Sustainable development and next generation's health: a long-term perspective about the consequences of today's activities for food safety

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Summary. Development is defined sustainable when it *meets the needs of the present without compromising the ability of future generations to meet their own needs*. Pivoting on social, environmental and economic aspects of food chain sustainability, this paper presents the concept of sustainable food safety based on the prevention of risks and burden of poor health for generations to come. Under this respect, the assessment of long-term, transgenerational risks is still hampered by serious scientific uncertainties. Critical issues to the development of a sustainable food safety framework may include: endocrine disrupters as emerging contaminants that specifically target developing organisms; toxicological risks assessment in Countries at the turning point of development; translating knowledge into toxicity indexes to support risk management approaches, such as hazard analysis and critical control points (HACCP); the interplay between chemical hazards and social determinants. Efforts towards the comprehensive knowledge and management of key factors of sustainable food safety appear critical to the effectiveness of the overall sustainability policies.

Key words: food safety, environmental health, nutrition, endocrine disrupting chemicals, HACCP.

Riassunto *(Sviluppo sostenibile e salute delle generazioni future: una prospettiva a lungo termine per le ricadute delle attività in sicurezza alimentare)*. Lo sviluppo è definito sostenibile quando soddisfa i bisogni del presente senza compromettere la possibilità delle generazioni future di rispondere ai propri. Considerando gli aspetti sociali, ambientali ed economici della sostenibilità della catena alimentare, viene presentato il concetto di sicurezza alimentare sostenibile basata sulla prevenzione dei rischi e dell'impatto sullo stato di salute per le generazioni future. In questo ambito è evidente la criticità della valutazione dei rischi a lungo termine e transgenerazionali, che è ancora limitata da significative incertezze scientifiche. Esempi di aspetti importanti sono: gli interferenti endocrini come contaminanti emergenti che colpiscono specificamente l'età evolutiva; la valutazione del rischio tossicologico nello scenario dei paesi in via di industrializzazione; la traslazione della conoscenza scientifica in indici di tossicità per lo sviluppo di azioni di gestione del rischio, come il sistema HACCP *(hazard analysis and critical control points)*; l'interazione tra pericoli chimici e determinanti sociali. Un impulso verso la conoscenza e la gestione di fattori critici per la sicurezza alimentare sostenibile è indispensabile per l'efficacia delle strategie per la sostenibilità.

Parole chiave: sicurezza alimentare, ambiente e salute, nutrizione, interferenti endocrini, HACCP.

INTRODUCTION

In the introduction to the first report of the Club of Rome *The limits to growth* (1972), Aurelio Peccei spelt out the problem of sustainability and the perspective of collapsing of myopic development [1]. Even not definitely addressed to health (including food safety) policies, Peccei argued that development and market are essential to allocate resources, balance demand, supply of goods and services and to stimulate innovation and competition; on the other side, the deficiency of global and intergenerational sense of responsibility, *i.e.* the deficiency of sustainability, was foreseen to get severe consequences.

Many definitions of sustainable development have been introduced over the years. The most widely accepted one comes from the report *Our common future*, known as the Brundtland Report (1987). It states that "sustainable" is the development that *"meets the needs of the present without compromising the ability of future generations to meet their own needs"* [2]. The key point of this approach is to avoid irreversible damages to natural capital in the long-term in turn for short-term benefits.

Simple in principle, the term "sustainable development" means meeting different objectives at the same time. It implies social progress recognising the needs

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of everyone, effective protection of the environment, prudent use of natural resources and waste, maintenance of high and stable levels of economic growth. Accordingly, long-term policies towards sustainability are recently approached from different angles and methodological approaches. Concepts such as transdisciplinary research and post-normal science [3], where important choices have to be made in face of scientific uncertainty and involvement of deep values, provide opportunities for novel ways to advance societies' capacity. In the real life, public health actors, with scientists at the front-line, work unavoidably amidst "imperfections", as they deal with risk, hence with probability, uncertainty, knowledge gaps and/or value-oriented choices [4, 5]. Even if practical answers to problems raised by risks and uncertainties can be shared by different value systems, it is important to name the values to which choices aspire and the consistency of goals as practical expression of these values. To evaluate choices and goals, uncertainty assessment is of paramount importance. Walker *et al.* [6] depict scientific uncertainty as consisting of level, nature and location. In particular, "level" refers to the knowledge degrees, as related to methodological uncertainties and/or to the weaknesses of the models applied. *Nature* refers to the question whether the uncertainties are due to a lack of knowledge or to inherent variability of the system itself. Finally, "location" depends essentially from what is within and what is without the conceptual system applied; for instance, to what extent a food safety system is designed to evaluate also long-term health risks.

FOOD PRODUCTIONS: THE CURRENT CONCEPTUAL FRAMEWORK OF SUSTAINABILITY

Food policies should aim at securing a sustainable future for farming and food industries, as viable productions contribute to a better environment as well as to healthy and prosperous communities. The concept of sustainability in food production entails many aspects, *e.g.* food chain (including feeds) management, innovation, affordability, eco-efficiency and competitiveness [7]. This has to be adapted to different contexts. For instance, in Europe relevant topics, as from the ongoing 7th Framework Research Programme, include: rural and coastal contexts, improved working and living environment, equity, as well as production, use and management of wastes and renewable resources, including biodiversity [8]. In China, where the huge rural environment has seen massive, often fully unbalanced changes in the last decades, a pragmatic approach considering the typical local potentials is being developed [9].

Within an industrialized, rich area such as the European Union, sustainable farming and food strategy seeks to address both increasing needs for nutritional food quality, free consumer's choice and demand for secure food in the context of growing population and increased land use [10]. Thus, mutually reinforcing benefits have to be achieved from ecology, economy and society. Key issues are also partly taken by the Slow Food Movement (www.slowfood.com/), expressing some consumers' reactions to environmental, ethical and health concerns associated with conventional, "long-chain" food systems, that widen the distance between consumers and the context(s) where food is produced. There are instances of government support to farmers meeting standards for environment, food safety, animal health and welfare, as in Austria [11]. This requires an overall system of farm management and food production, from preservation of natural resources through to animal welfare, as envisaged by the new vision on organic production [12]. Furthermore, short food supply chains, exploiting as far as possible local resources, may better support food safety as they reduce the number of critical hazard points between primary producer and final consumer; a comparative analysis of comprehensive hazards (*i.e.*, also including chemical long-term risks) according to the length and complexity of food supply chains might be warranted.

This approach does not mean at all to look back to "good-old times". Rather, it looks ahead in the wake of the improved responsibility awarded to actors in the food production systems. A substantial output of technological solutions is required to manage the effects of globalized, resource-intensive food system, including the identification of possible "hot spots", as well as to support an increasingly community-based food economy. Knowledge-based development is required in such fields as the full exploitation of fisheries and the production of less resource-intensive feeds, *e.g.*, with a reduced use of materials that could be directly utilized in human diet (see *e.g.* the EU Project AQUAMAX, addressing the use of novel ingredients in fish farming, www.aquamaxip.eu). Sustainability of food production is clearly a key issue for societal development [13]; nevertheless, there is one component of sustainability that appears to deserve more consideration, *i.e.* the interfaces between sustainability and food safety/public health issues.

FOOD SAFETY AND HEALTH SUSTAINABILITY

Amongst factors related to living environment, food is one shared by the whole general population. However, whereas food chain sustainability is a current issue, so far the sustainability concept has not, or scantly, been applied in the field of food safety. Food safety features prominently to guarantee and promote health and wellbeing of populations, and especially of such vulnerable groups as the unborn and the child. Food safety itself is a framework integrating the assessment and management of many factors, from the welfare of the living organisms used for food production, the quality of their living environment through to the management of production and distribution processes [14].

The "sustainability" concept framework implies insight into long-term consequences. Sustainability can imply also a public health standpoint; then, the "long-term capital" is associated to the prevention of risk factors spreading along generations. Progeny health, in fact, includes pre- and post-natal development as well as ability to lead a healthy adulthood; thus, it is inherent to sustainable development. The European Environment and Health Action Plan (2004-2010) puts emphasis on prevention of risks for children health, as they are both the most vulnerable population group and the future of society [15]. Indeed, the EU strategy stems from a number of international initiatives and statements. In the spirit of the Convention on the Rights of the Child of November 1989 [16], then emphasized at the United Nations General Assembly Special Session on Children in May 2002 [17] and at the World Summit on Sustainable Development (WSSD) in September 2002 [18], children are entitled to grow and live in healthy environments. Nearly two years after WSSD in Johannesburg, the World Health Organization (WHO) Ministerial Conference on Environment and Health expressed concern on the scant integration of health aspects into international and national initiatives, strategies and action plans on sustainable development [19]. Risk factors in early life are increasingly recognized to play a significant role in adult diseases. Thus, where food supply emergencies are overcame, improved access to and affordability of safe and nutritionally adequate food are major determinants to secure the health of next generations. Assessment of long-term risks deriving from chemical contamination and/or nutritional imbalances is a major component of the new food safety paradigm as implemented by international bodies, such as the European Food Safety Authority (EFSA, www.efsa.europa.eu/EFSA/). However, the current paradigm for toxicological risk assessment still lies mostly in the "hazard × exposure" scheme: as Paracelsus stated, indeed some time ago, "*dosis facit venenum*". A new and more complex paradigm based on the "hazard × exposure × susceptibility" scheme is recognized by the scientific community, but still awaits full implementation in the risk assessment framework [20]. Together with gender, life stage is a main factor modulating susceptibility to pollutants; so, one could envisage to extend Paracelsus paradigm as "amount *and timing* of exposure both make the poison". As a consequence, the whole testing and assessment process (from additives to pesticides to novel foods, etc.) should be evaluated also according to the ability to identify and characterize possible hazards in susceptible life stages. Along with this, exposure assessment should take into account, when appropriate, dietary patterns and/or pathways that are particularly relevant to the mother-infant dyad as well as to children and also adolescents.

Developing organisms, especially during embryonic and fetal periods and early years of life, are often particularly susceptible, and may experience a relatively higher exposure than adults to many environmental factors, such as polluted food [19]. At global scale, exposure to contaminated food can cause a range of long-term effects, including birth defects, metabolic, immune, reproductive and neuro-developmental disorders, as well as enhanced predisposition to cancer, overall accounting for one sixth of the total burden of disease [21]. As industrialization and social-economic growth go on, concern becomes greater regarding the potential for long-term adverse effects of low, continuous exposure to many chemicals.

The understanding of nature and amount of health effects produced on developing organisms, from the prenatal period to adolescence, by the exposure to environmental agents is still incomplete; even so, massive evidence-based literature reports the role played by several environmental factors in determining disease in children and in inducing effects that may become manifest only in adult life [21]. Depending on the risk's components (hazards × exposure × susceptibility), medium- or long-term effects on the next generation rising from genotoxicity and reproductive toxicity can take place even during intrauterine life; examples include the enhanced risk of hypertension related to low birth weight [22], and the testicular dysgenesis syndrome associated with poor fertility and testis cancer in adults [23]; for the latter, exposure to chemicals able to alter the endocrine function, so-called endocrine disrupting chemicals (EDCs), is suspected (see section below, "Food safety and developing organisms: the exposure to and the targets of the EDCs").

Outbreaks of acute poisoning from foods are frequently reported worldwide. In 2004, the WHO International Programme on Chemical Safety Team reported that 57% of chemical outbreaks of international public health concern were ascribed to food and/or drinking-water [24]. However, inadequate capabilities in monitoring, identifying, alerting, and tracking still do not allow a direct assessment of the expectedly far higher impact of chronic and transgenerational exposures. This may hold true particularly in developing/transition Countries; in such contexts efforts should be aimed at enabling the development of pilot models for the identification of food supply systems more sustainable from the point of view of long-term health and at exploiting new opportunities to address policies for sustainable health and primary preventive actions for generations to come.

NOVEL ZOONOSES: AN INTERFACE BETWEEN FOOD CHAINS' SUSTAINABILITY AND FOODBORNE DISEASES

Foodborne diseases are defined by WHO as *"diseases of an infectious or toxic nature caused by, or thought to be caused by, the consumption of food or water"* [25]. A major group is represented by foodborne zoonoses, *i.e.* diseases transmittable by farm animals or their products to humans. The awareness of long-term health risks through food has elicited a possible extension of the zoonoses concept; Adriano Mantovani formulated the following proposal *"Any detriment to the health and/or quality of human life deriving from relationships with (other) vertebrate or edible or toxic invertebrate animals"* [26]. Accordingly, chemical exposure through foods of animal origin is considered a "novel zoonosis". Bioaccumulation of xenobiotics is obviously more important in foods of animal origin, as they come from organisms that have a higher place in the food pyramid. When toxicants are able to bioaccumulate, a "body burden chain" may ensue: the body burden of toxicants in foods of animal origin is transferred to human tissues along life starting from the mother's womb; this may both induce, directly or indirectly, chronic diseases as well as be partly transferred to the next generation, either *in utero*, by breastfeeding or also through the living environment [27]. Novel zoonoses have to be viewed within the general frame of food safety. It might be inferred that minute amounts ingested via the diet would not cause, in most instances, concern in a "normal" individual. But this may not hold true for vulnerable subgroups. Short food chains may ease control of chemical exposure. However, on a global scale, the increase of the world population, the development of feed, animal and food trade and the spreading of polluting industrial activities make it difficult to keep under control contamination in individual Countries, with a long-range view to next generations. The food chain management must ensure safety, wholesomeness and soundness of food in all stages, from its primary production to its final consumption [28, 29]. As endorsed in the conceptual framework *from farm-to-fork* of the European food safety strategy [30], the whole food production chain contributes to the human total dietary intake of mixtures of chemicals. Contamination of animal feeds and human foods may arise in three ways: *i)* conscious (authorized chemicals used in the wrong way or insufficiently regulated to assure protection of susceptible population subsets); *ii)* fraudulent (use of unauthorized chemicals); or *iii)* involuntary (undesirable substances, including environmental pollution). In the production of foods of animal origin, feeds are a basic component of food safety. Healthy animals are the best guarantee to healthy foods, moreover animals carry over the quality of their living environment to consumers (and their progeny) [31, 32]. Accordingly, within the EFSA, one panel out of nine (Panel on additives and products or substances used in animal feed – FEEDAP, www.efsa.europa.eu/EFSA/ScientificPanels/efsa_locale-1178620753812_FEEDAP.htm) deals specifically with substances used in animal feeds, whereas a large part of the activity of the contaminants panel (Panel on contaminants in the food chain – CONTAM, www.efsa.europa.eu/EFSA/ScientificPanels/efsa_locale-1178620753812_CONTAM.htm) is devoted to the assessment of undesirable substances in feeds, including many persistent EDCs. The output of the food chain is also important for food safety: the food chain management interfaces directly with prevention of environmental pollution as it should address safe collection, storage, transportation, recovery, disposal and destruction of non-hazardous and hazardous waste, that are especially important in farm animal production [33].

Countries living the turning point in development may encounter serious problems due to new and/or insufficiently controlled chemicals introduced through rapid, unplanned and uncontrolled intensive farming, urbanization, industrialization, and dumping phenomena. In regions were income increases from a low level and urbanization occurs, the trade patterns and per capita demand for animal protein products (livestock and fisheries products) change rapidly. One major example is developing Asia, where projections indicate that a growing and urbanizing population with rising incomes will increase demand for meat by 47% between 1995 and 2020 [34]. As regards the urbanisation in sub-Saharan Africa, in 1995 projections showed that western and central African coastal populations would double by 2020 [35]. According to UN-HABITAT, the percentage of Africans living in cities is expected to rise from the present 37% level to 53% in 2030 [36]. Such increase of urban population means also increased dependency from external food supply. Rapid changes within the animal production in urban communities can drastically influence the control systems and the mixture of imported, processed, *semi*-processed and raw (fresh) foods increases complexity and centrality of primary food source quality [28]. Besides, an increasing fraction of population in such high-rate developing Countries is changing food preferences. As reported by the Food and Agriculture Administration (FAO), diet diversification is likely to have a significant effect on global food requirements by the year 2050 [37]. In developing Countries, where economic growth is robust, diets are expected to become lower in cereals and higher in animal-derived proteins and fats. Further, changing dietary habits may lead to the demand for foodstuffs with given taste, texture or colour; in its turn, this may lead to the use of feed and food additives (*e.g.* flavouring or colouring agents) not related to the disease prevention or production improvement in food-producing animals; also, these additives might be used to mask poor food quality [38]. Awareness and concern towards long-term risks may give rise to further problems. A public health approach needs being taken, as the ability to detect minute amounts of contaminants that may impair the use of food sources of substantial nutritional value. Health risk assessment, not merely chemical analysis, should be the driving force setting priorities for food control programmes. The debate on new models for comprehensive assessment of dietary impact on health was opened by the EFSA. In particular, the balance between food toxicological risk and nutritional benefit was discussed [39]. This new approach well fits the purposes of sustainable development. For instance, rice and fish are addressed when dealing with food production in developing Countries: from the toxicological risk point of view, they are known to accumulate environmental pollutants with long-term effects (*e.g.* arsenic and dioxins, PCBs, methyl-mercury, respectively) [40, 41]. In the meanwhile, nutritional characteristics and benefits of these foodstuffs, along with their relative low cost, make them staple food items in many Countries. Thus, there may be a conflict between food safety and food security, *e.g.* the insufficient availability of a staple food due to contamination should be considered as a possible adverse health effect. On the other hand, a diet rich in protective factors, such as antioxidants, may enhance the ability of the organism to cope with such chemicals as EDCs [42]. Risk-to-benefit analysis is mainly a field for scientific development; to date, it has to be performed to meet specific questions and to address regulators, policy makers and public choices; a clear and transparent problem definition is the first and key step for setting the process. Risk-to-benefit analysis should not lead to absolve or condemn a given food source or commodity; rather, it should identify critical points to improve the balance between toxic exposure and nutrition [39]. For instance, the EFSA risk-to-benefit assessment of wild and farmed fish identified aquaculture feeds as a critical point to improve the safety of fish production [43].

All in all, the Alma Ata Declaration stated that prevention and control of zoonoses is a most important function of public health [44]; as anticipated, the field of zoonoses, classically related to infectious agents, has to be extended to include foodborne diseases linked to the environment-to-food chains [45]. Considerations on critical contaminants relevant to zoonotic/food related disorders are detailed below.

CONTAMINATION OF THE FOOD CHAINS: FROM ACKNOWLEDGED TO NEW CONTAMINANTS

The global production chain of foods of animal origin is a particularly complex, as well as potentially vulnerable, context for contamination. Feeds are composed by several ingredients, coming from different sources; pastures (that can be treated with pesticides or exposed to environmental pollutants) are usually integrated with different kinds of concentrated feeds, including several kinds of additives [46]. Animals are good "tanks" of environmental hazard as well as good bio-indicators of biological uptake and consequences of pollution [31, 47]. Since animals are living organisms, consumers are often exposed to metabolites. Thus, food monitoring programmes should target the compounds that really matter for consumer (and environmental) exposure. Old, persistent contaminants are the heritage of the past to the current (and next) generations. In the meanwhile, new contaminants can be increasingly released as a legacy to the future. A glancing example of a major food production practice impacting on health sustainability is the agricultural insecticide dichlorodiphenyltrichloroethane (DDT); despite the international ban on DDT in agriculture, since the early 1970s, the food chain remains contaminated because of DDT persistence and fat solubility [48]; data show that a significant decrease of up to 90% in human exposure to DDT needs three decades following cessation of use [38]. Countries at the turning point in development are especially vulnerable to new contaminants due to rushing growth and insufficient strategies for exposure monitoring and control [38, 49]. For instance, emerging dumping grounds deal with the impact of importation of commodities which notoriously should have been dumped due to the content of additives banned in the Country of origin and informal waste of obsolete electronic material [50-52]. The e-waste piles can be toxic, with toxic metals including lead, cadmium, and mercury. What's more, electronic components are usually housed in plastic casings that spew carcinogenic dioxins and polyaromatic hydrocarbons when burned. Over these piles chickens and goats, further than kids, roam barefoot [51]. Again, in the absence of management measures, a serious impact on population health may occur, even though it may require years, and one more generation, to fully manifest.

Another issue is the dumping of poor quality and/or unwholesome food to rapidly growing areas. An example that has received recent media attention is the massive imports of frozen chicken in Cameroon. The product is sold at a very low price on local markets in disastrous sanitary conditions, creating severe problems to local poultry breeders. The Cameroonian ACDIC (Association for the defence of collective interests) campaigns against the import of frozen chicken meat (www.sosfaim.be/pages_be/en/partenairesSud/be_en_partenaires_cameroun_acdic.html) and, whereas attention has been provided to the immediate health risk associated with microbial contamination of thawed and refrozen chicken, no data exist on longer term risks such as those deriving from the use of preservatives.

Further, in industrialised Countries as well as in the developing and emerging/transition ones, cost-effective and timely production of meat, eggs and milk is supported by arguable feed composition. Contamination of feeds and carry-over to consumers may largely depend from feed composition, but also from environmental, including socio-economic, features. Animal feeds with ingredients like oil seed-, cotton seed- and coconut cakes, peanuts and corn grits, often contain natural contaminants, as mycotoxins [53]. Exposure to mycotoxins strongly depends from production practices. It is noteworthy that mycotoxins are not a problem of nomadic shepherds, rather of communities starting large-scale production of plant- and animal-derived foods with inadequate farming and harvesting practices, and/or improper storage, transport and marketing facilities. In developing Countries, where animals are likely to consume mycotoxins contaminated feeds and are milked individually at the household doorstep, the levels of toxins in feeds can be very high [38, 49]. Again, as mycotoxins are generally low-persistent compounds, the minute uptake through food of animal origin may not be a problem for general population, but a risk for vulnerable groups cannot be excluded, especially for carcinogenic compounds like aflatoxins. Mycotoxins are therefore old contaminants assuming new aspects. Since they may create substantial problems of food security [54], it is important to adopt strategies for prevention and, where possible, for recovery of contaminated commodities [53, 55]. To prevent long-term harms, one must cope with uncertainties, in particular, those related to the extrapolations from current knowledge, *e.g.* from experimental studies to predict potential humans harm. On the other hand, risk factors may be more complex than single chemicals administered in toxicological studies. As mentioned, the toxicants burden effects might interact with bioactive components (*e.g.* antioxidants) and nutrients (vitamins and trace elements) present in foods [42]. Inadequate nutrition may interact with susceptibility to toxicants and a diet satisfying the needs for calories and even protein but poor or unbalanced in protective factors, such as trace elements and vitamins, may be a critical situation. As mentioned above, underdevelopment and poverty are strongly related to the burden of environmentally attributable disease, and this is even truer for children [56, 57].

FOOD SAFETY AND DEVELOPING ORGANISMS: THE EXPOSURE TO AND THE TARGETS OF THE EDCs

EDCs represent a heterogeneous group of compounds, highly relevant to the food chain contamination, for which the life stage-related susceptibility is particularly important: in fact, EDCs affect, through various mechanisms and targets, the endocrine system, which is critical for tuning the whole development of progeny from implantation through to adolescence [32]. EDCs include well-recognized persistent pollutants, such as DDT and dioxins, compounds used in agriculture and farming (*e.g.* dicarboximide and triazole fungicides), as well as industrial compounds still largely used (*e.g.* phthalates, alkylphenols, brominated flame retardants, bisphenol A) and also plant compounds (*e.g.*, phytoestrogens, goitrogens) that may be present in high amounts, *e.g.* in soy-based milk or dietary supplements. The general population is exposed to complex mixtures of EDCs throughout life, according to varying scenarios. Recognized persistent pollutants are targeted by many national food control programmes, but in most cases the dietary exposure to new and emerging EDCs is insufficiently or not at all monitored in official food control, even though some of them can significantly bioaccumulate [58, 59]. Due to still limited attention to risk management, the ability to know and prevent EDC contamination of food chains remains inadequate. Indeed, it is difficult to monitor foods and feeds in the absence of consensus parameters (maximum residue limits, action levels, etc.) as well as without networks of reference laboratories providing validated analytical methods. An appraisal of existing literature suggests a significant role of uncontrolled EDCs exposure in the total burden of developmental health disorders, including reproductive, immune and neuro-behavioural impairments, as well as increased susceptibility to cancer of target organs, such as testis (see *e.g.* [60, 61]). Indeed, in the case of EDCs, there is the need for enhanced translation between increasing scientific evidence and effective risk assessment and risk management programmes.

Amongst chemical risk factors, EDC exposure during pre- and post-natal development features prominently [32, 62]. Numerous studies report a relation between exposure to EDCs and diseases as male infertility, pregnancy loss, diseases of uterus (*e.g.* endometriosis), malformations of the reproductive system (*e.g.* hypospadia and cryptorchidism), increased susceptibility to cancer of the testis and other target tissues, and developmental delays in children [62]. With reference to the definition adopted by the EU, an EDC is *"an exogenous substance or a mixture, that alters function(s) of the endocrine system, causing adverse health effects in an intact organism, or its progeny, or (sub)populations"* [63]. Thus, transgenerational effects were included since the very start within the EDC conceptual framework. It is noteworthy that one of the earliest public health concerns for residues in foods of animal origin was associated to the use of a peculiar group of EDCs, *i.e.* the hormonally active drugs administered to farm animals because of their anabolic effect. Due to possible long-term, endocrine effects of even very low levels of such potent compounds, hormone-like cattle anabolics are forbidden in the European Union, although some illicit use seems to persist, and allowed under controlled use conditions by other Countries (*e.g.* USA). Anabolics may represent a good example of risk management choices in the field of food safety: forbidding (requiring the support of efficient and up-to-date control systems) or allowing a controlled use (requiring ensuring adequate safety also to the most vulnerable population subsets) [64].

Several of these compounds are able to cross the placenta and to accumulate in the lipid portion of the organism with successive transfer to breast milk. The extent of hazardous dietary exposure occurred during intrauterine and early life create a body burden that may reveal later in life up to adulthood [41], thus generating a problem of health sustainability for next generation. Sustainable food safety requires that the assessment of compounds like EDCs should be supported by novel scientific approaches, including: 1) toxicological tests identifying relevant hazards, such as the long-term functional development of progeny and the specific effects of exposure in the peripubertal stages [32]; also basic research on a field such as epigenetics might be exploited to assess hazards extending trough generations [65]; 2) characterization of biomarkers for exposure and health surveillance of babies and children; this requires to prioritize issues such as predictiveness and social and personal acceptance (see, *e.g.*, the EU Integrated Project NewGeneris, www.newgeneris.org/). As mentioned above, such assessment should translate into regulatory limits and risk management (and risk communication) actions that take into due account the protection of next generation. What's more, social determinants of health are crucial when addressing sustainable development in food safety; this point is argued in the next section.

THE SOCIAL ROOTS OF HEALTH SUSTAINABILITY

In 2005 M. Marmot, Chairman of the WHO's Commission on Social Determinants of Health, reminded the inherent social basis of most chronic disease causation, highlighting that *"if the major determinants of health are social, so must be the remedies. Health status is the best measure of whether a population is thriving"* [56, 57]. Interdependent and mutually reinforcing pillars of sustainable development lay in environmental protection, economic development, and social development, which should include the protection of next generation's heath. Endocrine, metabolic and reproductive diseases have a major impact on the socio-economic status of a Country, even if not always represent direct major death causes; indeed, as indirect risk factors, they are involved in the major death causes of the industrialized world, *i.e.* cancer and cardiovascular disease [66]. Toxicity of most chemicals can be influenced by several factors as age, nutritional status, diseases and interactions with other substances [67]. The WHO Report *Eenvironmental burden of disease. Country profiles* highlights the 20-folds higher impact of chemicals on duration of healthy live in developing Countries [68], where rural and urban communities may experience a closer exposure to contaminated food chains and waste dumps. Further, in urban areas, where communities are entering the informal sector of economy, lower socioeconomic population groups face more constraints and limitations on making healthy choices. Particularly children are most likely enrolled in informal labour, including agriculture and food production in the most hazardous conditions and scavenging. The prevention of chronic diseases is not a *luxury* for industrialized Countries. Increasing of children obesity incidence is a warning in developing and emerging/transition areas. The worldwide prevalence of obesity has risen up to 3 folds in the last two decades [69]. The European charter on counteracting obesity acknowledged that obesity is no longer a syndrome of wealthy societies but also of developing Countries and Countries with economies in transition, particularly in the context of globalization [70]; the long-term consequences of children obesity could represent a significant burden to the health and social services of many Countries. A deeper understanding of the development course, progression and outcome of most endocrine, metabolic and reproductive diseases requires knowledge of social factors affecting potentially more susceptible individuals, *e.g.* infants, children, pregnant women and socio-economically disadvantaged communities. As highlighted by K. Olden and S. White [57], studies report that no more than one third of the cancer burden is attributable to genetics alone, only 15% of Parkinson's disease cases, and about a one third of autoimmune disease cases. Further, 90% of individuals with severe hearth disease present at least one risk factor related to diet, lifestyle or living environment. As the authors point out, *"the current view is that adverse health outcomes are caused by the combination of susceptibility genes with exposure to environmental triggers"*. In other words, the severity and time of expression of gene predisposition is modulated by environmental triggers; in the absence of triggering, the inherited predisposition remains silent. It is also accepted the vice versa: the genetic susceptibility to disease is modulated by the interplay of lifecycle stage and environmental (in the broader sense) factors. Thus, biologic and social processes underlie the genetic predisposition to diseases and adverse health outcomes from environmental exposure.

In fact, susceptibility is not only linked to age, sex, and genetic but also to social position. Often social factors are present concurrently with other risk factors, such as living and/or working in unhealthy environments with insufficient or unbalanced nutrition, illness-producing behaviours and lifestyle, reduced access to information and to proper health care services and social stigmatization. The most striking health implications cover shorter life expectancy and higher rates of birth defects, infant mortality, asthma, metabolic syndrome-related disorders (cardiovascular disease, diabetes, obesity) and cancer in socially deprived areas [71].

The close interplay of environmental conditions and unhealthy or uninformed behaviours in deprived areas calls for mutually supporting actions based both on reducing risk factors and on empowering the primary health care potential of people: under this respect, improved woman nutrition and supporting breastfeeding may be impressively cost-effective tools to increase children health [72]. Indeed, the need for "educating the educators" has also been pointed out, *e.g.* discussing how to strengthen sustainability-relevant topics in the science education process [72].

SUSTAINABLE FOOD SAFETY SHIELDING ALONG CRITICAL POINTS IN THE FOOD CHAINS

The EU has issued a directive on hygiene for foodstuffs [73], in which the hazard analysis and critical control points (HACCP) system is introduced as necessary mean to ensure that food processing and food-related industries comply with the relevant standards. The HACCP approach is based on a systematic analysis of each step of food production to identify critical hazard and control points for the whole food chain quality assessment and the food safety assurance. To date, the HACCP system is systematically applied throughout the food-chains for food microbiology and its benefits are recognized worldwide as well as its potential of enhancing food safety and preventing many cases of foodborne diseases. However, the new concept of sustainable food safety would require that HACCP strategies are prepared to include/consider/evaluate also hazards that are not related to acute foodborne diseases.

The European strategy for food safety is based on the risk assessment approach; accordingly, EFSA implements risk assessment concerning biological, chemical and nutritional hazards. In this context, a field systematic strategy combining HACCP and risk assessment appears necessary, covering the identification/control and, where possible, the removal of the risks due to toxicants along the food chains, covering food production steps or procedures at which a toxicological hazard can be identified, prevented, eliminated or reduced.

Some studies are already available in the literature. For instance, the phase of primary production represents a major interface between food safety and health sustainability; thus, actions for environmental remediation of contaminated agricultural land, soil, pastures and/or water sources [74-79] provide corrective actions in the food chain preventing long-term and transgenerational health risks. In fact, long-term hazardousness of chemicals is generated by toxicity, ability to accumulate and biodegradability; for instance, the environmental degradation of alkylphenols and the duration of the withdrawal period of livestock exposed to phthalates may represent key factors influencing contamination of edible tissues and milk by such EDCs [59, 80]. Currently, mycotoxins remain the toxic contaminants for which some hazard and critical control points are more consistently identified; strategies were developed to detect and remediate the presence of mycotoxigenic fungi as well as to inhibit mycotoxin biosynthesis during pre-harvest, harvest and post-harvest management [81]. Possible corrective actions are proposed during primary production [56]. In its turn, the widespread adoption of decontamination/detoxification strategies involving, *e.g.*, chemicals and/or irradiation would require a risk-to-benefit analysis, along the lines recently adopted, *e.g.*, for the assessment of the antimicrobial resistance in relation to the use of specific antimicrobial substances in foods (www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178697425124.htm). Finally, packaging materials and cooking devices may represent a critical point for sustainable food safety, due to the release of persistent, poorly characterized chemicals such as phthalates and perfluorinated compounds [82, 83].

Strengthening HACCP with sustainable food safety approach and managing risk factors (*e.g.* the vicinity of potentially polluting areas) should well combine with the EU strategy to reinforce, and support with new knowledge, both short chain productions and responsibility in waste management [10, 13], as well as with the FAO programme for local chains [83].

CONCLUSIONS

Development and sustainability implicate that the primary need for food security is satisfied [38]; in such a case, the establishment of a primary prevention framework is imperative, as food systems may be under threat from development-related activities. Safe and balanced nutrition is still an unmet need for too many children, and at the same time the prevalence of obesity and the risk of later development of metabolic disease, including diabetes, and cardiovascular disease are increasing. The scientific community is asked to improve efforts to ensure a healthier environment for children and to fill knowledge gaps on causal links, nature and magnitude of effects for effective interventions. This calls for enforcing the link between food safety and sustainability in a new framework that has to include several issues:

- the interaction between human activities, environment and human health is complex, and it is unfeasible to address the full range of health risks. Thus, it is necessary to build approaches to pool information, expertise and resources;
- the flows between knowledge and regulations should be strengthened;
- owing to finite resources, it is important that health risks are prioritized and tackled in an efficient manner. This requires the adoption of a consistent and transparent basis for decision-making across the responsible bodies. Duplication of efforts has also be minimized through the use of high-quality, integrated datasets, harmonized risk assessment and effective communication between those involved in the analysis, regulation and management of risks;
- as health is multifaceted, a wide range of issues must be taken into account. This necessarily involves the integration of sometimes competing objectives, such as evidence and precaution, within a single decision-making framework.

When developing the framework within the multi-faceted field of food safety, the potential and role of the different actors (public bodies, producers, citizens' organizations) should be exploited. Sustainability of production of foods of animal origin requires the local community and the developing veterinary services acting a pivotal role in the identification and adoption of good farming and agricultural practices; it also requires an insight on long-term impacts of manufacture, distribution, improper disposal and recycling of new and known hazardous chemicals, thus, to invest resources on next generation better health. In the case of developing Countries, a responsible management of food security issue should consider long range consequences also in terms of food safety, *e.g.* to minimize future social costs related to environmental remediation and/or problems with the export of food commodities. One recent case is the 2008 ban of thirty pesticides, including many chlorinated insecticides identified as EDCs, by the Nigeria's National Agency for Food and Drug Administration and Control, upon the recognition of many food poisoning cases (www.fc-international.com/viewitem.php?ItemID=1121).

To achieve an in-depth food safety shielding along the whole food chain and to match long-term and transgenerational food wholesomeness, a risk-based management of food processes, such as the HACCP system, should be implemented by toxicological indexes, as well as possible corrective actions in established toxicological critical points. Public bodies must define reference values and guidelines; whereas food safety is a community good, yet the private sector has to play an important role in risk management. Current food safety strategies highlight the issue of producer's responsibility in building a healthier environment, as well as for ensuring safe food processes [84, 85]. This entails transfer of knowledge in the whole food chain both vertically and horizontally between private actors, from primary producers through to retailers. Obviously, the promotion of awareness of health adverse effects and empowerment towards health-promoting behaviours is decisive, in the spirit of primary health care [45]. The importance of resources and attention moved by policy makers and media can not be overestimated, especially in Countries at the turning point of development that are called to make critical choices. Implementation of policies to minimize the burden of poor health for generations to come, *e.g.*, through the transgenerational flow from living environment to epigenetic modulation [86] is part of the precautionary framework; in its turn, this relies upon evaluation of consequences of exposures together with uncertainties hampering decision-making. Indeed, precautionary principle and sustainable development are strictly linked [87]. As pointed out by Godard [88] several aspects characterizing the precautionary principle are intrinsic to the sustainable development, such as the duties of early detection and intervention, of weighing both the magnitude and the probability of unacceptable harms, and of caring for future generations; the development of innovative, yet user-friendly and cost-effective, technologies can provide a significant support for monitoring strategies and risk assessment/management [89]. Accordingly, food safety systems should pivot on a common, both global and intergenerational, sense of responsibility in anticipating problems and trends in our own long-term interests and in those of our descendants.

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