO Food and Nutrition Paper 91. Rome, Italy: FAO. (10) Hauner H, et al. (2012) Evidence-based guideline of the German Nutrition Society: carbohydrate intake and prevention of nutrition-related diseases. *Ann Nutr Metab*. 2012;60(Suppl 1):1–58. (11) Malik VS, et al. (2013) Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am J Clin Nutr*. 98:1084–1102. (12) Malik VS, et al. (2010) Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. *Diabetes Care*. 33:2477–2483. (13) Malik VS, et al. (2006) Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr*. 84:274–288. (14) Vartanian LR, et al. (2007) Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis. *Am J Public Health*. 10:120. (15) Moynihan P, et al. (2004) Diet, nutrition and the prevention of dental diseases. *Public Health Nutr*. 7:201–226. (16) Sheiham A, et al. (2014) A reappraisal of the quantitative relationship between sugar intake and dental caries: the need for new criteria for developing goals for sugar intake. *BMC Public Health*. 14:863. (17) Sheiham A, et al. (2014) A new understanding of the relationship between sugars, dental caries and fluoride use: implications for limits on sugars consumption. *Public Health Nutr*. 2014:1–9.

6. US Health Status: Status Report of Healthy People 2020 Targets for Physical Activity, Obesity, and Nutrition

Good nutrition, regular physical activity, and a healthy body weight are important determinants of overall health and well-being.[1,2] Healthy eating patterns can help maintain healthy body weight and prevent and reduce the risk of chronic disease throughout periods of growth, development, and aging as well as during pregnancy. Healthy eating patterns consumed over time include a variety of vegetables from all of five vegetable subgroups—dark green, red and orange, legumes (beans and peas), starchy, and other—fruits; grains, especially whole grains; fat-free or low-fat dairy; and a variety of protein foods and oils (Figure 5).[1,2]

Figure 5. Healthy People 2020 Progress to Date



Source: Healthy People 2020.[3]

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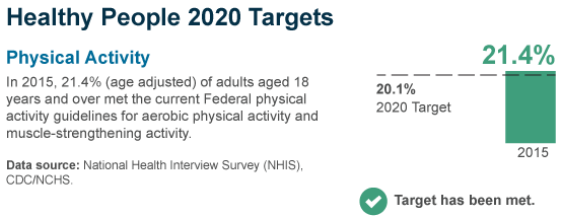
- **Physical Activity: Exceed 2020 Target.** From 2008 to 2015, the rate for adults aged ≥18 years who met the guidelines for aerobic physical activity and muscle-strengthening activity increased by 17.6%, from 18.2% to 21.4% (age adjusted), exceeding the Healthy People 2020 target of 20.1%. However, groups with some or no college education fall short of target (Figures 6 and 7).[1,2]
- **Obesity Rate: Below 2020 Target.** Between 2005–2008 and 2011–2014, there was no statistically significant change in the obesity rate among adults aged ≥20 years (33.9% in 2005–2008 and 36.2% in 2011–2014, age adjusted) and youth aged 2–19 years (16.1% in 2005–2008 and 17.0% in 2011–2014).[1,2]
- **Nutrition: Below 2020 Target.** Between 2005–2008 and 2009–2012, there was no statistically significant change in the mean daily vegetable intake of persons aged ≥2 years (0.76 cup equivalents of total vegetables per 1000 calories, age adjusted, in 2005–2008 and 0.77 in 2009–2012). The Healthy People 2020 target is 1.16 cup equivalents per 1000 calories (Figure 8).[1,2]
- **Additive Action.** By focusing on prevention, the Affordable Care Act promotes better health for adults and children. Two of the recommended preventive services without a copayment or coinsurance for all Marketplace plans because of the Affordable Care Act are directly related to nutrition and physical activity: dietary counseling for adults at higher risk for chronic disease, and obesity screening and counseling for all adults and for children aged ≥6 years.[1,2]

Implications: Most Americans do not eat a healthful diet and are not physically active at levels needed to maintain proper health. Fewer than 1 in 3 adults and an even lower proportion of adolescents eat the recommended amount of vegetables each day.[1] Compounding this, a majority of adults (81.6%) and adolescents (81.8%) do not get the recommended amount of physical activity. As a result, there is an increase in obesity. Today, approximately 1 in 3 adults (34.0%) and 1 in 6 children and adolescents (16.2%) are obese. Obesity-related conditions include heart disease, stroke, and type 2 diabetes, which are among the leading causes of death. In addition to grave health consequences, overweight and obesity significantly increase medical costs and pose a staggering burden on the US medical care delivery system.

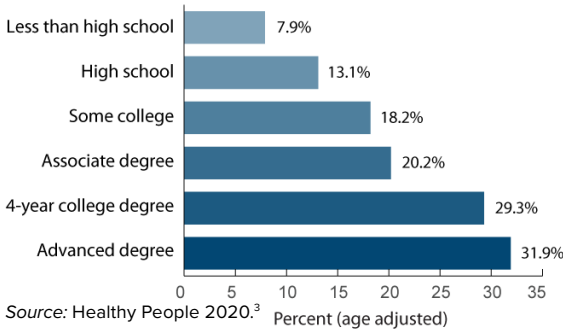
Figure 6. Healthy People 2020 Targets for Physical Activity



Source: Healthy People 2020.[3]

Figure 7. Education Level of Adult Respondents

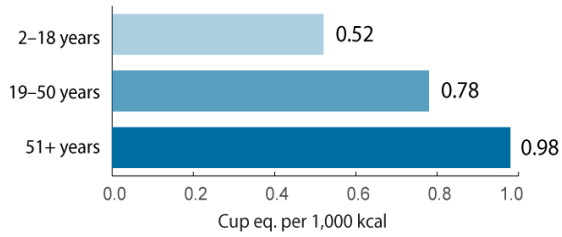
The proportion of adults aged 25 years and over who met the guidelines for aerobic physical activity and for muscle-strengthening activity in 2014 **increased as education level increased**.



Source: Healthy People 2020.[3]

Figure 8. Healthy People 2020 Targets for Nutrition

Mean daily vegetable intake increased as age increased.



Source: Healthy People 2020.[3]

Sources: (1) CDC (2009) *State Indicator Report on Fruits and Vegetables*. Atlanta, GA: CDC. (2) US Department of Health and Human Services (2008) *Physical Activity Guidelines for Americans*. Washington, DC: HHS. (3) HHS (2016) Healthy People 2020: Leading Health Indicators, Nutrition and Weight Status [Internet].

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2 Emerging Research

A. Healthy Aging

1. Delaying Aging: A New Strategy to Slow Disease Onset?

It is clear that directly targeting aging is theoretically superior to treating individual chronic diseases, but until recently, translation approaches to achieve this goal is just that—purely theoretical.

—Kaeberlin et al. (2015)[1]

Kaeberlin et al.[1] recently proposed that aging may play a critical role in disease pathogenesis. Traditionally, biomedical research has been singularly focused on pathogenesis and treatment of specific diseases, particularly those affecting morbidity and mortality. This disease-specific approach has resulted in many medical breakthroughs in treatments, improving quality of life and longevity. In spite of these advancements, delaying, ameliorating, or preventing disease onset has not yielded much progress.

These issues have raised questions regarding the role that the aging process plays in biological systems in disease pathogenesis and progression. Recent research in geroscience has led to the possibility that the aging process is pliable and that biological aging is modifiable, and that tangible approaches can be developed to enhance healthy longevity based on the premise that slowing the rate of biological aging would delay the onset and progression of each of these diseases, a prediction supported by experimental data in laboratory models.[2]

This translates as follows: (1) The biological effects of aging must be considered when developing therapies for chronic disease, especially in developing cancer immunotherapies.[3] (2) Delaying the rate of aging would increase longevity by controlling for multidisease onsets, compared to single disease treatment. (3) Multidisease delay would also delay later declines in function, now referred to as the "longevity dividend."[4] Research is underway to quantify this using projections from preclinical experimental data, to predict significant benefits in individual quality of life (health span), as well as important society-wide economic and productivity gains.[5]

Several interventional strategies have been proposed (Table 2).

Table 2. Interventional Strategies

Intervention	Description
Dietary restriction	Dietary restriction (DR), most studied for delaying aging.[6] Not universally effective. Many studies have indicated significant increases in both lifespan and health span in laboratory models, including non-human primates.[7] Limited human studies showed significant health benefits with DR, including reversal of disease risk factors.[6] Although not a viable translational approach at the population level, interest has shifted in search of alternative dietary modifications (e.g., low-protein diets) or small-molecule DR mimetics (e.g., mammalian target of rapamycin [mTOR] inhibitors, see below) that can provide health benefits of DR without requiring reduced food consumption.
Exercise	A broad body of literature supports the health benefits of exercise that are consistent with increased healthspan.[8,9] However, poor compliance, especially in the elderly population, inhibits widespread practice. Interest now focuses on developing pharmacologic interventions that would synergize with lower levels of exercise.
mTOR inhibitors	In mice and simpler organisms (worms), rapamycin is very effective in prolonging lifespan/promoting health span. Treatment beginning late in life is sufficient to extend lifespan, reverse cardiac decline, and improve immune function in mice.[10] A recent study also reported that a rapamycin derivative significantly boosts immune function in elderly people.[11]
Metformin and acarbose	Metformin and acarbose, used often as antidiabetes drugs, shown to also enhance health span in mice, and limited lifespan extension.[12] Acarbose robustly extends lifespan in male mice, with modest life extension in female mice.[13] In a nonrandomized retrospective analysis, diabetic patients taking metformin have lower mortality compared to counterpart controls not taking metformin and may live longer than nondiabetics not receiving metformin.[14]

continued

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Table 2. (*continued*)

Intervention	Description
NAD precursors and Sirtuin activators	Verdin[15] reported that NAD precursors such as nicotinamide riboside and nicotinamide mononucleotide improve health span in mouse models of muscle aging and cognitive decline. The mechanism of action is not known, although it may involve activation of sirtuin NAD-dependent protein deacetylases along with enhanced mitochondrial function.[16] Sirtuin activators also improve health span and extend lifespan in mice.[17]
Modifiers of senescence and telomere dysfunction	Senescent cells accumulate during aging and secrete factors that promote inflammation and cancer.[18] Telomere dysfunction is a major cause of cell senescence, and attempts to enhance telomerase function offer promise for improving health span, although the possibility of increased cancer risk must be addressed.[19,20] Other approaches using genetic and pharmacological strategies to target and kill senescent cells enhance both lifespan and markers of health in short-lived mice with high levels of senescent cells.[21,22]
Hormonal and circulating factors	Age-related changes occurred in sex steroids, growth hormone, and insulin-like growth factor (IGF)-1 although the risks and benefits of hormone supplementation in aging remain largely controversial.[23] Heterochronic parabiosis experiments in which the circulatory system of an aged mouse when shared with that of a young mouse resulted in age-associated declines in several tissues including brain, muscle, liver, and heart,[24,25] possibly a result of humoral factors. Some progress has been made to define these factors,[26] and an effort is underway to determine whether transfusion of young plasma can delay Alzheimer's disease.[27]
Mitochondrial targeted therapeutics	Wang and Hekimi et al.[28] proposed that mitochondrial dysfunction is a major contributor to aging and age-related diseases, although the mechanisms are more complex than initially suggested by the Harman's Free Radical Theory of Aging. Attention has now turned to interventions that augment mitochondrial function, energetics, and biogenesis, including mitochondrial targeted antioxidants and NAD precursors.

Data Source: Adapted from Kaeberlein M, et al. (2015) Healthy aging: the ultimate preventative medicine. *Science*. 350:1191–1193. Reprinted with permission from AAAS.

Implications: Further research is needed to investigate dietary and food constituents that may delay the onset of aging and disease development. Although caloric restriction has been studied, better controlled studies may be needed to better evaluate the effect of caloric restriction and the mechanism involved in modifying aging.

Sources: (1) Kaeberlein M, et al. (2015) Healthy aging: the ultimate preventative medicine. *Science*. 350:1191–1193. (2) Kaeberlein M (2013) Longevity and aging. *F1000Prime Rep*. 5:5. (3) Gravekamp C, et al. (2013) Aging and cancer vaccines. *Crit Rev Oncog*. 18:585–595. (4) Olshansky SJ, et al. (2007) Pursuing the longevity dividend: scientific goals for an aging world. *Ann N Y Acad Sci.* 1114:11–13. (5) Goldman DP, et al. (2013) Substantial health and economic returns from delayed aging may warrant a new focus for medical research. *Health Aff (Millwood)*. 32:1698–1705. (6) Omodei D, et al. (2011) Calorie restriction and prevention of age-associated chronic disease. *FEBS Lett.* 585:1537–1542. (7) Colman RJ, et al. (2014) Caloric restriction reduces age-related and all-cause mortality in rhesus monkeys. *Nat Commun*. 5:3557. (8) Mercken EM, et al. (2012) Of mice and men: the benefits of caloric restriction, exercise, and mimetics. *Ageing Res Rev*. 11:390–398. (9) Wang BW, et al. (2002) Postponed development of disability in elderly runners: a 13-year longitudinal study. *Arch Intern Med*. 162:2285–2294. (10) Johnson SC (2013) mTOR is a key modulator of ageing and age-related disease. *Nature*. 493:338–345. (11) Mannick JB, et al. (2014) mTOR inhibition improves immune function in the elderly. *Sci Transl Med.* 6:268ra179. (12) De Haes W. et al. (2014) Metformin promotes lifespan through mitohormesis via the peroxiredoxin PRDX-2. *Proc Natl Acad Sci USA*. 111:E2501–E2509. (13) Harrison DE, et al. (2014). Acarbose, 17-α-estradiol, and nordihydroguaiaretic acid extend mouse lifespan preferentially in males. *Aging Cell.* 13;273–282. (14) Bannister CA, et al. (2014) Can people with type 2 diabetes live longer than those without? A comparison of mortality in people initiated with metformin or sulphonylurea monotherapy and matched, non-diabetic controls. *Diabetes Obes Metab.* 16:1165–1173. (15) Verdin E (2015) NAD^+ in aging, metabolism, and neurodegeneration. *Science.* 350:1208–1213. (16) Imai S, et al. (2014) NAD+ and sirtuins in aging and disease. *Trends Cell Biol.* 24:464–471. (17) Mitchell SJ, et al. (2014) The SIRT1 activator SRT1720 extends lifespan and improves health of mice fed a standard diet. *Cell Rep.* 6:836–843. (18) Campisi J, Robert L (2014) Cell senescence: role in aging and age-related diseases. *Interdiscip Top Gerontol.* 39:45–61. (19) Bernardes de Jesus B, et al. (2012) Potential of telomerase activation in extending health span and longevity. *Curr Opin Cell Biol*. 24:739–743. (20) Blackburn EH, et al. (2015) Human telomere biology: a contributory and interactive factor in aging, disease risks, and protection. *Science.* 350:1193–1198. (21) Baker DJ, et al. (2011) Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. *Nature.* 479:232–236. (22) Zhu Y, et al. (2015) The Achilles' heel of senescent cells: from transcriptome to senolytic drugs. *Aging Cell*. 14:644–658. (23) Zouboulis CC, et al. (2012) Hormonal therapy of intrinsic aging. *Rejuvenation Res.* 15:302–312. (24) Goodell MA, et al. (2015) Stem cells and healthy aging. *Science.* 350:1199–1203. (25) Conboy MJ, et al. (2013) Heterochronic parabiosis: historical perspective and methodological considerations for studies of aging and longevity. *Aging Cell*. 12:525–530. (26) Bitto A, Kaeberlein M (2014) Rejuvenation: it's in our blood. *Cell Metab*. 20:2–4. (27) Scudellari M (2015) Ageing research: blood to blood. *Nature.* 517:426–429. (28) Wang Y, Hekimi S (2015) Mitochondrial dysfunction and longevity in animals: untangling the knot. *Science.* 350:1204–1207.

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B. Diet and Diseases

1. Dietary Reference Intakes for Chronic Disease Endpoints

Dietary reference intake (DRI) values are used in Canada and the United States in dietary assessment of healthy populations and they provide nutrient-based intakes to prevent nutrient deficiency. However, most DRI values have not been established for intakes that affect chronic disease outcomes, despite growing evidence that supports a link. The increasingly aging population and growing prevalence of chronic diseases, overweight, and obesity, which predispose to chronic disease, underscore the importance of providing DRI guidance for chronic disease prevention and control.[1–3]

In March 2015, the DRI Committees of the US and Canadian governments held a joint workshop titled "Options for Consideration of Chronic Disease Endpoints for Dietary Reference Intakes." This workshop aimed to identify and evaluate key issues related to using chronic disease endpoints for setting DRIs and to provide information on whether/how to include chronic disease endpoints in setting DRI levels. Members of the working groups were selected from diverse backgrounds and were asked to address three key questions[1,2]: (1) What are the important evidentiary challenges for selecting and using chronic disease endpoints in future DRI reviews? (2) What intake-response models can future DRI committees consider when using chronic disease endpoints? and (3) What are the arguments for and against continuing to include chronic disease endpoints in future DRI reviews?

In October 2016, the DRI Working Committee and the National Academies of Sciences, Engineering, and Medicine (NAS) Food and Nutrition Board (FNB) held a meeting to share key learnings from the "Options" report, delivered by Drs. Christine Lewis Taylor (Office of Dietary Supplements) and Amanda MacFarlane (Nutrition Research Division, Health Canada).[4] The FNB committee will address the following areas:

- Accepting a specified level of confidence and strength of the evidence
- Determining causality of the chronic diseases
- Assessing dietary intakes
- Establishing biomarker causality pathways

A report titled "Options for Basing Dietary Reference Intakes (DRIs) on Chronic Disease Endpoints: Report From a Joint U.S/Canadian-Sponsored Workshop Group" was published in December 2016.[3] This report was written in preparation for the new DRI committee that will develop the "guiding principles" for assessing chronic disease–based DRIs. The report outlined a range of options (not consensus recommendations), including challenges and opportunities. The following is a summary of the report conclusions:

> This report identified the evidence-related and intake-response relation challenges that have hampered the inclusion of chronic disease endpoints in the derivation of DRIs with the use of a traditional framework and approach. The report presents several potential options to address those challenges. The next step will be to make decisions about the feasibility of including chronic disease endpoints in future DRI reviews and to determine which options and/or their adaptations warrant inclusion in guiding principles for basing DRI values on chronic disease endpoints. Traditional DRIs have always been based on adequacy for the apparently healthy population. However, when DRI values are based on chronic disease endpoints, the target population or populations might be narrower (e.g., individuals with high blood pressure or obesity).
>
> Although beyond the scope of this report, further consideration of how to define target populations when DRIs are based on reduction in chronic disease risk may be needed. The report also highlights several research opportunities that are key to the derivation of future DRIs based on chronic disease endpoints. Among the most salient examples of those opportunities are the need for qualified biomarkers of long-term intakes for a large array of nutritional variables (i.e., nutrients and other food substances), tools specifically designed to assess the quality of evidence required for setting DRIs, and novel statistical and other analytic methods for integrating diverse relations linking specific food components to multiple outcomes of interest.

Next Steps: The Joint US-Canadian DRI Working Group is collaborating with NAS to develop guiding principles for inclusion of chronic disease endpoints to be used by committees setting future DRIs. The project will build on the March 2015 workshop, panel discussions, and the December 2016 published report.[2,3] The project was scheduled to begin in summer 2016, with a report to be completed by fall 2017.

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Implications: (1) Establishment of DRI values for chronic disease endpoints will provide target-level guidance, which is critical for developing future personalized food and dietary interventions targeted for different chronic disease end points. It will also provide more definitive guidelines and incentives for future research, exploration, and innovation of novel ingredients and food products. The establishment of agreed-upon biomarkers for different disease end points will simplify the process not only for furnishing evidence in support of health claims for food products/diet programs for the industry but also for developing new health claims for regulation. (2) Having DRIs for chronic disease endpoints will pave the way for advancing research on nutrigenomics and precision foods and dietary interventions, learning from and keeping pace with the NIH National Precision Medicine Initiative. On the other hand, if the DRI Committee decides at the end of deliberation that current evidence is not sufficiently robust to establish DRI values for chronic disease endpoints, one possible outcome is that the committee will either delay or recommend against using chronic disease endpoints for setting DRIs.

Sources: (1) HHS (2015) Dietary Reference Intakes and Chronic Disease Endpoints Workshop. (2) NIH. Workshop webcasts**:** March 10, 2015 (Day 1) webcast and March 11, 2015 (Day 2) webcast [Video]. (3) Yetley EA, et al. (2016) Options for basing Dietary Reference Intakes (DRIs) on chronic disease endpoints: report from a joint US-/Canadian-sponsored working group. *Am J Clin Nutr.* doi: 10.3945/ajcn.116.139097. (4) MacFarlane A (2016) Workshop presentation.

C. Sodium and Mortality

1. Sodium and Health: U-Shaped or Linear Relationship Between Sodium and Cardiovascular Disease Mortality?

Studies have shown that sodium (salt) intake is linearly associated with blood pressure in hypertensives, although such an effect is less obvious in prehypertensives and normotensives.[1,2] Whether salt reduction also translates into a beneficial effect for reducing cardiovascular disease (CVD) and all-cause mortality remains to be confirmed.[1–3] Data on the lower ranges of sodium intakes are limited, and many of these studies reported confounding error and inaccurate sodium intake measurement.

The DASH Sodium (Dietary Approaches to Stop Hypertension) trial used three sodium dose-response levels and the investigators concluded on a significant and direct relationship between sodium intake and blood pressure levels among hypertensives and normotensives.[4] A recent Cochrane meta-analysis involving 35 trials[1] reported that a 100-mmol reduction in 24-hour urinary sodium led to a reduction in systolic/diastolic blood pressure of 5.4/2.8 mmHg among hypertensive individuals and 2.4/1.0 mmHg among normotensive individuals. A 2013 Institute of Medicine report[5] concluded that there was a link between high sodium intake and risk of stroke. However, that report also found that data for the effects of sodium intake below 2300 mg/24 h were limited, inconsistent, and inconclusive.[5]

To address these questions, Cook et al. conducted a meta-analysis, published in the *Journal of the American College of Cardiology*, investigating the relationship of sodium intake to CVD risk and mortality.[6]

The researchers examined the relationship between urinary sodium excretion and long-term mortality using the TOHP (Trials of Hypertension Prevention) phase 1 trial from 1987 to 1988, over 18 months, and phase II from 1990 to 1995, over 36 months. Participants in TOHP had sodium reduction interventions. The studies included multiple 24-hour urinary collections from prehypertensive adults aged 30–54 years. Posttrial deaths averaged over a median 24 years, using the National Death Index. The results revealed the following:

> Among 744 phase I and 2382 phase II participants on sodium reduction or control, 251 deaths occurred, representing a nonsignificant 15% lower risk the active intervention (hazard ratio [HR], 0.85; 95% confidence interval [CI], 0.66 to 1.09; $P = 0.19$). Among 2974 participants not assigned to an active sodium intervention, 272 deaths occurred. There was a direct linear association between average sodium intake and mortality, with an HR of 0.75, 0.95, 1.00, and 1.07 ($P = 0.30$) for <2300, 2300–<3600, 3600–<4800, and >4800 mg/24 h, respectively; and with an HR of 1.12 per 1000 mg/24 h (95% CI, 1.00 to 1.26; $P < 0.05$). The HR per unit increase in sodium/potassium ratio was 1.13 (95% CI: 1.01 to 1.27; $P < 0.04$).[6]

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The authors concluded that the study provided support for a linear relationship and no evidence of a J-shaped or U-shaped curve between sodium intake and mortality risk and total mortality. There was an increased risk of mortality for high sodium intake and a direct relationship with total mortality, even at levels below 2300 mg. The authors indicated that the results supported a benefit of reduced sodium and sodium/potassium intake on total mortality over a 20-year period.

- ***Implications:*** This study supports previous findings of a linear relationship between blood pressure and sodium intakes across a wide range of sodium intakes (<2300 to >4800 mg). Such linearity was also confirmed using the Na/K ratio measure. This study, unlike others, used urinary sodium excretion to measure sodium intakes, instead of food records as used in other studies. The 24-hour urine test is widely accepted but still has limitations for estimating sodium intake. Limitations of this study include its lack of power at the lower and higher sodium dosages. More research is needed to confirm this finding. Reducing sodium in foods as part of a dietary strategy to reduce blood pressure, CVD risk, or mortality may have added benefits from increasing potassium levels as well.

Sources: (1) He FJ, et al. (2013) Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *BMJ*. 346:f1325. (2) Aburto N, et al. (2013) Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ*. 346:f1326. (3) Whelton PK, et al. (1998) Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA*. 279:83946. (4) Sacks FM, et al. (2001) Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med*. 344:3–10. (5) Institute of Medicine (2013) *Sodium Intake in Populations: Assessment of Evidence*. Washington, DC: National Academies Press. (6) Cook NR, et al. (2016) Sodium intake and all-cause mortality over 20 years in the Trials of Hypertension Prevention. *J Am Coll Cardiol*. 68:1609–1617.

2. Blood Pressure and Vascular Risks: Reducing Blood Pressure Is Effective in Lowering Vascular Risk and Comorbidities Independent of Starting Baseline Blood Pressure

Lowering blood pressure is widely used to prevent development and progression of CVD and premature death.[1] However, less is known about the extent of the impact of blood pressure lowering as influenced by various factors, including individual variations in baseline blood pressure, presence of comorbidities, age, gender, or drug class. To address some of these questions, Ettehad et al. conducted a systematic review and meta-analysis of large-scale randomized controlled trials (RCTs) of blood pressure–lowering treatments performed between 1966 and 2015.[1] The study, supported in part by NIH, included all RCTs of blood pressure–lowering treatment with a minimum of 1000 patient-years of follow-up in each study group. No trials were excluded because of presence of baseline comorbidities, and trials of antihypertensive drugs for indications other than hypertension were eligible. Outcomes of major CVD events, coronary heart disease (CHD), stroke, heart failure, renal failure, and all-cause mortality were collected, and an inverse variance weighted fixed-effects meta-analysis was used to pool the estimates.

Findings of the study were published in the *Lancet* in 2016.[1] The authors identified 123 studies with 613,815 participants for the tabular meta-analysis. Some key findings are as follows[1]:

- Relative risk (RR) reductions were proportional to the magnitude of the blood pressure reductions obtained.
- Every 10-mmHg reduction in systolic blood pressure significantly reduced the risk of major CVD events (RR, 0.80; 95% CI, 0.77–0.83), CHD (0.83; 0.78–0.88), stroke (0.73; 0.68–0.77), and heart failure (0.72; 0.67–0.78), which, in the populations studied, led to a significant 13% reduction in all-cause mortality (0.87; 0.84–0.91).
- The effect on renal failure was not significant (0.95; 0.84–1.07). Similar proportional risk reductions (per 10-mmHg lower systolic blood pressure) were noted in trials with higher mean baseline systolic blood pressure and trials with lower mean baseline systolic blood pressure (all $P_{trend} > 0.05$).
- There was no clear evidence that proportional risk reductions in major CVD differed by baseline disease history, except for diabetes and chronic kidney disease.

These studies reaffirm that blood pressure lowering significantly reduces vascular risk across various baseline blood pressure levels and comorbidities, supporting a strong case for reducing systolic blood pressures below 130 mmHg and for providing blood pressure–lowering treatment to individuals with a history of CVD, CHD, stroke, diabetes, heart failure, and chronic kidney disease.

- ***Implications:*** This study raises an interesting research question regarding whether the magnitude of change in blood pressure is influenced by (1) different starting baseline sodium intake levels and (2)

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different magnitudes of sodium reduction required to achieve targets. In addition, questions remain as to whether these effects are influenced by age, gender, ethnicity, baseline blood pressures, comorbidities, diet patterns, and drug treatments. To date, little is known about the benefit of sodium reduction to reduce blood pressure when used as an adjunct intervention when different drug treatments (beta blockers, diuretics, calcium channel blockers, statins) are used for reducing vascular risks.

Source: (1) Ettehad D, et al. (2016) Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet.* 387(10022):957–967.

D. ICHNR Releases First United States National Nutrition Research Roadmap for 2016–2021

In March 2016, the Interagency Committee on Human Nutrition Research (ICHNR) released the first Nutrition Research Roadmap for 2016–2021 with the purpose to guide federal nutrition research focus on research that can lead to more individualized advice for promoting health and preventing disease.[1] The roadmap is the result of more than a year of interagency collaboration among government, academia, and the private sector and integration of public comments.

The roadmap, co-chaired jointly by Catherine Woteki, PhD (USDA Under Secretary for Research, Education, and Economics & Chief Scientist), and Karen B. DeSalvo, MD (HHS Acting Assistant Secretary for Health), involved representatives from 20 separate federal agencies with an interest in nutrition research, including HHS, USDA, the Department of Defense (DoD), Department of Commerce, the Federal Trade Commission (FTC), the National Aeronautics and Space Administration, the US Agency for International Development, the Environmental Protection Agency (EPA), the Veterans Health Administration (VHA), and the White House Office of Science and Technology Policy.

According to ICHNR, the roadmap underscores the importance of understanding the role of nutrition for optimal performance and military readiness.[1] The timely release of the roadmap is important at a time when public policies and guidelines on diet and nutrition are under criticism of constant changes.

The roadmap identifies research gaps concerning nutrition-related chronic diseases and health disparities, including among pregnant women, children, and older adults. It provides a unified approach to addressing research needs and funding priorities to address these research needs. The roadmap identified the following:

- Three priority nutrition research questions and critical topics for focus in 2016–2021 (Box 1).

Box 1. Three Priority Nutrition Research Questions for 2016–2021

Question 1. How can we better understand and define eating patterns to improve and sustain health?

- How do we enhance our understanding of the role of nutrition in health promotion and disease?
- How do we enhance our understanding of individual differences in nutritional status and variability in response to diet?
- How do we enhance population-level food- and nutrition-related health monitoring systems and their integration with other data systems to increase our ability to evaluate change in nutritional and health status, as well as in the food supply, composition, and consumption?

Question 2. What can be done to help people choose healthy eating patterns?

- How can we more effectively characterize the interactions among the demographic, behavioral, lifestyle, social, cultural, economic, occupational, and environmental factors that influence eating choices?
- How do we develop, enhance, and evaluate interventions at multiple levels to improve and sustain healthy eating patterns?
- How can interdisciplinary research identify effective approaches to enhance the environmental sustainability of healthy eating patterns?

Question 3. How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?

- How can we enhance innovation in measuring dietary exposure, including use of biomarkers?
- How can basic biobehavioral science be applied to better understand eating behaviors?
- How can we use behavioral economics theories and other social science innovations to improve eating patterns?
- How can we advance nutritional sciences through the use of research innovations involving Big Data?

Source: ICHNR.[1]

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Box 2. Federal Agencies Addressing Each Nutrition Area

Agency	Commerce	DoD	EPA	FTC	HHS	NASA	USAID	USDA	VHA
Question 1. How can we better understand and define eating patterns to improve and sustain health?									
Q1T1: Health promotion and disease prevention and treatment	X	X		X	X	X	X	X	X
Q1T2: Individual differences including "omics"		X			X	X		X	X
Q1T3: Population-level monitoring	X	X	X		X		X	X	X
Question 2. What can be done to help people choose healthy eating patterns?									
Q2T1: Influences on eating patterns	X	X		X	X	X	X	X	X
Q2T2: Interventions		X		X	X	X	X	X	X
Q2T3: Systems science					X				X
Q2T4: Environmental sustainability	X	X					X	X	X
Question 3. How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?									
Q3T1: Assessing dietary exposures	X	X	X	X	X	X	X	X	X
Q3T2: Biobehavioral science		X			X	X	X	X	X
Q3T3: Behavioral economics		X		X	X			X	X
Q3T4: Big Data	X	X		X	X		X	X	X

Source: ICHNR.[1]

Box 3. Example of Short- and Long-Term Research Needs Identified for Question 1, Topic 1

Question 1. How can we better understand and define eating patterns to improve and sustain health?

Question 1, Topic 1 (Q1T1). How do we enhance our understanding of the role of nutrition in health promotion and disease prevention and treatment?

Research and Resource Needs

Short-Term Initiatives

- Incorporate the examination of food, nutrition, eating, and activity patterns in research on the management of multiple complex comorbid diseases including the assessment of malnutrition.
- Support mechanistic research in humans to establish causal relationship between nutrition and disease pathophysiology.
- Support mechanistic research to understand how nutritional status affects individuals' response to different types of physical activity across the lifespan.
- Examine the role of nutrition, physical activity, and other health habits during pregnancy/gestation and early childhood in the support of good health and the avoidance of adverse health outcomes throughout the lifespan.
- Explore the potential to incorporate research on the role of nutrition in brain function within the context of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative.
- Expand the exploration of the association of eating patterns with cause-specific morbidity and mortality within large epidemiologic cohorts.
- Explore the potential to merge dietary and nutritional data across multiple existing prospective cohort studies, including efforts such as the National Cancer Institute (NCI) Cohort Consortium, to conduct meta-analyses on the association of nutrition, food, and eating patterns with multiple disease outcomes.

Long-Term Initiatives

- Encourage collection of nutrition and activity-related data within the health care delivery systems for the integration of long-term clinical care information and health information systems with data for disease outcomes including the assessment of malnutrition.
- Examine the role of nutrition, physical activity, and other health habits in the support of good health and the avoidance of adverse health outcomes in older individuals, including those who are healthy with minimal chronic conditions, as well as those with complex comorbid conditions, and cognitive and physical disabilities.

Source: ICHNR.[1]

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- Federal agencies with human nutrition programs that have relevance to addressing each topic area (Box 2).
- Short and long term research initiatives (examples of select short- and long-term research needs identified for Question 1 by the agencies are shown in Box 3)

Each topic has proposed short- and long-term initiatives. For a complete list of all short-term and long-term research needs identified for all four questions including those by the various agencies, please refer to the reference source provided below.

Implications: The roadmap nutrition questions and short- and long-term initiatives can, for the first time, provide a unified and common foundational food and nutrition framework from which to build research that can improve and promote healthier diet patterns. ILSI North America has collaborated with NIH and USDA on initiatives related to establishment of guiding principles for public-private partnerships, as well as the development of a pilot test project on a "branded food products database for public health."

Source: (1) ICHNR (2016) *National Nutrition Research Roadmap 2016-2021: Advancing Nutrition Research to Improve and Sustain Health*. Washington, DC: ICHNR.

E. NIH Charts 10-Year Nutrition Science Path

In 2016, NIH established a Nutrition Research Task Force (NRTF), which comprises members from NIH agencies such as the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Heart, Lung, and Blood Institute (NHLBI), the National Cancer Institute (NCI), the National Institute on Aging (NIA), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).[1] "We hope that the strategic planning will encourage scientists to conduct innovative and really ground-changing studies in nutrition as they relate to health," stated Griffin P. Rodgers, MD, NIDDK director and NRTF co-chair.[1]

In an interview with *JAMA*, Dr. Rodgers emphasized the importance of cross-cutting disciplinary approaches to research, stating that[1]:

> The formation of the NIH Office of Nutrition Research aimed to help NIH develop a strategic plan to expand its nutrition research. One of the many tasks that will be tackled by this new office will be to review published nutrition research. And we're looking at the strategic planning effort really to guide nutrition research for the next 10 years and to identify priorities and to help guide NIH institutes and centers to build research initiatives and collaborations to fill some of the gaps and follow on advances that suggest promising opportunities. The strategic planning effort will be over the next 2 years with the final plan in October 2018, which will not only include the plan but also the implementation and communication strategy.

Dr. Rodgers[1] identified the following preliminary areas of interest for the NRTF:

- Dietary and physical activity assessments currently rely on recall, which is an unreliable method of data collection. "This is currently the state of the art, so we've not been able to measure accurately what and how much we're eating," said Dr. Rodgers. He added that researchers are currently developing innovative smartphone apps and other technologies that could lead to more objective and accurate ways to measure food intake and physical activity.
- Development of a strategic planning effort that cuts across a wide range of diseases, such as diabetes, cancer, obesity, and heart disease.
- Studies on the effects of certain food intake on human growth and development.
- Genetic influence on human nutrition and metabolism.
- The effect of the gut microbiome and its likely role in nutrition.
- An emerging and very interesting basic science research area is food intake as it relates to the timing of the meal. Studies in mice suggest that restricting eating to shorter periods during the day might lead to metabolic benefits that could promote weight loss, if calories remain unchanged. We know from several studies that healthy metabolism is tied closely to circadian rhythms and that our bodies more effectively process and digest foods during the day. The mouse studies may help to explain metabolic problems observed in people who, for example, work night shifts in which their circadian rhythms and their eating are out of sync.
- Physical activity has many beneficial effects on health and weight control, as well as metabolic and cardiovascular health.
- Insulin resistance and its role in obesity and diabetes may be involved in other conditions, such as certain types of cancers or polycystic ovary syndrome and perhaps in the brain. Animal models of Alzheimer's

disease show a pattern of insulin resistance. In fact, some people call this Alzheimer's disease type 3 diabetes.

- Another area covered was the intergenerational transmission of type 2 diabetes risk, where environmental influence may begin *in utero*. What the mother is exposed to in terms of her metabolic status and her nutrition may imprint on the developing infant, something that will be played out decades later in terms of diseases like diabetes, obesity, and so forth.

Finally, Dr. Rodgers mentioned that although the NIH Nutrition Plan is not involved in the Dietary Guidelines process, NIH does provide comments to the DGAC and review its recommendations.

Implications: The NRTF will benefit from input from the food and nutrition communities to identify areas of public health issues and opportunities. Many of the potential areas identified by Dr. Rodgers at NIDDK are also areas of similar interest to many of ILSI's members, such as improvement of technologies to better assess dietary intake and physical activity, the diet-gut microbiome relationship in health and diseases, diet and chronic diseases (obesity, type 2 diabetes, CVD), child-maternal health and nutrition (including neonatal development), diet (macronutrients), and obesity.

Source: (1) Abbasi J (2016) NIH charts a path for nutrition science. *JAMA*. doi:10.1001/jama.2016.18217.

F. Effects of Circadian Rhythm on Eating Patterns, Sleep, and Health

Understanding the mechanisms by which food, light, and ambient temperature affect the daily sleep-wake cycle and metabolism has increasing importance for humans who are living under diverse work schedules, lifestyles, and food preferences,.

—Satchidananda Panda (2016)[1]

Most species, including humans, undergo rhythm changes in their behavior and physiology regulated by the daily dark/light cycle governed by a biological clock located in the two brain suprachiasmatic nuclei. The circadian cycles have periodicity of approximately 24 hours and they can be synchronized to environmental time signals but can also function in the absence of such signals. The internal "clock" consists of an "array of genes and the protein products they encode."[1] These chemicals regulate cellular metabolic and physiological functions throughout the body. Disruptions of the circadian rhythm (CR) can interfere with normal function and impacts an organism's health and well being (Table 3).[1] Recent interest in research has focused on the effect of CR on nutrition and energy metabolism, as well as factors that disrupt the biological clocks and subsequent consequences on health. To date, many factors have been identified, including alcohol, sleep, diet, fasting duration, physical activity, medications, body weight, and so forth.[2–5]

Panda and his team at the Salk Institute have contributed to recent knowledge on the link between CR and eating patterns, time-restricted feeding (TRF), and sleep-wake cycles on health. Using a method involving mobile devices that provided a 24-hour data feed on eating, sleep, and food pattern behavior, these investigators were able to link eating behavior and sleep patterns to physiological outcomes in animal and human models. The scientists believed that cyclical expression of cell-autonomous circadian clock components and key metabolic regulators often coordinate discordant and distant cellular activities to maintain efficient metabolism. Disruptions to these cycles, either by genetic alterations or light/dark cycles (as in humans) via eating patterns, contribute to obesity and metabolic dysfunction (Figure 9).

TRF and Metabolism

TRF usually refers to time of access to food reduced to a few hours without caloric restriction. TRF maintains normal metabolic cycles and reduces blood lipid, glucose, and body weight, risk factors of obesity and dysmetabolism. The mechanism by which TRF imparts its benefits is not fully understood but "likely involves entrainment of metabolically active organs through gut signaling. Understanding the relationship of feeding pattern and metabolism could yield novel therapies for the obesity pandemic."

TRF and the Gut Microbiome

With regard to the effects of TRF on the gut microbiome, Panda et al. proposed that a cascade of events are involved in regulating feeding rhythms: for example, dynamic fluctuation of the gut microbiome could induce changes in the levels of gut short-chain fatty acids (SCFAs), causing cyclical fluctuation of GPR43 activation, which then downregulates insulin signaling in adipocytes, promoting the utilization of lipids in other ways, hence maintaining metabolic homeostasis. Dynamic fluctuations in the gut microbiome can also trigger cyclical fluctuation of

Table 3. Effects of Circadian Rhythm Disruption

Circadian Rhythm Disruption or DIO	Time-restricted feeding	Potential mechanism
Obesity	↓Fat, ↑Lean mass	↓Plasma- and ↓Liver- triglycerides
Glucose intolerance/ Insulin resistance	Improved glucose homeostasis	↓Gluconeogenesis ↑PPP and ↑ TCA cycle
Gut Dysbiosis	Diverse and dynamic	Altered digestion, absorption, and excretion of nutrients and bile acids
Cardiovascular Diseases	↓Arrhythmia and improved cardiac function*	ATP dependent chaperone and improved mitochondria function
Chronic inflammation	↓Tissue inflammation	↓Macrophage infiltration of WAT ↓ IL6 and TNFα
Liver diseases	↓Fibrosis and ↓hepatic fat deposit	↓ Fatty acid synthesis, ↑ β oxidation mitochondria volume
Increased cancer risk	↓Risk for breast cancer# and ↑ breast cancer prognosis	Improved metabolic homeostasis reduced inflammation
Hypercholesterolemia	↓Cholesterol	↑Cholesterol metabolism to bile acids
Sleep disorders	↑Sleep quality# and ↑quantity*	Consolidation of activity and rest
Compromised muscle function	↑Endurance and ↑flight index*	Ketone bodies, creatine metabolism

Source: Adapted from Dr. Satchidananda Panda (Salk Institute), with permission from the author. Based on Panda.[1]

Figure 9. Effects of Food on Circadian Rhythm

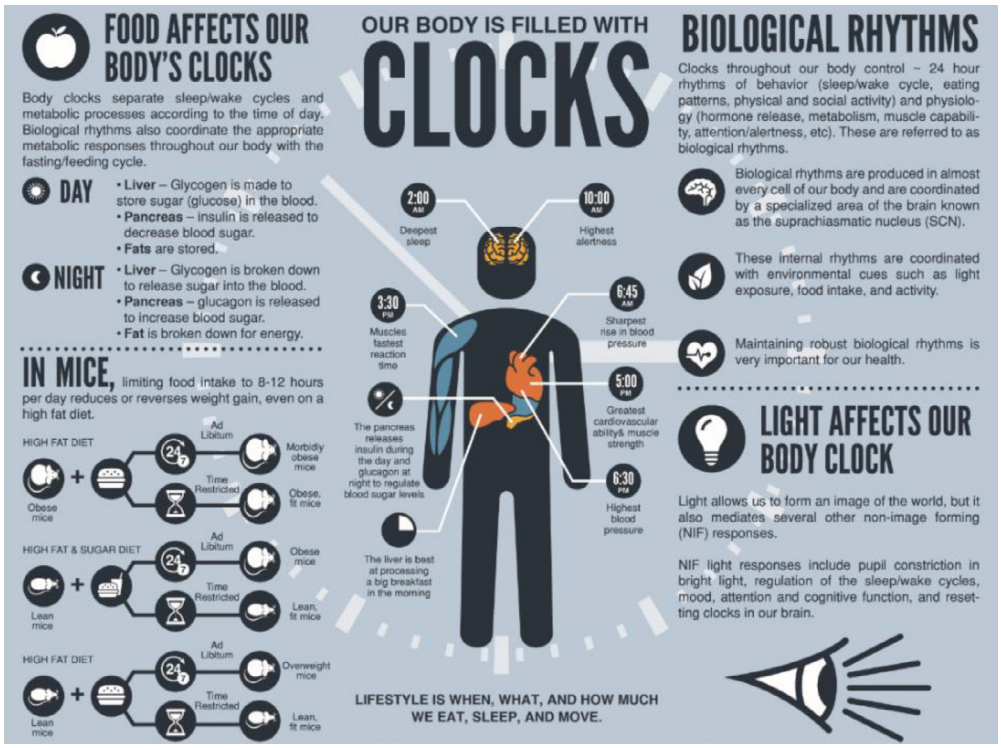

Image courtesy of Satchidananda Panda (Salk Institute).

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primary and secondary bile acids (BAs), which can modulate FXR and TGR5 activation and downstream signaling, affecting energy expenditure and influencing cholesterol, lipid, and glucose homeostasis. When normal feeding rhythms are perturbed with DIO, this leads to a cascade of disrupted cyclical fluctuations of the gut microbiome that, in turn, alter the luminal SCFA profile or BA profile, leading to constant suppression of GPR43 signaling and a continuous increase in insulin-mediated lipid uptake in adipocytes. Few studies have investigated how each single agent discussed can affect circadian biology. It will be exciting to determine, by investigating each of these complex and intertwined pathways, the mechanism by which meal timing can promote optimal metabolic health.

- ***Implications:*** Research on CR effects on eating patterns and health is noteworthy for nutrition and food research. Maintaining CR is critical for normal metabolic (nutrient) homeostasis. Disruption of CR has been shown to negate health outcomes. TRF research needs further support, as it has direct relevance to food and eating pattern behavior especially when targeting diets toward subpopulations. Panda et al. proposed a pathway whereby dietary components and the gut microbiome may affect CR and vice versa. This field warrants further research.

Sources: (1) Panda S (2016) Circadian physiology of metabolism. *Science*. 354:1008–1015. (2) Vitaterna MH, et al. (2016) Overview of circadian rhythms. (3) Ray LB, et al. (2016) On the clock. *Science*. 354:986–987. (4) Zarrinpar A, et al. (2016) Daily eating patterns and their impact on health and disease. *Trends Endocrinol Metab*. 27:69–83.

G. Gut Microbes and the Brain: Paradigm Shift in Neuroscience

Research has shown the complexity, diversity, and active role that the gut microbiome may play in multiple organ functions beyond the gut (skin, immune system, reproductive system, brain, etc.).[1–3] There is ongoing interest in understanding (1) the role of the human gut microbiome, (2) what derivatives of microbial activities may be involved in chronic disease pathogenesis, and (3) what effect preventive measures (e.g., diet, including prebiotics and probiotics, as well as exercise and stress management) might play to reduce the pathogenic effects of microbial activities. Recent interest has turned to whether the gut microbiome has a mediating role in brain function. Mayer et al.[3] reported that a "growing body of preclinical literature demonstrated bidirectional signaling between the brain and the gut microbiome, involving multiple neurocrine and endocrine signaling pathways. While psychological and physical stressors can affect the composition and metabolic activity of the gut microbiota, experimental changes to the gut microbiome can affect emotional behavior and related brain systems."[2–6]

These findings have led to some postulations that manipulating changes (e.g., antibiotics, stressors, dietary, probiotics) to the gut microbiome may present opportunities to alter the pathophysiology of some human brain diseases, including autism spectrum disorder, anxiety, depression, and chronic pain. Ongoing large-scale population-based studies of the gut microbiome and brain imaging studies looking at the effect of gut microbiome modulation on brain responses to emotion-related stimuli are seeking to validate these speculations.[4–10]

Mayer et al.[3] concluded that:

> Not only is the concept of gut-microbiome-brain interactions in health and disease paradigm breaking, the emerging data-driven, analytical methodologies that are required to pursue the integration of massive amounts of data are equally revolutionary. It is difficult to predict the trajectory of [this] exciting period of discovery: Will the gut microbiome add paradigm-transforming insights to our existing understanding of human brain function in health and disease, resulting in novel therapies, or will it represent an incremental step in understanding the inner workings of our brains? The next few years of research hold the potential of uncovering intriguing connections between gut bacteria and neurological conditions that may possibly impact human health.

- ***Implications:*** The possibility that dietary and food components can influence brain function and disorders modulated via the gut microbiome presents an intriguing opportunity to explore food-based interventions for brain dysfunction. However, more well-controlled and human studies are needed to further advance this intriguing early gut-brain relationship. Additionally, any potential of magnitude of effect needs to be considered to avoid extrapolating to implausible impacts.

Sources: (1) Gonzalez A, et al. (2012) Advancing analytical algorithms and pipelines for billions of microbial sequences. *Curr Opin Biotechnol*. 23:64–71. (2) Kuczynski J, et al. (2012) Experimental and analytical tools for studying the human microbiome. *Nat Rev Genet.* 2012;13:47–58. (3) Mayer EA, et al. (2014) Gut microbes and the brain: paradigm shift in neuroscience. *J Neurosci.* 34:15490–1549. (4) de Theije CG, et al. (2014) Autistic-like behavioural and neurochemical changes in a mouse model of food allergy. *Behav Brain Res.* 261:265–274. (5) Diaz Heijtz R, et al. (2011) Normal gut microbiota modulates brain

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development and behavior. *Proc Natl Acad Sci USA*. 108:3047–3052. (6) Dinan TG, et al. (2013) Psychobiotics: a novel class of psychotropic. *Biol Psychiatry*. 74:720–726. (7) Distrutti E, et al. (2014) Modulation of intestinal microbiota by the probiotic VSL#3 resets brain gene expression and ameliorates the age-related deficit in LTP. *PLoS One*. 9:e106503. (8) Messaoudi M, et al. (2011) Assessment of psychotropic-like properties of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in rats and human subjects. *Br J Nutr*. 105:755–764. (9) Moayyedi P, et al. (2010) The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Gut*. 59:325–332. (10) Moloney RD, et al. (2014) The microbiome: stress, health and disease. *Mamm Genome*. 25:49–74.

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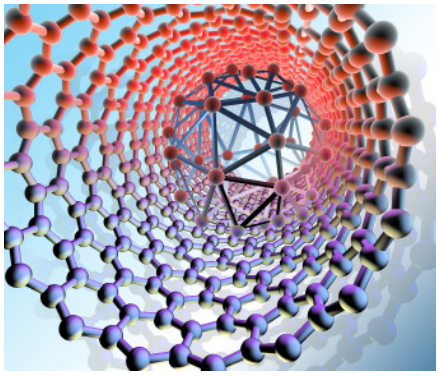
3 Emerging Technology Innovations and Discoveries

A. Technologies Are Reshaping Life Science Research and Approaches to Human Health



"Life sciences" is an umbrella term to describe loosely the study of living organisms, their processes, interrelationships, and connections to the environment. In recent years, life sciences have become progressively more cross-disciplinary: exploring the potential of technology to improve the quality and longevity of physical, social, and mental health both for individuals and populations...

—Remi Erikson, CEO of DNV-GEL (2016)

1. Top 10 Technologies Impacting Biomedical and Energy Innovation

In 2016, the World Economic Forum (WEF) convened an expert panel of executives from diverse background experience (business, science, medicine, physical sciences, engineering, social sciences) and identified the top 10 technology trends that will have profound future impact in the scientific fields and will be instrumental in future biomedical, health, and energy research, and breakthroughs.[1]

1. Nanosensors and the Internet of Nanothings (tiny sensors that can connect to the web)
2. Next-generation batteries with large-scale power storage
3. Blockchain A revolutionary decentralized trust system
4. Two-dimensional materials (these "wonder materials" are becoming increasingly affordable)
5. Autonomous vehicles (self-driving cars coming sooner than expected)
6. Organs-on-chips (using chips instead of organs for medical testing purposes)
7. Perovskite solar cells (making progress toward ubiquitous solar power generation)
8. Open artificial intelligence (AI) ecosystems (from artificial to contextual intelligence)
9. Optogenetics (using light to control genetically modified neurons)
10. Systems metabolic engineering of chemicals from sources' microorganisms

Implications: Transformation in bioinspired technologies is not feasible if advances in data and computational sciences have not continued to progress, paving the way for next-generation bioinspired technologies to develop more intelligent products.

Source: (1) World Economic Forum (2016).

B. The Emergence of Convergence in Technology Innovation and Science

In 2016, we interviewed Dr. Andrew Maynard, a member of the WEF Global Futures Council on the Future of Technology, Values, and Policy and currently Director of the Risk Innovation Lab and Professor in the School for the Future of Innovation in Society at Arizona State University, on his insights into the future of technology trends in the life sciences. Dr. Maynard highlighted the emerging importance of "convergence" between multiple technology platforms as the new approach for breakthroughs in manufacturing, processing, and biomedical research. The integration of Big Data, AI, computational sciences, sensor advancement, systems biology, cellular genomics, and nano- and material technologies has opened new doors for combination technologies targeted to customized applications.

The 10 technologies identified above by the WEF have a common theme—the result of unified research contributions from cross-cutting disciplines converging on common goals. According to the Wyss Institute at Harvard University, "Convergence science is now the new norm approach to solve multicomplex problems."[1] The convergence science approach is gaining popularity as an efficient and effective way to solve complex multidisciplinary problems. The Wyss Institute has successfully applied convergence science in its bioinspired research programs. Advances in bioengineering and computational and data science have transformed life science by applying physical and engineering principles to solve biomedical problems. Often, the convergence science approach

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in research produces unexpected and synergistic transformations. Examples of such breakthroughs include nanotechnology, genomics, cell engineering, photonic tools, and data science/mathematical modeling. Recent advances in material sciences combined with physical and chemical sciences have enabled research at the atomic, molecular, and system biology levels exemplified in stem cells, bioengineered synthetic organs, micro-devices, and computational modeling to study cell function, tissue regeneration, and complex organ physiology.

- ***Implications:*** Convergence science is breaking ground for breakthroughs in biological sciences and digital systems. It has enabled the proliferation of a new field of "biologically inspired engineering," an offspring of unification between life sciences, engineering, and physical sciences. This integration is transforming the biomedical areas and leading to a better understanding of living beings. In the food and nutrition fields, a convergence science approach has not yet been fully applied, and the tools and technologies from bioinspired research programs have yet to be taken advantage of for food and nutrition research and technology programs.

Source: (1) Wyss Institute at Harvard (2016).

C. Emerging Technologies to Watch

Through the applications of biological principles to develop new engineering solutions for medicine, and other nonmedical fields never before touched by the biology revolution. In the near future, it is conceivable that the boundary between living and nonliving systems is slowly becoming an integrated entity.

Wyss Institute at Harvard University (2016)

1. Next-Generation Optogenetics: Exploring Aging Plasticity and Alzheimer's Pathogenesis

With optogenetics, for the first time in history neuroscientists can tune the activity of specific brain circuits to determine their contribution to functions such as perception, attention, memory and decision-making.

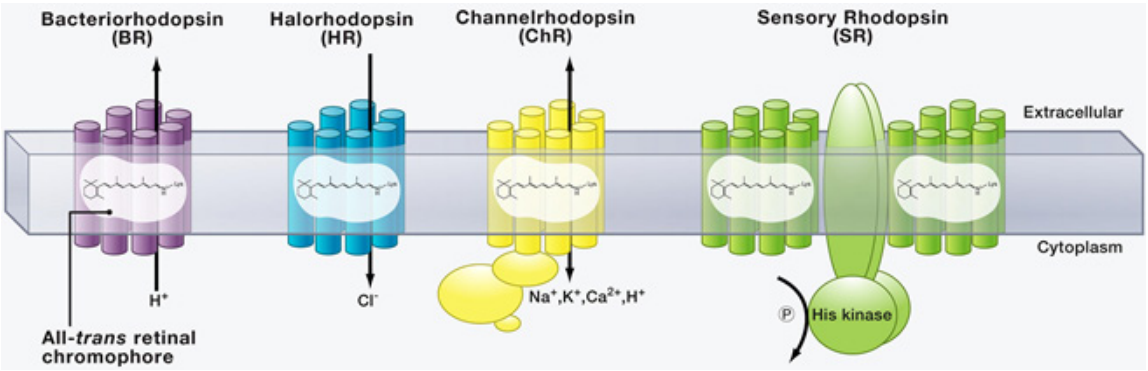
—Bill Newsome, Director of the Stanford Neurosciences Institute and Professor of Neurology (2014)[1]

It recent years, optogenetics has captured the interest of NIH to advance this technology for research on brain plasticity and neural activities. The principles behind optogenetics technology can be explained in Figure 10.[2,3]

Neural activities undergo profound changes as individuals age that significantly affect behavioral changes in older adults. According to the NIH National Institute on Aging (NIA),[4]

> Such neural plastic changes include a decrease in inhibition of unnecessary or undesirable neural activity or an increase of neural activities in additional brain regions presumably in response to functional declines in primary neural circuits. However, empirical evidence has been lacking to determine the causal relationships between these neural activity changes and the behavioral outcomes. In addition, it is not known whether reversing these neural activity changes would alter the associated age-related

Figure 10. Principles of Optogenetics



Source: Reprinted from *Cell*, Volume 147, Edition 7, Zhang F, Vierock J, Yizhar O, Fenno LE, Tsunoda S, Kianianmomeni A, Prigge M, Berndt A, Cushman J, Polle J, Magnuson J, Hegemann P, Deisseroth K, The microbial opsin family of optogenetic tools, Pages 1446–1457, Copyright 2011, with permission from Elsevier.

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behavioral outcomes. Recent development and advances in optogenetic technologies has enabled the ability to control the level of neural activities at a single neuron level in living model organisms through the control of light at appropriate wavelengths.

To study neural systems, the approach relies on single-component microbial light-activated regulators of transmembrane conductance, called opsins. These opsins can either activate neuronal firing by light, such as channel rhodopsin, or inhibit neural activities in response to light, such as halo rhodopsins, bacteriorhodopsins, or archae rhodopsins. They can be expressed in neurons using cell type–specific promoters, and fiber optic- and laser diode–based *in vivo* light delivery. With the switch-on of light at an appropriate wavelength, neural activity in molecularly defined circuits or ensembles can be elevated or suppressed in living organisms, including rodents and nonhuman primates, in a well-controlled manner. New-generation optogenetic systems allow for multicolor and sophisticated spatial and temporal control of neural activity, thus enabling a broad array of applications of optogenetic tools to study neural systems at multiple levels, either *in vitro* or *in vivo*. Although optogenetic technologies have been utilized to address many fundamental questions in a variety of neuroscience disciplines, their application to aging and/or AD research remains limited.

As a result, the NIA has provided funding support since 2013 to "encourage broad applications of optogenetic-based technologies to study basic and/or translational questions in aging neural systems (including sensory, motor, cognitive, emotional, sleep/circadian, epileptogenic, neurovascular and autonomic) and AD. Applicants are encouraged to develop and/or incorporate optogenetic tools particularly suitable for aging and/or AD research. Studies combining optogenetics with other cellular, molecular, genetic, neurophysiological, neuroimaging, and/or behavioral methodologies are also encouraged. Study of a wide variety of cellular systems and model organisms of aging or AD, preferably in mammalian systems, (rodents and nonhuman primates) is encouraged."[5]

- ***Implications:*** Although optogenetics technology has not yet gained much headway in food and nutrition, it certainly warrants further monitoring as a probe for future research on the impact of diet and nutrition intervention on brain development, plasticity, and aging.

Sources: (1) Stanford University (2014). (2) Zhang F, et al. (2011) The microbial opsin family of optogenetic tools. *Cell.* 2011;147(7):1446–1457. (3) Guru A, et al. (2015) Making sense of optogenetics. *Int J Neuropsychopharmacol.* 2015;18(11):pyv079. (4) NIA (2016). (5) NIA (2012).

2. DNA Nanostructures for Target Compound (Drug) Delivery

Customizable nanostructures can be built using DNA. Investigators at the Wyss Institute at Harvard University have developed a method that can build arbitrarily shaped nanostructures using DNA, with a focus on translating the technology toward nanofabrication and drug delivery applications.[1,2]

"DNA-brick self-assembly" is currently a proprietary technology that uses short, synthetic strands of DNA that work like interlocking jig jaw pieces. It utilizes the ability to program DNA to form into preset shapes based on DNA base pairs, such that binding A (adenosine) only binds to T (thymine) and C (cytosine) only binds to G (guanine).

Another DNA nanofabrication method, DNA origami, uses rules of programmable self-assembly in which strands of DNA are directed to form custom, specific shapes of tightly cross-linked double helices using a single strand of DNA as a "scaffold." The scaffold is formed using base pairing from numerous short, chemically synthesized DNA strands that are specially designed using computer software. In this manner, DNA origami is now being used to create 3D structures, with the goal of building nanoscale tools and drug delivery devices.

The combination of DNA nanostructures is precise at the nanoscale and can be rapidly assembled within hours, and its capability to integrate DNA components into complex architectures all make it an attractive method for nanofabrication.

- ***Implications:*** Can nutrients and bioactive compounds be delivered using this method for understanding nutrient-DNA/gene interaction?

Sources: (1) Wyss Institute (2009). (2) Wyss Institute (2012).

3. Genetically Engineered Biofilms: Potential Probiotics?

Biofilms, produced by communities of bacteria, are slimy tough matrices consisting of extracellular materials of mucopolysaccharides, proteins, and others. During biofilm formation, individual bacteria release proteins that

self-assemble outside the cell. This process can be controlled by using genetic engineering to harness it to target for specific therapeutics and biologics applications (e.g., potentially a new generation of probiotics targeted for specific health applications).[1–3]

A novel protein engineering system, BIND (Biofilm-Integrated Nanofiber Display), developed by scientists at the Wyss Institute, could be used for future probiotic therapies and foundry templates for synthesizing biomaterials. These biofilms of microbes could be customized as probiotic pills. Ingestion of this probiotic would colonize microbiota in the gastrointestinal tract in patients with chronic inflammatory diseases. There, the bacteria would produce and secrete anti-inflammatory factors. These biofilms could be designed for use in treating inflammatory bowel diseases, cleaning up polluted rivers, manufacturing pharmaceutical products, fabricating new textiles, and more.

- ***Implications:*** This approach presents opportunity for biofilms to be consumed or integrated into food systems as well. However, whether these biofilms can be modified to withstand food processing and shelf-life conditions needs further research in addition to regulatory approval.

Sources: (1) Wyss Institute (2014). (2) Wyss Institute (2015). (3) Nguyen PQ, et al. (2014) Programmable biofilm-based materials from engineered curli nanofibres. *Nat Commun*. 2014;5:4945.

4. Mannose Binding Protein: A New Way to Capture Pathogens

Genetically engineered mannose-binding lectin (MBL) protein, called FcMBL, is used to capture viruses, fungi, parasites, toxins, and dead pathogen fragments released after antibiotic killing. A broad base of FcMBL platforms can be developed to trap various pathogen combinations.[1]

Pathogenic contaminants are found in foods, in the environment, and in manufacturing processes, requiring early detection, confirmation, identification, characterization, and removal options (i.e., therapeutics, decontaminants, etc).

Native MBL binds to multiple microbial classes (Gram-positive/negative bacteria, fungi, viruses, and parasites). Scientists at Wyss Institute[1] genetically engineered MBL by deleting complicating complement activation and coagulation-promoting domains and fusing it to an antibody Fc fragment (FcMBL), which stabilizes the molecule and enables rapid purification. FcMBL retains the ability of native MBL to bind to the same broad spectrum of pathogens, and it is easily coupled to surfaces for pathogen capture or biologically active therapeutics or diagnostic markers; it also can be produced with a thousand-fold lower cost and exhibits higher stability. Importantly, FcMBL captures not only live and intact pathogens, but also toxic fragments and toxins released by dead pathogens, known as pathogen-associated molecular patterns (PAMPs), which trigger the inflammatory cascade that leads to organ injury and sepsis.

- ***Implications:*** This approach has potential applications in food safety. It offers a broad-spectrum, pathogen-extracting method that simulates the pathogen- and toxin-removal functions of the human spleen.

Source: (1) Wyss Institute (2016).

D. Emerging Discoveries

1. Reducing Time From Discovery to Applications in Half: The 2011 White House Material Genome Initiative

In 2011, President Obama mandated that the United States must have a plan to accelerate the speed to market from discovery to application to stay competitive as a leader in a global environment.[1] The Material Genome Initiative (MGI) was launched as a result.

According to President Obama, "To help businesses discover, develop, and deploy new materials twice as fast, we're launching what we call the Materials Genome Initiative. The invention of silicon circuits and lithium ion batteries made computers and iPods and iPads possible, but it took years to get those technologies from the drawing board to the market place. We can do it faster."[1]

The MGI provides a working framework focusing on infrastructure, process, and workforce skill identification and training to accelerate the materials continuum (Figure 11). The initiative has four cross-cutting themes and three goals (Table 4).

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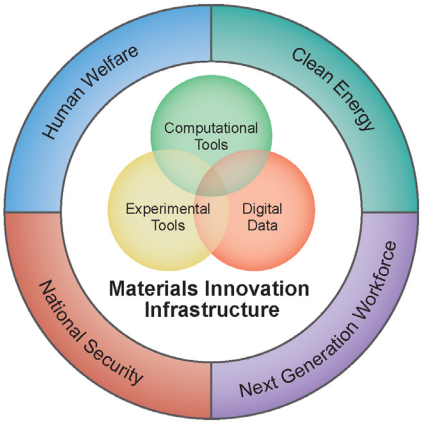
Figure 11. The Material Genome Initiative



Source: White House Office of Science and Technology Policy.[1]

Table 4. Cross-Cutting Themes of the MGI

Cross-Cutting Themes[1]	Goals[2]
1. Incentivizing open data and access of tools 2. Structuring public-private partnerships 3. Driving innovation across computation, data informatics 4. Moving the community to a different cultural norm	1. Developing a materials innovation infrastructure 2. Achieving national goals with advanced materials 3. Equipping the next-generation materials task force

Source: White House.[1,2]

According to the White House Office of Science and Technology Policy, "A genome is a set of information encoded in the language of DNA that serves as a blueprint for an organism's growth and development. The word genome, when applied in non-biological contexts, connotes a fundamental building block toward a larger purpose."[1]

Implications: This initiative is a springboard for speed to market, reducing time from discovery to application, the principles of which can be applied to many research and technology programs (drugs, novel ingredients, food ingredients, materials, devices). Such an infrastructure, initiated at the federal level, has the advantage of encouraging more public-private collaboration in addition to open-source data sharing. Many bioinspired discoveries and public-private partnerships have benefited from the MGI. However, the final measure of the success and challenges of this initiative is not available at this time.

Sources: (1) Wadia C; White House Office of Science and Technology Policy (2012) *The Materials Genome Initiative.* Washington, DC: OSTP. (2) White House Executive Office of the President (2011) *Materials Genome Initiative for Global Competitiveness.* Washington, DC: Executive Office of the President.

2. Beyond 3D Printing: 4D Printing for Shapeshifting Devices?

Investigators are examining 3D-printed hydrogel composite architectures that provide the ability to change shape over time for use in smart textiles, soft electronics, medical devices, and tissue engineering.

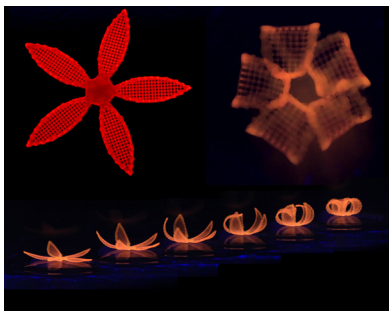


Image courtesy of Wyss Institute at Harvard University.

Organisms have dynamic morphologies that can change shape in response to environmental changes such as humidity, temperature, and light. Wyss Institute researchers have mimicked a variety of such dynamic shape changes in innovative 4D-printed hydrogel composites.[1] They describe their work as follows:

> By aligning cellulose fibrils from wood using predicted configurations from a proprietary mathematical model in the 4D-printing process, [the] composite ink encodes anisotropic swelling and stiffness properties that can be patterned along the printing path. With this technology, local swelling behaviors become programmable in water-immersed composites, which as a result produce intricate and highly predictable shape changes. In addition, a variety of hydrogel materials can be used interchangeably resulting in different stimuli-responsive behaviors, while the cellulose fibrils can be replaced with other anisotropic fillers of choice, including conductive fillers. These materials may be used to fabricate medical devices that take on programmed shapes when placed in contact with body fluids, as well as smart textiles, responsive building materials and novel electronic sensors and actuators.[1]

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- ***Implications:*** Can such 4D composite architectures be applied to predict changes in food during shelf-storage where changes in food texture, shape, color, moisture content, and nutrient composition are influenced by storage temperature, humidity, color, light, and packaging containers?

Source: (1) Wyss Institute (2016).

3. Beyond 3D: 3D Bioprinting for Thick-Tissue and Organs

This research will help to establish the fundamental scientific understanding required for bioprinting of vascularized living tissues.

—Zhijian Pei, National Science Foundation Program (2016)[2]

The typical bioprinting technique creates thick 3D tissues composed of human stem cells and embedded vasculature. With potential applications in drug testing and regenerative medicine, bioprinting sets the stage for future tissue and organ replacement.[1]

This is a new method for 3D bioprinting thick vascularized tissue constructs, made from human stem cells, extracellular matrix, and circulatory channels lined with endothelial blood vessel cells. The resulting network of vasculature contained within these deep tissues enables fluids, nutrients, and cell growth factors to be controllably perfused uniformly throughout the tissue. The advance was reported in *Proceedings of the National Academy of Sciences* in 2016.[1]

A technique developed by Alan Feinberg at Carnegie Mellon University extends the use of 3D printing technology to print heart and other thick tissues or organ structures.[2] The 3D-printed object may comprise any material of choice allowing the master scaffold framework for cells to grow into the desired organs. Bioprinting when coupled with imaging provides a powerful tool for surgeons to study the 3D layout of structures of organs and vessels prior to surgery.

- ***Implications:*** 3D printing of food products is in testing stages. With use of desired ingredients, new food products can be created conforming to desired shape, color, and contour.

Sources: (1) Wyss Institute (2016). (2) NSF (2016).

E. Tissues on Chips (Organs-on-Chips)

1. Organs-on-Chips for Toxicological and Disease Screening

The NIH National Center for Advancing Translational Sciences (NCATS) has led research in the Tissue Chips (Chip) Initiatives program in collaboration with other NIH institutes and centers, the Defense Advanced Research Projects Agency (DARPA), and the Food and Drug Administration (FDA). The Tissue Chip Project is now being applied for rapid drug screening, focusing on developing human tissue chips that "accurately model the structure and function of human organs—such as the lung, liver, and heart—to help predict chemical and drug safety in humans more rapidly, effectively, and efficiently. Currently, this program is focused on toxicity testing with plans underway to renew focus on disease modeling and efficacy testing."[1]

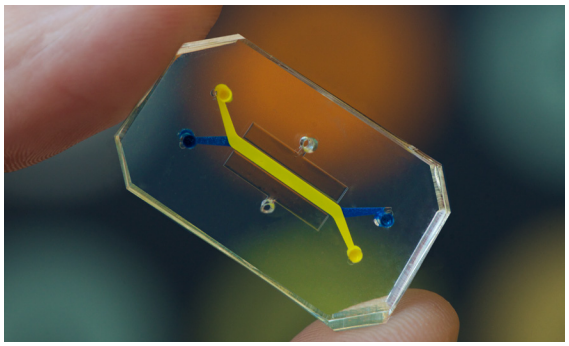


Image courtesy of Wyss Institute at Harvard University.

The Tissue Chips (or Organs-on-Chips) Platform centered on building 3D platforms designed to simulate functions of the human body and support living human tissues and cells. These devices are designed to be accurate models of the "*in situ*" structure and function of human organs, such as the lung, liver, and heart. Among the chips developed to date and tested with compounds already known to be safe or toxic in humans, the majority of these chips have been validated.

Implications: Modular design allows multiple chips to connect with another to mimic effects of potential drugs on several organ systems at a time. A "human body on a chip" is the ultimate goal of the program, enabling researchers to test the potential effects of a substance across the entire body before involving human clinical participants.

Source: (1) NCATS (2016).

2. Progress of the NIH Tissue-on-Chips Program

a. Tissue Chips for Drug Screening

The first 2-year funding phase of the Tissue Chip for Drug Screening program (2012–2014) supported the development of 3D cellular microsystems designed to represent a number of human organ systems.[1]

Renewable cell sources and bioengineered microsystems that successfully demonstrated physiological function moved into the next 3-year phase (2015–2017) to further refine the technology and begin organ chip integration, with the first 5 years of the program drawing to a close in July 2017. Projects that explored the use of stem and progenitor cells to differentiate into multiple cell types that represent the cellular architecture within the organ were also awarded through this initiative.[1]

Since 2012, NCATS has funded 19 chip studies, 12 of which met objectives. These studies provide the foundations for current and future advancement in the field:

- 2014 projects to integrate tissue chips
- 2012 projects on model systems
- 2012 projects on cell resources

The first organ-on-chip effort focused on the lungs. The lungs are where oxygen from the atmosphere is transported to the bloodstream. Blood flows through tiny vessels in the lungs, receiving oxygen when breathing in and releasing carbon dioxide when breathing out. From the lungs, oxygen-rich blood flows to the heart, then out to the rest of the body. Scientists need better ways to test how the lungs and their sensitive vessels respond to drugs and chemicals.

On October 18, 2016, NCATS announced a new funding opportunity for the next phase of the Tissue Chip for Drug Screening program.[2] For the Tissue Chips for Disease Modeling and Efficacy Testing initiative, the center and its collaborators plan to commit an estimated total of $13.5 million in fiscal year 2017 for 10–12 awards. NCATS funds its Tissue Chip for Drug Screening program through the Cures Acceleration Network.[2]

The new support will enable researchers to create models of human disease using tissue chip technology for testing the effectiveness of candidate drugs. Failure to demonstrate efficacy accounts for approximately 65% of drug failures during clinical trials. Ultimately, these disease models will help scientists to better assess biomarkers, bioavailability, efficacy, and toxicity of candidate therapeutics prior to entry into clinical trials.[3]

b. Tissue Chip Testing Centers

NIH Tissue Chip Testing Centers are based at independent institutions and provide a way to test and validate tissue chip platforms developed through the program.[4] These efforts will help to validate tissue chip technology and promote the adoption of this technology by the broader research community.

- 2016 testing center awards

c. Tissue Chips in Space

NCATS is partnering with the Center for the Advancement of Science in Space (CASIS) on its Tissue Chips in Space initiative.[5] Through this initiative, NCATS and CASIS will collaborate to refine tissue- and organ-on-chip platforms for on-flight experiments at the International Space Station US National Laboratory so that scientists can better understand diseases and translate those findings to improve human health on Earth.[3]

d. Advancing Tissue Chips From Chemical Screening to Disease Modeling and Efficacy Testing

The Tissue Chips for Disease Modeling initiative will support further development of tissue chip models of human disease that mimic the pathology in major human organs and tissues.[6] The goals are to (1) support studies

to develop *in vitro* disease models using primary tissue or induced pluripotent stem cell (iPSC)–derived patient cell sources on tissue/organ-on-chip platforms, (2) determine disease relevance of these models by preliminary testing of key experimental features, and (3) test the effectiveness of candidate drugs.

Under this platform, three disease models will be tested:

- Metastatic breast cancer in the liver
- Rare heart and muscle condition
- Tumor with blood vessels

Sources: (1) NCATS (2016). (2) NCATS (2016). (3) NCATS (2016). (4) NCATS (2016). (5) NCATS (2016). (6) NCATS (2016).

3. From Organs-on-Chips to a Human Chip Network

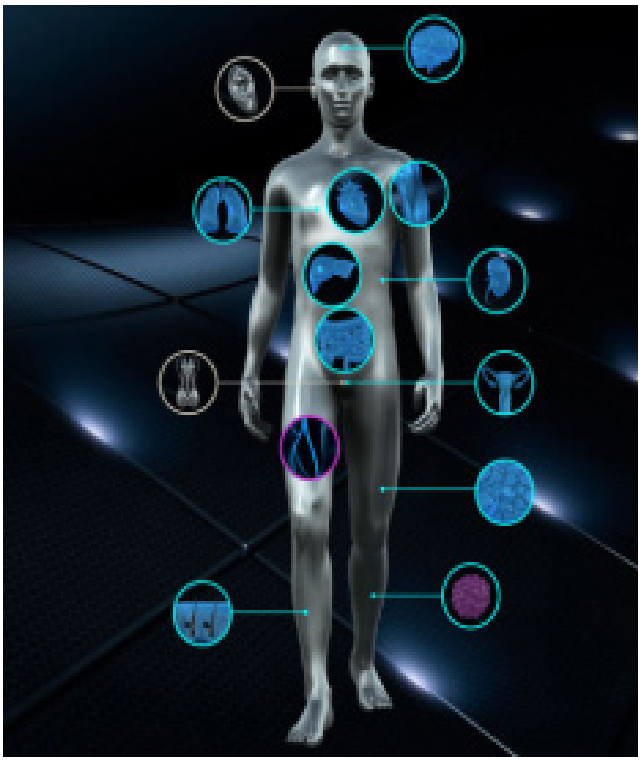
NIH has invested in technology and research to develop a whole human network of chips that mimic organs of interest. Some chips are further along in development than others. The Chip diagram in Figure 12 shows chips currently under development.[1]

The current chips are designed to be modular, meaning scientists can connect one chip with another to test the effects of potential drugs or other compounds on several organ systems at a time. A "human body on a chip" is the ultimate goal of the program, enabling researchers to test the potential effects of a substance across the entire body before involving human clinical participants.[1]

NCATS envisions that the tissue chips will help scientists generate data on drug safety and effectiveness to predict more accurately how specific drugs will respond in people.[1] The new technology ultimately could help accelerate the drug development and approval process and, most important, enable health professionals to make new treatments available sooner to patients.

Once these models are integrated with chips based on other human organs, scientists will be able to learn more about how other body systems affect diseases. For example, scientists could study how the immune system affects the activity and growth of metastatic tumors or how experimental treatments for heart failure affect other organs.

Figure 12. Chip: Advancing Drug Testing



From the NIH: Chip can help you learn about the innovative developments of the Tissue Chip for Drug Screening program at NCATS. Clicking on Chip's icons allows readers to learn more about the tissues and organ systems they represent, and read more about the entire project below. Note: Gray icons represent tissue chips that are not currently in development.

- Brain
- Lungs
- Heart
- Muscles
- Liver
- Kidney
- Gastrointestinal
- Female
- Blood
- Adipose
- Skin
- Disease

Source: NCATS.

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Ultimately, scientists might use this technology for precision medicine to predict which treatments would be most effective against a person's specific disease while minimizing side effects. Scientists might use the LiverChip to identify optimal conditions for administering chemotherapy drugs, for example, during morning or evening, in a fasting state, or on a full stomach.

Implications: The organs-on-chips technologies present vast potential applications for food and nutrition research, particularly in food safety and nutrient metabolism in specific organs or combinations of organs. The future human chip networks may offer better insight into whole system biology functions/effects from by-products of pathogens, chemical toxicants, bioactives, and nutrients.

Source: (1) NCATS (2016).

F. Next-Generation Gene Editing: Base Editing Building on CRISPR-Cas9

A study by Komor et al., published in *Nature*,[1] reported an enhancement to the CRISPR gene editing technology. The current method requires breaking double-stranded (ds) DNA at a target locus as the first step to gene correction,[2,3] which is inefficient, potentially introducing an abundance of random insertions and deletions (indels) at the target locus resulting from the cellular response to dsDNA breaks.[2,3] The researchers developed a new approach using "base editing" to genome editing that enables the following:

> ...the direct, irreversible conversion of one target DNA base into another in a programmable manner, without requiring dsDNA backbone cleavage or a donor template. By combining CRISPR/Cas9 and a cytidine deaminase enzyme that retain[s] the ability to be programmed with a guide RNA, this reduces dsDNA breaks, and mediate[s] the direct conversion of cytidine to uridine, thereby effecting a C→T (or G→A) substitution. The resulting 'base editors' convert cytidines within a window of approximately five nucleotides, and can efficiently correct a variety of point mutations relevant to human disease. In four transformed human and murine cell lines, second- and third-generation base editors that fuse uracil glycosylase inhibitor, and that use a Cas9 nickase targeting the non-edited strand, manipulate the cellular DNA repair response to favor desired base-editing outcomes, resulting in permanent correction of ~15–75% of total cellular DNA with minimal (typically ≤1%) indel formation. Base editing expands the scope and efficiency of genome editing of point mutations.[1]

Source: (1) Komor AC, et al. (2016) Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage. *Nature.* 533:420–424.

G. Data Visualization

2015 and 2016 were turning points with large growth in Big Data with the expansion of the Internet of Things (IoT). What used to be novel is now the norm, as more businesses and researchers use data in all forms and sizes in order to make the best possible decisions. In 2016, there was large growth in systems that support a large volume of nonrelational or unstructured data. These systems will evolve to operate well inside of enterprise IT systems and standards.

In 2015, Michelle Wallace of Tableau stated[1]:

> The Internet of Things is a powerful ecosystem. Devices or "things"—which encompass everything from pedometers to seismographs—are producing unprecedented amounts of data about the world around us. When put in the hands of everyday people, this information can make every area of life more data-driven. "Things" aren't really a new concept. After all, we've been using sensors to collect scientific data for centuries. What's different now is the interconnectedness of all these devices—plus the fact that they're producing ever more granular data sets... *all* while that data is getting more and more accessible to everybody. But once we have all this data, what do we do with it?
>
> The Internet of Things is changing the game for data access. And when real people can actually visualize and interact with this data—even blend it with their organization's other data assets—entirely new insights can be reached. From jet engines bolted on airliners to pacemakers embedded in hearts, the increasingly interconnectedness of devices around us mean we can see our world in completely new ways. Ultimately, this empowers innovation that's not only data-driven but deeply human-centric.

Chris Selland, Vice President of Marketing and Business Development for Tableau, stated that "What's really going to make big data go mainstream is the ability to connect not just with data scientists and technologists but business people. And absolutely one of the keys to that is visualization, is being able to show people—not just tell people,

not just show numbers or even show charts—but to have those charts and graphs and visualizations come alive."[2]

- ***Implications:*** This is a critical question for nutritionists and food researchers using data from the Internet of Things. This information is valuable if it is designed to provide transformational decisions; to do this will require clear and useful visualization of complex and massive databases.

Sources: (1) Wallace M (2015) . (2) Tableau (2015).

H. Other Discoveries

1. Insects Allied Program: New Generation of Technology for Environmental Security Sources

DARPA announced in 2016 that it is initiating a program to explore use of vector-mediated modification technologies for rapidly countering environmental and biological threats to plant crops. Threats of interest might include pathogens, pests, drought, salinity, and others.

DARPA's Biological Technologies Office hosted a Proposers Day meeting on November 18, 2016, in Arlington, Virginia, which aimed to provide further information for potential applicants on the structure and objectives of the new Insect Allies program. Insect Allies will seek to develop vector-mediated modification technologies for mature plants to rapidly counter environmental and biological threats to crops. Threats of interest might include pathogens, pests, drought, and salinity, among others. DARPA believes that the high specificity of genetic modification coupled with quick plant gene uptake could allow crops to be protected from threats within a single growing season.

- ***Implications:*** Such research would enable future advancement in technology approaches to combat crop insect infestations that would improve and maximize crop yields and protect against changing food environments and threats..

Source: (1) DARPA (2016).

4 Forecast and Predictions

It is said that the present is pregnant with the future.

—Voltaire (1694–1778)

A. The Increasingly Virtual and Digitized World

1. Strategic IT Trends for 2020 Forcasted by Gartner Inc.

Gartner's top 10 strategic technology trends will shape digital business opportunities through 2020.

—David Cearley, Vice President and Gartner Fellow (2016)[1]

Gartner, a leading IT research and advisory company, has identified its top strategic technology trends in 2016 that will have an impact on the future. Gartner states that "A strategic technology trend is one with potential to significantly impact an organization as measured by a high potential for disruption to the business, end users or IT, the need for a major investment, or the risk of being late to adopt. These technologies may interrupt an organization's long-term plans, programs and initiatives."[1]

The organization predicts that by 2020, our world will become even more virtual and digitized. Some examples of these trends relevant to food and nutrition research are highlighted below.[1]

1. The Device Mesh

The device mesh refers to applications and information collected and connected through various systems includes mobile devices, wearable, consumer and home electronic devices, automotive devices and environmental devices—such as sensors in the Internet of Things (IoT).

While devices are increasingly connected to back-end systems through various networks, they have often operated in isolation from one another. As the device mesh evolves, connection among models to expand and greater cooperative interaction between devices to emerge.

2. Ambient User Experience

The ambient user experience preserves continuity across the device mesh, time, and space. The experience is seamless across multiple devices and interaction channels merging physical, virtual, and electronic environment as the user moves from one place to another.

"Designing mobile apps remains an important strategic focus for the enterprise," said Mr. Cearley. "However, the leading edge of that design is focused on providing an experience that flows across and exploits different devices, including IoT sensors, common objects such as automobiles, or even factories. Designing these advanced experiences will be a major differentiator for independent software vendors (ISVs) and enterprises alike by 2018."

3. 3D Printing Materials

Advances in 3D printing have already enabled 3D printing to be used in a wide range of materials, including advanced nickel alloys, carbon fiber, glass, conductive ink, electronics, pharmaceuticals, and biological materials. These innovations are driving user demand, as the practical applications for 3D printers expand to more sectors, including aerospace, medical, automotive, energy, and the military. The growing range of 3D-printable materials will drive a compound annual growth rate of 64.1 percent for enterprise 3D-printer shipments through 2019. These advances will necessitate a rethinking of assembly line and supply chain processes to exploit 3D printing.

"3D printing will see a steady expansion over the next 20 years of the materials that can be printed, improvement in the speed with which items can be printed and emergence of new models to print and assemble composite parts," said Mr. Cearley.

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4. Information of Everything

According to Mr. Cearley, "Everything in the digital mesh produces, uses and transmits information. This information goes beyond textual, audio and video information to include sensory and contextual information. Information of everything addresses this influx with strategies and technologies to link data from all these different data sources. Information has always existed everywhere but has often been isolated, incomplete, unavailable or unintelligible. Advances in semantic tools such as graph databases as well as other emerging data classification and information analysis techniques will bring meaning to the often chaotic deluge of information."

5. Advanced Machine Learning

The explosion of data sources and complexity of information makes manual classification and analysis infeasible and uneconomic. DNNs automate these tasks and make it possible to address key challenges related to the information of everything trend.

DNNs (an advanced form of machine learning particularly applicable to large, complex datasets) are what makes smart machines appear "intelligent." DNNs enable hardware- or software-based machines to learn for themselves all the features in their environment, from the finest details to broad sweeping abstract classes of content. This area is evolving quickly, and organizations must assess how they can apply these technologies to gain competitive advantage.

Additional analysis can be found in the Gartner report here.

Implications: As food and nutrition research data captures are provided by multiple sources and in many forms, keeping pace with IT advances and end users' expectations is critically important for constructive knowledge building and decision making.

Source: (1) Gartner (2016).

B. Predictions for the Future: Today to 2025

1. Prediction of Changes in the Global Environment by 2025

DNV-GL launched its *Technology Outlook 2025* in April 2016. This report captures changes in the global environment across many areas, including society, health care, life sciences, food technology, and the food supply. We highlight some of the organization's findings below.[1]

a. Societal Changes

Global societal structures are changing at a rapid pace, driven in part by a growing global population, poverty, increasing lifespan and health, and improved employment. By 2025, the global population will have more access to opportunities, higher income, and personal wealth. This shift is fueled by increasing global digital connectivity, personal and manufacturing technology innovations, and rising productivity. In the next decade, more than half of the world's population will have access to the Internet, renewable power, and remote health care.[1]

Three key drivers of societal structural change will include: demographic shifts, smart cities, and mobile health care.

b. The Rise of the Fourth Industrial Revolution Will Drive Breakthroughs in the Health Care and Life Sciences

By 2025, access to safe, effective, and efficient health services as a fundamental human right will become increasingly difficult, which in turn will make it difficult to meet the needs of humanity. Global population increases, shifts in the aging population, emerging diseases, climate change, rising costs, inequitable access, food and nutrition security, the environment, and food safety all will make the development and deployment of traditional health care methods in their current forms more difficult to sustain between now and 2025.

Development and deployment of technology, through collaboration between the health care and life sciences fields, may be one pivotal approach to overcoming these challenges. DNV-GL identified that the following would continue to have an impact on technology advances by 2025: activity trackers, remote diagnostics, sensors, drones, social media, electronic health records, additive manufacturing, robotics, and clinical genomics.[1] It is conceivable that the combination of personalized medicine, surgery and additive manufacturing (3D printing),

and nanotechnology may afford physicians the ability to make cellular repairs or produce prostheses and organs tailored to individual needs,lifestyle, and behavior. Mobile health (mHealth) technology will enable rapid access to health care that is made feasible by remote means.

c. Predicted Change in the Food Supply

The food supply chain is threatened on many fronts: new weather patterns, increasing populations, human migration, and pollution of land and water. By 2025, the global food supply will continue to be driven by emphasis on food security, food safety, health, and sustainability.[1] As the millennial generation matures, there will be increased demand for customized/personalized foods that meet tastes, lifestyle practices, and ecological beliefs and practices. Consumers will demand foods to be produced and distributed in a safe, equitable, and sustainable manner. Social media and social networks will influence consumers' decisions on food shopping and diet planning, as well as decisions on health care and nutrition practices.

The food system of the future will have to integrate many food and production attributes—higher yields, less material and water wastage, efficient distribution, early contamination screening and detection, and clarity and transparency in food safety and health communication. Increasingly, there will be more demand for food safety, transparency, trust in processing and food origin, and authenticity. Regulations will be a driver for new solutions and at the same time a barrier to rapid technology innovation and implementation. There will be more availability and accessibility to healthier foods to developing nations, triggered by more countries adopting national nutrition guidelines for foods (WHO guidelines to restrict free sugars, salt, saturated fats, and energy-dense foods; Pan-American Health Organization [PAHO] guidelines to limit ultra-processed foods). Sustainability will take precedence as a guiding principle throughout the food chain. By 2025, additional labeling will be incorporated in the food system, including documentation and verification of food sustainability associated with climate change, ethics-related requirements, and resource efficiency.[1]

d. Advances in Food Technologies

DNV-GL predicts that the following areas will impact future advances in food technologies: genomics, sensors, tracking, automation, and packaging and processing. For further details, read the full DNV-GL report online.

Source: (1) DNV-GL (2016). *Technology Outlook, 2025*. Oslo, Norway: DNV-GL.

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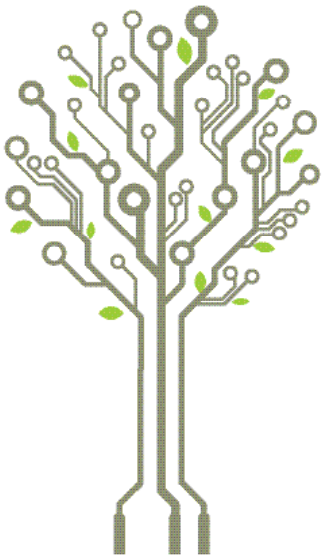
2. Ten Skills Critical for the Future Workforce of 2020: A Forecast by the Institute for the Future

Multiple forces are shaping the future workforce. The Institute for the Future (IFTF) describes the contrasts between the workforces of the past and future[1]:

> In the 1990s, IBM's Deep Blue beat grandmaster Gary Kasparov in chess; today IBM's Watson supercomputer is beating contestants on *Jeopardy*. A decade ago, workers worried about jobs being outsourced overseas; today companies such as ODesk and LiveOps can assemble teams "in the cloud" to do sales, customer support, and many other tasks. Five years ago, it would have taken years for NASA to tag millions of photographs taken by its telescope, but with the power of its collaborative platforms, the task can be accomplished in a few months with the help of thousands of human volunteers. Global connectivity, smart machines, and new media are just some of the drivers reshaping how we think about work, what constitutes work, and the skills we will need to be productive contributors in the future. This report analyzes key drivers that will reshape the landscape of work and identifies key work skills needed in the next 10 years. It does not consider what will be the jobs of the future.

IFTF has identified the following six drivers that will influence new skills that the workforce will need by 2020.[1]

1. Extreme longevity
2. Rise of smart machines and systems
3. New media environment
4. Computational world
5. Superstructured organizations
6. Globally connected world



These drivers will change the future of workforce skills needed. According to IFTF,[1] the 10 most critical skills for the future workforce are:

1. Sensemaking
2. Novel and adaptive thinking
3. Social intelligence
4. Transdisciplinarity
5. New media literacy
6. Computational thinking
7. Cognitive load management
8. Design mindset
9. Cross-cultural competency
10. Visual collaboration

- ***Implications:*** The skills needed for the future workforce will have significant impacts on the hiring, training, and retention of candidates/employees in the various sectors (e.g., academia, business, educational institutions, and granting offices).

Source: (1) IFTF (2016). *Future Work Skills, 2020*. Palo Alto, CA: IFTF.

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5 Emerging Food Safety Trends

A. United States

1. National Strategy for Combating Antibiotic-Resistant Bacteria

In September 2014, the White House put forth the following vision for the National Strategy for Combating Antibiotic-Resistant Bacteria: "The United States will work domestically and internationally to prevent, detect, and control illness and death related to infections caused by antibiotic-resistant bacteria by implementing measures to mitigate the emergence and spread of antibiotic resistance and ensuring the continued availability of therapeutics for the treatment of bacterial infections."[1]

One goal of the cross-agency strategy is to advance the development and use of rapid diagnostics for highly resistant bacterial infections. NIH is putting aside $20 million for point-of-care testing for rapid use by health care professionals in real-world settings and has identified the following research priorities and anticipated outcomes.[1]

Research Priorities

1. Identify environmental factors that facilitate the development of antibiotic resistance and the spread of resistance genes that are common to animals and humans.
2. Increase research focused to understand the nature of microbial communities, how antibiotics affect them, and how they can be harnessed to prevent disease.
3. Intensify research and development of new therapeutics and vaccines, first-in class drugs, and new combination therapies for treatment of bacterial infections.
4. Develop nontraditional therapeutics and innovative strategies to minimize outbreaks caused by resistant bacteria in human and animal populations.
5. Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates.
6. Enhance opportunities for public-private partnerships to accelerate research on new antibiotics and other tools to combat resistant bacteria.
7. Create a biopharmaceutical incubator—a consortium of academic, biotechnology, and pharmaceutical industry partners—to promote innovation and increase the number of antibiotics in the drug development pipeline.

Some Anticipated Outcomes

- FDA, USDA, CDC, DOD, and NIH will convene a joint summit to evaluate the status of ongoing research into mechanisms of resistance and its spread among zoonotic pathogens and commensal microbiota. The research projects may make use of whole-genome sequencing (WGS), proteomics, metagenomics, structural biology, and bioinformatics.
- Data sets on antibiotic resistance generated through federally funded research, including genomic and proteomic data sets, are publicly available through searchable online databases in a manner that is consistent with protecting personally identifiable information.
- The gut microbiome of at least one animal species raised for food will be sequenced and characterized to advance our understanding of the structure and function of gastrointestinal microbial communities. This research may help identify new growth promotants, antibacterial interventions that do not disrupt the normal gut intestinal microbiota of food animals, and may provide insight into management of the human microbiome.

Source: (1) White House (2014) *National Strategy for Combating Antibiotic-Resistant Bacteria.* Washington, DC: White House.

2. NSF and NIH Are Funding Research for Novel Antibacteriosides: Exploring Soil and Dirt!

The emergence of antibiotic-resistant human pathogens has spurred new and urgent searches for alternative compounds. Traditional antibiotics have targeted against cell mechanisms such as DNA replication as well as protein and cell wall synthesis. Alternate sources from mineral-based therapies against pathogens, such as clays used for medicinal purposes throughout millennia, have not yet been studied for their ability to treat bacterial

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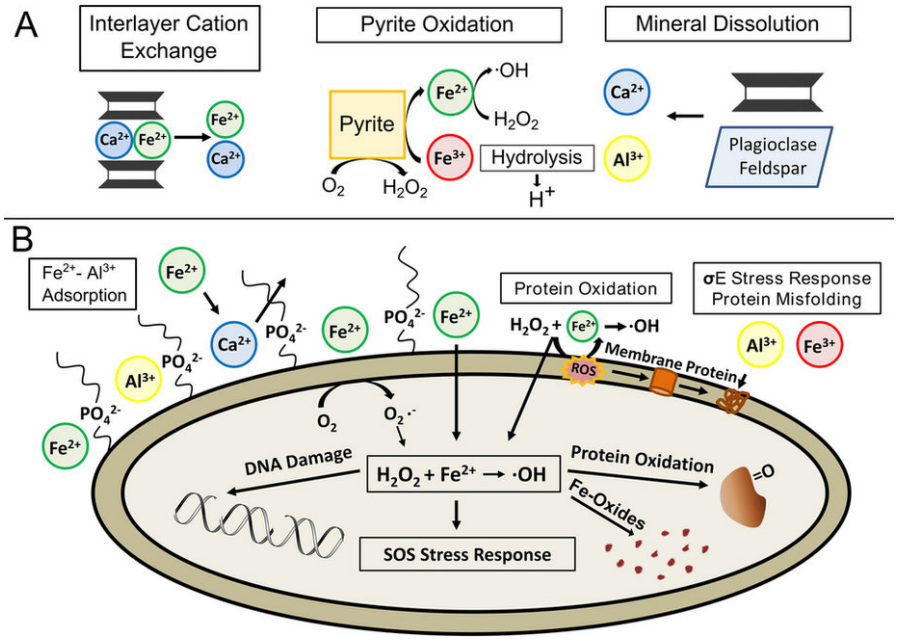
Figure 13. Antibacterial Mechanism



Source: Reproduced from Morrison et al.[2] with permission.

infections. Documented use of reduced metal-rich clays in healing necrotizing fasciitis,[1] or "flesh eating bacteria," led Morrison et al.[2] to investigate the geochemical properties of antibacterial minerals. They found that, when tested against a broad spectrum of human pathogens, certain clays also kill antibiotic-resistant pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA).[2]

Natural antibacterial clays, when hydrated and applied topically, kill human pathogens, including proliferating antibiotic-resistant strains. Only clays containing soluble-reduced metals and expandable clay minerals are bactericidal. Clays that absorb cations and have the ability to release metals and produce toxic hydroxyl radicals have this function.

The critical antibacterial components in Oregon Blue clays are soluble Fe^{2+}, Fe^{3+}, and Al^{3+}, which work synergistically to attack and overcome multiple cellular systems in pathogens. The hydrated antibacterial clays generate a low pH (<4.6) environment, through mineral oxidation, dissolution, and hydrolysis reactions, sustaining metal release and reactive oxygen species (ROS) production throughout the antibacterial mechanism (Figure 13). This geochemical process offers an alternative antibacterial strategy to traditional antibiotics. Advanced bioimaging methods and genetics show that Al^{3+} disrupts cell membrane proteins, whereas Fe^{2+} evokes membrane oxidation and enters the cytoplasm inflicting hydroxyl radical attack on intracellular proteins and DNA. The lethal reaction precipitates Fe^{3+} oxides as biomolecular damage proceeds. The mechanism of action is shown in Figure 13.

To note, the term "clay" refers to <2-µm minerals of any type, and this size fraction commonly contains discrete clay minerals (smectite, illite, kaolinite), which provide an enormous surface area (100′ s m^2/g) for cation exchange reactions when hydrated.[3] Only a few clays have been identified as antibacterial, completely killing a broad spectrum of human pathogens

- ***Implications:*** Discovery of this bactericidal mechanism demonstrated by natural clays offers new opportunities for the design of future mineral-based antibacterial agents found in soil and other environmental sources.

Sources: (1) Williams LB, et al. (2004) Killer clays! Natural antibacterial clay minerals. *Miner Soc Bull.* 139:3–8. (2) Morrison KD, et al. (2016) Unearthing the antibacterial mechanism of medicinal clay: a geochemical approach to combating antibiotic resistance. *Sci Rep.* 6:19043. (3) Moore DM et al. (1997) *X-Ray Diffraction and the Identification and Analysis of Clay Minerals*, 2nd ed. Oxford, UK: Oxford University Press.

Click here for the *2017–2019 Emerging Science Brief*, which provides highlights of topics in this report.

3. USDA Food Safety Research Priorities

The USDA set new research priorities for 2017–2021, as described below.[1,2]

a. 2017–2021 Areas of Focus

- Rapid in-field screening for chemical and microbial hazards with positive samples sent for rapid laboratory confirmation to expedite compliance decision making.
- Develop a new real-time analytical tool for Food Safety and Inspection Service (FSIS) inspectors to make faster regulatory decisions related to adequacy of sanitary operations by identifying potential pathogen contamination of regulated products.
- Whole-genome sequencing (WGS) use by FSIS to characterize bacterial genomes will provide greater precision and granularity than previous methods:
  - Allows for more rapid and accurate pathogen identification than traditional methods for more rapid responses to outbreaks, through conducting efficient trace backs, knowledge of environmental harborage and movement of pathogens in regulated establishments
  - Provides in-depth understanding of harmful traits, such as bacterial virulence and antimicrobial resistance.
- WGS will be useful in making inspection decisions as well as future policy development and will be applied to samples from "farm to fork," a tracking process already in motion to generate real-time analysis for food safety and public health regulatory decisions.
- WGS analytics will be applied to develop individualized inspection strategies for certain food pathogens and to inform the need for establishments to enhance sanitary practices and programs.
- FSIS will share what it learns about the harmful traits of pathogens with collaborating partners to track and potentially prevent these pathogens from adulterating food throughout the farm to fork continuum. This approach will specifically provide a more in-depth understanding of antimicrobial resistance in bacteria and further help FSIS, APHIS, CDC, and ARS efforts to protect the effectiveness of antibiotics for the US population and animal agriculture.
  - Metric Measure: percentage of all isolates that FSIS sampling generates that are subject to WGS.

b. FSIS Research Priorities

The 2017 goals for research priorities build upon the FSIS 2011–2016 Strategic Plan research interests summarized below. [2]

- Emerging screening technologies for enhanced subtype/virulence characterization of pathogens.
- Screening technologies to provide multi-analyte detection from a single analytical sample portion. Screening technologies that are applicable to FSIS-regulated products (meat, poultry, egg products, and foods containing these products).
- Rapid methods for screening of "high-risk" compounds such as environmental contaminants. Testing methods for *quantifying* target pathogens in meat, poultry, and egg products.
- Develop physiologically based pharmacokinetic (PBPK) models to estimate chemical concentrations in beef, pork, and chicken tissues.
- Identify and/or develop emerging technologies for real-time testing for higher levels of pathogen contamination prior to slaughter.
- Develop nontargeted methods to detect chemical contaminants in FSIS-regulated products
- Develop the use of indicator/surrogate organisms in processing establishments to validate and monitor intervention effectiveness.
- Evaluate the potential effectiveness of pre-harvest pathogen interventions on finished products.
- Develop a screen for the detection of hormone and hormone-like compounds.
- Determine retail use statistics/practices which could contribute chemical (insecticide, rodenticide, fungicide, antimicrobial) or pathogen contamination to FSIS-regulated products.
- Determine the magnitude and significance of migration of chemicals (e.g., endocrine disruptors) from packaging into FSIS-regulated products.
- Determine the presence and contributing factors for antimicrobial-resistant bacterial strains in poultry and cattle.
- Develop or refine cooking and cooling models.
- Develop or refine dose-response curves for pathogens (including specific subtypes) of interest.

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- Determine (validate) the effectiveness (log-reduction) of interventions used by industry to reduce levels of pathogens on FSIS-regulated products.
- Identify consumer practices which compromise the safety of FSIS-regulated products and/or generate data to develop public education and outreach to improve food-handling practices.
- Identify and/or develop pre- and post-harvest interventions to reduce levels of pathogens and chemical hazards for each class of veal (bob veal, non-formula-fed, formula-fed, and heavy calves).
- Identify unique attributes of pathogen outbreak strains that may increase the probability of foodborne illness.
- Determine the contribution of endogenous extra-intestinal sources of pathogens to contamination of FSIS-regulated products.

Sources: (1) USDA (2016) *FSIS Strategic Plan, 2017–2021*. Beltsville, MD: USDA. (2) USDA (2010) *FSIS Strategic Plan, 2011–2016*. Beltsville, MD: USDA.

B. Global Food Safety Challenges

1. Global Trends

In August 2016, we interviewed Dr. Mike Doyle, Professor of Microbiology at the University of Georgia. We asked for his unfiltered thoughts on global food safety trends. Dr. Doyle shared with us the talk he gave as an invited speaker at the W.C. Frazier guest lecture at the University of Wisconsin in May 2016. Highlights are shown in Table 5.

Table 5. Global Food Safety Trends

Emerging Trend	Potential Implications
1. Whole-genome sequencing (WGS) of foodborne pathogens is revolutionizing microbial outbreak detection and traceback globally. As a result, there will likely be more outbreaks detected with small numbers of cases (3–10)	• The average number of cases in listeriosis outbreaks is now 4 for 2016
2. More companies and specific food vehicles will be identified; food processing facilities will be WGS fingerprint profiled	
3. Pathogens obtained from retail food samples will implicate food processors in foodborne outbreaks. Especially vulnerable in fresh produce	• Need for "bullet-proofing" fresh produce from foodborne pathogen contamination • Produce is a leading vehicle of foodborne illness, with fresh-cut leafy greens and melons of particular concern • Cantaloupe is prone to pathogen contamination, and many commonly used sanitizers are not fully effective in mitigating pathogen contamination, especially at the stem scar
4. Aquaculture farming is gaining prominence and will become a dominant global food production practice	• Excessive use of antimicrobials critical to human therapy for disease control and use of raw animal manure and human feces as primary nutrient source has global ramifications regarding antimicrobial-resistant microbes and pathogen contamination
5. Adulterating foods with fraudulent and even unsafe additives by some exporting countries will continue to be an issue	• This is being accelerated by the use of social media disseminating misinformation
6. Consumer: Unintended consumer uses of foods will continue to increase with growing consumer interest in raw or undercooked, natural (no preservatives) foods that can be prepared quickly or are not cooked sufficiently	• "Natural" foods that do not contain antimicrobial preservatives may be a disaster in the making, depending on the food's ability to support the growth of pathogens and spoilage microbes and storage temperature and time. As a result, consumer abuse is going to be unavoidable

Source: Doyle M (May 18, 2016) "Unprecedented Challenges in Producing and Serving Safe Foods." W.C. Frazier Memorial Lecture at University of Wisconsin-Madison.

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2. Peanut Allergy

a. LEAP Study: Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy Suggests Early Small Dose Introduction Can Mitigate Later Allergy

"Prior to 2008, clinical practice guidelines recommended avoidance of potentially allergenic foods in the diets of young children at heightened risk for development of food allergies," said Daniel Rotrosen, MD, director of the NIH National Institute of Allergy and Infectious Diseases (NIAID) Division of Allergy, Immunology, and Transplantation.[1] "While recent studies showed no benefit from allergen avoidance, the LEAP study is the first to show that early introduction of dietary peanut is actually beneficial and identifies an effective approach to manage a serious public health problem."[1]

"Food allergies are a growing concern, not just in the United States but around the world," said NIAID Director Anthony S. Fauci, MD. "For a study to show a benefit of this magnitude in the prevention of peanut allergy is without precedent. The results have the potential to transform how we approach food allergy prevention."[1]

The prevalence of peanut allergy among children has been on the rise (doubled) in Western countries and prevalence is apparent in Africa and Asia. In 2015, a collaborative study led by Du Toit et al.,[2] under the LEAP (Learning Early About Peanut) Initiative and funded by the NIAID-funded Immune Tolerance Network (ITN), reported the findings of a large multiyear study evaluating whether a strategy of early introduction of peanut consumption or avoidance is "most effective in preventing the development of peanut allergy in infants at high risk for the allergy."[2]

The study randomly assigned 640 infants between 4 and 11 months of age with severe eczema, egg allergy, or both to consume (6 g peanut protein/week) or avoid peanuts for 60 months.[2] Participants were assigned to separate study cohorts based on preexisting peanut sensitivity screened via the skin-prick test and were evaluated by appearance of no measurable wheal after testing or with a wheal measuring 1–4 mm in diameter. The primary outcome was the number of participants with peanut allergy at 60 months of age. A dietary food record was also collected to check compliance.

Results of the LEAP study indicated the following[2]:

- Among the 530 infants in the intention-to-treat population with initial negative results on the skin-prick test, the prevalence of peanut allergy at 60 months of age was 13.7% in the avoidance group and 1.9% in the consumption group ($P < 0.001$).
- Among the 98 participants in the intention-to-treat population who initially had positive test results, the prevalence of peanut allergy was 3 times higher in the avoidance group compared to the consumption group (35.3% and 10.6%, $P = 0.004$), respectively.
- There was no significant group difference in the incidence of serious adverse events.
- Increases in levels of peanut-specific IgG4 antibody occurred predominantly in the consumption group; a greater percentage of participants in the avoidance group had elevated titers of peanut-specific IgE antibody.
- Peanut allergy was associated with larger skin wheal and a lower ratio of peanut-specific IgG4:IgE.

The authors concluded that "The early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk for this allergy and modulated immune responses to peanuts."[2]

b. LEAP-On Study

In a follow-up LEAP study (LEAP-On), Du Toit et al.[3] examined the effect of avoidance on peanut allergy after early peanut consumption. Their results confirm that the long-lasting effect of regularly consuming peanut-containing foods early in life prevents later development of peanut allergy even after stopping peanut consumption for 1 year. In the LEAP-On study, the rate of peanut allergy remained low after 12 months of peanut avoidance among participants who had consumed peanuts during the primary trial (peanut-consumption group), as compared with those who had avoided peanuts (peanut-avoidance group). Participants from the LEAP study were told to avoid peanuts for 12 months.

The LEAP-On study enrolled 556 of 628 eligible participants (88.5%) from the LEAP study, and 550 participants (98.9%) completed the study. The compliance rate to avoid peanut consumption was 90.4% in the peanut-avoidance group and 69.3% in the peanut-consumption group.

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Results of the LEAP-On follow-up study were as follows:

- Peanut allergy at 72 months was significantly higher in the avoidance group compared to the peanut-consumption group (18.6% versus 4.8%, $P < 0.001$).
- After 12 months of avoidance there was no significant increase in the prevalence of allergy among participants in the consumption group at 60 months (3.6%) and 72 months (4.8%; $P = 0.25$).
- Fewer participants in the peanut-consumption group than in the peanut-avoidance group had high levels of Ara h2 (a component of peanut protein)–specific IgE and peanut-specific IgE, a higher level of peanut-specific IgG4, and a higher peanut-specific IgG4:IgE ratio.

The investigators concluded that children at high risk for peanut allergy and introduced to peanut protein in the first year of life for 60 months did not have an increase in the prevalence of peanut allergy even after a 12-month period of peanut avoidance.[3] Longer-term effects are not known.

Implications: These two studies confirmed that consuming a low dose of peanut protein from birth to 60 months prevents development of peanut allergy later in childhood. Although the study was successful in children, it is not clear whether this effect would apply to older children and currently allergic adults. It will also be interesting to see whether the model used in testing peanut allergy could be applied to other food allergies (e.g., seafood, eggs, and dairy products).

Sources: (1) NIAID (February 23, 2015) Study finds peanut consumption in infancy prevents peanut allergy [Internet]. (2) Du Toit G, et al. (2015) Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 372(9):803–813.(3) Du Toit G, et al. (2016) Effect of avoidance on peanut allergy after early peanut consumption. *New Engl J Med.* 374(15):1435–1443.

C. Global Food Science Trends

1. Additive Manufacturing (3D Printing)

Additive manufacturing is a 3D printing manufacturing method used to build objects by laying down successive thin layers of material until the object takes a designated form.[1] Rapid advances in 3D printing technology are transforming product design, prototyping, and manufacturing. With fewer design restrictions and constraints and more precision than conventional manufacturing processes, 3D printing has improved efficiency and has reduced cost. In this respect, 3D printing has helped make great inroads in shipping, aircraft, and lightweight prototype designs, reducing manufacturing time for some applications by almost a third.

The technology is already being used for rapid prototyping, but it is now gradually being integrated into the existing manufacturing infrastructure, such as in the automotive and aircraft-manufacturing industries.

Implications: 3D printing in the last decades has made inroads into medical applications (organ prototypes). This technology is beginning to make headway in the food industry. The value is not only in applying 3D printing in just early product or packaging prototyping but in also integrating it into the existing food manufacturing infrastructure, as is being done in the automotive and aircraft industries. Food products are complex systems that often require great customization to meet different consumer tastes and preferences. Additive manufacturing can also improve responsiveness to market demands and generally uses only the material necessary to produce a component, thereby driving down the amount of waste and overall material use. This aspect becomes useful in packaging design and manufacturing (i.e., to reduce packaging material). Although additive manufacturing presents many future possibilities in innovative manufacturing, challenges remain that must be considered, such as qualifications and certifications because of variability in specified application needs.

(1) *Source:* (1) DNV-GL (2016). *Technology Outlook, 2025*. Oslo, Norway: DNV-GL.

2. Packaging Technologies

a. Shrilk (Insect Cuticle) Biodegradable Plastic

A fully degradable bioplastic derived from shrimp shells and silk protein could replace regular plastic and be more environmentally friendly.[1] A new degradable bioplastic developed by Wyss Institute used chitosan from shrimp shells laminated with silk fibroin protein, mimicking the microarchitecture of the natural insect cuticle.

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Chitosan is found in the hard shells of crustaceans, armor-like insect cuticles, and flexible butterfly wings. The new material ("Shrilk") can be used to manufacture bioplastics or other materials that are easily degraded during composting, releasing nitrogen-rich nutrient fertilizer.[1] Because chitosan and fibroin are both used in FDA-approved devices, Shrilk may have potential for developing implantable foams, films, and scaffolds as well for surgical closure, wound healing, tissue engineering, and regenerative medicine applications.

- ***Implications:*** Today, about 300 million tons of plastic are produced per year and only 3% are recycled, leaving 97% to break down in oceans and landfills and impacting the food chain and environment. Most current bioplastics are derived from plant cellulose and are used in food and drink packaging. Cellulose is a rigid and difficult material to shape. Shrilk, on the other hand, is flexible and can be used in complex 3D shapes while retaining the hardiness of conventional plastics.

Source: (1) Wyss Institute (2016).

6 Regulatory Science, Science Policy, and Movements

A. United States

1. Healthy People 2030 Planning Is Underway

HHS convened the first meeting of the 2030 Healthy People expert committee in December 2016.[1] The planning committee comprised experts from health promotion, disease prevention, epidemiology, health literacy, communication, law, and state and local public health practice. Committee members are tasked to perform a "...review of the nation's health promotion and disease prevention objectives and accomplishments and... recommend goals and objectives to improve the health status and reduce health risks for Americans by the year 2030."[1] The committee will advise the HHS Secretary on the Healthy People 2030 mission, vision framework, and organizational structure.

Implications: Challenges for the new committee may include a potential change of mission and infrastructural framework in an administration change. In addition, the unaccomplished targets of the 2020 Healthy People goals will need to be an important component of decisions influencing the 2030 mission (e.g., obesity goals for underserved populations, vegetable intake targets for younger populations, or saturated fat targets).

Sources: (1) HHS (2016) November 14, 2016 and March 17, 2016 HHS Federal Register Notices, March 22, 2016 HHS NTP News e-mail update. (2) HHS (2016) *Healthy People 2020*. Washington, DC: HHS.

2. FDA Final Rule on Substances Recognized as GRAS in Foods

The long-awaited FDA final ruling on substances recognized as GRAS in foods was issued in August 2016 and amended on September 8, 2016. According to the FDA, "The final rule eliminates the petition process to affirm that a substance is GRAS under the conditions of its intended use and replaces that petition process with a GRAS notification procedure. We estimate that over 10 years with a 7 percent discount rate, the present value of the total costs of the final rule range from $0.9 million to $3.3 million; with a 3 percent discount rate, the present value of the total costs range from $0.9 million to $3.4 million. The annualized costs of the rule range from $0.1 million to $0.4 million with a 7 percent discount rate and range from $0.1 million to $0.5 million with a 3 percent discount rate."[1]

The major provisions of the Final Rule will help clarify (1) the criteria for classifying food substances as GRAS, and (2) the new administrative process for submitter to provide FDA the needed basis for a conclusion that a substance is GRAS under the conditions of its intended use.

Criteria for eligibility for classification as GRAS in the final rule include the following[1]:

- A substance cannot be classified as GRAS under the conditions of its intended use if the available data and information do not satisfy the safety standard for a food additive under the FD&C Act;
- General recognition of safety requires common knowledge, throughout the expert scientific community knowledgeable about the safety of substances directly or indirectly added to food, that there is a reasonable certainty that the substance is not harmful under the conditions of its intended use;
- "Common knowledge" can be based on either "scientific procedures" or on experience based on common use of a substance in food prior to January 1, 1958; and
- General recognition of safety through scientific procedures must be based upon the application of generally available and accepted scientific data, information, or methods, which ordinarily are published, as well as the application of scientific principles, and may be corroborated by the application of unpublished scientific data, information, or methods.

Further details on the procedure for submitting a GRAS notice and administration of such notices are available online.

Implications: The GRAS process has drawn much debate and was the subject of a lawsuit brought by the Center for Science in the Public Interest. This final ruling will help clarify and address many of the questions raised in GRAS review and approval of ingredients placed in this category.

Source: (1) FDA (2016) *Fed Regist,* p. 54960.

3. FDA Issued New Guidance for Claim "Healthy" on Food Labels

On September 15, 2016, FDA released guidance for use of the implied nutrient content claim "healthy" on food product labels.[1,2] The agency stated that these recommendations in the guidance are nonbinding and are intended to advise for use on food labels. Claiming a product is healthy is allowed if the product complies with the following:

- If the product is not low in total fat but has a fat profile makeup of predominantly mono- and polyunsaturated fats; or
- If the product contains at least 10 percent of the Daily Value (DV) per reference amount customarily consumed (RACC) of potassium or vitamin D.

These recommendations came about in recognition of evolving research evidence. FDA intends to "exercise enforcement discretion with respect to the current requirement that any food bearing the nutrient content claim 'healthy' contain at least 10 percent of the Daily Value (DV) per reference amount customarily consumed (RACC) of vitamin A, vitamin C, calcium, iron, protein, or fiber, if the food instead contains at least 10 percent of the DV per RACC of potassium or vitamin D. The regulations updating the Nutrition Facts label have provided for new DVs for potassium and vitamin D and manufacturers have been given some time to come into compliance with these regulations."[1,2]

FDA indicated that this guidance is effective immediately because the agency has determined that prior public participation is not feasible or appropriate (21 CFR 10.115(g)(2)). FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. FDA guidance reflects current thinking on a topic and should be viewed only as a recommendation, unless specific regulatory or statutory requirements are cited.

Sources: (1) FDA (September 2016). *Guidance for Industry: Use of the Term "Healthy" in the Labeling of Human Food Products.* Rockville, MD: FDA. (2) FDA (August 2016). *Guidance for Industry: Use of the Term "Healthy" in the Labeling of Human Food Products.* Rockville, MD: FDA.

4. USDA Seeks Comments on Reducing Sodium in School Meals

The USDA Food and Nutrition Service is seeking additional public comments associated with its study to "... identify, among schools that are successfully meeting the sodium targets, 'best practices' that could be used to provide technical assistance to School Food Authorities (SFAs) for developing lower sodium menus."[1,2]

> The purpose of this study was to identify the best practices employed by SFAs that have successfully met or exceed[ed] sodium requirements in their schools. The findings will be helpful for SFAs and schools that have difficulty meeting the sodium targets, by providing insight into ways that other similar SFAs have overcome obstacles to successfully serve school meals that meet the sodium requirements. Other important considerations for identifying best practices include the acceptability of meals to children and the additional cost (if any) of providing lower sodium meals. The study will also provide information about the availability of, and strategies for, procuring lower sodium foods for schools to purchase and serve.

Sources: (1) USDA (November 3, 2016) Submission for OMB Review. Beltsville, MD: USDA. (2) USDA (March 16, 2016) Agency Information Collection Activities: Proposed Collection; Comment Request—Successful Approaches To Reduce Sodium in School Meals. *Federal Register Notice.*

5. FDA Seeks Public Input on Long-Range and Cutting-Edge Research Scientific Areas to Help the Agency Fulfill Its Mission

On October 16, 2016, FDA announced that it is establishing a public docket (Docket No. FDA-2016-N-2406 for "Emerging Issues and Cross-Cutting Scientific Advances" here) to receive input on emerging issues and cross-cutting scientific advances that will enhance FDA preparedness and interagency activities.[1]

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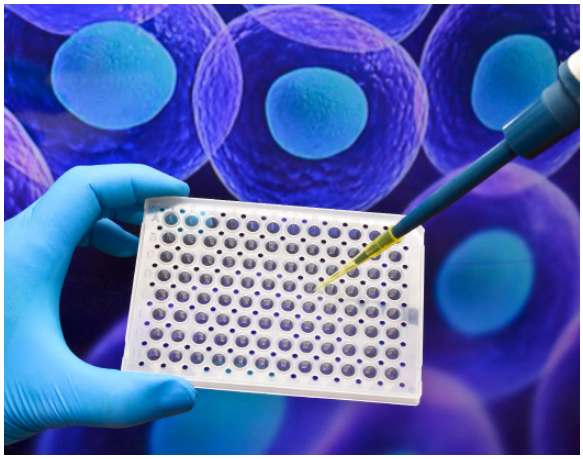
This solicitation for external inputs came as a result of a 2007 report of the FDA Science Board, which raised concerns about FDA's "weak scientific base and inadequate scientific workforce" and "highly doubtful" ability to ensure the rapid entry of new technologies and life-saving new medical therapies. As a result, the board created a multidisciplinary committee to explore the identified weaknesses. The committee noted areas that needed improvements:

- Medical product quality control procedures had not kept pace with advances in research, product development, and biomedical innovation.
- A need exists to "facilitate the qualification of biomarkers, including surrogate endpoints, for evaluation of new therapies and providing guidance on how new biomarkers can be qualified as surrogate endpoints."
- The use of clinical trial networks and master protocols should be encouraged, access to external experts in emerging technologies should be expanded to expedite approvals ,and data-mining and analytical tools should be used to further evaluate the safety and efficacy of new drugs and devices.

Since the 2007 report, the Science Looking Forward Subcommittee of the Science Board has noted several improvements in FDA's collaborations with outside groups and support of a culture of science, which Zachary Brennan[2] described as follows:

- The creation of the Office of the Chief Scientist, strengthening areas related to regulatory science, health informatics, professional development, and bioterrorism
- Initiatives that deal with new technology innovations, including stem cells, 3D printing, predictive toxicology, genome sequencing, computer simulation, and, more recently, organs-on-chips
- Collaboration with NIH on the Precision Medicine Initiative
- Advancing regulatory science that promotes the lifecycle approach to regulation for drugs, devices, biologics, and foods
- Enhanced focus on postmarket surveillance (e.g., new Sentinel active surveillance system)



The 2016 *Federal Register* announcement[1] called for public submissions for comments on longer-term emerging technologies and cross-cutting scientific advances that would help advance FDA's ability to fulfill its mission. The agency stated that "FDA's ability to achieve its mission relies on awareness of, and proactive preparedness for, emerging issues and scientific advances, which will impact the development of regulated products well in advance of formal FDA regulatory submissions (e.g., 5–10 years). Of particular interest are the emerging areas such as synthetic biology and bio-inspired technologies [that] are expected to impact FDA regulated products in the relatively near term."[1]

Inputs will be evaluated by FDA's Emerging Sciences Working Group. According to FDA, "The group would provide FDA a wide science-based forum to identify and communicate scientific regulatory approaches, in order to prepare for anticipated high impact emerging science and technology that could impact regulatory policy development."[1]

Implications: Many of the emerging research areas and technologies identified will have importance in current and future food and nutrition research for developing better diagnostic dietary assessment tools, more specific guidelines targeted for diseased populations, and improved criteria for customized dietary intervention (e.g., personalized foods and dietary interventions).

Sources: (1) FDA (2016) Emerging Issues and Cross-Cutting Scientific Advances; Establishment of a Public Docket. *Federal Register*. (2) Brennan Z (September 21, 2015) FDA Science board calls on agency to find new ways to stimulate biomedical innovation [Internet]. *Regulatory Affairs Professional Society*.

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6. Regulations Must Be Streamlined to Reduce Burden, Confusion, and Conflicts, According to a 2016 National Academies Report

A new report released in 2016 by the National Academies of Sciences, Engineering, and Medicine (NAS) concludes that the continuing growth of federal research regulations and requirements is "diminishing the effectiveness of the nation's research investment" by forcing investigators to spend more time on administrative and compliance matters, rather than research.[1] The report proposes a new regulatory framework for the 21st century, titled "Optimizing the Nation's Investment in Academic Research: A New Regulatory Framework for the 21st Century: Part 1."[2]

The study was mandated by Congress and supported, in part, by funds from NIH and the US Department of Education. The report includes specific proposed actions to reduce the regulatory burden for various stakeholders, such as Congress, the White House Office of Management and Budget (OMB), federal agencies, and academic research institutions, citing the following call-outs[1]:

- The need for "strengthening the partnership between the government and university research and urges the establishment of a government-enabled, private-sector Research Policy Board to support this partnerships and work to streamline research policies."
- The "different, and sometimes conflicting, sets of policies and regulations among the various federal agencies especially on guidance on compliance in areas such as financial conflict of interest, animal care, grant proposals, and the like."

Recommendations include the following:

- Congress should work with OMB to conduct a review of agency research grant proposal documents for the purpose of developing a uniform format to be used by all funding agencies.
- Congress should work with the White House Office and Science and Technology Policy (OSTP) and research institutions to develop a single financial conflict-of-interest policy to be used by all research funding agencies.
- Congress should instruct OSTP to convene representatives from federal agencies that fund animal research and from the research community to assess and report back to Congress on the feasibility and usefulness of a unified federal approach to policies and regulations pertaining to the care and use of research animals.
- OMB should require that research funding agencies use a uniform format for research progress reporting.
- Federal agencies should limit research proposals to the minimum information necessary to permit peer evaluation of the merit of the scientific questions being asked, the feasibility of answering those questions, and the ability of the investigator to carry out that research.
- Universities should conduct a review of institutional policies developed to comply with federal regulations of research to determine whether the institution itself has created excessive or unnecessary self-imposed burden.

Implications: Although the call-outs have been targeted to stakeholders that include congress, government, and academia, industry participation to streamline the regulatory burden was not included or limited and was not explicit.

Sources: (1) NAS (September 22, 2015) Inconsistent, duplicative regulations undercut productivity of U.S. research enterprise; actions needed to streamline and harmonize regulations, reinvigorate government-university partnership [Internet]. (2) NAS (2015) *Optimizing the Nation's Investment in Academic Research: A New Regulatory Framework for the 21st Century*. Washington, DC: National Academies Press.

7. 2017 HHS Budget Focuses on Targeted Key Priorities

The president's FY 2017 Budget provides $82.8 billion in discretionary funding for HHS to continue and to expand critical science initiatives in the safety and health areas.[1] Examples include the following:

- Increase access to early intervention for mental and behavioral health programs.
- Address opioid abuse, misuse, and overdose through a $1 billion initiative to expand access to treatment.

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- Support research/intervention initiatives to combat bacteria antibiotic resistance.
- Modernize the current food safety system to reduce foodborne illness outbreaks and position the nation to meet the challenges of the global market. The NIH budget includes $1.6 billion, an increase of $212 million. The budget also includes $52 million for CDC activities, which will help address the critical unmet needs in the nation's food supply safety system by focusing on monitoring, surveillance, data analysis, and dissemination of technical guidance, training, and technology to state health departments.
- Support US and global efforts to meet the needs of natural and human-made threats, disasters, outbreaks, and epidemics. Supports emergency preparedness aimed at addressing chemical, biological, radiological, and nuclear threats, outbreaks, and epidemics.
- Maintain historic investments in Head Start and child health and education.
- Invest in programs for older adults including nutrition services. The FY 2017 budget provides $151 million for family caregiver support services; a $2 million increase for the lifespan respite care program; and an additional $10 million for a total of $358 million, to fund in-home and community-based services. The FY 2017 budget provides $849 million in funding for the Administration for Community Living (ACL) Nutrition Services programs, $14 million more than FY 2016 to provide an estimated 205 million meals to over 2 million older Americans nationwide. Within the nutrition budget, a 1% set-aside is included for evidence-based innovations that will help make future funding for nutrition services more cost-effective through improved quality and efficiency.
- Invest in scientific research and medical innovation. Scientific, technological, and medical breakthroughs will be on the forefront of several scientific efforts:
  - The Cancer Moonshot Program, focusing on causes of cancer, new prevention strategies, early detection, diagnosis, and treatment and modernization of regulatory pathways.
  - Scale up of the National Precision Medicine Initiative, including a dedicated research cohort of a million or more individuals.
  - BRAIN Initiative; and support of research to reduce and treat Alzheimer's disease.
  - Agency for Healthcare Research and Quality efforts to build an evidence base to drive systemic health care improvement.

Implications: Current NIH research priorities and resources tended toward medical (pharmacological and devices) discoveries and interventions. More future resources may need to be put into food and nutrition research. Perhaps once the NIH Nutrition Research Task Force completes its 10-year nutrition strategic plan, a clear path on funding and research priorities will emerge. It is important that the nutrition and food research communities continue to work to support NIH's mission in areas such as individual variabilities, precision and personal, nutrigenomic nutrition, mechanisms of taste, and research in healthy and aging populations.

Source: (1) HHS (2016).

B. European Union

1. Health Claims

The EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) has approved health claims on calcium and bone health. The opinion of panel members was published in the *EFSA Journal* in 2016.[1] The claim was reviewed following a 2008 application from Specialised Nutrition Europe (formerly IDACE) seeking authorization for a health claim on calcium in accordance of Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of France. The NDA was asked to provide an opinion on the scientific substantiation of a health claim related to calcium and its impact on normal development of bones.

The panel concluded based on data presented that[1]:

- Calcium as a food constituent has been sufficiently characterized for health claims.
- The panel agrees that calcium contribution in normal bone development is a beneficial physiological effect and supports the claim that the calcium effect 'is important for the development of bones for infants (from birth) and young children up to 3 years of age. A cause and effect relationship has been established between the dietary intake of calcium and contribution to the normal development of bones.'
- The following wording reflects the scientific evidence: 'Calcium contributes to the normal development of bones.'

- In order to bear the claim,
  - Follow-on formulae should comply with the criteria for the composition of follow-on formulae as required in the Directive 2006/141/EC.
  - Nutritionally complete foods for special medical purposes intended for use by infants and nutritionally complete foods for special medical purposes other than those intended for use by infants should comply with the criteria for the composition of these foods as laid down in Directive 1999/21/EC.
  - Processed cereal-based foods for infants and young children should comply with the criteria for the composition of these foods as laid down in Directive 2006/125/EC.
  - Other foodstuffs intended for infants and young children should provide at least 15% of the reference values for the nutritional labeling of foods intended for infants and young children as laid down in Directive 2006/141/EC. Such amounts can easily be consumed as part of a balanced diet. The target population is infants and young children up to 3 years of age.
  - No tolerable upper intake levels have been set for calcium for this age group of infant and children.

Source: (1) Turck D, et al.; EFSA NDA Panel (2016) Scientific opinion on calcium and contribution to the normal development of bones: evaluation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006. *EFSA J.* 14:4587, 9 pp. doi:10.2903/j.efsa.2016.4587.

2. Dietary Reference Values

EFSA's NDA issued a draft of its Scientific Opinion on Dietary Reference Values for vitamin B_6 in 2016.[1] Following a request from the European Commission, NDA derived a dietary reference value (DRV) for vitamin B_6, concluding that:

- Plasma 7 pyridoxal 5′-phosphate (PLP) concentration is a suitable biomarker of status for deriving DRVs for vitamin B_6.
- A plasma PLP concentration of 30 nmol/L, as a population mean, is indicative of an adequate vitamin B_6 status. The panel proposes this cut-off value to set average requirements (ARs).
- Population reference intakes (PRIs) are derived for adults and children from ARs, assuming a coefficient of variation (CV) of 10%.
- For women, the AR and PRI are set at 1.3 and 1.6 mg/day. For men, the AR of 1.5 mg/day is derived by allometric scaling from the AR for women, and a PRI of 1.7 mg/day is set.
- For all infants aged 7–11 months, an AI of 0.3 mg/day is set, averaging the results of two extrapolation approaches based on allometric scaling: upwards extrapolation from the estimated intake of vitamin B_6 of exclusively breastfed infants from birth to 6 months, and downwards extrapolation from the ARs for adults applying a 16 growth factor.
- For all children, ARs are derived from adult ARs using allometric scaling and growth factors.
- For children of both sexes aged 1–14 years, ARs range between 0.5 mg/day and 1.2 mg/day. For children aged 15–17 years, the panel derives the same ARs as for adults.
- PRIs for children aged 1–17 years range between 0.6 and 1.7 mg/day. Extrapolation of ARs by allometric scaling considered differences in reference body weight.
- For pregnant and lactating women, additional requirements are considered, based on the uptake of vitamin B_6 by the fetal and maternal tissue and the losses through breast milk, and PRIs of 1.8 and 1.7 mg/day, respectively, derived.

Source: (1) EFSA NDA Panel (2016) Scientific Opinion on Dietary Reference Values for vitamin B6. *EFSA J.* 14:4485, 79 pp. doi:10.2903/j.efsa.2016.4485.

C. Canada

1. Emerging Challenges in Regulatory Science

a. Changing Food Environment

Canadian regulatory science is evolving to respond to multiple changes in the Canadian food environment that are contributed by many concurrent factors. These factors include changing consumer food purchasing behavior, an aging population, changes in ethnic populations, administrative changes, social and economic shifts, rapid advances in emerging science in systems and synthetic biology, genomic research, and novel food ingredients and technologies (gene editing, CRISPR, stem cells, high-throughput screening), all of which will influence regulatory science decisions.

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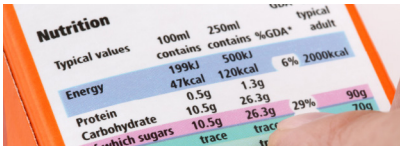
b. Emergence of Deliverology

Deliverology is the science of delivering on goals and promises made by governments, in which the promises are implemented using tax monies for programs.[1] It relies on clearly identifying priorities, setting targets and collecting data related to those priorities, and exercising central oversight through a unit reporting directly and regularly to the leader.[1] The deliverology concept was developed by UK educator Michael Barber and a team at McKinsey and has been extensively applied in several countries. Deliverology science was first applied to evaluate the effectiveness of government-funded initiatives and policies under UK Prime Minister Tony Blair's administration in order to provide the checks and balances of tracking deliverables of government-funded services, programs, and policies using taxpayer dollars.

- ***Implications:*** The adoption of deliverology will have broad implications for scientific research and public health policies. This approach would instill an increased need for scientific accountability and clear outcome measures. This means increasing scientific substantiation of policy decisions as well as identifying the intended/unintended consequences of policy decisions, including the cost, timing, and evaluations of implementation and compliance. Governments are employing a methodical approach to define, assess, and report on the results produced; emphasis is now on delivered measurable progress. All policy decisions will need to clearly define the target segments for which policies are reaching with clear articulations of desired outcomes, types of outcome measures, and how to measure success. How deliverology science will affect nutrition and food safety programs needs further study. A case example is how to measure whether regulations banning *trans*-fat in the diet have any impact on health. Do national food guides/eating recommendations impact eating behaviors? How do we develop consensus regarding biomarkers?

c. Food Labels

There is increasing discussion on whether food disclosures should be mandatory or voluntary. This raises several questions in areas related to (1) how to inform and educate consumers on food processing and production, (2) what is in food, (3) how it is regulated for safety, (4) efficacy of claims, and so forth.[2]



d. Erosion of Trust

There is public confusion on scientific research and recommendations, resulting in erosion of trust in scientific research and findings. More effective ways are needed to inform and educate consumers about what a food contains and how the food is produced. Use of alternative information sources (e.g., the QR method) is driven, in part, by a variety of factors, including the desire to provide access to more information, limitations in packaging space, inability to communicate scientific information clearly and concisely, and inability of governments to enforce non-health and safety information requirements. The explosion of nongovernment, third-party assurance/certification agencies providing symbols and statements for use on product labels and websites may work to increase or decrease trust in the food supply.

- ***Implications:*** More research is required to determine how consumers perceive nongovernment labeling statements and alternative information sources to using the label; enforcement/compliance resources are focused solely on food safety/health (not consumer fraud).

e. Approval of New and Novel Ingredients

- Approval of alternative nontraditional protein sources—insects, meat grown in labs, fermented grains, and algae-microbials. Alternative protein crystals produced by *Diploptera punctata* (cockroach milk). Contribution to nutritional intake/impact on iron status and other minerals
- Risk assessment protocols for nontraditional food processing technologies—What evidence is required? When is there adequate evidence to support their application to food processing? What are the opportunities for global review panels for scientific assessment using internationally accepted protocols (e.g., Cochrane Reviews)?

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f. Guidance and Regulation of New Technology

- Challenges related to the process and substantiations needed for approval of new regulations on new technologies for foods (e.g., 3D printing for foods) and in manufacturing (additive manufacturing); novel ingredients (i.e. alternative proteins; fibers); bioengineered foods; biofortification; CRISPR as a gene-editing tool for food use.

Sources: (1) Curran R (April 27, 2016) Will "deliverology" work for the federal government? *Policy Options*. (2) Health Canada (2016) Consultation on front-of-package nutrition labelling [Internet].

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7 Consumer, Food, and Marketplace Trends

A. Global Consumer Trends

Global consumer food trends were taken from research reports from three sources: Euromonitor International, Mintel, and Innova Research from Thomson Reuters.

1. Changing Consumer Shopping Trends

Euromonitor conducted a global assessment of trends from multiple studies.[1] Highlights are as follows.

- **Rise of the "Agnostic Shoppers."** This is symbolic of today's contradictory shopper. These consumers are very well informed with savvy-shopping zeal, and they like to compare prices using the Internet or visiting multiple stores in search for values (not always based on price but also on utility and needs). They are less bothered by labels and brands.
- **"Saving Time" Means "Buying Time."** This is no longer just about convenience. Time is "luxury" and consumers are looking for time-saving solutions by outsourcing. Thirty percent of UK households would rely on ready-made food options to save time/stress in the kitchen. Seventy percent of affluent Indians, aged 18–35 years, see luxury as "how much free time one enjoyed," rather than purchasing power. This compared with 68% of respondents in South Korea and 59% in China. Saving time has been reported among US and Canadian shoppers as well and is a key driver behind the surge in shopping for food locally and online, eating ready meals, and eating locally.
- **Defying Aging.** In 2016, old age is about a mature lifestyle, as more people are living a busier, more satisfying, and extended "third age," starting after middle age—anywhere from 55 to 65 years. Post-middle-age consumers are more energetic, work more, enjoy maintaining good physical health, pay attention to mental well-being, and are able to lead fuller lives.
- **Change Makers.** Making life better through social causes is gaining mainstream priority. Younger consumers (especially millennials) are setting the lead in a crusade to embrace social causes. Consumer expectations regarding corporate environmental issues are growing; millennials especially, with recent greenwashing scandals in mind, want brands they buy to behave responsibly.
- **Seeking Greener Foods**. This trend is no longer a niche but is going mainstream worldwide. Attributes of green foods include all-natural, organic, supported by organic certification, locally grown, vitamin rich, no additives, and no added fat or less fat, sugars, and salt.
- **Preserving Mental Well-Being**. This is a move toward mindfulness in all aspects of daily activities.
- **Overconnected Shoppers**. There is increasing concern regarding digital and device overconnectivity.
- **Surge in Security Devices and Home Protection Services**. This concern for personal and family security/safety is also transferring to food purchases and preservation.
- **Increasing Spending by Singles**. There is an increase in the number of single individuals with no children and in the number of empty nesters, which translates to a need for smaller portions. Upwardly-moving younger singles are more inclined to indulge in luxury and higher-priced products.

Source: (1) Euromonitor International (2016).

2. Global Trends in Food and Drinks

Mintel's team of global analysts have identified 12 key trends that will impact the global food and drink market in 2016 and beyond[1]:

1. **Alternatives Everywhere.** The growing appeal of novel and alternate protein sources will profoundly change the marketplace, in which what was formerly "alternative" could take over the mainstream. This is clearly seen in the results of the National Restaurant Association's "What's Hot in 2016" survey of chefs (described below), in which the vegetable is replacing protein as the center of the plate.
2. **Artificial: Public Enemy Number 1.** Consumer demands for natural and "less processed" food and drink are forcing companies to remove artificial ingredients.

3. **Eco Is the New Reality.** Climate change is permeating consumers' daily concerns worldwide. Drought, food waste, and natural disasters not only impact agriculture production and interrupt the food supply, but they also influence availability, preparation, and production.
4. **From the Inside-Out.** Consumers are recognizing that nutrition and diets can connect with the way they look and feel, as well as with quality of life and longevity.
5. **Increasing Performance.** Increasing promotion of fitness and athletic programs is encouraging consumers to get and stay active and presents a parallel need for food and drink that helps consumers interested in performance and sports nutrition.
6. **Communicating Based on True Stories.** These messages are found to be more compelling and impactful with product origin, ingredients, or inspiration stories.
7. **e-Revolution: From Carts to Clicks.** While the Internet has not yet vastly changed the landscape of grocery shopping, innovations encourage consumers to think outside traditional physical retailers.
8. **Diet by DNA.** Interest in natural products and "getting back to basics" has boosted interest in ancient grains and superfoods, fostering a principle that age-old staples are better than today's manufactured options.
9. **Good Enough to Tweet.** The rise of food-centric media has sparked new interest in cooking, not only for the sake of nourishment but also for the purposes of sharing one's creations via social media.
10. **Table for One.** Across age groups, more consumers are living in single-person households or occasionally eating meals alone.
11. **Fat Sheds Its Stigma.** Consumer awareness of the many sources of good and bad fats is ushering in a paradigm shift in which fat content is not the first and foremost consideration in the search for healthy products.
12. **Eat With Your Eyes.** Flavor has long been the core of innovation, but more visual and share-focused societies call for innovation that is boldly colored and artfully constructed.

Source: (1) Global Food Forums (2016).

3. Emerging New Trends in Food and Drinks on Health and Practice

In 2015, the Innovation Group (J. Walter Thompson Intelligence's think tank) outlined some key trends that will impact the food and beverage industry of the future.[1]

- **Food and Health Converging.** Health-conscious millennials are gravitating toward healthier mixers and combining exercise with hedonism when it comes to alcohol.
- **Technology Changing the Way We Eat.** The future promises curated delivery, delivery-only restaurants, and even zero-cost delivery by self-driving car. A FoodBev editor noted "Last month, we reported on a survey that claimed the way in which we ordered food was directly influencing the cuisines we opted to eat."

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- **The Rise of "Post-Artisan."** The cloying cocktails of the 1970s and 1980s—long considered passé—are reemerging in a comeback for sophisticated, modern palates.
- **Sharing Our Food With Others.** Sharing pictures of foods, recipes, and eating locations is now made feasible by mobile devices and increasing digital access globally. Some 72% of British and American millennials are likely to share pictures of their food and drink if it is different or unique, compared with just 22% of baby boomers. The Internet and smart devices are making virtual sharing of foods and cuisines eaten a norm.
- **Cannabis in Beverages.** Nearly three-quarters of consumers surveyed across the millennial, generation X, and baby boomer generations agree that marijuana will be as socially acceptable as alcohol over the next decade.

Source: (1) FoodBevMedia (2015).

4. Baby Boomers and Millennials–A Clash of Age and Food Preferences

Current restaurant sales for the baby boomer and millennial markets are estimated at $783 billion. Both segments are passionate about foods, cuisines, and great service. But expectations are quite different, according to a Restaurant Hospitality report.[1]

Millennials are drawn to trendy cuisines, tableside payment, bolder flavor and taste (spicy, salty, combinations), and social media technologies for communicating with restaurants. They are two to three times more likely than boomers to use a restaurant electronic ordering tablet or a tableside payment terminal. In contrast, boomers are more likely to prefer familiar foods and staples, keeping with traditional technologies such as phones and e-mail, based on findings from the 2016 Restaurant Industry Forecast conducted by the National Restaurant Association.

- ***Implications:*** This learning is useful when targeting behavior change in the two groups, especially when related to restaurant food decisions, meal selections, and mode of access to restaurant dining and payment. A restaurant catering to both population segments will need to strike a balance in the types of foods and service offerings. As stores evolve to more online shopping, they must also balance the needs of baby boomers that tend to prefer to shop for products in person. Similar messages apply to communicating nutrition, food, and health information to millennials' taste preferences and the shopping habits of baby boomers.

Source: (1) Flynn M (2016). How to engage both millennials and boomers. *Restaurant Hospitality.com*.

5. Generation Alpha: Children of Millennials, Where the Virtual World Is a Daily Reality

Dan Schawbel, director of Future Workplace, defines Generation Alpha as persons who were born after 2011 (aged ≤5 years). Generation Alpha comprises the children of millennials and is predicted to grow to 35 million in the next 2 decades. These individuals will be very comfortable in a virtual world of smartphones, electronic readers, wearables, IoT, and more.[1]

"Using these technologies will feel very natural to them, and their behavior will influence older generations, as we've seen in the past with millennials and [Generation] Z. …We believe their tech adoption, and the advancements in technology, will make them lonely, detached and have less direct human contact," Schawbel warns.[1]

- ***Implications:*** There is growing concern among health professionals that prolonged and constant exposure to digital reliance may have harmful effects on effective communication and maintaining relationships.

Source: (1) Schawbel D (2014).

B. US Food Trends

1. Restaurant Food Trends

a. Top 20 Foods for 2016

The National Restaurant Association's "What's Hot in 2016" survey of chefs predicts food and menu trends for the coming year to find the hottest menu trends that will be served in restaurants.[1]

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The online study, conducted in late 2015 by the National Restaurant Association, surveyed 1575 chefs who were all members of the American Culinary Federation. Participants were asked to rank a list of 221 items as a "hot trend," "yesterday's news," or "perennial favorite" on restaurant menus in 2016.[1] Results of the study showed an increasing interest in locally grown foods and ingredients, natural and environmentally sustainable foods, artisan foods, healthy kids' meals, and reduction in food waste.

1. Locally sourced meats and seafood
2. Chef-driven fast-casual concepts
3. Locally grown produce
4. Hyper-local sourcing
5. Natural ingredients/minimally processed food
6. Environmental sustainability
7. Healthful kids' meals
8. New cuts of meat
9. Sustainable seafood
10. House-made/artisan ice cream
11. Ethnic condiments/spices
12. Authentic ethnic cuisine
13. Farm/estate branded items
14. Artisan butchery
15. Ancient grains
16. Ethnic-inspired breakfast items
17. Fresh/house-made sausage
18. House-made/artisan pickles
19. Food waste reduction/management
20. Street food/food trucks

Source: (1) National Restaurant Association (2015). *What's Hot: 2016 Culinary Forecast.*

b. Disrupting the Norms: New Restaurant Food Signals

The National Restaurant Association study[1] also identified some new food menu signals with potential to disrupt the norm:

- **More Fresh Vegetables.** More fresh vegetables as the protein center of the plate, but in disguise.
- **Sriracha = The New Ketchup?** This sauce will break ground for new and novel condiments and spices to create bolder flavors.
- **Emergence of African Flavors.** African flavors are gaining traction among millennials but have a long way to go in North American cuisine.
- **The Restaurant–Grocery.** "Grocerants" are grocery stores increasingly focusing on foodservice with their fresh produce. Hybrid concepts like food halls and market restaurants are leading the way.
- **Simplicity.** Simple, back-to-basics cooking, with classic dishes and few ingredients.
- **Molecular Gastronomy.** Molecular gastronomy is turning more mainstream, losing the "foam."
- **Pickling, Fermenting, and Smoking.** Pickling, fermenting, and smoking are regaining popularity.
- **Gluten-Free and Kale.** Gluten-free and kale are going mainstream. Both are losing novelty but are likely to evolve into perennial favorites over time (e.g., kale salads).

Source: (1) National Restaurant Association (2015). *What's Hot: 2016 Culinary Forecast.*

2. New Food Signals Predicted for 2017

a. Ten Cutting-Edge Food Trends for 2017: Chocolate for Breakfast, Sardines for Lunch, and Goat for Dinner!

Consumers are seeking to rediscover traditional cooking methods and explore global cuisines.

—Liz Moskow, Culinary Director at Sterling-Rice Group (October 2016)[1]

"With nutrition, sustainability, and authenticity top of mind, consumers are seeking to rediscover traditional cooking methods and explore global cuisines, and restaurants and packaged food companies are taking note," says Liz Moskow.[1] Many of these cutting-edge food trends are being combined to create new novelty food offerings.

1. **Chocolate.** Chocolate can be eaten at all occasions.
2. **Turmeric.** Turmeric has been trending over the past couple of years and is widely accepted. It is a good balancing additive for food.
3. **Plant Butchery**. Chickpeas, corn, legumes, and fungi are standing in for steaks in an emerging crop of butcher shops with products designed to appeal to vegans and carnivores alike. "Plant butchery really focuses in on the fact that meat eaters are exploring plant-based options," says Moskow.

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4. **Food Waste Frenzy.** Consumers and companies are creatively reducing food waste by repurposing typically tossed-out stems, skins, and rinds. "This is driven by millennials' desire to make the earth a better place," Moskow said. "They're finding ways to repurpose and use things that would ordinarily be discarded. For example, watermelon rinds being made into pickles, or making cauliflower rice using the stem, something that ordinarily would end up in the garbage." A company called Forager Project has identified a use for the wasted pulp from production of cold-pressed juices—by manufacturing organic tortilla chips containing the nutritious byproduct.
5. **Snackin' Sardines.** Present-day trends for sardines support a move to the protein-rich fish. In restaurants, the rise of toast's popularity presents an opportunity to offer sardines as a topper. "Sardines are high in omega-3 fatty acids, high in protein, high in umami flavor, all things that are trending," Moskow said.
6. **Hand-Pulled Noodles.** Offering authentic taste and showmanship, hand-pulled noodles are hot in big-city Chinese restaurants.
7. **Mocktail Mixology.** Mocktails are getting a modern makeover, with such offerings featuring fresh-pressed juices, flavored teas, sipping vinegars, and muddled herbs and spices. According to Moskow, "It's sort of like the next incarnation of soda. People don't want to view it as soda, but as a cocktail. It's like an adult Shirley Temple."
8. **Goat for Dinner.** Goat is potentially the next hot protein to hit plates in the United States.
9. **Cook and Connect.** Like Uber and Airbnb, a new app and website called EatWith connects home cooks with hungry strangers. "This is really all about people craving interaction in an increasingly disconnected world," Ms. Moskow said.
10. **Migratory Meals.** Immigrants are playing changing food palate in their new home countries, inspiring unique fusions of flavor and heritage. "Where we're seeing this now the most is in war-torn Middle East, with Afghanis, Syrians, Persians all fleeing the area and their food culture trickling down and out," Ms. Moskow said.

Source: (1) Watrous M (2016) Ten cutting-edge food trends for 2017. *Food Business News.*

3. Changing Consumer Trends Among Americans

The International Food Information Council Foundation (IFIC) *2015 Food & Health Survey: Consumer Attitudes toward Food Safety, Nutrition & Health* identifies the following trends that are changing among US consumers.[1]

1. Taste has more impact on decisions in food shopping than price, healthfulness, convenience, and sustainability.
2. Dieticians, health professionals, and government institutions are the most trusted sources of nutrition information by consumers.
3. Regarding food safety, consumers are more likely to trust food that is grown locally or served in local restaurants.
4. Moderation, portion-size control, variety, and inclusion of healthy foods are the building blocks consumers define for healthy living.
5. A healthy diet is defined as one of moderation with inclusion of healthy foods.
6. Consumers are making dietary improvements through small gradual changes by including more fruits and vegetables (however, the 2020 Healthy People targets on increasing vegetable intakes are not being met; consumer intake is 0.77 cups but the target is 1.13 cups).
7. Sixty-six percent of adults are confident that the US food supply is safe.
8. Consumers are avoiding foods that have high sugars, high fructose corn syrup, and preservatives.
9. Consumers are concerned with food waste: (1) 6 out of 10 consumers take food home from restaurants. (2) The top contributor to food waste is buying too much fresh produce, forgetting about perishables.
10. Four out of 10 consumers believe that conserving nature and reducing use of preservatives in food is an important approach to producing sustainable foods.

Source: (1) IFIC (2015) *2015 Food & Health Consumer Survey: Consumer Attitudes Toward Food Safety, Nutrition & Health*. Washington, DC: IFIC.

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C. Canada

1. Changing Consumer and Food Trends Among Canadians

A study sponsored by Agriculture and Agri-Food Canada identifies changing environmental drivers that could impact Canadian food trends in the future. Key findings from the report, *Changing Canadian Environmental Trends: A Long-Range Look at Food Trends to 2020*, indicated the following drivers that will have a relevant impact on Canadian food trends.[1]

- **Population.** The Canadian population will continue to age, with more seniors and fewer children projected between 2004 and 2020. This finding will have implications for the type and quantity of food demanded as well as where it will be consumed.
- **An Evolving Society.** Shrinking household size, participation in the workforce, globalization, environmental awareness, and media fragmentation. Brands become less of a status symbol and more an expression of individualization.
- **The New Face of Canada.** Increasing immigration.
- **Changing Meal Patterns.** Less food preparation. Shopping and eating habits will be sporadic; meal planning cycles will be shorter, snacking will replace courses as well as whole meals, and food will become even more portable. These trends will have implications for both food and package waste.
- **Shifting Expenditures.** The move to spending less disposable income on food will continue. Retail food purchases will still dominate, while food service will see only modest growth in expenditures. The real shift will be in prepared meals and takeouts.
- **Food for Health.** The most significant health driver will be obesity, with its associated medical conditions such as CVD and diabetes. One in two adults and one in three children were considered overweight or obese in 2001. The move to adopt healthier lifestyles will be slow. Adults faced with serious health concerns related to their weight may be motivated to change their diet and activity patterns, but it may take a concerted effort to educate this group and the next generation of children, in order to achieve significant lifestyle and diet improvements within the population.
- **No Trade-Off for Convenience**. Fresher, tastier, ready-to-go products.
- **Organic Foods.**
- **More Indulgence**. Taste is still a top driver of food purchase. Gourmet food represents a small indulgence, an affordable luxury, and a reward. Canadians will embrace gourmet foods and boutique brands. Slow foods, high quality, smaller portions, and nutritious foods will gradually replace demand for fast, big, and cheap.
- **Food Safety and Product Concerns.**
- **More Veggies, More Meatless Meals.** Growth will be gradual.
- **The Educated Consumer... Fads or Trends**? By raising a generation of label readers, more consumers are becoming conscious of nutrition and food ingredients, with a focus on zero *trans*-fats, low sodium, healthy/high fiber carbohydrates (the low-carb fad is nearly dead), reduced sugar, allergen identification, fortification, and health claims. Foods with a function beyond just energy will be in demand.
- **Sustainability**. Closed loop systems; carbon footprint; local, smaller portions; new processing techniques such as vertical hydroponics, aquaculture; recycling water and its impact on food safety regulations.

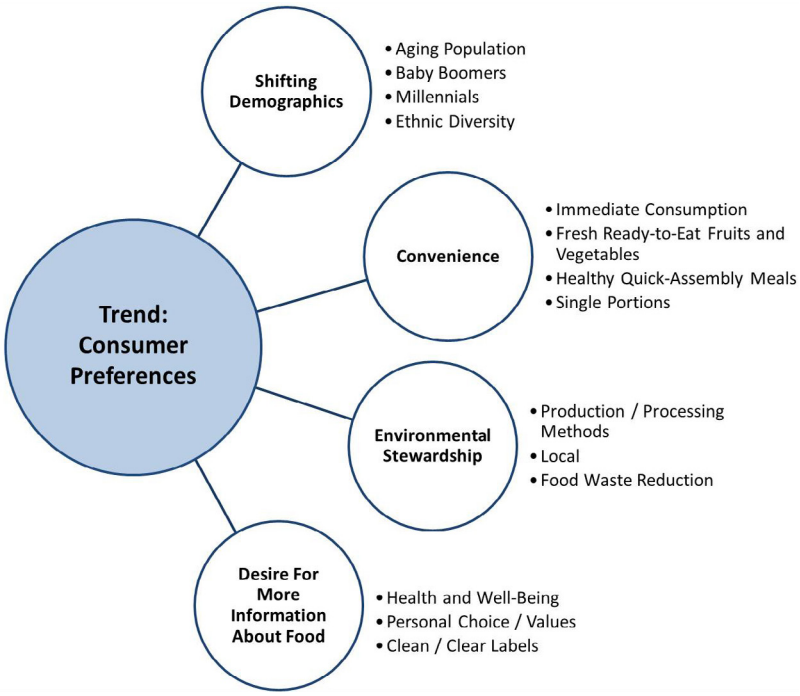
Source: (1) Serecon Management, Consulting Ltd. and Agriculture and Agri-Food Canada (2005) *Canadian Food Trends to 2020—A Long-Range Consumer Outlook*. Ottawa, Canada: Agriculture and Agri-Food Canada.

2. Canadian Consumer and Market Trends

Increasingly, consumer food preferences are influenced by changing demographics (aging population, ethnic diversity, and population segmentations), demand for convenience (time savers, healthier convenience, ready-to-go fresh produce, and single servings), environmental stewardship (local grown and served; natural/no chemical products; reducing food waste; minimal processing), and demand for more information (health and healthy information; personalized and customized products and services, clear label and transparency) (Figure 14).

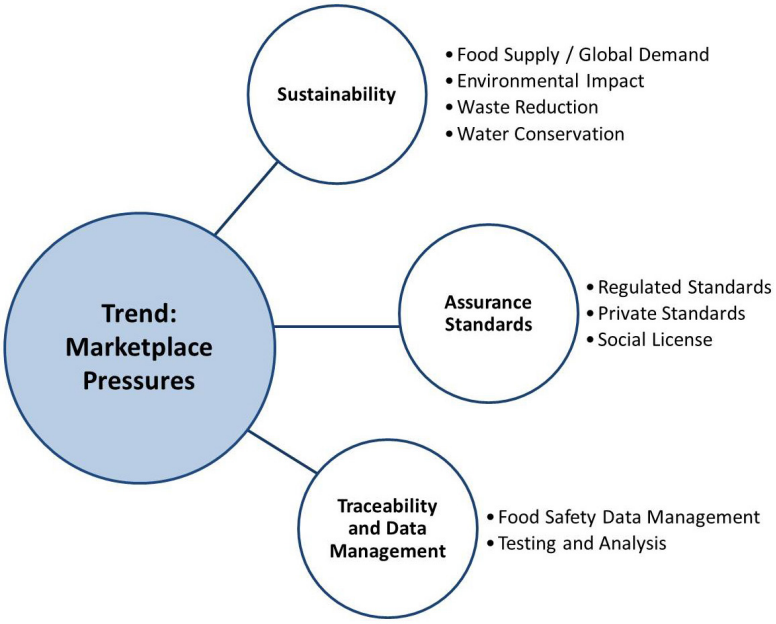
At the same time, the marketplace is experiencing enormous pressure from environmentalists calling for increased attention to sustainability, food component and ingredient product traceability, food safety, and assurance of quality and standards, including the following (Figure 15):

Figure 14. Consumer Preferences in Canada



Source: Agriculture and Agri-Food Canada.[2]

Figure 15. Marketplace Pressures in Canada



Source: Agriculture and Agri-Food Canada.[2]

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- Third-party assurance and certification programs (e.g., Non-GMO Project, Whole Grains Council, etc.), role of government in monitoring/assessment, and science-based and maintaining consumer trust in food supply.
- Food waste. Along the entire food value chain from field to consumer—logarithmic waste of inputs (energy, labor, leading to new production practices; new distribution [gleaning] and social outreach).

a. Changing Canadian Food Environment

The changing Canadian food environment is increasing the tension in the consumer–market equation, revealing new issues yet creating new opportunities for ingredient and technology innovations and nutrition.

b. Food and Food Safety Trends

- Active packaging with sensors when product packaging has been breached or visual change if temperatures have not been maintained in safety zone. Requires scientific assessments and consumer education
- Rapid testing. Faster, more reliable methodology for in-field assessments and compliance monitoring
- DNA fingerprinting for product origin, tracking and tracing, fraud prevention
- Nanotechnology. Identification of small particles in food and food packaging to assess their safety as well as their use in developing rapid testing applications of nanotechnology and nanobiosensors to food processing and packaging (how do you know they are there?); impact on quality and safety
- Adulteration. Intentional and unintentional

c. Nutrition Trends

- Cognitive function and nutrients/fortification/supplementation
- Eye degeneration and nutrients/fortification/supplementation
- Sugar substitutes
- Novel fibers
- Protein. Has the distribution of protein/carbohydrate/fat changed? Role of protein with satiety and weight loss
- Personalized nutrition. Knowing your genetic disease risk profile and being able to customize your intake using 3D printed foods and other technologies
- Alternative protein sources (e.g., biofabricated “meat”)
- Biofortification
- Medical/dietary foods for aging population; performance; chronic disease conditions
- Regulatory approvals for emerging technologies—3D printing; novel ingredients (i.e., alternative proteins)
- Bioengineered foods

d. Regulatory Trends

- Regulatory trends are discussed in Section 6.C.

Implications: The changing food and consumer environment present many issues and opportunities for innovations and research in several shorter and longer-term needs

Source: (1) Serecon Management, Consulting Ltd. and Agriculture and Agri-Food Canada (2005) *Canadian Food Trends to 2020—A Long-Range Consumer Outlook*. Ottawa, Canada: Agriculture and Agri-Food Canada. (2) Agriculture Canada (2016) Emerging Food Innovation: Trends and Opportunities [Internet].

Acknowledgments

Dr. Khoo extends thanks to and acknowledges the contributions from the following individuals:

- Stephanie Atkinson, PhD, FACHS, Professor, Health Sciences Center, McMaster University, Hamilton, Ontario, Canada
- Gary Beauchamp, PhD, Distinguished Member and Emeritus Director and President, Monell Chemical Senses Center, Philadelphia, Pennsylvania
- Kathryn J. Boor, PhD, Dean, College of Agriculture and Life Sciences, Cornell University, Ithaca, New York
- Ray DeVirgiliis, MPH, Science Program Communications Manager, ILSI North America, Washington, DC
- Michael Doyle, PhD, Regents Professor, Center for Food Safety, University of Georgia, Griffin, Georgia
- George Dunaif, PhD, DABT, President, ToxPro Solutions LLC, Clyde, North Carolina
- Suzanne Harris, PhD, Executive Director, International Life Sciences Institute, Washington, DC
- Eric Hentges, PhD, Executive Director, ILSI North America, Washington, DC
- Anne Kennedy, Deputy Director, Food Industry Division, Agriculture and Agri-Food Canada/ Government of Canada, Ottawa, Ontario, Canada
- David Klurfeld, PhD, National Program Leader for Human Nutrition, US Department of Agriculture, Agricultural Research Service, Beltsville, Maryland
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About ILSI North America

The North American branch of the International Life Sciences Institute (ILSI North America) is a public, non-profit scientific foundation that advances the understanding and application of science related to the nutritional quality and safety of the food supply.

ILSI North America carries out its mission by sponsoring research programs, professional and educational programs and workshops, seminars, and publications, as well as providing a neutral forum for government, academic, and industry scientists to discuss and resolve scientific issues of common concern for the well-being of the general public. ILSI North America's programs are supported primarily by its industry membership.

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