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Review

Critical Review of the Effects of Glyphosate Exposure to the Environment and Humans through the Food Supply Chain

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Abstract: Glyphosate is a synthesis product and chemical substance that entered in the global market during the 70s. In the beginning, the molecule was used as an active principle in a wide range of herbicides, with great success. This was mainly due to its systemic and non-selective action against vegetable organisms and also to the spread of Genetically Modified Organism (GMO) crops, which over the years were specifically created with a resistance to glyphosate. To date, the product is, for these reasons, the most sprayed and most used herbicide in the world. Because of its widespread diffusion into the environment, it was not long before glyphosate found itself at the center of an important scientific debate about its adverse effects on health and environment. In fact, in 2015 the IARC (International Agency for Research on Cancer, Lyon, France), an organization referred to as the specialized cancer agency of the World Health Organization (WHO, Geneva, Switzerland), classified the substance as "likely carcinogenic" to humans. This triggered an immediate and negative reaction from the producer, who accused the Agency and claimed that they had failed to carry out their studies properly and that these conclusions were largely contradictory to published research. Additionally, in 2015, just a few months after the IARC monography published on glyphosate, the EFSA (European Food Safety Authority, Parma, Italy), another WHO related organization, declared that it was "unlikely" that the molecule could be carcinogenic to humans or that it could cause any type of risk to human health. The conflict between the two organizations of the World Health Organization triggered many doubts, and for this reason, a series of independent studies were launched to better understand what glyphosate's danger to humans and the environment really was. The results have brought to light how massive use of the herbicide has created over time a real global contamination that has not only affected the soil, surface and groundwater as well as the atmosphere, but even food and commonly used objects, such as diapers, medical gauze, and absorbent for female intimate hygiene. How human health is compromised as a result of glyphosate exposure is a topic that is still very debatable and still unclear and unambiguous. This paper is a review of the results of the main independent recent scientific studies.

Keywords: glyphosate; food chain; toxicity; alternative technologies

1. Introduction

This review paper deals with a topic that to date is not yet fully investigated, to enable certain conclusions to be drawn and be accepted by all authorities. Glyphosate is the chemical substance of debate in the present work, which comprises a huge question mark for science, as well as for medicine, governmental institutions, and current legislative authorities.

The central theme of the present review study is the effects that the massive use of glyphosate has caused both to the ecosystems that come into contact with it and to human health. As far as the environment is concerned, glyphosate is the most sprayed and distributed chemical substance in human history [1–7]. Therefore, over the years of its use a global contamination has occurred, which has not only affected the soil, the surface and underground waters, and the atmosphere, but even food and objects of common use, such as diapers, medical gauze, and absorbents for female intimate hygiene—all materials in which glyphosate has been found in significant quantities [8].

On the other hand, as human health is compromised due to glyphosate exposure, it remains a controversial subject and for this reason numerous research studies have been carried out, both by public and private organizations [9–11]. However, what triggered the real scientific debate was the classification of glyphosate in 2015, by the IARC (International Agency for Research on Cancer, Lyon, France), as a substance "probably carcinogenic substance for humans" and the subsequent negative reaction of the Monsanto company, the glyphosate product manufacturer [12].

For greater clarity, the different classifications to which the substance has been classified over the years have been reported in the text, as well as the opinions of various scientific organizations regarding its dangerousness and some of the operating procedures through which the results have been obtained.

Furthermore, this paper also addresses the need to find valid alternative technologies to the use of glyphosate. For this reason, the paper describes various agricultural methods that substitute the use of glyphosate, such as biological agriculture.

2. Environmental Criticism and Effects on Human Health

2.1. Characteristics and Environmental Contamination

Glyphosate, being a phosphoric amino derivative of glycine, tends to behave like the inorganic phosphates naturally present in the soil and as such is generally persistent. The reported Biochemical Oxygen Demand (BOD) and Chemical Oxygen Demand (COD) values are less than 2 mg/g and 0.53 g/g respectively, thus the molecule cannot be considered easily biodegradable. Also considering the glyphosate density of about 1.7 g/cm^3 and its limited volatility, it is fairly straightforward to deduce that it will be difficult for the substance to evaporate or to remain suspended in the air for a long time after its application [13].

Glyphosate is a strong chelating agent. Thus, it creates, through physical chemical links, the complexes that immobilize the mineral micronutrients of the soil (calcium, iron, magnesium, manganese, nickel, zinc . . . etc.) making them unavailable to plants [14].

The elimination of glyphosate from the environment through physical processes is very limited. Microbial degradation can significantly eliminate glyphosate from the soil, which can be performed in the presence or absence of oxygen and can vary greatly according to the characteristics of the soil and the pH range at which the reaction takes place [15]. The time, estimated in the laboratory, necessary to degrade 50% of glyphosate present in the water is less than 14 days in aerobic conditions and about 14–22 days in anaerobic conditions. While for the glyphosate present in the soil the degradation time in aerobic conditions is about 2–3 days (estimated time in laboratory tests) [13,15].

Biological degradation and associated times are often described and calculated using the models and equations related to first-order kinetics [13].

The degradation of the herbicide molecule can follow two paths; the first is based on the breakdown of the carbon-nitrogen bond and leads to the formation of Aminomethylphosphonic acid (AMPA, main metabolite of glyphosate), while the second way is based on the splitting of the carbon- phosphorus bond, resulting in the formation of sarcosine and glycine [16].

What may affect the degradation rate of the herbicide in the earth is the presence of inorganic phosphates, which inhibit the action of some strains of bacteria from entering into competition with the molecule [17,18]. In fact, glyphosate is absorbed from the ground as well as through metal complexes and through the bonds created by the phosphorus atom.

In general, the total concentration of glyphosate in the ground varies from 4 to 180 days, making it therefore a potentially contaminating substance for soil and likely for groundwater as well [17,19]. Numerous laboratory studies have shown that the absorption constant of the molecule in the soil varies between 8 and 377 dm^3/kg, depending on the characteristics and composition of the soil (clay, sand, or gravel). This coefficient value indicates a high absorption in the soil. In water, the half-life of glyphosate varies from a few days to 91 days [17,19].

In contact with water, glyphosate quickly transforms into its main metabolite, AMPA, which maintains all the toxic characteristics of its precursor and is even more persistent, with a half-life that ranges from 76 to 240 days. The highest amount of AMPA detected in soils corresponds to about 20% of glyphosate applied under aerobic conditions and to 0.5% under anaerobic conditions. As for the soil matrix, the maximum amount of AMPA detected corresponds to 25% of glyphosate used under aerobic or anaerobic conditions [19].

Glyphosate, as reported in the recommendations for use and the toxic phrases contained in the safety data sheet (P273 and H411), must not be dispersed in the environment and is toxic to aquatic life, with long lasting effects. Consequently, it can be deduced that its uncontrolled use provokes, almost with certainty, damage to the environment, especially to the aquatic one. In general, all habitats characterized by the presence of plants and plant organisms of all kinds, which are located near the sprayed fields, are exposed to the effects of glyphosate [15,20,21].

The environmental contamination by the herbicide in sites that are not considered a target during the application of the product is mainly caused by the unwanted loss of substance during the various phases of transport, handling and storage, and by the action of the wind. The undesirable presence of glyphosate, especially in drinking water, is mainly caused by the contamination of surface water rather than groundwater. Glypshosate has low mobility in the soil, as shown by its value of constant absorption in the soil, and therefore a rather low probability of contamination of the stratum [22].

In order to detect the presence and quantity of glyphosate dispersed in the environment, various laboratory analyses are performed on samples taken in situ. The most common methods are the use of fluorine-based substances and chromatographic techniques, such as liquid chromatography or gas chromatography. The limits for which the molecule is detectable in water, plants, soil, and human urine are respectively 0.02–3.2 μg/L, 0.01–0.3 mg/kg, 0.05–1 mg/kg and 0.1 mg/L [23,24].

The most important processes to which glyphosate can fight, once dispersed in the environment, are the formation of complexes with some ions, which include calcium and magnesium, its presence in the soil water, its absorption from part of the particles and seeds in the soil, the degradation performed by various strains of microorganisms, the absorption of the plants and the resulting degradation in water and by the light (photodegradation). It has been found in some laboratory tests that more than 45% of the glyphosate applied on the soil is absorbed by the plants on which it is sprayed. Once in the water, the oxidation takes about 28 days to eliminate 50% of the glyphosate present, based especially on the type of light radiation [20].

2.2. Human and Animals Health

The relationship between herbicide use and harm to human health has been extensively studied. Although there is still an open debate on the subject, it has been found that the levels of risk of death are generally higher for workers in the agricultural sector compared to other sectors. The causes of this situation are to be found in the changes that have occurred in the agricultural world in recent years: namely, the introduction of very high doses of synthetic chemicals (herbicides, insecticides, fungicides, etc.). For example, in Italy every year about 130,000 tons of plant protection products are used in agriculture. Obviously, the risk that these substances entail cannot be limited only to the agricultural field, as the pesticide and herbicide molecules, including glyphosate, have now completely entered into human habitats, contaminating water, soil, food and much more [25].

Contained in plants and the soil, the herbicide has taken over the food chain of herbivores and omnivores, exposing animals and humans to contamination by glyphosate through ingestion [26].

Many laboratory tests have demonstrated the possible absorption of glyphosate in the gastro-intestinal tract of humans and mammals, as well as absorption through inhalation, ingestion, and dermal contact. In addition, numerous studies [15,20,27] have been performed on mice and rats by administering high doses of glyphosate. The results show that the substance causes growth delays, kidney damage, liver enlargement and inflammation, and gastric disease [15,20,21]. Also, for aquatic plant organisms, glyphosate is considered toxic and acts by altering the vital functions related to photosynthesis, respiration, and the synthesis of essential aromatic amino acids.

Numerous laboratory analyses conducted through the cultivation of bacteria present in the soil have highlighted the effects of glyphosate on nitrogen fixation processes, such as nitrification and denitrification, yet despite these results the analyses carried out directly in the field have shown milder effects and only some species of bacteria are considered to be directly affected by the negative effects of the herbicide [28].

The application of glyphosate in large quantities can also cause effects on insects, such as bees, and on birds, for which the herbicide is toxic [29].

3. Outcome of Research Studies

Several traces of herbicide have been found in various foods, especially those based on cereals, in everyday objects, in drinking water, and even in human urine through a series of studies conducted in recent years. The following is a schematization of the analyses and the results obtained:

- In 2012 the German magazine Oko-Test found traces of glyphosate in wheat flour, oats, and bread in 14 samples out of 20 analyzed [30].
- In 2014 the Moms Across America group and the Sustainable Pulse information website reported the presence of glyphosate in human milk in 3 out of 10 samples, with levels ranging from 76 to 166 μ/L (levels considered acceptable by the Environmental Protection Agency) [31].
- In 2015, the National University of La Plata in Argentina detected traces of glyphosate in 85% of the sample tampons purchased in supermarkets and all analyzed samples of medical gauze and cotton [8].
- Between 2015 and 2016, the BioCheck laboratory in Leipzig, Germany, analyzed the urine of 48 European parliamentary representatives and found traces of glyphosate in each sample. The levels of substance that have been recorded range from 0.17 to 3.5 μ/L [32].
- In the same year, a study by the Heinrich Boell Foundation found that 99.6% of Germans (analyzing the samples of 2009 people) showed traces of glyphosate in the urine and the highest values were found in children and young people who had worked in the agricultural sector [33].
- In 2016, research conducted by Boston University and Abraxis LLC revealed the herbicide's presence in 62% of conventional honeys and in 45% of organic honeys [34].
- In 2016, another two studies conducted by the Munich Institute of the Environment and the Consumer Magazine 60 Millions de Consommateurs found traces of glyphosate in 14 beers, among the best known in Germany (Beck's, Paulaner, Warsteiner, etc.) and in panty liners from the feminine hygiene company Organyc. [35].

3.1. Salvagente (Lifebelt) Test Research

Particularly in Italy, 100 food products based on flour and 26 samples of drinking water were analyzed by the magazine Test-Salvagente, finding traces of glyphosate in half of the food and in two samples of water. This molecule is not easy to identify, especially in low quantities [36,37].

Based on these studies, the following are the products and quantities of substance detected in the research:

- Corn flakes, Kellogg's, All Bran Plus Sticks: 0.140 mg/kg
- Rusks, Gentilini, Whole wheat Slices: 0.130 mg/kg
- Flour, La Conte, Manitoba Magic Flours: 0.023 mg/kg
- Pasta, Colavita, Spaghetti: 0.019 mg/kg
- Pasta, Del Verde, Spaghetti: 0.083 mg/kg
- Pasta, Divella, Lined Ziti Pens: 0.033 mg/kg
- Pasta, Divella, Spaghetti: 0.038 mg/kg
- Pasta, Garofalo, Short Safalda: 0.043 mg/kg
- Pasta, Italiamo Lidl, Spaghetti: 0.070 mg/kg
- Pasta, La Molisana, Striped Butterflies: 0.160 mg/kg
- Pasta, La Molisana, Spaghetti: 0.056 mg/kg

As far as glyphosate research in drinking water is concerned, samples were taken from house faucets and public drinking fountains, thus studies were focused on the everyday water resources with which people come into contact. The molecule in question was detected in two samples, one from Brusnengo (Biella, Italy), and one in Campo Galliano (Modena, Italy), both located in Northern Italy. In these samples the presence of glyphosate was not detected, however its metabolite, AMPA, which retains the toxicity and persistent characteristics of its precursor, was detected. The measured doses were respectively 4.6 μ/L in the first sample (Brusnengo, Italy) and 2.3 μ/L in the second sample (Campo Galliano, Italy). Considering that the tolerable limit for pesticides in drinking water is 0.5 μ/L, the values found in the research conducted by the Test-Salvagente are clearly beyond those of the law. The two interested Municipalities, once the results were published, carried out new research on their water two months later. They found no trace of glyphosate and AMPA.

3.2. ISPRA Research (Italian Water Report: May 2016 Edition)

Important data on the state of water contamination in Italy were also provided by the ISPRA (Italian Higher Institute for Environmental Protection and Research) in the "*National Report of Pesticides in Water*", published in May 2016 [38]. It is important to consider that the monitoring of pesticides requires the preparation of a network covering a large part of the national territory, the control of a large number of substances, and continuous updates due to the introduction of new substances on the market. The Report was made using the 2013–2014 two-year period as well as the data provided by regional environmental protection agencies (Agenzia Regionale Protezione Ambientale-ARPA). In these two years, 29,220 samples were analyzed for a total of 1,351,718 analytical measurements, with an increase respectively of 4.3% and 11.8% compared to the previous two-year period. The Report highlighted the presence of pesticides and contaminants in 63.9% of the 1284 surface water monitoring points (rivers, lakes, streams) and in 31.7% of the 2463 groundwater monitoring points. Compared to the previous biennial, the contaminants detected went from 335 to 365. Glyphosate and AMPA were detected in surface waters in 4 cases out of 10 and in 7 out of 10 cases, respectively. In surface waters, 274 points of monitoring (21.3% of the total) show glyphosate concentrations above the limits imposed to guarantee environmental quality standards. The contaminant substances above the limit are: glyphosate and its metabolite AMPA, metolachlor, triciclazole, oxadiazon, terbuthylazine and its main metabolite, desethyl-terbuthylazine. In groundwater, 170 points (6.9% of the total) have concentrations above the environmental limits. The substances most frequently found above the limit are: bentazone, metalaxyl, terbuthylazine and desethyl-terbutylazine, atrazine and atrazine-desethyl, oxadixil, imidacloprid, oxadiazon, bro-macile, 2,6-dichlorobenzamide, metolachlor [25].

Furthermore, in surface waters the percentage of contaminated points has increased by about 20%, and in underground areas by about 10%.

The concentrations of measured substances are generally fractions of μg/L, but this does not render the results more reassuring. The harmful effects of pesticides are in fact also found for very low concentration exposures.

The overall result of the ISPRA Report indicates a widespread diffusion of contamination. Levels are generally lower in groundwater, but pesticide residues are also present in the deep layers although they are naturally protected by poorly permeable geological layers. A total of 224 different substances were found during the analyses, a higher number of previous years (there were 175 in 2012) [39].

The herbicides are still among the most found substances, above all because of their direct use on the ground and often coinciding with periods of higher rainfall at the beginning of the spring, which determine a faster transport in the surface and underground water bodies. The presence of fungicides and insecticides has also increased significantly compared to the past.

Overall, the contamination is more widespread in the Po Valley-Veneto plain. This is a direct consequence of the fact that surveys are generally more representative in the Northern regions. The checks carried out are not complete and do not homogeneously cover all of the Italian regions. No data has been sent from Molise and Calabria (Southern Italy) and for five regions there is still no analysis of the groundwater. Furthermore, only in Lombardy and in Tuscany are the ARPAs equipped with a monitoring system for glyphosate and AMPA, thus making research in the remaining regions limited to some areas. From the results obtained it becomes clear the need to include in the regional protocols the research of some substances responsible for the most cases of non-conformities, such as daredals and AMPA, but also imidacloprid, me-tolachlor-hex, triadimenol, oxadixil.

The boost given by this research led Emilia Romagna to start monitoring the levels of glyphosate and AMPA by testing and analyzing samples from twenty surface water stations in the regional network between May and October 2016.

In some areas the contamination is much more widespread than the national data, reaching over 70% of the surface water points in Veneto, Lombardy, Emilia Romagna, with peaks of 90% in Tuscany and 95% in Umbria. In underground waters the spread of contamination is particularly relevant in Lombardy, affecting 50% of the points considered, 68.6% in Friuli, and 76% in Sicily.

Contamination from pesticides is a very complex and difficult to predict phenomenon, mostly due to the large number of substances used, the modalities of release, and to the multiplicity of routes and migration routes that can follow in the environment. Furthermore, the toxicity of a mixture is always higher than that of its more toxic component. Humans and other organisms are often exposed to mixtures of chemical substances, whose composition is not known a priori. For this reason, it is forbidden to act directly on limits regarding authorizations for the production and sale of the products in question.

ISTAT data indicate a significant decrease in the sales of plant protection products in the period 2001–2014, from 147,771 to 129,977 tons/year (−12%), with an even more marked decline for active ingredients, from 76,343 to 59,422 tons (−22.2%). In the same period the quantity of very toxic and toxic products was reduced by 30.9%.

The most sold substances, in addition to inorganic pesticides, such as sulfur and ray compounds, are 1,3-dichloropropene, glyphosate, mancozeb, metam-sodium, fosetil-aluminum, chlorpyrifos, with annual volumes of more than 1000 tons [40].

3.3. Diffusion Due to GMO Crops

As already mentioned, the actual diffusion of glyphosate was due to the increase in transgenic crops, specially made to resist disease. Initially, with the creation of the first GMO seeds, many manufacturers and producers ensured that the spread of this new variety of products would lead to a decrease in dependence on toxic chemicals in the agricultural world. To date, using the data collected and reported on in the research, we know with certainty that exactly the opposite happened [41]:

- 11% herbicide use between 1996 and 2011;
- In 2002, the use of glyphosates on GMO soybeans increased by 21%;
- American farmers have increased the use of Roundup herbicide to 19 million pounds a year;
- In 2011, farmers who cultivated corn, soya and cotton GMO crops used 24% more glyphosate than those who grew the same but non-GMO varieties.

The same technical source [41] highlighted the correlation between glyphosate use and GMO crop diffusion (such as soybean and wheat planted) and grew with the same trend.

4. Classification as Carcinogenic

The debate on the dangers of glyphosate on humans is, to date, still open. Given the conflicting terms of the various scientific bodies on the subject, we will now try to clarify some of the definitions and various classifications that have been given over the years to this substance.

In 1985, the US Environmental Protection Agency (EPA) classified glyphosate as a suspected human carcinogen and labeled it a Category C substance, which show limited evidence of carcinogenicity to animals and an absence of negative data or inadequate data on humans [34]. This decision was made after assessing the effects of the long-term administration of the substance in rats and considering some epidemiological studies conducted on farmers in Canada and Sweden. The latter also indicated the association between the prolonged use of glyphosate over time and the increase in the occurrence of cases of non-Hodgkin lymphoma.

In 1991, the EPA [42], based on the same study conducted six years earlier, decided to include glyphosate in the E category, which are substances that do not show carcinogenic potential in at least two animal studies, properly conducted on different species, or in both animal and epidemiological studies. The reason for this decision was an incorrect assessment, from six years earlier, of the results of the studies. The cases of tumors in animals were too rare to consider glyphosate a potentially carcinogenic substance.

In March 2015, the Agency for Research on Cancer or IARC (International Agency for Research on Cancer, Lyon, France), a department of the World Health Organization based in Lyon, classified glyphosate as "probably carcinogenic to humans", inserting it in the 2A category, which are substances with limited evidence of carcinogenicity to humans and sufficient evidence for animals [12]. Exceptionally, substances for which there is only limited evidence for humans or only sufficient evidence for animals is supported by other relevant data. It is advisable to specify that within category 2A there are 66 substances, among which include acrylamide, red meat, bitumen, wood combustion fumes, etc. The conclusion of the investigation, concerning the herbicide, to which the agency arrived was as such, the evidence that glyphosate caused cancer in animals was considered "sufficient" and the evidence concerning the genotoxicity of the product, or its ability to damage DNA, was considered "strong". Laboratory studies also demonstrated the ability of glyphosate to induce genetic damage and oxidative stress in cells.

The study, performed by 17 international experts, considered the exposure of humans and animals to glyphosate (pure or mixed with other substances), and was published in the journal "The Lancet Oncology" [12]. In general, it consisted of a 92-page report, in which 5 substances extensively used in agriculture were considered. In particular, the international organism examined a herbicide, glyphosate, and four insecticides: malathion, diazinon, tetrachlorvinphos, and parathion. Among the latter, the first two were declared as probable carcinogens for humans and included in category 2A, while the others were recognized as possible human carcinogens and classified in category 2B, which are substances with limited evidence for humans in the absence of sufficient evidence for animals or with sufficient evidence for animals and inadequate evidence or a lack of data for humans. In some cases substances with only limited evidence for animals can be included in this group as long as this is strongly supported by other relevant data. The use of the two insecticides falling into category 2B was subsequently banned in the European Union, while they are still used in the United States.

In the years before the study published by the IARC, exposure to the pesticides listed above was often related to an increase in cases of childhood leukemia and neurodegenerative diseases, such as Parkinson's disease, while after the research emerged a close relationship between glyphosate use and the increasingly relevant onset of non-Hodgkin's lymphoma was identified. The same agency declared the need for new independent experimental and epidemiological studies to be able to say with certainty whether the pesticides considered were or were not carcinogenic to humans, thus seeking to identify the target organs, the predictive markers of the exposure, and the biological transformations that occur in detail in our organism [43].

The Government of the United States, until the publication of the IARC monographs that declared glyphosate as "probably carcinogenic to humans", had always supported the safety of the active ingredient, based on the statements of the main manufacturer of the product, Monsanto. The latter, in 2013, requested and even obtained, by the EPA, the approval to increase the tolerance thresholds for Roundup [42].

Monsanto's reaction to the IARC statements, having always declared glyphosate as safe, was naturally very hard, decreeing in a press committee that the WHO agency had not taken into account all the new data and that it was impossible to table a conclusion so distant from what had already been established by all of the regulatory agencies of the world.

In November 2015, the European Food Safety Authority (EFSA, Parma, Italy), a WHO institution, published [44] an article entitled "*Conclusion on the peer review of the pesticide*" in the technical journal of the same agency, on the risk assessment of the glyphosate. The conclusion was that it was "improbable" that the pesticide was genotoxic or carcinogenic to humans. The research undertaken by the EFSA was carried out by following a procedure that included a technical assessment by an institution of a member state, in this case the German Federal Institute for Risk Assessment (BfR), which after conducting six different studies, pronounced the non-carcinogenicity of glyphosate. The final evaluation of EFSA was based largely on the studies conducted by the BfR.

Also in the same period, the European Food Safety Authority [45] proposed new toxicological safety thresholds in order to improve the control of glyphosate residues in food:

- Increasing the ADI (Acceptable Daily Intake) or DGA, that is the daily human consumption limit, from 0.03 mg/kg to 0.05 mg/kg, in line with the acute reference dose (ARD), always fixed at 0.05 mg/kg body weight.
- The admissible exposure level of the operator (Laeo) was fixed at 0.01 mg/kg of body weight per day.

In May 2016, a joint meeting of experts from the World Health Organization and FAO (Food and Agriculture Organization of the United Nations) on pesticide residues in the environment and food, concluded that "*glyphosate is unlikely to lead to carcinogenic risk for humans as a consequence of exposure through the diet*" [46].

5. Scientific Debate

The discord of opinions on the subject concerning the dangerousness of glyphosate is evident and for this reason each institution, technical journal or scientific magazine express and still declare their own opinion. A review of the scientific articles, evaluation methods and conclusions drawn from the technical literature is presented below.

The scientific journal, Test-Salvagente, published in May 2016 [36,37], initially maintains that the study conducted by the EFSA appears to have a low level of independence. In fact, some scholars have shown the direct involvement of some pesticide-producing companies that, under the name of the Glyphosate task force, have conducted studies and defined their own conclusions.

It also highlights the doubt about the change of decision by the WHO and the FAO with respect to what the IARC had communicated, in addition to the WHO-based agency. It is clear that there are no clear reasons for this decision, as the long work of the IARC, which lasted exactly two years, was the only and last study on which the assessments that took place in May 2016 were based.

However, scientists and FAO-WHO experts argue that there has never been evidence of a direct association between glyphosate ingestion and cancer at any level of exposure. In particular, they declare that an exposure up to 2000 mg/kg body weight has not been associated with some genotoxic effects in most of the cases conducted on mammals. Therefore it does not become necessary to establish a dose for glyphosate and its metabolites that may give rise to diseases.

The article in Test-Salvagente focuses on the great conflict of interests that lies behind the WHO and its declaration of the non-carcinogenicity of glyphosate. Thanks to a complaint made by Greenpeace, the relationship between the WHO and ILSI (International Life Sciences Institute, Washington, DC, USA) became evident. ILSI is currently considered one of the largest agribusiness lobbies in the world and funded mainly by private companies, including Monsanto and Dow, who both produce glyphosate. It was discovered that some members of the ILSI, who were also a part of the EFSA, had to resign because they had not declared a financial interest in the assessment of chemicals. In 2006, for this reason, the WHO prevented the ILSI from intervening and taking part in an assessment of microbiological and chemical standards for food and water. In Europe, the practice with which the experts and technicians pass from the controlled companies to the controllers and then return to the former is very widespread and obviously leaves important doubts on the ability to assess these institutions.

The WHO decision was questioned, again by Greenpeace, who claimed that the experts who took care of the study were only pronouncing effects related to diet, such as taking glyphosate by ingestion, without making any reference to the combined effects of diet, exposure through environmental contamination, and the effect of the compound on the fauna.

The Ramazzini Institute (RI) or National Institute for the Study and Control of Tumors and Environmental Diseases, addresses the issue of pesticides and has expressed its opinion regarding the dangers of glyphosate [47,48]. The RI clearly shows its concerns about the EFSA report, especially regarding the way in which the conclusions were drawn. In fact, according to the Institute, there are no accurate scientific exams in the evaluation of the data currently available and the final verdict is devoid of plausible motivations in its favor. Contrary to what was reported by the IARC, EFSA's statements lack the necessary investigations and scientific literature to be able to express such a large consideration, going further to disprove, after only a few months, another international organization.

According to the Ramazzini Institute, in order to reach their conclusion EFSA may have refused to consider human studies, which were instead taken by the IARC and considered by the Lyon Agency to comply with the standards of quality and methodological soundness required for this type of study. Moreover, the investigations carried out on the animals and on the toxicological effects of glyphosate are excluded from the ESFA assessment, as they are considered to be of an academic nature and not in line with the methodologies adopted in the studies of the industries. This decision was widely criticized by the Institute, which considers some studies that have not been considered very valid.

Because of their unwillingness to consider that the EFSA had discarded the evaluation of these researches a priori, the Institute affirmed the inability of the experts to examine in an objective way the available scientific literature. This is also a result of the conflict of interests of the involved experts, some of whom are also consultants of the herbicide-producing industries. A poor evaluation based on the toxicity of the active substance and not of the commercial form itself occurred, which neglected the role of the adjuvants that allow for a faster and simpler penetration of the active substance into the cells.

The Ramazzini Institute has started a study in recent years together with other international partners in order to establish the most suitable experimental plan for assessing the effects of the substance on human health. Independent research has been requested not only by the IARC but also by the EFSA and the industry, so that a certain and safe classification can be reached in the shortest possible time and appropriate precautions can therefore be taken.

Another opinion regarding the conclusion reached by the IARC and the ESFA is expressed by the International Society of Doctors for the Environment (ISDE), who consider it paradoxical that the two agencies can arrive at opposite evaluations [49]. It also accuses the EFSA's panelists who wrote the document of putting forth a work that is essentially empty and does not contain any mention of new and specific scientific studies nor new evidence, especially when compared to what was included in the IARC monographs. Finally, the non-genotoxicity of glyphosate declared by the EFSA cannot be considered a valid reason because there are several carcinogenic substances that have never been shown to be genotoxic.

Glyphosate was indicted by a new scientific study [50], which highlighted the correlation between the use of the substance and the onset of non-alcoholic fatty liver disease through studies carried out in the laboratory. It would therefore be fundamental, in subsequent studies, to understand if the herbicide is also capable of damaging the human liver. In fact, according to research on the prolonged consumption over time, even in minimum doses, glyphosate can cause significant damage to the liver, including non-alcoholic steatosis and even necrosis. For this reason, more control is required from the competent authorities and more restrictions on the use of toxic substances are required.

Reuters [51] reports a statement about the USDA (United States Department of Agriculture, Washington, DC, USA) and the failure to execute accurate glyphosate testing. A spokesman for the department says that the methods for testing the substance are very expensive and time-consuming and for this reason they opt to not carry out the tests directly. Moreover, in other studies, the effect that the herbicide would have on human health is declared to interfere with many metabolic processes and cause a series of serious diseases, such as hypertension, diabetes, obesity, senile dementia, inflammatory disease, renal failure, thyroid and liver cancer, etc.

An above mentioned work [20], highlights the relationship between glyphosate and the development of chronic disease. The researcher assumes that intestinal bacteria are the fundamental component to understand the severity of glyphosate damage. Monsanto, considering that the molecule in question inhibits the EPSPS enzyme, has always supported the safety of the molecule for humans and animals. However, this is not entirely correct, since the enzyme is also contained in some bacteria and especially in intestinal bacteria within the human body. The glyphosate is therefore able to destroy the microorganisms present in the human digestive system and the intestinal villi, inhibiting the ability to absorb vitamins, minerals, and even some proteins. Furthermore, the exposure to the molecule is always greater and the main cause is an increase of the dried cultures, such as cultures in which the herbicide is used before the harvest to increase the release of seeds. This practice is exploited above all in fields where wheat is cultivated, but also for the cultivation of barley, beans, peas, peanuts, brown sugar, oats, lentils, flax, etc. On these products the glyphosate contamination grows and, together with the grain, there are diseases associated with it, such as celiac disease. A specific evaluation, provided by the USDA, CDC (Centers for Disease Control and Prevention, Atlanta, GA, USA), and NASS (National Agricultural Statistics Services, Washington, DC, USA) shows the relationship between the diagnosis of celiac disease and glyphosate applications to wheat in the United States [20].

The research also demonstrated [20] the correlation between exposure to the herbicide Roundup and autism. In 1975, 1 child out of 5000 developed the disease, in 1985, it became 1 in 2500, in 1995 1 in 500, in 2005 1 in 166, and today it is 1 in about 68 children. With this growth rate it is estimated that in 2025 there will be one in three children affected by autism. The causes for the increase of this disease are to be found in various fields, but Samsel and Seneff [20] argue that one of the most relevant causes of the increase is the use of pesticides. Knowing the effect that glyphosate can have in the human body, particularly in the gastrointestinal tract, and comparing it with the autism bio-markers, such as the alteration of intestinal bacteria, intestinal inflammation, lack of serotonin and melatonin, disorders to the mitochondria and iron and zinc deficiencies, the correlation between the two factors is evident.

Related to the above research, studies conducted by the University of California, Davis [52] highlight that the risk of having autistic children increases in mothers who have come into contact with or have been exposed to chemicals during pregnancy. In fact, two out of three autistic children are born from women whose residence is near a field. This data obviously applies to California, where the survey took place. Despite the growing concerns of the various scientific bodies after the results of research and studies conducted were published, the EPA, in 2013, increased the permissible levels of glyphosate in food, at values 15–20 times higher than previous levels [52].

In Denmark [53], Monsanto was indicted by scientists at Aarhus University after studies showed that Roundup could have an effect on mammalian gastrointestinal health. In particular, they found that glyphosate, when sprayed on genetically modified soybean feeds, came into direct contact with livestock through diet and compromised their health. In particular, they found that the pesticide destroyed the bacteria of the gastrointestinal tract that acted as guarantors of the natural balance of the intestine of the animals. This is also shown in studies [20,21,53], which consider cattle infections and show their dramatic increase over the past decade. The cause is due to the fact that the debilitated gastrointestinal tract in animals favors the onset of infectious diseases. Other research [21,27] has shown how the Roundup herbicide and, more precisely, glyphosate, can cause damage to human health. Only a small part of glyphosate ingested through contaminated food is metabolized to AMPA (2%), while the rest enters the bloodstream and is finally eliminated through the urine. The product was originally marketed as absolutely non-toxic for humans, as acting on the shikimate path present only in plants did not go on to affect our body. However, what has not been considered is the presence of this path in the bacteria in our intestine, which help digestion, synthesize vitamins, detoxify harmful chemicals, improve intestinal permeability and increase the defenses of the immune system. Furthermore, the active substance contained in Roundup, by inhibiting the cytochrome P450 enzymes, also called CYP enzymes, in humans, further compromises the natural detoxification capacity of unhealthy chemicals coming from outside (drugs or environmental). In this way, harmful molecules of animal origin are allowed to remain permanently in the human body, depleting it with minerals and thus lowering its immune defenses. Inflammatory bowel diseases, such as juvenile onset Crohn's disease, have become more widespread in the last ten years, and it is reasonable to suppose that it is also the fault of glyphosate and its increasingly widespread use in agriculture [20].

Following the conclusions drawn by the IARC that classified glyphosate as "probably carcinogenic" for man, Monsanto decided to commission Intertek Scientific & Consultancy Regulatory to conduct critical and detailed research into the herbicide and to its dangerousness. A total of 15 experts were assembled, divided into four groups based on their skills, their scientific publications, and their relevance to the studies to be performed. They were tasked with examining four basic points: exposure to the molecule, its carcinogenicity, genotoxicity, and epidemiological studies in the scientific literature concerning the herbicide.

Two meetings were held, dated August 2015 at the Intertek facility in Mississauga, Canada. During the first meeting the group of experts discussed and examined data on human epidemiological studies and research on glyphosate exposure, while in the next meeting the remaining two subjects of the survey were addressed. It was decided that they would author four separate specialized papers on the methodologies adopted, the results, and the final decisions [54–57]:

1. Exposure to glyphosate: the evidence regarding the amount of glyphosate to which workers or citizens are exposed every day implies the use of much higher doses than the real quantities that are dispersed in the environment. The results obtained showed that the exposure to glyphosate levels was much lower than any legal limit (RfD) and in any case did not constitute any danger to human health.
2. Carcinogenicity to animals: animal studies, in particular mice and rats, have provided sufficient evidence to the experts to state that there is no correlation between certain diseases developed in rats and their exposure to glyphosate. This is defined on the basis of the lack of statistical reports, of consistency between the data obtained, of specificity and of do-and-response models. Glyphosate is therefore not carcinogenic to laboratory animals.
3. Genotoxicity: glyphosate, being a chemical substance widely used by man, has been subjected to various genotoxicity tests to assess whether or not it could damage human DNA. In the studies

carried out by the panel of experts, it is highlighted how some test results can be "false" positive or "misleading" results, causing an incorrect conclusion. In fact, a positive result can also be obtained from carcinogens that, for this characteristic, are also considered genotoxic, or from extreme treatments during the various phases of the tests that alter the DNA response, or also from human errors during the carrying out of an analysis or final evaluation. A "*weight of evidence*" (WoE) is then used by the expert group. This method includes an assessment of the weights related to the different available information, considering the strengths and weaknesses for each. In order to define this approach the relevance, reliability and adequacy of every available data must be analyzed. In particular:

(a) analyses that report mutations or chromosomal damage have greater weight than analyses that report DNA damage. Each type of test has a different weight;
(b) the quality of the tests, their reproducibility and the rigidity with which they were performed involves different weights;
(c) the number of tests in an analysis also changes the weight that will be attributed to the analysis itself;
(d) analyses with more evidence for humans will have greater weight than in vitro or analyses conducted in animals other than mammals.

The panel of experts, once all the data were analyzed using the methods described above, concluded that glyphosate did not represent any genotoxic risk or oxidative stress for humans, thus disproving also in this case the conclusions reached by the IARC.

4. Epidemiological studies: epidemiological studies indicated a close correlation between glyphosate use and the onset of two serious pathologies: non-Hodgink's lymphoma and multiple myeloma. The scientists carried out a purely qualitative work, based only on scientific evidence and data published up to that time, with the conditions that they had broad and proclaimed scientific validity and that they were recognized by scientific institutions. It was also specified that, in the case of conflicting articles or opinions, only the one published more recently was considered. This evaluation method, adopted by the group of experts, is based on the so-called PRISMA guidelines, which is a type of approach to perform systematic reviews of research or studies already published. The conclusions were, as in the other cases, in disagreement with what was published by the IARC. In fact, glyphosate was not considered responsible for the onset of multiple myeloma or non-Hodgink's lymphoma.

In addition to the study just reported, the panel of experts was given the task of carrying out a critical evaluation of the conclusions drawn from the IARC and the methodologies adopted in its research. In this regard, the experts clarified the fundamental differences between the evaluation methods adopted by the IARC and those they would use in the course of the research [9,10,54,55]. The Lyon Agency, according to the panel of scientists, did not take into account some important studies and this also led to a completely different approach to evaluating available data. Furthermore, the experts argued that, by analyzing the data available until before the publication of the IARC, there was no such document that would allow the Agency to change the conclusions on the carcinogenicity of the glyphosate disclosed up to that time. The conclusions of the research clearly stated that glyphosate did not pose any risk to humans [54,55].

Monsanto also published the data obtained by itself during the investigations on the product during its use in the fields and showed that the levels of glyphosate detected in the air, in water and in food were much lower (several orders of magnitude) to the limits tolerated by law [56–58]. The company stated that, from the results obtained, it was evident that, despite the worst conditions of exposure, there was no risk associated with exposure through the normal use of the product in agriculture or to manage weeds along roadsides or in domestic and industrial areas [54–57].

In 2004, two studies related to the monitoring of the concentration of glyphosate present in the urine of some families of farmers after coming into contact with the herbicide, were published [59,60]. The families that were part of the research were initially chosen based on the list of farmers authorized to use the pesticide in South Carolina and Minnesota and focusing on some aspects, among them:

(1) the farmer and family, including children (aged between 4 and 18 years old) lived in a farm;
(2) the cultivated fields had to have an extension of 10 acres and had to be located within 1 mile of the family residence;
(3) all family members had to be willing to collect samples of their urine for five consecutive days (the day before, the same day and three consecutive days for the application of the herbicide);
(4) the farmer and his wife had to be willing to complete pre and post-research questionnaires and had to allow authorized personnel to support them during the glyphosate application phases in the field.

Families who accepted these conditions and were chosen to participate in the project, financed by the University of Minnesota, also receiving a sum of money. Finally, there were 48 approved farmers' families, with 79 children in total. The participants were given the task of collecting urine samples in 500 mL containers. The results of the analyses showed that 60% of the farmers contained detectable traces of glyphosate in the urine on the day of the application of the herbicide, and the average concentration found was 3 ppb, while the maximum value was 233 ppb. A higher level of glyphosate was observed in the farmers who, during the use and handling of the product, had not worn the appropriate rubber gloves. 4% of the wives showed detectable levels of glyphosate in their urine, always on the day of application, with a maximum value of 3 ppb of substance, while 12% of the children, always in the same conditions and on the same day, had detectable values of glyphosate in their urine, with a maximum concentration of 29 ppb. The scientists who carried out the study concluded that the levels of glyphosate found in the farmers and their families did not reach or exceed the reference doses that could be tolerated by law, but they nonetheless recommended minimizing exposure to the pesticides [59,60].

Another study was conducted selecting 15 participants, who had the task, as in the previous study, to collect urine samples for five consecutive days (the day before, the same day and three days after the application of the product) in order to detect the presence of glyphosate. The results showed that 4 of the 15 subjects had detectable levels of glyphosate in their urine, with a maximum value of 14 ppb. Also in this case, the conclusions could affirm that these levels were not above the limits fixed by law [58].

However, it is necessary to take into account that these studies are not based on applications with different methods or prolonged exposures, but are limited to only one week of exposure to the product. Also, the presence of external personnel could cause changes to the normal agricultural practices adopted by the workers, thereby also modifying the results of the analyses.

6. Alternative Solutions to Glyphosate

Clearly, a critical review of a herbicide such as glyphosate is not easy, even considering the considerable differences that the behavior of the herbicide presents in different geographical, environmental and climatic contexts. Since glyphosate is used all over the world, it ranges from applications in very hot or tropical climates to very cold and icy areas. Therefore, the outcomes can not be generalized. Also, the analysis of the alternatives cannot be exhaustive. Alternative agronomic techniques are more easily applied in limited agricultural settings and not in extremely large spaces (both due to technical difficulties and costs). It will take many years to obtain effective measures in large fields. However, it is good to make a critical analysis and try to make strategic choices with the aim of preserving human health [61].

The high consumption of glyphosate is related to the rather low cost of the product compared to other herbicides on the market and its high efficacy against any type of plant. However, due to concerns about the dangerousness of the substance, it is appropriate to consider the various alternatives that exist for its use.

However, we should not think about replacing glyphosate with a new, less harmful synthetic molecule, we must to change the type of agriculture and introduce new agricultural techniques to better manage unwanted herbs.

The various solutions that can be used for domestic use or for road maintenance are natural methods of weed control, such as:

- Preventive measures: regularly clean the garden and avoid the accumulation of fine materials, delimit the areas where there is more weeds by removing the material and dirt that remain in the vegetation and cover the empty cracks or microspaces in which the fine material could potentially accumulate.
- Soil processing in order to eliminate weeds and prevent their re-growth: this practice can be carried out through weeding, that is the removal of weeds by working the soil and cutting the green surfaces.
- Soil coverage: the ground is covered with sheets, barks, or straw in order to prevent it from being reached by light, a fundamental component for the growth of plants.
- Use of natural substances such as cooking salt, diluted vinegar (around 10%) and products based on herbal extracts.

The most common alternatives in the agricultural field are pyroherbicide, biological agriculture, biodynamic agriculture, mulches (covering the soil with biodegradable plastic sheets or with dry leaves, barks and sticks in order to protect the crops from exposure to the sun and thus avoid the growth of weeds. This practice is widely used in the fruit and vegetable sector), soil processing (the only valid alternative, to date, for herbaceous crops), and high volume water (physical action is used against the seeds of the lower plants). Some of these alternatives to glyphosate inevitably lead to a cost increase. Here below, we provide a short description of pyroherbicide (PH), biological agriculture (BA), biodynamic agriculture (BDA), which are the most interesting practical applications.

6.1. Pyroherbicide

PH is defined as the technique that uses fire to obtain direct physical control over the elimination of weeds, fungal diseases, and insects. The first patented PH apparatus was used in the US in 1852 [62]. Initially, the burners contained oil or gasoline, thus resulting in high operating costs. During the '40s and '50s, large quantities of liquefied petroleum gas (LPG) began to be available on the market at very low costs, causing a rapid spread of PH and its related equipment. The practice is based on the production of heat, dry or wet, by electromagnetic waves, electricity, water vapor or thermal energy (free flame). To date, the use of a direct flame is certainly the most widespread among the various methods. The principle on which the practice is based on is connected to thermal shock. The application time is as such that it does not involve the carbonization of the vegetables but only a rapid increase in temperature. This causes the rapid expansion of the cell plasma and the consequent destruction of the outer membrane within the plant. In this way the protein coagulation cycle, the ionic and gaseous exchange control systems and the nutritive mechanisms of the plant tissues are modified. The plant will no longer be able to feed itself and for this reason it dies within 1–3 days, depending also on the climatic conditions, the type of plant, and its growth phase once it has undergone treatment [62].

The PH does not burn the weeds directly, but acts in plant cells through high temperatures. It is therefore necessary to know the time interval and the temperatures to be used in order to achieve maximum effectiveness. In this regard, in the juvenile stage (20–25 days from the emergency) it is possible to work with temperatures of 90–95 °C for a time of 0.1 s, while in plants in advanced stages, it is used at temperatures of 110–120 °C for 1 s. Immediately after the treatment, the plant assumes the typical green color, then changes after a few days to the yellow, classic coloring of dried plants.

The PH equipment can be manually operated, therefore it is rather simple, or more complex when combined with mechanically operated parts. The simplest tools, used for small areas, are not cumbersome and easy to use. The mechanical equipment consists instead of ventilation openings that allow a better control of the flame and an electronic control unit equipped with a magnetic connection for controlling the burners [62].

Regarding the environmental impact, PH is not considered dangerous, as the burning of LPG releases only carbon dioxide and water vapor. Moreover, the flame, being transparent, does not involve the release of fumes or an alteration of the color of the surfaces on which it is used. As for the direct impact on the soil and on the microfauna present in it, the temperatures reached during the treatment are around 50–60 °C, temperatures that are easily reached even naturally during the hot season. If the treatment is carried out in a longer time than established, the temperatures could reach 70–80 °C, leading to a sterilization action of the soil with the elimination of pathogenic microorganisms [62].

PH is more effective for annual broad-leaved plants than for grasses. It is also applied more in specific crops, such as maize and horticulture, in tree crops, and also in non-agricultural areas (parks and public places, roads) [62].

6.2. Biological Agriculture

BA is a method of cultivation and breeding based only on the use of natural substances already present in nature, completely excluding synthetic chemicals. The main characteristic that distinguishes BA from conventional practices is the energy resource from which it draws. The organic substance contained in the ground is mainly exploited as a source of energy, thus creating an agricultural system at low cost and with a low environmental impact, and one that does not introduce any type of external human energy (mechanical, thermal, chemical, extractive, etc.). The organic substance used consists mainly of manure or fertilizers, such as compost or a mixture of earth, plant remains, wood and all that is bio-degradable and non-polluting [63–65].

BA has the task of protecting biodiversity, protecting the natural fertility of the land, as well as the desire to eliminate all sorts of pollution from agriculture and to produce foods with high nutritional quality. In order to achieve these objectives, very specific rules are followed, namely [66]:

- organic crops are rotated, alternating crops that improve soil fertility and others that impoverish it, thus ensuring a more efficient use of resources;
- the use of pesticides, herbicides, synthetic chemicals, and genetically modified organisms is prohibited;
- specially resistant, disease-resistant and environmentally friendly plants are preferred for cultivations;
- the farms are organized in a closed cycle, so that the farms supply the agricultural fertilizers and the agriculture supplies the food for the animals;
- mulching is practiced, that is the covering of the ground that aims to protect crops from excessive heat and to avoid the growth of weeds;
- green manure is used, that is the sowing of some plants, such as clover, spinach, etc., which once flowered and buried improve the fertility of the soil and avoid the phenomenon of erosion.

To date, in spite of the numerous advantages of organic farming and the absence of an environmental impact deriving from its use, criticisms are still numerous and mainly aim to disprove the concept that organic products are necessarily good and uncontaminated products. The disadvantage of organic farming consists in having yields lower than those of conventional agriculture, thus causing an increase in cultivated land to compensate for losses and to produce the same quantities of product. Moreover, it has been observed that often the effectiveness of biological production is linked to the use of fertilizers that derive from conventional production, making the two practices closely linked and dependent on each other in terms of sustainability.

Regarding organic products, some independent studies have stated that it is not univocally determined that organic food and healthy food is free of traces of pesticides, for this reason they are widely criticized for funding this sector [66].

6.3. Biodynamic Agriculture

Biodynamic agriculture is a method of agricultural cultivation based on the knowledge of Rudolf Steiner, who in 1924 held lessons in which the fertility of the soil was related to the cosmic and spiritual forces present in the world. This practice has as its objectives the protection of biodiversity and the environment, the production of foods with a high nutritional quality, and the activation of life on the ground. In fact, BDA is today a registered trademark of the German company Demeter International, which allows its use exclusively on the products obtained following the guidelines of Rudolf Steiner [67]. This knowledge is, in part, without scientific basis and at the practical level consists of the application of organic agriculture added to "esoteric" practices that take into account the phases of the lunar cycle, some concepts of astronomy, of the position of the planets, and the zodiac. Basically, the bases on which biodynamic agriculture is based are the use of "magic" rites that involve the burial of parts of animals in the ground according to a specific calendar (following the phases of the moon and the positions of the stars and planets), the use of compost, or a mixture of earth, plant and animal remains, food waste, and water to keep the fertile land and plants healthy, and the absolute prohibition of products that are not completely natural. The disadvantage of BDA is that some of its methods, not having scientific validity, are not recognized as actually competitive with traditional agriculture and often, as an alternative, organic farming is preferred, being instead a more established practical practice.

7. Conclusions

Despite numerous studies regarding the dangers resulting from the extensive use of glyphosate, it is not possible to attribute a clear and unambiguous definition to glyphosate, especially regarding its potentially harmful effects on humans. Resuming and analyzing each treated subject, it is concluded that the massive use of glyphosate, given its chemical-physical properties and its presence in many commercial products, even in the form of more toxic mixtures than the single molecule, should be reduced. This could be achieved by implementing resources and funding dedicated to alternative solutions to the herbicide. However, diffusion is unfortunately not yet advanced due to the huge economic interest in the market for herbicides.

It is also evident that new studies and independent research must be performed in order to clearly define the seriousness of glyphosate exposure to carcinogenicity and genotoxicity. In fact, there is a too great a discrepancy between the opinions of the various scientific institutions, mainly because of their different economic and social interests. The controversy and the debate are expected to continue. Recently, the European Union Appeals Committee, made up of representatives of all the member states, approved a further five years authorization for the use of glyphosate (December 2017). The decision was marked by debate and there was a split in the vote within the Commission (for example, Italy and France not favorable, Germany favorable).

It is certain, however, that the population and the environment must be better protected, especially through the endorsement of new rules and limitations regarding the chemical in question. It is the duty of the institutions to place the "precautionary principle" before economic interests, namely the protection of citizens and the environment from exposure to a substance whose side effects are not yet known.

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