Position Paper

PESTICIDES, AGRICULTURAL PRACTICES AND ENVIRONMENTAL HEALTH

by the ISDE Italy working group on pesticides

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This document summarises the position of ISDE Italia with regard to the environmental and public health risks associated with exposure to pesticides. It presents relevant scientific data on the risks posed by agro-industrial practices to human and animal health and ecosystems in general.

On the basis of the main arguments presented, ISDE Italia recommends informing and raising the awareness of the public and the authorities responsible for public health, taking on the priority task set out by the European Parliament in Article 7 of Directive 2009/128/EC: "Member States shall take measures to inform the general public and to promote and facilitate information and awareness-raising programmes and the availability of accurate and balanced information relating to pesticides for the general public, in particular regarding the risks and the potential acute and chronic effects for human health, non-target organisms and the environment arising from their use, and the use of non-chemical alternatives."

Rigorous protection and prevention measures need to be adopted, pending definitive bans, as the evidence of the acute and chronic toxicity of many pesticides studied to date is scientifically sound. There is a need for stricter regulation based on the precautionary principle for all substances whose effects are not yet clear, are being studied or are completely unknown.

ISDE Italia promotes policies, expertise, technologies and culture to protect the legitimate right of all citizens to high quality, uncontaminated foods.

The development of local networks of farmers, citizens, local institutions and cooperative sales channels is a starting point towards the aim of completely eliminating the use of pesticides from Italy's and Europe's agri-food systems.

In the light of current knowledge about the risks to human health, individuals are also called on to make a change. All consumers can adopt responsible behaviours and take simple steps to reduce exposure to pesticides, thus minimising the risks to themselves and to their families. Finally, rural communities, working with stakeholders and local organisations, have the right and the duty to require public institutions to put in place suitable health prevention and chemical contamination reduction programmes, within a mandatory framework of intervention for the protection of public health.

BACKGROUND

The production and release into the environment of synthetic pesticide compounds represented a fundamental stage in the green revolution – the transformation of agriculture into an industrial sector today controlled primarily by the chemicals industry. This radical transformation of the agricultural sector into an extractive and industrial sector like so many others has been widely presented as an undisputed step forward in the development of advanced societies.

However, since the end of the 1950s, there has been growing evidence of the negative impact of this revolution, thanks to scientific research more attuned to the costs, rather than the presumed benefits, of agricultural industrialization. Over the same period, the first international treaties to protect the world's resources and natural environments from chemical contamination and other damaging human activities were adopted.

The current mass spread of pesticides into the natural environment (water, air, soil and foods) would suggest that serious consideration should be paid to biological exposure to these substances and their metabolites. The scientific community has widely recognized that contamination by synthetic chemical agents now affects the entire biosphere, i.e. the totality of terrestrial and aquatic ecosystems and the entire human population.

The damage caused by these compounds can vary depending on the type of molecules, their quantity, the presence of multiple active agents, the environmental contexts in which they spread and the diversity of the organisms exposed. It follows that a detailed empirical evaluation of the ecological and health impact of pesticides is often difficult to perform and very time consuming.

The scale of the spread of this contamination has largely exceeded our ability to monitor its impact and assess the associated risks. In the meantime, the legitimate concerns of citizens are being downplayed by the chemicals industry and its proxies in government, using spurious arguments based on a presumed "insufficiency of evidence" of the environmental and health toxicity of pesticides.

THE TRADE IN PESTICIDES

There is no certain data available on the number of toxic or potentially toxic synthetic substances traded at global level. According to UNEP estimates, based on REACH (Regulation on Registration, Evaluation, Authorization and Restriction of Chemicals) data, there could be some 150 000 (1). According to the IARC (International Agency for Research on Cancer), 1 500 pesticides (commercial formulations) were formally registered in 1991 around the world, with several hundred active molecules known; however, 75% of total consumption of pesticides related to just 50 or so active molecules (2). In 2009, the WHO listed around 550 active molecules in use and some 150 obsolete ones (3). Every year, around 2.5 million tonnes (t) of synthetic pesticides are released into the environment around the world, mainly for agricultural use. 40% of this figure relates to herbicides, sales of which far surpass those of insecticides and fungicides (4). In Europe, Italy is the country using the greatest amount of pesticides (active substances), in both absolute terms (61 890 t), and in terms of consumption per unit of cultivated land (5.6 kg/ha) (5, 6, 7). A comparative approach limited to the EU shows that, in 2006, Italy consumed 81 450 t of pesticides (active substances), compared to 71 612 t in France, 31 819 t in Germany and 21 151 t in the UK (5). In 2005, Italy accounted for 39% of the fungicides, 36% of the insecticides, 10% of the herbicides and 37% of other compounds used in the EU (5). It should be noted that an analysis carried out half way through the period 2002-2012 showed a decreasing trend, with an overall reduction of 33 000 t (-19.8%) of pesticides (active substances) used in agriculture at national level. Over the same period, the use of very toxic and toxic products fell by 33.6% together with the use of non-classified products (-26.1%), whilst there was an increase in noxious products (+57%). The use of products for organic agriculture also increased significantly (from 11.9 to 289.9 t) (7).

As already mentioned, in 2012 Italy's mean consumption per hectare of fungicides, insecticides, herbicides and other synthetic compounds (active substances) was 5.6 kg (6). The highest consumption figures were in Trentino Alto Adige (42.33 kg/ha), Veneto (12.62 kg/ha), Campania (10.93 kg/ha), Liguria (9.86 Kg/ha), Sicily (9.8 kg/ha), Emilia-Romagna (7.78 kg/ha) and Friuli Venezia Giulia (7.32 kg/ha), whilst the lowest were in Mo-

lise (1.07 kg/ha) (7).

As pesticide consumption per hectare in Italy is the highest in the EU, the fall in Italy's consumption of pesticides during the period 2002-2012, although welcome, is far from guaranteeing a healthy environment propitious to public health. The environmental matrices assume an environmental health picture which has, for some time, been critical as a result of large-scale contamination which has been continuing for more than half a century. This deterioration of the quality of the environment will not be reversed by partial reductions in the burden of agricultural contaminants over the past few years.

ENVIRONMENTAL DRIFT AND DISSEMINATION

Data from ISPRA (Istituto Superiore per la Protezione e la Ricerca Ambientale) (9) on chemical contamination of Italian waters show how pesticides have spread throughout Italy's surface water and groundwater. Monitoring has shown that Italian waters contain 175 different pesticides, more than in previous years. Compared to the past, we have seen a significant increase in fungicides and insecticides, above all in groundwater.

Pesticide residues were found at 55.5% of the 1 469 sampling points of surface waters (2011-2012), in 17.2% of cases at concentrations above the limit values in the Environmental Quality Standards. Groundwater was found to be contaminated in 31.8% of the 2 404 sampling points, in 6.3% of cases at concentrations above legal limits. The ISPRA report confirms that, of the many substances currently in use, some 200 are not included in the monitoring programme, even though 44 of them are classified as hazardous (38 specifically for aquatic environments).

At national level, the limits set for drinking water are exceeded in surface waters in 33.7% of cases, while these limits are exceeded in 9.5% of cases in groundwater. This is relevant to public health as these waters are often intended for human consumption (9).

Synthetic pesticides are designed to remain unchanged over time in the environment with regard to their toxicological properties; this is a very important technological characteristic because it influences both the environmental impact and the economic value of each substance placed on the market. As compounds with these properties are not altered by the normal environmental decomposition mechanisms, they can remain in ecosystems for an indeterminate period, and are thus described as "persistent". It should be noted that the persistence of pesticides in environmental matrices can vary depending on the compound, the chemical classification, the temperature, the nature of the environments in which they are to be found and the characteristics of their metabolites. Moreover, there are certain active substances which are particularly persistent, more toxic and very mobile. The combination of these properties raises concerns about the spread of active substances considered to be most hazardous which, thanks to their volatility and other features, can spread surprisingly long distances. These substances are on the list of POPs (Persistent Organic Pollutants) drawn up by the Stockholm Convention in 2001 which are now banned from most countries in the world (10). It should not be forgotten that Italy is the only country in Europe to have signed the Convention but not yet to have ratified it.

FOOD CHAINS

Pesticides, like other hazardous substances, can enter animals (including humans) by inhalation, ingestion and cutaneous (or mucosal) absorption. Another important property which characterizes them is their capacity to be incorporated into individuals (bio-accumulation) – which, in turn, form the biomass of biological communities – increasing their concentration in the food chain (bio-magnification) (11). Being highly lipophilic, many pesticides tend to accumulate in specific animal tissues and fluids - first of all in fat tissue and breast milk and, to a lesser extent, in the nervous tissue, muscle tissue, liver and the reproductive organs - where their concentration increases gradually as one moves from the bottom of the food chain to higher levels. On each occasion when biomass and biochemical energy are transferred along the chain, there is a considerable loss of both: the ratio between one level and the next one along the chain is, on average, 10:1

(11). Consequently, the concentrations of pollutants in the food chain, for example at the level of primary production (plants) increase as a result of the drastic and progressive loss of biomass which can be seen between the various levels of the chain (animals). Animals at the top of the food chain - usually predators - are exposed to very high and potentially lethal concentrations of pesticides.

From the point of the view of environmental exposure, the food chain and drinking water are probably the most widespread sources of risk for human beings. As humans are at the top of the food chain which they themselves control, by means of agriculture and animal rearing, exposure to pesticides through foods represents a potential threat to public health. It should be remembered that children are most exposed to food contamination by pesticides, above all during pregnancy and breastfeeding, because of the process of bio-magnification described above (12). Because of their physiological status (growth and development) and low body weight, children are without doubt the most at-risk category.

In 2013, EFSA (the European Food Safety Authority) published its latest report on the monitoring of pesticides in food (data from 2010), which showed that 1.6% of samples contained several of the 178 pesticides studied at concentrations above the MRL (maximum residue level). Moreover, pesticide residues within the legal limits were found in 47.7% of samples, and the presence of mixtures containing several pesticides were found in 26.6% of samples, a figure which has been rising over recent years. Inspections of products of animal origin have found residues of particularly dangerous pesticides in a significant percentage of cases. For example, DDT, use of which has been banned in Europe for more than 30 years, was found in 13.4% of samples (13). A study conducted in Italy (14) found that a ready meal contains, on average, between 8 and 13 pesticides, with the greatest number found being 91.

BIODIVERSITY

Up-to-date estimates put the current species extinction rate at more than 1 000 times faster than would be the case due to natural processes and phenomena alone (15). Intensive agriculture, with its high input of synthetic products and fossil fuels, together with climate change and the fragmentation of habitats, have all played a fundamental role in accelerating this huge loss of biodiversity. There is widespread agreement that the factors involved in the loss of biodiversity not only add up but also interact to provoke a rapid deterioration of the health of ecosystems, leading to a reduction in the quality of natural resources, to the detriment of economies throughout the world (16, 17).

The huge quantities of pesticides used around the world have an ecological impact which cannot always be monitored precisely. This impact is the subject of a sound corpus of scientific literature which documents a serious loss of biodiversity, the repercussions of which on the environment and on agriculture are already being felt. It is enough to recall the serious crisis in the populations of pollinating insects which has been seen throughout Europe, including Italy (7).

The normal functioning of ecosystems, which provide essential "services" to agriculture (pollination, fertility of soils, containment of parasites, etc.) and to economic systems more generally, is being significantly degraded by chemical pollution (18, 19, 20). Aquatic systems are also suffering from the toxic effects of pesticides, even where the contamination is caused by molecules which have been banned for decades. An example of this is DDT, the concentration of which, because of the complexity and unpredictability of ecological and climatic processes, has recently started to increase again in the waters of several sub-Alpine lakes (21). The serious impact of pesticides on aquatic biocoenosis must be added to the damage caused by synthetic fertilisers, which are responsible for eutrophication (22, 23).

ISDE Italy is concerned that such dangerous substances are still being used without due attention being paid to the impact on natural systems, the balance of which is essential as they provide us with irreplaceable resources.

TOXICITY

The biological and health effects of pesticides can take various forms, representing equally important aspects of toxicity. In general, two types of effect on health can be defined: i) acute effects which arise quickly as a result of sudden high dosage exposure (acute toxicity); ii) long-term effects due to low-level exposure over time (chronic toxicity). In the second case, the ability to monitor and analyze the biological damage depends on the period between the exposure and the damage, which may require years or even decades (latency period). The latency period is at the root of the methodological difficulties faced by researchers trying to reconstruct exposure which has led to biological damage and is a serious obstacle to the identification of the causal factors involved. The difficulties in monitoring the impact on ecosystems are similar to those in monitoring the health impact, except that, in an environmental assessment, the typology and spatial/temporal scale of the impact present greater problems, because the impact assessment relates not only to individuals and populations but, above all, to biological communities, in other words infinitely more complex systems (8). This means that the impact on ecosystems may take decades or centuries to become clear, which increases the uncertainty of forecasts made using even state-of-the-art scientific methods.

The important fact remains that the toxicological and eco-toxicological studies on the health and environmental impacts of many pesticides are now incontrovertible. Not having absolute scientific proof does not mean that we do not have sufficient information to make technical, policy recommendations and rules. Neither does it justify playing down the problems caused by pesticide pollution.

EFFECTS ON HUMANS

A growing body of scientific evidence, both experimental and epidemiological, shows that chronic exposure to pesticides may lead to changes that have a detrimental effect on various structures in the human body, including the nervous, endocrine, immune, reproductive, renal, cardiovascular and respiratory systems. A substantial contribution, in terms of scientific evidence based on up-to-date knowledge, comes from the Agricultural Health Study (AHS). The AHS is an ongoing prospective cohort analysis which, between 1993 and1997, recruited thousands of subjects from farming families in one of the regions of the USA most characterized by intensive agriculture and the use of pesticides. Exposure to a range of noxious substances, including pesticides, among farmers is at the root of a clear increase in the risk of developing certain neoplasms and neuro-degenerative diseases.

CANCER

Monograph IARC 53, published in 1991, stated that the "spraying and application of nonarsenical insecticides entail exposures that are probably carcinogenic to humans"(2). Since then, at least 21 pesticides (organochlorine pesticides, organophosphorous compounds, carbamates and phenoxy herbicides, triazine) have been identified in epidemiological studies monitoring potential confounding factors and observing a relationship between dosage and response.

The AHS cohort has shown significant correlations between exposure to the main functional categories of pesticide (insecticides, herbicides, fungicides) and the onset of cancer of the breast, prostate, lung, brain, colon/rectum, testicle, pancreas, oesophagus, and stomach, as well as melanoma and non-Hodgkin's lymphoma. In particular: exposure to organochlorine pesticides, organophosphorous compounds, carbamates, phenoxy herbicides and triazine has been linked to a higher risk of tumours of the lung, prostate, lymphatic system and haemopoietic systems (24). Even children, especially the offspring of farmers or other persons regularly exposed to pesticides, show a greater incidence of certain tumours. The literature suggests that exposure to pesticides in utero, during infancy and adolescence significantly increases the risk of leukaemia, lymphoma and brain tumours. The risk is particularly high when the mother has been exposed, during pregnancy, to pesticides in a domestic environment (gardens, vegetable gardens, etc.). The risk of brain tumours has been found to be linked to the use of pesticides during the pre-natal period, also by the father (25). Certain data from the AHS cohort relating to farmers' children aged between 0 and19 years clearly show a 36% higher cancer risk and a statistically significant increase in non-Hodgkin's lymphoma (26). Moreover, a signif-

icant increase in the risk of leukaemia related to levels of metabolites of certain insecticides (pyrethroids) in urine has been documented in children (27). Of particular interest is that Sweden, where chlorophenols and other phenoxy herbicides have been banned since the 1970s, is now seeing a significant fall in the incidence of non-Hodgkin lymphoma after 20 years, despite the incidence of this disease rising in every other western country, above all in young people and adolescents (28).

NON TUMORAL PATHOLOGIES

Various studies suggest a positive link between exposure to pesticides and diabetes, cardiovascular disease, obesity, reproductive disorders, congenital malformations, development defects, endocrine diseases and renal pathologies (29, 30). Moreover, pesticides are suspected of being a factor in falling male fertility, which is now a serious health problem around the world (31, 32, 33, 34).

Neurotoxicity, however, remains one of the most relevant health problems linked to exposure to pesticides and, in particular, insecticides. The main neuro-degenerative diseases linked to exposure to these compounds are Parkinson's, amyotrophic lateral sclerosis (ALS) and Alzheimer's.

Multiple exposure to insecticides and herbicides brings an overall increase in the risk of developing Parkinson's disease. It should be remembered that, in 2013, the French health institutes officially recognized Parkinson's as an occupational disease affecting farmers (35, 36, 37).

EFFECTS ON BRAIN DEVELOPMENT

In 2006, the influential journal The Lancet (38) published an alarming article listing 202 substances known to be toxic to the human brain, of which 90 were pesticides. Recently, the same authors reiterated that many insecticides (e.g. chlorpyrifos) are associated with this risk and recommended a global prevention programme to contain what could become an epidemic caused by exposure to these compounds (39).

Other insecticides (such as organophosphorus ones) are already known for their impact on neuro-development, and in particular sensory, motor and cognitive development and cerebral morphology (40, 41). It should be emphasised that these studies were conducted using rigorous bio-monitoring methods, for example measuring contaminant levels at birth in blood from the umbilical cord or in the mother's urine during pregnancy and then following the children's neuro-psychomotor development.

There is growing evidence that exposure to insecticides in utero is linked to the onset of autism, in particular when the exposure is coincident with the phase of gestation when the brain develops (42).

Grave concerns have been expressed about this issue, as the epidemiological studies which show links between neuro-cognitive development and pesticides are consistent with the experimental toxicology results. Moreover, many synthetic compounds currently sold in Europe, including organophosphates, carbamates, pyrethroids, dithiocarbamates and chlorophenyl silicate herbicides, can compromise neuro-development, with serious and irreversible effects on children's health (43).

VULNERABLE PERIODS: PREGNANCY AND LACTATION

Exposure to a series of pesticides during pregnancy, breast-feeding and childhood can have a very significant impact, even at tiny doses. Specifically, exposure during the first trimester of pregnancy is associated with a greater risk of low birth weight, compromised brain development, and cognitive and behavioural anomalies (42). Even the period before conception is considered today to be a vulnerable period (see more below) when prospective parents should take particular care.

Food-related exposure, through the everyday consumption of contaminated foodstuffs, and the subsequent transfer to the child via the placenta or breast milk, is a significant route for the exposure of foetuses or neonates. Breast milk is the ideal indicator of the quality of the environment in which the mother lives, as lipophile contaminants such as many pesticides, dioxins or polychlorinated biphenyls (PCBs) accumulate in

it. Precautionary measures in these phases of life are absolutely vital and can be taken through deliberately avoiding the main vectors for exposure to pesticides: in food, at home and at work.

Recent studies suggest that eating organic food during pregnancy significantly reduces the risk of complications like eclampsia and malformations such as hypospadia (44, 45).

ENDOCRINE INTERFERENCE AND LOW DOSE EXPOSURE

A growing body of experimental evidence suggests that chronic exposure to endocrine disruptors can lead to changes to various apparatus and organs, for example the nervous, endocrine, immune, reproductive, renal, cardiovascular and respiratory systems. The term endocrine disruptors was coined in 1991 and refers to all substances able to interfere with the synthesis, secretion, transport, action, metabolism and elimination of hormones. A complex mechanism can affect the ability of cells to communicate between themselves, producing a vast range of negative impacts on health, such as: congenital defects, reproductive defects, developmental problems, changes in metabolism, immune diseases, neuro-behavioural disorders and hormone-related tumours.

These substances can have a negative impact not only on the individuals directly exposed but also on their offspring, with an impact down the generations (which, obviously, is very worrying). The trans-generational effect can in turn cause potential neoplastic processes through biological mechanisms different to those associated traditionally with carcinogenicity. The main groups of pesticides responsible for this action are chloro-organic compounds, triazoles, imidazoles, trazines, dithiocarbamates and coformulants. The scientific community has widely accepted that these risks are greater if the exposure occurs in the early stages of life, starting from the embryo/foetal stage. At the same time, evidence is accumulating that low dose exposure even before conception may also have an impact, with trans-generational effects through mutations at the level of the reproductive cells. The health risks of preconception exposures manifest themselves mainly in congenital malformations and chronic degenerative pathologies which, later on, can flare up in the descendants of the individuals originally exposed. Mutations to the germinal line can be found in the genome or in non-genomic factors which regulate the expression of the genes (the epigenome). In the case of both genetic and epigenetic changes, the damage to the reproductive cells can be permanent and potentially lead to inherited diseases passed down from generation to generation.

A case of trans-generational pathology has been well studied in an experimental context in rodents. Certain fungicides (e.g. vinclozolin) increase the incidence of metabolic pathologies, tumours and reproductive disorders in rats (Rattus norvergicus), which can even be seen in subsequent generations. Studies conducted among human populations exposed to dioxins or pesticides, in particular DDT, also find thyroid problems, infertility and cardiovascular problems in individuals not directly exposed (29).

It should be noted that, overall, there are few studies on the impact of pre-conception exposure to pesticides in humans. This is because such studies are recent and subject to methodological difficulties which cannot always be overcome. In any event, the available evidence indicates that parental exposure to pesticides before conception is associated with childhood cancers of the blood and central nervous system. In this context, the literature mentions in particular acute lymphoblastic leukaemia, acute myeloid leukaemia and brain neoplasm (46, 47, 48, 49, 50).

EXPOSURE TO MULTIPLE RESIDUES

Pesticides are often used as mixtures, and multiple exposure to these chemical substances poses serious problems in terms of assessing their safety, as confirmed by the Council of the European Union (Council document 17820/09), which emphasizes that EU law recognizes the combination effects of exposure to multiple chemicals and that new methods of assessment need to be developed. Regarding acute toxicity, the synergies of such mixtures and the potential for them to exacerbate each other's effects has already been documented. Particularly concerning is the interaction between the various molecules and metabolites at cellular and sub-cellular levels, the dynamics of which appear to be somewhat complex: genetic and epi-

genetic modifications, imbalances in receptor function with endocrine disruption, mitochondrial dysfunction, perturbation of neuronal conduction because of the alteration of ion channels, alteration of enzyme activity (in particular, interference with the acetyl-cholinesterase), oxydative stress. Moreover, the information available suggests that mixtures of pesticides can modulate or interfere with the function of the immune system. It is therefore very difficult to translate the results of experimental studies into primary prevention and public health decisions and/or measures. Another important aspect is that the toxicity of commercial formulations may be different to that of the active ingredients. Experimental and environmental research shows that commercial formulations may be even more toxic than their individual active ingredients and that the combined action of the main active substance and adjuvants must be considered as a specific case of multiple exposure, the repercussions of which on human and environmental health have so far been underestimated or completely disregarded (51).

EUROPEAN POLICY AND MANAGEMENT OF FOOD RISKS

EU pesticides policy has recently been updated with the entry into force of new provisions. These replace, to a certain extent, Directive 91/414/EEC and are intended to make the procedures for the authorization of pesticides more effective, whilst leaving the Member States sufficient autonomy to make different choices at national level.

In order to create a legislative framework able to ensure the sustainable use of pesticides in Europe, Directive 2009/128/EC was adopted in 2009, followed several years later by the relevant implementing decree (Legislative Decree 150/2012). In Italy, the above Directive was transposed by the PAN (Piano di Azione Nazionale - National Action Plan), with the aim of reducing the risks and impact of agrochemical products on human health, the environment and biodiversity and promoting organic agriculture, integrated plant protection and other approaches which provide alternatives to conventional agriculture. The PAN provides, among other things, for information and awareness-raising campaigns aimed at the general public, illustrating the potential risks of plant protection products. It has not yet been possible to determine the specific impact of Directive 2009/128 and the PAN. However, in the light of the above, it is clear that these provisions should act purely as a starting point for developing new programmes able to launch a real sea change in the use of synthetic chemicals in agriculture.

Legislative instruments able to provide sufficient food safety guarantees are being implemented in the EU to manage the food safety risk posed by pesticides. It should be mentioned that, on this particular point, the most important reference remains Directive 91/414/EEC, which states unequivocally that a pesticide can be authorized only if "it has no harmful effect on human or animal health, directly or indirectly". Unfortunately, this provision is not always applied consistently in the context of EU policy.

Managing the food safety risk caused by pesticides is implemented by way of the minimum safety requirements for food products (MRL, Maximum Residue Limits), which indicate the maximum acceptable amounts of each pesticide in the various types of food. At EU level, EFSA considers the application of MRLs to be the most useful tool for ensuring food safety, in line with the recommendations of the Codex Alimentarius and the joint WHO/FAO food standards programme.

EFSA establishes the MRLs, also taking into account good agricultural practices (GAPs): in other words, the MRL defines the maximum quantity of pesticides allowed in a particular foodstuff on condition that the GAP requirements are also met. The EU applies another risk assessment parameter in addition to MRLs: ADI (Acceptable Daily Intake), which defines the amount of a substance which may be ingested in food without damaging health. It is clear that the ADI depends on both the MRL and the amount of pesticide-containing food consumed by individuals - an aspect which is far more difficult to assess and monitor, given the evident variability in individuals' food consumption.

It should be stressed, as outlined above, that pesticides authorized for sale should not be considered merely in terms of their main active substance but contain a whole series of other substances, such as adjuvants, which are normally excluded from official safety assessments: this is significant and, in several cases, has been the subject of objections on the part of public health researchers and operators (51, 52).

ISDE Italia takes the view that the European model for managing the risks of pesticides is overly complex, difficult to apply and thus unreliable. The risk posed by the use of pesticides remains an unresolved problem, not only because of the objective difficulty of integrating safety parameters such as the MRL and ADI but also because of the insurmountable methodological obstacles to understanding the health impact of mixtures of pesticides present in foodstuffs and active molecules at low doses. This is illustrated perfectly by the case of the endocrine disruptors described above, in relation to which European risk management is sorely lacking. Moreover, MRL and ADI are rigid parameters which cannot take account of these difficulties or other factors mentioned above, such as those associated with the time period of exposure. This point refers to the technical and policy responsibilities of the regulatory bodies, primarily. EFSA, often accused of not complying with the obligation to perform exclusively scientific and independent evaluations and thus of not fully meeting its own obligations in the context of the institutional mandate delegated to it by European citizens. EFSA's role is in fact to guarantee food safety in the countries of the European Union, not to protect the interests of industry and pressure groups (52, 53).

ECOLOGY AND AGRICULTURE

Only a rational and targeted overhaul of the rules of agricultural production, the dynamics governing the markets and the consumer behaviour of citizens can guarantee food safety.

ISDE Italia promotes policies, expertise, technologies and types of cultivation to protect the legitimate right of all citizens to have access to high quality, uncontaminated foods. In this respect, the European directive on the sustainable use of pesticides, despite its limitations and ambiguities, still represents a legislative starting point to launch the transition from a form of agriculture based on chemicals and fossil fuels to a genuinely ecological form of agriculture. Local ecological and ethical commerce networks already provide a concrete example of environmentally sound and sustainable agriculture which can be further promoted and developed and may provide the outlines of a way to reduce and, eventually, completely eliminate pesticides from the production of foods. However, for these changes to be made organically, it is important for the entire agri-food chain to be involved, first and foremost by raising awareness among operators, technicians and producers. It is becoming increasingly evident that current methods of agricultural production are unsustainable. Courageous legislative intervention is therefore needed, consistent with the expectations of an aware and informed public.

Many studies show that the consumption of organic/biodynamic food produced without the use of pesticides leads to a clear reduction in these substances and their metabolites in the human body (54, 44). These foods are more nutritional and have more antioxidants, phenolic acids, stilbenes, flavonoids, anthocyanins and other nutrients able to prevent a whole series of health issues. It is currently believed that a diet attentive to toxicological and nutritional quality can protect against chronic tumoral, cardiovascular, metabolic and neuro-degenerative ailments.

Moreover, ecological (organic/ biodynamic) agriculture respects biodiversity and does not threaten the physical, chemical and biological integrity of the soil and water. It also provides benefits in terms of productivity. It is being found that the yield gap between organic and conventional agriculture is much less than used to be believed. In particular, if specific crop diversification techniques are adopted, such as polyculture, inter-cropping, crop rotation etc, the gap closes significantly (55). Boosting agronomic research based on ecological principles could therefore lead to unexpected economic/productive and environmental/health gains.

CONCLUSION

For the above reasons, ISDE Italia is calling for a sea change in Italian and EU agri-food policy and is extremely concerned by developments in the context of the TTIP (Transatlantic Trade and Investment Partnership). The TTIP aims to remove definitively the few remaining principles of justice and environmental standards which, with great effort, we can still enforce.

The evidence of acute and chronic toxicity (e.g. tumoral and neurodegenerative diseases) associated with exposure to pesticides is much sounder and more convincing than the evidence for these substances being safe documented in studies carried out or financed by producers. For this reason, there are well founded reasons for calling for the application of the precautionary principle with regard to all substances whose effects are still unclear, being studied or completely unknown. With respect to all substances whose toxicity has already been documented scientifically, rigorous protection and prevention measures must be adopted and, in the most serious cases, total bans or strict limitations on use, as well as i) withdrawal from the market, ii) the imposition of sanctions proportionate to the environmental/health/economic damage caused by the producers and users of the pesticides in question and iii) financial compensation for damage to persons, property and public and private resources.

The position outlined here relates not only to the agricultural use of pesticides but also to their use in urban contexts, e.g. the use of glyphosates for the maintenance of urban parks, and civil, industrial, zootechnical, domestic and any other type of use which causes damage which can be proven in whole or in part.

RECOMMENDATIONS

In the light of the information outlined above, ISDE Italia recommends the following:

- **At the level of the public institutions**
  - Require full compliance with the provisions of the Legislative Decree of 14 August 2012 on the sustainable use of pesticides, exercising appropriate vigilance (i.e. providing timely information to the public with regard to buffer zones, the scheduling of treatments, procedures intended to contain drift, etc.).
  - Ban any type of herbicide and pesticide from public land.
  - Introduce organic food in schools, nursery schools and other mass catering establishments in both the public and private sectors.
- **At the level of individuals and families**
  - Encourage the consumption of organic/biodynamic food in all phases of life, avoiding in particular non-organic whole meal cereal products.
  - Ensure that both mothers and fathers are not exposed to any risk during pregnancy and lactation, taking into account that exposure before conception may well also have an impact on the health of any descendants.
  - Ensure, as far as possible, that children are not exposed to pesticides through their food, housing or domestic environment.
  - Ensure, as far as possible, that pets are not exposed to pesticides through their food, housing or domestic environment.
  - Limit, as far as possible, the consumption of food products of animal origin (both land and aquatic animals).
  - Wash thoroughly or peel fruit and vegetables of unknown origin, and always remove the skin and fat from meat, whilst remembering that these precautions do not guarantee that all contaminants are being removed.

- Avoid the use of synthetic pesticides in the home, both indoors and outdoors (house plants, gardening, greenhouses, pets, for disinfection, etc.), replacing them with manual, physical, mechanical or biological measures.
- Regularly check living environments, especially during the warmer seasons of the year, in order to avoid infestations of parasites (lice, cockroaches, etc.).

If pesticide use is inevitable:

- Always keep children and animals away from areas being treated, remove toys and all other consumer objects, and ensure good ventilation.
- Do not store pesticides in the home or in places within the reach of children, pets or wild animals.
- Never store pesticides in containers which may be mistaken for containers for domestic use which may store food or other household objects.
- Never allow children or pets to play or remain in gardens, vegetable patches, orchards, cultivated fields etc. which have been treated with pesticides.
- Remember that pesticides can be fatal to many wild animals and animals living in and around human communities which are harmless or even useful for maintaining a balanced environment, such as spiders, small scorpions, worms, insects, birds, large and small mammals (including rodents), amphibians, reptiles and all aquatic fauna.

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