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The relevance of the food production chain with regard to the population exposure to chemical substances and its role in contaminated sites

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Abstract
Food may be contaminated with many chemical substances at any level along the production chain. Chemicals that may be found in food items can simultaneously be present in other matrices, as air, water, soil and dust; therefore, human exposure to chemicals via food has to be summed to the exposure through all the other possible routes. The role played by the food production chain with regard to the population exposure to chemicals assumes amplified proportions when considering contaminated sites. Indeed the link between environment and food production is undeniable and consequently, when population chemical exposure is considered, an integrated approach assessing the contribution of the different routes of exposure, including dietary exposure, is needed. Such integrated approach allows a realistic and comprehensive risk assessment of chemical substances in order to identify and deploy effective prevention and intervention measures to protect human health.

Key words
- food chain
- food safety
- chemical contamination
- contaminated sites

INTRODUCTION

Chemicals can end up in food either intentionally added for a technological purpose (*e.g.* food additives), as residuals of pesticides and veterinary drugs or due to the contamination arising from environmental pollutants of the air, water and soil, from both natural or anthropogenic origin. Moreover chemical substances may be present in food added voluntarily as a result of an illegal action.

Food, both vegetables and of animal origin, may be contaminated with many chemicals at the same time, that pose potential concern for the toxicological consequences in humans. Chemicals that may be found in food items can simultaneously be present in other matrices, as air, water, soil and dust; therefore, human exposure to chemicals via food has to be summed to the exposure through all the other possible routes. If this step is not performed, it will not be possible to have a complete estimate of the total exposure, thus compromising the completeness of the risk assessment.

Food contamination can arise at any level of the food chain. Contaminations at primary production level are those that occur directly in the field or in farm due to contaminated soil and/or water, as well as through polluted air. For example, vegetables cropping along major highways represent a serious concern since they are significantly more exposed to metal accumulation (in particular lead and cadmium) compared to plants growing in fields away from highways, thus representing a consistence route of exposure to metals for consumers [1]. The problem of chemicals entering the food chain has become more and more important with the industrialization: in fact the risk of contamination of the food chain increases proportionally with the concentration of the chemical substances in the environment.

Apart from primary production, contamination can occur at any level along the food production, transformation and distribution. Paradigmatic is the example of Perfluorooctanoic Acid (PFOA): a long-chain perfluorinated chemical of synthetic origin. Animal data evidenced that PFOA exposure may cause several types of tumors and neonatal death exerting toxic effects also at immune, liver, and endocrine systems levels [2]. Due to its special properties, PFOA is used for hundreds of manufacturing and industrial applications, in particular, it is widely used in non-stick coatings (polytetrafluoroethylene – PTFEg) for cookware and in paper coatings for oil and moisture resistance. PFOA may leach from cooking instruments to food, especially when high temperatures are reached, so that secondary contamination may happen [3]. Since PFOA persist indefinitely in the environment, environmental contamination at

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primary production level may also occur: indeed PFOA has been found in water, food of animal origin and vegetables [4]. Consequently, when estimating dietary exposure to PFOA both primary and secondary food contamination should be taken into account.

The scientific awareness that contaminants can enter the food chain at any step, has led in the last decade to the development of the so called "farm-to-fork" approach, which can be described as a holistic concept including all elements which may have an impact on food safety throughout the food chain, and consequently, that can represent a risk for public health. This approach requires the assessment and control of the major components of the food chain, with emphasis on primary production. It is evident that such holistic approach cannot ignore the strong link between environment and food production: considering that foods are produced by living organisms, plants and animals, the environment in which these organisms live is an essential determinant of the quality of the food [5].

In contaminated sites the relation between quality of the environment and the food chain assumes amplified proportions. Bioaccumulation and biomagnification along the food chain of certain chemical compounds, as persistent organic pollutants, result in higher concentrations in food products than those present in the environment. The characteristics that each food ingredient has concerning the level of contamination may impact on the quality of the final food product, therefore, within a contaminated site, foods containing locally produced ingredients may eventually represent an important exposure route for the population. On the other hand, it is worth also to highlight the level of complexity that the food chain has reached in the last decades: nowadays it has taken global features, food products are constantly exchanged between continents and thus may carry chemical contaminants from one part of the globe in virtually no time. In those countries where structured food monitoring programs are in place, it could be extremely useful to integrate these data with those obtained from environmental monitoring plans, in order to have a complete vision of chemical presence and levels of contamination.

In the following sections we will illustrate the relevance of the food production chain with regard to the population exposure to chemical contamination. Specific emphasis will be given to the role of food chain production through the contaminated sites, considered as polluted environment and production site, as well as highlighting the possible role of "sentinels" that food products may have. Some case studies will be discussed.

BIOACCUMULATION AND BIOMAGNIFICATION

When considering the importance of the food chain in the context of human chemical risk assessment it is necessary to introduce the concepts of bioaccumulation and biomagnification, since humans are at the top of the food pyramid. Bioaccumulation refers to an accumulation of a substance in an organism and occurs when the organism absorbs a toxic substance at a higher rate than that at which the substance is cleared. In parallel, the term biomagnification indicates the sequence of processes in an ecosystem by which higher concentrations of a particular chemical are reached in organisms higher up in the food chain, generally through a series of prey-predator relationships. Biomagnification is the result of bioaccumulation and biotransfer processes by which tissue concentrations of chemicals in organisms at one trophic level exceed tissue concentrations in organisms in the lower trophic level of a food pyramid.

As mentioned earlier, the persistent organic pollutants (POPs) tend to be extremely stable and thus persistent in the environment, having long half-lives in soils, sediments, air or biota. For this reason POPs bioaccumulate and magnify in the food chain with bigger health impact at the higher levels of the food pyramid, so in humans [6]. That's why human exposure to most of the POPs is mainly attributable to foods of animal origin, which in turn may arise from the presence of these contaminants in animal feeds. POPs accumulate mainly in fat, so even extremely low levels of POPs in feed may become significant over the lifetime of an animal and result in unacceptable residues in human food commodities such as meat, milk, and eggs [7].

Also heavy metals may bioaccumulate and magnify in food of animal origin. Paradigmatic is the case of methylmercury (MeHg), a highly toxic organic compound of mercury that derives from industrial processes. Indeed, MeHg has toxic effects on the nervous, digestive and immune systems and on lungs, kidneys, skin and eyes [8, 9]. It is well known that MeHg bioaccumulates and magnifies in fish and shellfish with concentrations that can be over a million-fold higher than in the surrounding water [10]. A sadly well known historical example is represented by the accident of Minamata Bay, Japan. In the 1950's a chemistry plant dumped an estimated 27 tons of mercury compounds in Minamata Bay. Considering that local fish and shellfish represented a main component of the residents' diet, thousands of people living in the areas surrounding Minamata Bay started developing symptoms due to MeHg poisoning. The chemistry plant actually stopped its production in 1968 and till then it is estimated that over 2000 patients have been affected by MeHg poisoning, of which more than half died [11]. In this context, the population's exposure through environment to MeHg was irrelevant while the main route of exposure was in fact represented by food, primarily fish and shellfish, which had significant higher MeHg concentrations compared to those measured in the water.

Bioaccumulation of chemical substances occurs also in humans just as in other animals and these substances can be eliminated through different routes including milk. This aspect deserves special attention when breast-fed infants' dietary exposure is assessed since they can be exposed through the mother's milk to contaminants. This route must be summed to infants' other possible routes of exposure. Perfluorinated compounds (PFC), polychlorinated biphenyls (PCBs), p,p'-Dichlorodiphenyltrichloroethane DDT and its metabolites, dioxins, dibenzofurans, polybrominated diphenyl ethers (PBDEs), and heavy metals are among the toxic chemicals most often found in breast milk [12]. It is therefore extremely important to investigate occurrence and levels of contaminants in human milk, in order to estimate infants' dietary exposure.

Plants are also able to absorb and accumulate a number of elements from soil, some of which are known to be toxic at low concentrations, such as heavy metals, contributing to the total human exposure [13, 14]. Well known is the example of inorganic arsenic which derives from both natural and anthropogenic sources and is a well-established human carcinogen [15, 16]. The inorganic arsenic may enter the food chain through plants, in particular cereals, that absorb it through their roots according to its bioavailability in the soil. Food is a primary source of inorganic arsenic for populations not exposed to elevated concentration though drinking water. Indeed, compared to dietary exposure, non-dietary exposure to arsenic is likely to be of minor importance for the general population in the European Union [15].

THE LOCAL FOOD CHAIN AS MAJOR SOURCE OF EXPOSURE IN AREAS CHARACTERIZED BY PCB, PCDD/PCDF INDUSTRIAL CONTAMINATION

When assessing chemical exposure of people living in contaminated sites, it is essential to include also the dietary route since food may represent an important source of exposure being also crucial for preventive action.

In contaminated sites it is important to evaluate the characteristics of the local environment and analyze the specific land use. Indeed, the site-specific risk assessment should be different if the land is used for agricultural activities or assigned to other human activities (industries or urban development). In particular in case of land addressed to food production, the exposure of the local population due to food consumption could be even more important because of local produced foods could be more contaminated compared to imported food, and the probability to consume locally produced foods is higher than imported food items.

The key role played by the local food chain in the exposure of the population living in contaminated sites has been investigated in the case of Brescia, in Northern Italy, declared contaminated site due to a polychlorinated biphenyls (PCBs) producing plant operating in the period 1958-1983. This plant diffused the contaminants in the environment mainly through a water channel used for irrigation of agricultural fields [17].

PCBs are synthetic organic chemical compounds that result from the incomplete burning of coal, oil, gas, wood, garbage, or other organic substances [18]. PCBs have been demonstrated to cause a variety of adverse health effects, especially affecting the immune, reproductive, nervous, and endocrine systems. Moreover, PCBs are considered potential carcinogenic substances [19]. The study area was characterized by PCBs' soil levels far higher than those established as acceptable for the EU legislation (legal limit: 10 pgTE(I)/g). The analyzed exposure pathway started by measuring the total PCBs' concentration in the forage grown in that area. The levels varied from 26 to 6 ng/g dry forage, confirming the capability of the crop to absorb the contaminant from the environment [20]. Since the study area was characterized by the presence of small farms producing meat and milk mostly for familiar consumption, the following step was to measure PCBs concentration in cows' milk and kidney fat. PCB's concentrations higher than background level were found in both the analyzed matrices [21]. Finally, PCBs exposure assessment in serum samples highlighted that farmers and their families had significantly higher levels compared to the general population [17, 22, 23]. The study concluded that the main source of exposure affecting farmers and their families was food of animal origin produced at home, thus highlighting the crucial role of dietary exposure and putting in evidence that the risk assessment conducted without including this route of exposure would have been misleading, underestimating the effective total exposure of such population sub-group.

THE FOOD CHAIN AS VECTOR OF LONG DISTANCE CHEMICAL DISSEMINATION

Nowadays the food chain is longer and more complex than ever before, in fact demographic, cultural, economic and environmental developments, along with globalized trade, travel and migration, have increased health risks related to food. As declared by Zsuzsanna Jakab, WHO Regional Director for Europe, "A failure in food safety at any link in this chain, from the environment, through primary production, processing, transport, trade, catering or in the home, can have significant health and economic consequences" [24]. The agriculture and food industries have now joined the list of "global" sectors, supplying a world-wide market. Nowadays, food ingredients often come from multiple countries, with each item having travelled thousands of kilometers from a field, farm or factory.

The so called "Belgian PCB/dioxin crisis" can be considered a suitable example of the complexity of the food chain and how it can contribute to the diffusion of contaminants. In Belgium, in the latest '90, a mixture of PCBs contaminated with dioxins was accidentally added to a stock of recycled fat used in the production of feedstuffs [25]. As a consequence of such contamination, exceptionally high levels of dioxins and PCBs were found in feed, meat and eggs. The Belgian authorities found that the contaminated fat could have been sold to nine manufacturers of animal feeds which supplied more than 2500 Belgian farms, including bovines', pigs' and chickens' farms, and some farms in the Netherlands, France, and Germany [26-28]. The uncertainty about the real extent of the contamination resulted in an embargo on all Belgian food products of animal origin, and, for a short period, USA banned all European poultry and pork imports [27]. Belgium economic losses due to the PCB/dioxin crisis approximated 1.5-2 billion Euro, to be added to the social and economic consequences of the temporary disturbance of the food sector. At EU scale, also the additional costs for the controls carried out by the other member states during the crisis, in order to identify, and eventually destroy, at risk products directly or indirectly linked to Belgian production, have to be considered [27, 29]. Since then the European Commission has established a set of instruments, including the rapid alert system for food and feed (RASFF), tight control measures, and maximum limit values in food, feed and raw materials produced within the EU and imported from non-EU countries [30]. Assessments of the human health risk caused by this major accident produced contradictory results. Scientist disagree on the magnitude of the impact that this event had on the general population: several authors sustain that it was too limited in time and in scale to have increased the PCB/dioxin body burden of the general population, while others estimated that the total number of cancer cases resulting from this accident would have ranged between 40 and 8000 and that neurotoxic and behavioral effects in neonates were also to be expected but couldn't be quantified [25, 26]. This example shows that contamination from a single source, irrespective of its origin, may become widespread and have enormous health, social and economic consequences because of the global trade of food supplies and the increased complexity of the food chain. Given the interaction of multiple actors involved in the global food chain that are separated by vast distances and potentially delayed impacts, multisectoral and international cooperation is essential. This is why food safety in general, and chemical food safety in particular, has become a matter of increasing international concern [31].

FOOD CHAIN CONTAMINATION: AN "EARLY ALARM BELL" FOR ENVIRONMENT CONTAMINATION

The so called "Sacco river valley scandal" may be considered a paradigmatic example of the use of food and feed products as bioindicators of environmental contamination, like a "sentinel product". In Italy, a national monitoring system has been in place since 1991 for detection of residues of both illicit and authorized substances and environmental contaminants in feed and food of animal origin, namely National Plan for Residues (PNR) [32]. Within the PNR activities, in spring 2005 the analysis of bovine milk from several dairy farms located in the Sacco river valley, Lazio Region, showed β-hexachlorocyclohexane (β-HCH) levels far exceeding the expected values (legislation limit 0.003 mg/kg) [33, 34].

The Sacco river is one of the main rivers of the Lazio region in Italy and runs north to south in an open and densely populated valley. Since the beginning of 1900 to the end of the '90s, industrial settlements located in the north of the Sacco valley produced a wide range of chemical products, including explosives, industrial chemicals and pesticides, in particular technical DDT and Lindane (β-HCH) [33, 35, 36]. The β-HCH is a persistent chlorinated organic compound, formed as a reaction product during the synthesis of the insecticide β-HCH. Plants are able to absorb and bioaccumulate HCH in their tissues. The extent of bioaccumulation depends on the concentration of the contaminant in the soil, plant species, and the physicochemical properties of each isomer: in particular, β-HCH is the most accumulated in plants [37]. The epidemiological investigation to trace the source of contamination highlighted that contaminated milk was mainly from farms that used forage and feed locally grown in the Sacco river valley. β-HCH was found in soil samples at decreasing concentration when the distance from the river increased. It was therefore concluded that the Sacco river served as the vehicle for the contamination and that the distribution of the contaminants in neighboring land, and consequently the contamination of the fodder, had occurred following overflow and/or irrigation with water from the river [35]. Finally a human biomonitoring study in the Sacco valley population highlighted that high β-HCH serum concentrations were strongly associated with the consumption of locally produced food [34].

Since 2005, Sacco river valley has been classified as a site of national interest for environmental remediation and represents an example of how results of the monitoring of food products, not only can be used for integrated risk assessment, but can also be a useful "early alarm bell" for environmental contamination.

CONCLUSIONS

From the examples presented in this work it emerges that the food chain plays a role of fundamental importance when it comes to chemical contaminants. We showed that the bond environment-animals-humans is undeniable and one of the main interactions among these three actors is indeed the food chain. This fundamental aspect in recent years has been developed in the concept of "One Health" which, through a collaborative effort among multiple disciplines, aims to obtain optimal health of humans ensuring in the first place the healthiness of the environment and thus of the animals that live in it, since they represent the main source of nutrition for humans. The awareness that plants and animals are constantly exposed to chemicals present in the environment and that foods, both vegetables and of animal origin, may be an important vehicle of such chemicals to humans has become increasingly solid. In the whole food production process the environment influences the qualities of the final food products and it is evident that only ensuring a healthy environment it is possible to guarantee a reduction of chemicals' dietary exposure. In recent years more active cooperation between actors involved in public health, environment and food safety has been widely promoted by international organizations in order to reach the common goal of "One Health" [38].

This work highlights how different matrices, air, soil, water, and foods, very often share the same contaminants, thus, a risk assessment based on exposure estimate through one route is incomplete unless scientific evidence of the absence of that specific substance in any other matrices is supplied. Once again collaboration between sectors committed to ensure human health is needed in order to achieve an integrated risk assessment.

The environment-humans interaction through food becomes even more complex when considering the complexity of international food trade. Nowadays foods originated everywhere are commonly available on the market and people may be exposed to substances present in the environment from which the foods derive, even if at far distance [24].

In Italy and other EU member states the food monitoring system, is a structured system that provides data which indirectly describe the environment from which foods derive. These data have proved their usefulness also as early warnings of environmental contamination.

Moreover data driven from food controls are a useful tool to ensure dissemination of information to consumers that are more aware of risks related to the food chain. Risk communication is indeed a key action in the support of health protection actions. Consumers express higher concerns about chemicals, as compared with microbial, contaminants mainly because of potential long-term negative effects on human health [39]. Nineteen percent of the EU citizens consider chemicals as the major food related concern, ranking chemical residues from pesticides, antibiotics and pollutants like mercury and dioxins as the main hazards [40]. Consumer attitudes toward food related risks may differ significantly across countries, creating the potential for trade disputes, which could have huge economic consequences.

In conclusion, when population chemical exposure is considered it is essential to adopt an integrated approach assessing the contribution of the different routes of exposure, including dietary exposure, moreover taking into account the environment characteristics in which people, animals and plants live. Such integrated approach allows a realistic and comprehensive risk assessment of chemical substances in order to identify and deploy effective prevention and intervention measures to protect human health.

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Conflict of interest statement

The authors declare that they have no conflicts of interest.

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REFERENCES

1. Atayese MO, Eigbadon AI, Oluwa KA, Adesodun JK. Heavy metal contamination of amarathus grown along major highways in Lagos, Nigeria. *African Crop Science Journal* 2008;16(4):225-35.
2. Steenland K, Fletcher T, Savitz DA. Epidemiologic Evidence on the Health Effects of Perfluorooctanoic Acid (PFOA). *Environ Health Perspect* 2010;118(8):1100-8.
3. Schlummer M, Sölch C, Meisel T, Still M, Gruber L, Wolz G. Emission of perfluoroalkyl carboxylic acids (PFCA) from heated surfaces made of polytetrafluoroethylene (PTFE) applied in food contact materials and consumer products. *Chemosphere* 2015;129:46-53.
4. European Food Safety Authority. Perfluoroalkylated substances in food: occurrence and dietary exposure. *EFSA Journal* 2012;10(6):2743. DOI:10.2903/j.efsa.2012.2743.
5. Mantovani A, Frazzoli C, La Rocca C. Risk assessment of endocrine-active compounds in feeds. *Vet J* 2009;182(3):392-401.
6. Jones KC, de Voogt P. Persistent organic pollutants (POPs): state of the science. *Environ Pollut* 1999;100(1-3):209-21.
7. Muntean N, Jermini M, Small I, Falzon D, Fürst P, Migliorati G, Scortichini G, Forti AF, Anklam E, von Holst C, Niyazmatov B, Bahkridinov S, Aertgeerts R, Bertollini R, Tirado C, Kolb A. Assessment of dietary exposure to some persistent organic pollutants in the Republic of Karakalpakstan of Uzbekistan. *Environ Health Perspect* 2003;111(10):1306-11.
8. Hachiya N. The history and the present of Minamata Disease – entering the second half of the century. *Japan Medical Assoc J* 2006;49(3):112-8.
9. Yorifuji T, Tsuda T, Takao S, Harada M. Long term exposure to methylmercury and neurological signs in Minamata and neighboring communities. *Epidemiology* 2008;19(1):3-9.
10. Du H, Igarashi Y, Wang D. Transmembrane transport of inorganic mercury in microorganisms – a review. *Wei Sheng Wu Xue Bao* 2014;54(10):1109-15.
11. Harada M. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Crit Rev Toxicol* 1995;25(1):1-24.
12. Landrigan PJ, Sonawane B, Mattison D, McCally M, Garg A. Chemical contaminants in breast milk and their impacts on children's health: an overview. *Environ Health Perspect* 2002;110(6):A313-5.
13. Jolly YN, Islam A, Akbar S. Transfer of metals from soil to vegetables and possible health risk assessment. *SpringerPlus* 2013;2:385. DOI:10.1186/2193-1801-2-385
14. Peralta-Videa JR1, Lopez ML, Narayan M, Saupe G, Gardea-Torresdey J. The biochemistry of environmental heavy metal uptake by plants: implications for the food chain. *Int J Biochem Cell Biol* 2009;41(8-9):1665-77.
15. EFSA. Panel on Contaminants in the Food Chain (CONTAM). Scientific Opinion on Arsenic in Food. *EFSA Journal* 2009;7(10):1351. DOI:10.2903/j.efsa.2009.1351.
16. Hong YS, Song KH, Chung JY Health Effects of Chronic Arsenic Exposure. *J Prev Med Public Health* 2014; 47(5):245-52.
17. Donato F, Magoni M, Bergonzi R, Scarcella C, Indelicato A, Carasi S, Apostoli P. Exposure to polychlorinated biphenyls in residents near a chemical factory in Italy: the food chain as main source of contamination. *Chemosphere* 200;64(9):1562-72.
18. Centers for Disease Control and Prevention (CDC). Third National Report on Human Exposure to Environmental Chemicals. July 2005. Available from: www.jhsph.edu/research/centers-and-institutes/center-for-excellence-in-environmental-health-tracking/Third_Report.pdf.
19. Carpenter DO. Polychlorinated biphenyls (PCBs): routes of exposure and effects on human health. *Rev Environ Health* 2006;21(1):1-23.
20. Turrio-Baldassarri L, Abate V, Alivernini S, Battistelli CL, Carasi S, Casella M, Iacovella N, Iamiceli AL, Indelicato A, Scarcella C, La Rocca C. A study on PCB, PCDD/PCDF industrial contamination in a mixed urban-agricultural area significantly affecting the food chain and the human exposure. Part I: soil and feed. *Chemosphere* 2007;67(9):1822-30.
21. Turrio-Baldassarri L, Alivernini S, Carasi S, Casella M,

Fuselli S, Iacovella N, Iamiceli AL, La Rocca C, Scarcella C, Battistelli CL. PCB, PCDD and PCDF contamination of food of animal origin as the effect of soil pollution and the cause of human exposure in Brescia. *Chemosphere* 2009;76(2):278-85.
22. Apostoli P, Magoni M, Bergonzi R, Carasi S, Indelicato A, Scarcella C, Donato F. Assessment of reference values for polychlorinated biphenyl concentration in human blood. *Chemosphere* 2005;61(3):413-21.
23. Turrio-Baldassarri L, Abate V, Battistelli CL, Carasi S, Casella M, Iacovella N, Iamiceli AL, Indelicato A, Scarcella C, La Rocca C, Alivernini S. PCDD/F and PCB in human serum of differently exposed population groups of an Italian city. *Chemosphere* 2008;73:S228-34.
24. WHO regional office for Europe. Available from: www.euro.who.int/en/media-centre/sections/press-releases/2015/complex-food-chain-increases-food-safety-risks.
25. Bernard A, Fierens S. The Belgian PCB/dioxin incident: a critical review of health risks evaluations. *Int J Toxicol* 2002;21(5):333-40.
26. van Larebeke N, Hens L, Schepens P, Covaci A, Baeyens J, Everaert K, Bernheim J L, Vlietinck R, De Poorter G. The Belgian PCB and dioxin incident of January-June 1999: exposure data and potential impact on health. *Environ Health Perspect* 200;109(3):265-73.
27. Covaci A, Voorspoels S, Schepens P, Jorens P, Blust R, Neels H. The Belgian PCB/dioxin crisis-8 years later An overview. *Environ Toxicol Pharmacol* 2008;25(2):164-70.
28. Bernard A, Fierens S. The Belgian PCB/dioxin incident: a critical review of health risks evaluations. *Int J Toxicol* 2002;21(5):333-40.
29. Olsson EK. *"Chapter 3: The Dioxin Scandal Crisis". In: Decision making in the European Union*. Larsson Sara, Olsson Eva-Karin, Ramberg Britta (Eds). ISBN: 91-85401-02-1 ISSN: 1650-3856. A Publication of the Crisis Management Europe Research Program. Stockholm: Elanders Gotab; 2005.
30. Brouwer A, Benisch P. Systematic surveillance for management of Dioxin contamination risks in the food chain: Germany and related cases. *Act Vet Scand* 2012;54(Suppl. 1):S3.
31. Negri S. *Food Safety and Global Health: An International Law Perspective. Global Health Governance*. Volume III, No. 1 (Fall 2009). Available from: www.ghgj.org.
32. Draisci R, Falcone E, Patriarca M, Purificato I, Macrì A. Workshop. Residui negli alimenti di origine animale: analisi del rischio, prevenzione e sorveglianza. Roma: Istituto Superiore di Sanità; 19-20 dicembre 2005. (ISTISAN Congressi, 05/C15).
33. Sala M, Caminiti A, Rombolà P, Volpe A, Roffi C, Caperna O, Miceli M, Ubaldi A, Battisti A, Scaramozzino P. Beta-hexachlorocyclohexane contamination in dairy farms of the Sacco River Valley, Latium, Italy, 2005. A Retrospective cohort study. *Epidemiol Prev* 2012;36(5) Suppl. 4:1-52.
34. Porta D, De Felip E, Fantini F, Blasetti F, Abballe A, Dell'Orco V, di Domenico A, Fano V, Ingelido AM, Perucci CA. Population Exposure to a Persistent Organic Pollutant (β-HCH) Following Waste Disposal from a Chemical Plant (Sacco River Valley, Italy). *Epidemiology* 2009;20(6)S30.
35. Fano V, Porta D, Dell'Orco V, Blasetti F, De Felip E, Di Domenico A, Fantini F, Corbo A, D'Ovidio M, Forastiere F, Perucci CA. Esperienza del Lazio sulla valle del fiume Sacco: studi epidemiologici in un'area contaminata da composti organoclorurati persistenti. In: Indagini epidemiologiche nei siti inquinati: basi scientifiche, procedure metodologiche e gestionali, prospettive di equità. Bianchi F, Comba P (Eds). Roma: Istituto Superiore di Sanità; 2006. (Rapporti ISTISAN, 06/19).
36. Ingelido AM, Abballe A, Marra V, Valentini S, Ferro A, Porpora MG, Barbieri PG, De Felip E. Serum concentrations of beta -hexachlorocyclohexane in groups of the Italian general population: a human biomonitoring study. *Ann Ist Super Sanità* 2009;45(4):401-8.
37. Calvelo Pereira R, Camps-Arbestain M, Rodríguez Garrido B, Macías F, Monterroso C. Behaviour of alpha-, beta-, gamma-, and delta-hexachlorocyclohexane in the soil-plant system of a contaminated site. *Environ Pollut* 2006;144(1):210-7.
38. Gibbs EPJ. The evolution of One Health: a decade of progress and challenges for the future. *Veterinary Record* 2014;174:85-91.
39. Kher SV, De Jonge J, Wenthol MTA, Deliza R, de Andrade JC, Cnossen HJ, Luijckx NBL, Frewer LJ. Consumer perceptions of risks of chemical and microbiological contaminants associated with food chains: a cross-national study. *Inter J Cons Stud* 2013;37(1):73-83.
40. European Food Safety Authority. *Special Eurobarometer 354 / Wave 73.5 – TNS Opinion&Social. Food related risks*. Parma: EFSA; 2010. Available from: www.efsa.europa.eu/en/factsheet/docs/reporten.pdf.