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Review

Critical review: regulatory differences among countries expose the permissiveness in the use of hazardous pesticides in Brazil

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Abstract

This critical review warns of differences in pesticide registration and approval among major agricultural nations and classifications based solely on acute toxicity, which masks the risk of exposure to unapproved hazardous pesticides. It presents (a) the approval status of active pesticide ingredients (AI) in Brazil (BR) compared to other agricultural nations (e.g. European Union, USA and China); (b) the toxicological reclassification scenario of commercial pesticides in BR, and (c) the toxicological category of commercial pesticides in BR, with AI not approved for use in the three analyzed nations. A list of approved and not approved AI for use in Brazilian agriculture was compiled from the ANVISA website, and a comparison of the approval status among the agricultural countries was performed. Additionally, the number of commercial pesticides in classes/categories was compared before and after the toxicological reclassification from the ANVISA toxicological reclassification list. Among AI approved in BR, approximately 46.6% are "not approved" for use in at least one analysed nation. In addition, 43 pesticides (22,6%) were identified as approved in BR and not approved for use in two of the three nations. It is also noteworthy that nine pesticides (4,7%) are not approved for use in any of the three nations compared. Category 5, currently incorporated (product unlikely to cause acute harm), is the one that most absorbed products previously classified in Classes I (extremely toxic), II (highly toxic), and III (moderately toxic) (46.9%). Most formulations containing not approved active ingredients are classified in Categories 4 (slightly toxic) and 5 in BR. The negative effects that agrochemicals bring to the nation, such as on human health, or in wildlife, polluting water sources, and promoting a global problem by producing contaminated food, do not outweigh the economic benefits obtained by agribusiness.

Keywords: Acute toxicity; agricultural nations; approval status; hazardous pesticides; toxicological reclassification.

THE APPROVAL STATUS OF PESTICIDE ACTIVE INGREDIENTS IN BRAZIL AND DISCREPANCY WITH OTHER AGRICULTURAL NATIONS

Brazil is the fifth largest country in the world by territory and has the sixth largest population in the world. It stands out as one of the largest agricultural producers in the world (Donley, 2019). The introduction of pesticides was a significant milestone in the modernization of this sector in Brazil. The 1960s and 1970s saw the large-scale use of pesticide formulations, the main form of management in monocultures used to this day. Because the Brazilian economy is based on agriculture and livestock, these economic activities are considered important to maintain a positive balance in the economy. However, despite high production rates, it is estimated that hunger continues to grow, as 59% of Brazilian families are in a situation of food insecurity (Brito & Baptista, 2021; Galindo et al., 2021; Da Silva et al., 2020).

In the maintenance of monoculture crops, chemical inputs such as fertilizers and pesticides are intensively used, in addition to transgenic seeds (Pignati et al., 2017). There is currently a concern about the excessive

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use of hazardous pesticides in Brazil, as well as the alarming release of new active ingredients and new formulations of ingredients that have already been approved for use. Furthermore, the excessive use of dangerous pesticides associated with acute poisoning, as well as chronic exposure, are environmental risk factors that may be implicated in the cause of different diseases such as Alzheimer's, Parkinson's disease, cancer, diabetes, kidney or respiratory diseases and congenital malformations (Han et al., 2019; Loomis et al., 2015; Mostafalou & Abdollahi, 2013; Sekhotha et al., 2016; Tang, 2020).

In global terms, the European Union (EU), the United States of America (USA), and China (CHN) join Brazil (BR) as the group of the four largest producers and users of agricultural products in the world. Each of these nations, or blocs of nations, has its regulatory system for the use of pesticides to protect human health and the environment. In the EU, the European Commission supervises and decides on the approval, restriction, and cancellation of pesticides based on the report on the active ingredient prepared by the European Food Safety Authority (EFSA). These Directives can them become even more restrictive in each country but never more less than the established in the Directives. EFSA ensures that the industry demonstrates that substances or products produced or placed on the market have no detrimental effect on human or animal health or any unacceptable environmental effects (European Parliament, 2005; 2009). In the USA, the regulation and inspection of pesticides are supervised by the United States Environmental Protection Agency (US EPA), under the Federal Food, Drug and Cosmetic Act (FFDCA), and the Federal Insecticide Act, Fungicides and Rodenticides (FIFRA), (US EPA, 1996; 2002). In China, the responsibility to assess safety, and establish the requirements for registration, licensing, and marketing, in addition to establishing the prohibition or elimination of highly toxic pesticides, is carried out by the Institute for the Control of Agrochemicals (ICAMA), which directly subordinate to the Chinese Ministry of Agriculture, through the Pesticide Management Law (CHINA, 1997). In BR, the Federal Pesticides Law (Law No. 7,802, 1989) and Decree No. 4,074 of 2002 (BRASIL, 1989; 2002) regulate the tripartite authority for the evaluation, inspection, and registration of pesticides, which is exercised by: The Ministry of Health, which assesses the level of toxicity to human health through the Brazilian Health Regulatory Agency (ANVISA); The Ministry of the Environment, which carries out the ecotoxicological assessment through the Brazilian Institute of the Environment and Renewable Natural Resources (IBAMA); and the Ministry of Agriculture, Livestock and Supply (MAPA), which assesses agronomic effectiveness (BRASIL, 1989).

The tripartite evaluation carried out by the three agencies of the Federal Government of BR seeks to ensure that no individual interest prevails since each agency performs analysis according to its respective area (Folgado, 2016). However, bill of law PL 6.299/2002, known as the "Poison Bill" or "Poison Package" (Bassani et al., 2018; Braga et al., 2020; Porto, 2018), was approved by the parliament. Among the highlights of this bill of law is the exclusion of tripartite authority by transferring the power to decide on the approval of a pesticide to MAPA alone. Thus, the need for safety evaluations for human health and the environment by ANVISA and IBAMA, respectively, will no longer be necessary for registration approval, which facilitates the release and consumption of pesticides in the country (Fernandes et al., 2022). Now, if it gets approved in the senate, the bill of law 6.299/2002 will replace the current legislation (Law 7.802), which was an important milestone for public health and environmentalism and has been in force since 1989 in Brazil.

The objectives of the regulations are to ensure the protection of human, animal, and environmental health, maintain high levels of agricultural yield and facilitate international trade, which in turn requires greater control of pesticide residues in food. Comparing the ability of different regulatory agencies to ban or eliminate pesticides that have the greatest potential to cause harm to humans and the environment can provide a glimpse of each country's regulatory laws and supervision of pesticides.

Therefore, this review presents (a) the approval status of pesticides' active ingredient in BR compared to the other major agricultural producers in the world; (b) the scenario of toxicological reclassification of commercial pesticides in BR, and (c) the toxicological category of commercial pesticides in BR, with active ingredients not approved for use in the EU, USA and/or CHN. We believe that information on such compounds should be easily obtained and transparent, especially for the consumer population of products from agribusiness, as well as for agricultural workers and rural communities exposed to such compounds.

Pesticide active ingredients approval status

Approval status of pesticides' active ingredient is standardized according to international criteria and can be used to identify the effectiveness of each country's regulatory laws to ensure the protection of health and the environment. Although it follows international criteria, a comparison of pesticide approval status among the four largest producers and users of agricultural products in the world exposes significant differences between these countries regulations.

In order to perform a critical review of pesticides used in Brazilian agriculture, a search of the ANVISA website was performed (https://www.gov.br/agricultura/pt-br/assuntos/insumos-agropecuarios/insumos-agricolas/agrotoxicos). A list of pesticides that have been used in agriculture was compiled from the active ingredients listed by ANVISA as approved and not approved for use in BR. Afterwards, a comparison of the approval status was performed among BR, EU, USA and CHN (Figure 1). From this survey, A survey of active ingredients approved for use in BR and not approved by EU, USA and/or CHN regulatory agencies was listed

(Supplementary material 1).

The approval status of each pesticide was verified on the following pesticide regulatory agencies' websites: Brazilian Health Regulatory Agency (ANVISA, 2020a, 2020b); European Commission (EC, 2022); United States Environmental Protection Agency (US EPA, 2022) and China Pesticide Information Network, Institute Control of Agrochemicals, Ministry of Agriculture (ICAMA, 2022). The statuses were considered as "approved","not approved", or when the information was not available in the databases as "not found". For this study, an active ingredient was considered "not approved" when (i) the decision was taken by the regulatory agency to prohibit such active ingredient from entering the market, (ii) its approval was cancelled, (iii) it was never approved for use; (iv) when a pesticide registrant voluntarily withdrew its registration application for the active ingredient or requested deregistration; (v) when the registration expired and renewal was not requested, or (vi) when the registration has expired, and the renewal has not been approved.

Currently, there are 509 active ingredients approved for use in BR among active ingredients of pesticides (408 products - herbicides, insecticides, fungicides, acaricide, nematicide, rodenticide, molluscicide and growth regulator), biological products for pest control (59 products) and hormones synthetic (42 products) evaluated by the inspection agencies ANVISA and IBAMA regarding their harmful effects on human or animal health or any unacceptable effects on the environment. Among the 408 active ingredients of pesticides approved in BR, 190 products (approximately 46.6%) are not approved for use in the EU, USA and/or CHN. Among these, 43 pesticides (22,6%) were identified as approved in BR and not approved for use in two of the three nations. It is also noteworthy that nine pesticides (4,7%) are not approved for use in any of the three compared countries, namely: allethrin, asulam, azimsulfuron, cadusafos, fenamiphos, fenarimol, pencycuron, sulfluramid and tepraloxydim (Supplementary material 1).

When comparing the approval status of all pesticides registered at ANVISA, both approved and not approved for use in BR, with the status of the EU, USA and CHN, it was found that the EU has a lower number of pesticides approved for use (32%), with BR having the highest number (72%), followed by CHN (60%) and USA (60%). Regarding pesticides not approved for use, the EU stands out with the greatest restriction on the use of these products (59%) and CHN with the lower restriction (9%). It is also interesting to note that concerning approval status not found, the CHN has the highest percentage (31%), followed by the US (16%). In Figure 1, the list of pesticides on ANVISA's website was used for comparison. For this reason, BR did not have the status not found (Fig 1).

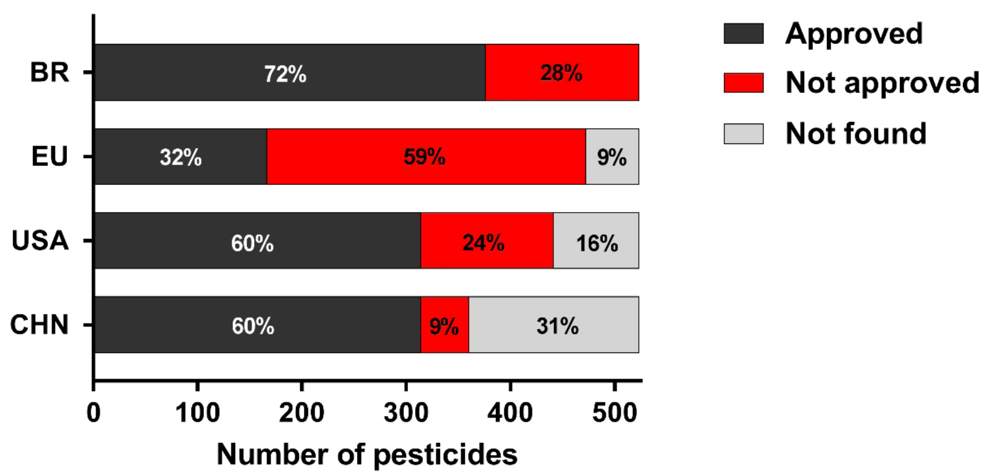

Figure 1 Comparison of the approval status of all pesticides registered at ANVISA, approved and not approved for use in Brazil (BR), with the status of the European Union (EU), United States of America (USA) and China (CHN). When the status was not found in the databases was considered "not found".

Most commercial pesticides have been reclassified into less hazardous categories in Brazil

The current regulatory framework for pesticides published by the ANVISA, Resolution - RE nº 2080/2019 (ANVISA, 2019), established the toxicological reclassification of commercial products already on the BR market. Taking as a reference the toxicological reclassification list obtained on the ANVISA website (https://www.gov.br/anvisa), a survey was carried out to (i) classify the total number of commercial pesticides in the classes/categories before and after the toxicological reclassification; and (ii) show the distribution of each pesticide for each current category. Pesticide products were previously classified into: Classes I - Extremely toxic; Class II - Highly toxic; Class III - Moderately toxic; and Class IV – Slightly toxic. Now, the categories of the current toxicological classification were expanded from four to five: Category 1 - Extremely toxic; Category 2 - Highly toxic; Category 3 - Moderately toxic; Category 4 - Slightly toxic; and Category 5 - Product unlikely to cause acute harm. In addition to these five categories, some products are now indicated as Not classified product and Not informed by the company totalizing seven categories. The data was presented as a percentage of the total number of commercial pesticides in each class and category before and after toxicological reclassification, and the distribution percentages of commercial pesticides for each previous class, in the current categories.

The toxicological reclassification list presents 1,942 commercial pesticides with respective previous and current toxicological classifications for each product. Among these commercial pesticides, 1,919 were previously registered in Classes I to IV, with the remaining 23 pesticides not included in this classification, listed as not informed by the company (6 pesticides); registrant's process was not found (2 pesticides) and not determined due to the nature of the product (15 pesticides). The distribution of commercial pesticides in classes or categories, respectively, before and after the toxicological reclassification carried out by ANVISA in BR in 2019 is shown in Fig. 2.

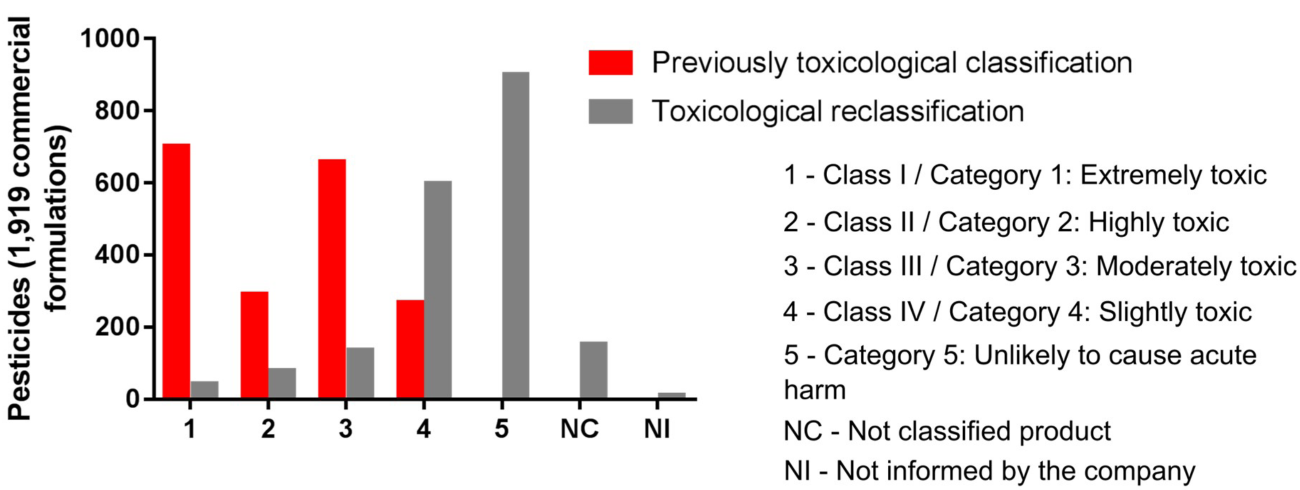

Figure 2 Distribution of toxicological classes or categories of the 1,919 commercial pesticides before and after the toxicological reclassification by the National Health Surveillance Agency (ANVISA) in Brazil. The previous distribution of pesticides in Classes I to IV in the toxicological classification the current distribution of pesticides after toxicological reclassification in Categories 1 to 5, not classified, and not informed by the company, are presented in columns.

Of the 1,919 previously registered pesticide products, 36.6% (702 pesticides) were classified as Class I (extremely toxic) representing the majority. In contrast, in the current classification, only 2.2% (43 pesticides) are classified as Category I (extremely toxic) among the total of reclassified pesticides (Table 1).

Table 1 Toxicological classification: Distribution of commercial pesticides in Classes/Categories before and after toxicological reclassification in Brazil.

Classes / Categories	**Previous toxicological classification**	**Toxicological reclassification**
Class I / Category 1 – Extremely toxic	36.6% (702 pesticides)	2.2% (43 pesticides)
Class II / Category 2 – Highly toxic	15.1% (290 pesticides)	4.1% (79 pesticides)
Class III / Category 3 – Moderately toxic	34.3% (659 pesticides)	7.1% (136 pesticides)
Class IV / Category 4 – Slightly toxic	14.0% (268 pesticides)	31.2% (598 pesticides)
Category 5 – Product unlikely to cause acute harm	_	46.9% (900 pesticides)
Not classified	_	8.0% (153 pesticides)
Not informed by the company	_	0.5% (10 pesticides)
Total	1,919 pesticides	1,919 pesticides

Most of these products were distributed in less-dangerous categories, as shown in Fig. 3A, as 39.4% were reclassified as slightly toxic products (Category 4), and 34.6% as products unlikely to cause acute harm (Category 5). A decrease in the number of commercial pesticides classified as highly toxic was also observed, changing from 15.1% (290 pesticides) to 4.1% (79 pesticides) in the currently toxicological classification (Category 2). The distribution in the lower toxicity ranges of pesticides previously classified as highly toxic was identified (Fig. 3B). There was a decrease in the number of commercial pesticides classified as moderately toxic, which previously totalled 34.3% (659 pesticides) and currently represent only 7.1% (136 pesticides) of the total pesticides. The same pattern of reclassification into less toxic categories also applies to products classified as moderately toxic and the distribution in the new categories can be seen in Fig. 3C. However, the analysis of the number of pesticides previously classified as slightly toxic (Class IV) showed an increase in pesticides in this category, from 14.0% of the total (268 pesticides) to 31.2% (598 pesticides) in the current classification (Category 4). The distribution of pesticides previously classified as slightly toxic can be seen in Fig. 3D. In general, the currently incorporated Category 5 is the one that most absorbed the products previously classified in Classes I to III, with almost half of all pesticides used in BR today being classified as unlikely to cause acute harm (46.9% - 900 pesticides). In addition, 153 pesticides (8.0% of the total) previously classified as Class I (5 pesticides), Class II (16 pesticides), Class III, (34 pesticides), and Class IV (98 pesticides), currently do not have a toxicological classification assigned by ANVISA (non-classified product). Furthermore, ten pesticides (0.5% of the total) previously classified as Class I (four pesticides), Class III (two pesticides), and Class IV (four pesticides) are currently listed as the data were not informed by the company.

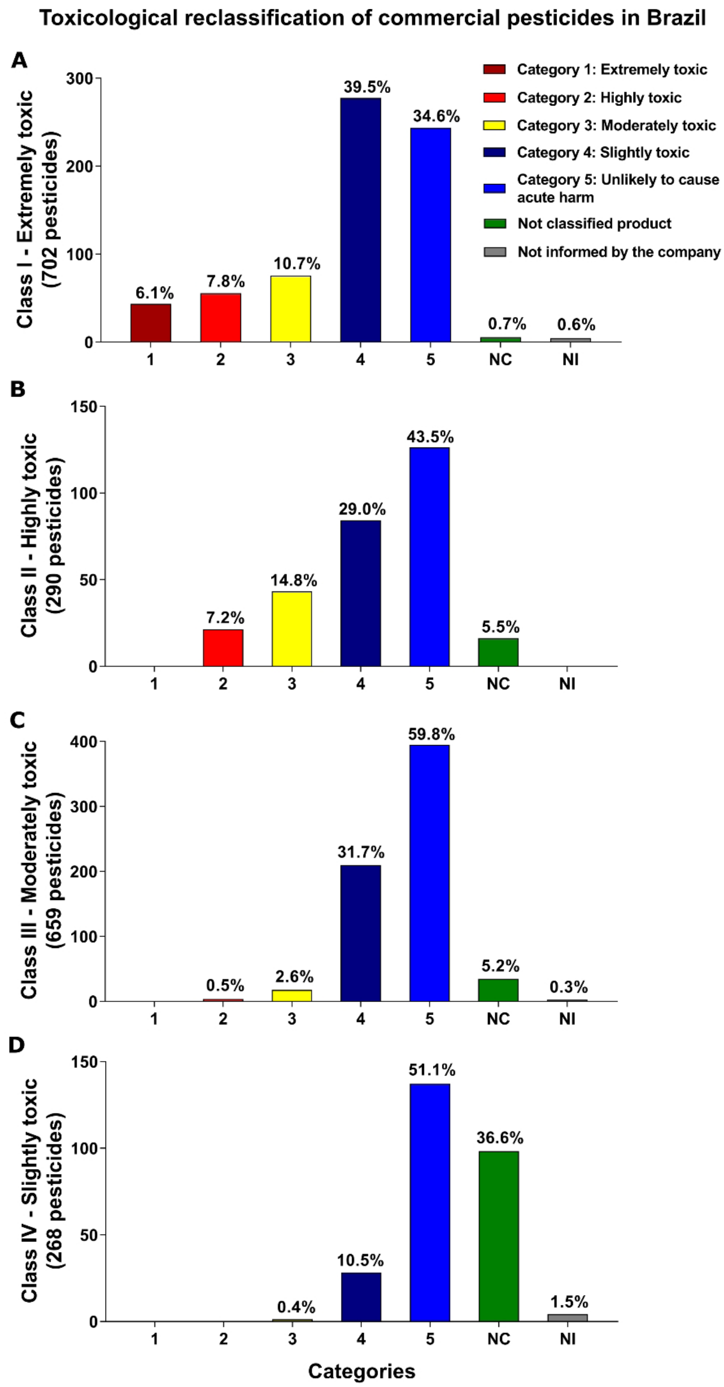

Figure 3 Toxicological reclassification of commercial pesticides in Brazil. Distribution in currently categories after toxicological reclassification of the (A) 702 commercial pesticides previously classified as Class I – Extremely toxic, (B) 290 commercial pesticides previously classified as Class II – Highly toxic, (C) 659 commercial pesticides previously classified as Class III – Moderately toxic, and (D) 268 commercial pesticides previously classified as Class IV – Slightly toxic. Current categories: Category 1 – Extremely toxic; Category 2 – Highly toxic; Category 3 – Moderately toxic; Category 4 – Slightly toxic; Category 5 – Unlikely to cause acute harm; NC – Not classified, and Not informed by the company.

Most formulations containing not approved active ingredients are classified in Categories 4 and 5 in Brazil

Regarding the toxicological classification of commercial pesticides containing not approved active ingredients in the compared nations, variations in the toxicological category in BR were observed, depending on the commercial product.

Many new commercial formulations and new active ingredients of pesticides have been launched in BR in recent years, mainly from the year 2016. Due to this, data on these compounds' previous classification and toxicological reclassification are not yet available on the ANVISA website. Clearly, there is a delay in updating data on the toxicity of these compounds based on the scientific knowledge available in reliable databases and journals. Thus, based on the information available on the products, the survey carried out presents the description of the previous toxicological classes and current categories after toxicological reclassification by ANVISA with the active principles of pesticides used in BR and not approved for use in two and/or three nations (Table 2). Based on this review, it was found that most commercial pesticides containing active ingredients not approved in two and/or three countries (EU, US and/or CHN) were reclassified into the low toxicity categories in BR (Categories 4 and 5).

Table 2. Pesticide active ingredients approved for use in Brazil that are not approved in two or three nations [European Union (EU), United States of America (USA) and/or China (CHN)] and its toxicological reclassification from Classes to Categories.

Pesticide active ingredients	**Not approved**	**Previous toxicological classification**	**Toxicological reclassification by formulation**
ALACHLOR	EU; USA	Class III	Category 5
ASULAM	EU; USA; CHN	Class III	Category 4
AZAMETHIPHOS	EU; USA	Class III	Category 5
AZIMSULFURON	EU; USA; CHN	Class III	Category 5
BENALAXYL	EU; USA; CHN	Class III	Category 5
CADUSAFOS	EU; USA; CHN	Class I	Category 4
FENAMIPHOS	EU; USA; CHN	Class I	Category 1 e 2
FENITROTHION	EU; USA	Class II	Category 3
FENTIN HYDROXIDE	EU; CHN	Class II	Category 4
FENVALERATE	EU; USA	Class II	Category 4
FLUMICLORAC-PENTYL	EU; CHN	Class IV	Category 5
METHIDATHION	EU; USA	Class I	Category 2
IOXYNIL OCTANOATE	EU; USA	Class II	Category 4
PENCYCURON	EU; USA; CHN	Class IV	Not classified
PROCYMIDONE	EU; USA	Class III	Category 5
PROFENOFOS	EU; USA	Class I, III e IV	Category 4
PROFOXYDIM	EU; USA	Class IV	Category 4 e 5
SULFLURAMID	EU; USA; CHN	Class IV	Category 4
TEFLUBENZURON	EU; USA	Class IV	Not classified
TERBUFOS	EU; CHN	Class I	Category 2
THIACLOPRID	EU; USA	Class II	Category 4
THIAZOPYR	EU; USA	Class III	Category 4
TRIADIMENOL	EU; USA	Class II	Category 5
TRICYCLAZOLE	EU; USA	Class II	Category 4
TRIFLUMURON	EU; USA	Class IV	Not classified

Critical assessment of toxicological regulation of hazardous pesticides

The use of pesticides to increase agricultural yields is a widespread practice worldwide. However, alongside the benefits of these products, there is also the potential for adverse effects on people and the environment (Veiga, 2007). Hazardous pesticides may have acute and/or chronic toxic effects and are recognized as a matter of global concern due to the risks they pose (Ruths & Simch, 2021; Sabarwal et al., 2018). The greatest exposure to dangerous pesticides is by agricultural workers during handling, dilution, mixing and application, and for people living in areas close to crops (Agostini et al., 2020; Niemann et al., 2015; Zoller et al., 2020). But the general population may be exposed to the consumption of pesticide residues in food and drinking water (Carneiro et al., 2015). To minimize risks to living beings and the environment, potentially toxic pesticides must be easily identified by their labels, with clear and objective information on health, environmental and physical risks, in addition to strict control and inspection of pesticide residues in food and water (United Nations, 2019).

Many countries follow the internationally harmonized approach to classifying and labelling chemicals. This form of classification presupposes facilitating the international trade of chemicals whose hazards have been assessed and identified at an international level, increasing the protection of human health and the environment by providing an internationally understandable system for communicating hazardous chemicals (United Nations, 2019). The new regulatory framework for pesticides, ANVISA, published RE No. 2080/2019, with the toxicological reclassification of products that were already on the market in BR, adopting parameters based on the standards of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) and follows the classification according to acute toxicity. For this, the categories of the toxicological classification were expanded from four to five, in addition to the item not classified, theoretically valid for products with very low hazardous potential, such as products of biological origin, for example (ANVISA, 2019).

The classification based on acute toxicity refers to the adverse effects that occur after oral or dermal administration of a single or multiple doses of a substance are administered in 24-hours or 4-hours inhalation exposure. Substances can be allocated to one of the five hazard categories based on acute toxicity by oral, dermal, or inhalation, according to the numerical cutoff criteria described by the GHS. However, in addition to the acute toxicity criterion, other measures are used within the health hazard group, such as carcinogenicity, germ cell mutagenicity, reproductive toxicity, and specific target organ toxicity for single exposure or repeated exposure (United Nations, 2019). Because physical and environmental hazards are also considered when assessing a chemical compound (WHO & FAO, 2016), the pesticide risk assessments for human health must be carried out correctly following scientific progress (Topping et al., 2020). According to the United Nations (2019), all available evidence, and relevance to human health, must be considered in the classification process of chemical compounds. Thus, the classification of acute toxicity in some cases underestimates the real risk to humans (Dawson et al., 2010), and disregards the effects of morbidity or death resulting from repeated or long-term exposure, which can occur even at relatively low doses/concentrations due to the bioaccumulation of the substance or its metabolites, or to the exhaustion of the detoxification process by repeated exposure.

In BR, many pesticide registration approvals have occurred in recent years, with an emphasis on the years 2020-2021 (Hess et al., 2021), which was record-breaking in the number of approvals. Most of these records are for new formulations of active ingredients that had already been released on the market, but more companies can now commercialize that. However, new active ingredients unprecedented in BR have also been released. Among the most recent active ingredients released are dinotefuran, pyroxasulfone, tolfenpyrad, and cyclaniliprole all of which are not approved for use in the EU (ANVISA, 2021; EC, 2022).

A large number of newly registered formulations and active ingredients released in recent years, and Bill 6.299/2002, called the Poison Package, are of great concern, since together they make control difficult and favor the release and marketing of hazardous products. Bill 6.299/2002 makes it possible to register harmful and carcinogenic pesticides by excluding the prohibition in this regard contained in current legislation. Moreover, confers Temporary Special Registrations and Evaluation of pesticides that are not analyzed within the established period (Bill 6299/2002). That is, the evaluation of environmental and health safety is left for after approval. In summary, the current bill violates several articles of the Constitution and agreements and treaties that BR has ratified, provides for the release of carcinogenic pesticides; greater power to MAPA, and disallowance of ANVISA and IBAMA; and opens space for an industry of Temporary Special Registrations. Since 2016, the Federal Government has accelerated changes in legislation that weaken the current regulatory framework on pesticides and expose the environment and people of all ages to hazardous substances with devastating consequences for our health and well-being. Research institutions, scientific societies and organized civil society are on their feet, calling on the Brazilian government to reject the "Poison Package" and warning that its approval will mark a monumental setback for human rights and environmental policy in the country (Friedrich et al., 2021a). Furthermore, it is very important to bring this debate to an international audience since Brazilian food products are distributed to many countries. A possible approval in the senate will bring setbacks in food security, leaving the country further from achieving the 2030 Agenda for Sustainable Development (Fernandes et al., 2022).

In the present study, an analysis of the scenario of toxicological reclassification of commercial pesticides in BR is presented, focusing on identifying pesticides considered hazardous for use by different regulatory systems and comparing the nations of EU, USA, and CHN. A considerable number of not approved pesticides in the compared agricultural countries due to the unacceptable risks they pose to human health and the environment have been found among commercial pesticides reclassified in BR. Warnings and advisories must be issued regarding the current toxicological categories of these products, as most of them (46.9%) have been reclassified to Category 5 - unlikely to cause acute harm, and products classified in this category do not receive the danger warning on the label. However, they can pose severe risks of intoxication. For example, specific pesticide formulations reclassified by ANVISA as Category 5 contain the active ingredient alachlor, included by the Rotterdam Convention as severely hazardous pesticide formulations (SHPF - PAN, 2021), banned in EU, and not approved in the USA.

Attention is especially drawn to active ingredients such as terbufos (Bonner et al., 2010; Lizé et al., 2022), methidathion (Le et al., 2010, Rooney et al., 2010), cadusafos (Malhat & Nasr, 2011; Wada & Toyota, 2008) and fenamiphos (Albuquerque et al., 2020; Čadež et al., 2021), which are not approved for use in two or three of the compared nations. In addition, it was possible to verify the change in the toxicological classification of commercial pesticides that contain these active ingredients, which, like the vast majority, have recently been classified in the categories of less toxicological danger. For example, cadusafos is not approved in the EU, USA, and CHN, but in BR was reclassified from Class I (extremely toxic) to Category 3 (moderately toxic).

Our study showed that hazardous pesticides already not approved in developed countries are still used in BR, where the risk of human and environmental exposure is high, mainly due to the lack of means for inspection. It is also worrisome that most formulations containing these active ingredients have been reclassified as Category 4 (slightly toxic product) or 5 (unlikely to cause acute harm), since mainly agricultural workers handling these products are being exposed to hazardous products. It also includes commercial pesticides with the active ingredients hexazinone and trifluralin, which are not approved in the EU, and are included in the item not classified in the list of products reclassified by ANVISA, valid for products with meager hazardous potential (Cecconi et al., 2013; Jonsson et al., 2020; Oliveira et al., 2020; Stefano et al., 2022).

The use of products that have discrepancies concerning the toxic potential among regulatory bodies can facilitate the occurrence of serious accidents compromising human and animal health, as well as the environment, especially in countries that have been openly hostile to environmental regulations. In contrast, the EU's policy of protecting human health and the environment was evident when the highest number of not approved pesticides in the block countries was observed. For example, the EU has already issued a complete and permanent ban on all outdoor uses of the three most used neonicotinoid pesticides: clothianidin, imidacloprid, and thiamethoxam, the most widely used insecticides in the world (EFSA, 2018). Neonicotinoids are very persistent in soil and water, and substantial waste are commonly found in the environment, including wildflowers. A growing body of evidence strongly suggests that existing levels of environmental contamination are causing large-scale adverse effects on bees and other beneficial insects, in addition to insectivorous bird populations (Pisa et al. 2015; FAO & WHO, 2019), which can promote damage to plantation pollination as well as an environmental imbalance.

In contrast, according to IBAMA (2022), the most commercialized pesticides in BR during 2019 and 2020 were those formulated based on glyphosate, 2,4-D, mancozeb, acephate, atrazine, chlorothalonil, malathion, paraquat dichloride, sulfur, and chlorpyrifos active ingredients. Acephate and atrazine, with more than 58,415 and 56,350 tons of active ingredients marketed in 2019 and 2020, respectively, are among the active ingredients not approved in the EU (Donley, 2019). Paraquat dichloride also stands out in eighth place, with more than 24,518 tons and is among the most commercialized active ingredients. Despite being banned in BR and banned by the EU and CHN for being a potentially highly hazardous pesticide, it continues to be used in large quantities in BR. In tenth place, with almost 19,692 tons of active ingredient marketed in 2019 and 2020 (IBAMA, 2022; Supplementary material 2), is chlorpyriphos, which is currently not approved for use in the EU, as it did not have the standard regulatory renewal approved due to concerns related to human health, possible genotoxicity, and developmental neurotoxicity (EFSA, 2019) and is banned for use in vegetables by CHN (CIRS, 2017).

Pesticides are at the same time agricultural inputs and dangerous products. Therefore, they must be regulated by the State. If the scientific evidence on the impacts of pesticides is universal, their regulation should not vary from country to country. In general, there is an urgent need for greater transparency from international regulatory agencies on the reasons for authorizing or not the active ingredients of pesticides, subsidizing protection actions, and stimulating the global market to develop less harmful and more sustainable technologies (Friedrich et al., 2021b). Regulatory agencies can increase safeguards for any pesticide, including limiting in which plantations the pesticide can be used, requiring safety equipment to be used by workers, and requiring management practices to minimize off-target movement, among others (Donley, 2019). Nevertheless, pesticide regulations are not created and implemented by politically neutral state bodies—they result from the relative influence of organized groups that have something to gain or lose from them, especially in the case of BR (Coelho et al., 2019; Moraes, 2019) as well as the USA (see Donley, 2019), both lagging other agricultural nations in banning harmful pesticides.

The presence of pesticide residues above permissible levels calls for a reevaluation of the current regulations at an international and national level (Abou Zeid et al., 2020). It seems to be urgent to rewrite and tighten the pesticide laws and regulations in Brazil, taking into account the various studies that have recursively demonstrated the risks to human health associated with the use of those products, as well as by using global criteria from countries where the use of pesticides has successfully been reduced (Nunes et al., 2021). Guidelines from organizations such as FAO, Pan American Health Organization and WHO also guide the importance of promoting other models of agriculture, whether by reducing the use of pesticides or even transitioning to organic and agroecological production modes (HLPE, 2019).

EFSA provides an annual report that analyzes pesticide residue levels in food on the European market. The analysis is based on data from official national control activities carried out by EU Member States, Iceland and Norway and includes a subset of data from the EU coordinated control program using a random sampling strategy (EFSA, 2020). Due to the strict control of pesticide residues in EU legislation, a strategy may be implemented in which the registration of unauthorized products in at least three OECD member countries or the European Community is reviewed. Following these guidelines, in Brazil, in cases where the non-authorization of use has occurred due to damage to the environment or human health, one would expect the registration to be immediately cancelled (Friedrich et al., 2021b).

Finally, while the number of regulatory approvals for pesticides has been falling in the EU, the reality in Brazil shows an increase in the number of approvals associated with the growing demand for these hazardous chemicals. However, while the EU bans these products in its territories, it produces and exports them to Latin American countries (Sarkar et al., 2021). This reveals a gap in pesticide regulation worldwide, exacerbated by the supply of hazardous pesticides produced in developed countries and the high demand for use by developing countries.

CONCLUSIONS

Pesticide Regulation in Brazil has enabled the intense use of hazardous pesticides, unlike in other countries more concerned with protecting human health and the environment. In this sense, this study sought to expose the differences in regulation between countries and alert to the problem of classifications based on acute toxicity, which underestimate the real risk of exposure to potentially toxic compounds. The toxicological reclassification in Brazil based on acute toxicity has enabled the redistribution of most commercial formulations into lower hazard categories (Categories 4, 5 and not classified), with many of these containing not approved active ingredients for regulatory actions that were taken to protect human health and the environment in other agricultural nations. The widespread use of agrochemicals will lead to long-term damage to the environment, human health, and the economy. The accumulative effects that agrochemicals bring to the nation, such as the preservation of wildlife, the pollution of water sources, and the promotion of a global problem by the production of contaminated food, do not outweigh the benefits obtained by agribusiness, which stimulates economic development at any price, for the benefit of a few and to the detriment of the vast majority of the population.

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CREDIT AUTHOR STATEMENT

All authors contributed to the study's conception and design. Material preparation, data collection and analysis were performed by Aline Guimarães Pereira, Carla Eliana Davico, Breno Raul Freitas Oliveira and Geison Souza Izídio. The first draft of the manuscript was written by Aline Guimarães Pereira, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

Supplementary material 1. List of active ingredients of pesticides approved for use in Brazil that are not approved for use in the European Union (EU), United States of America (USA) and/or China (CHN), and their classes of use.

Pesticide active ingredients	Classes of use	EU	EUA	CHN
ACEPHATE	Inseticide and acaricide	Not approved	Approved	Approved
ACETOCHLOR	Herbicide	Not approved	Approved	Approved
ACIFLUORFEN	Herbicide	Not approved	Approved	Approved
ACIFLUORFEN SODIUM	Herbicide	Not approved	Approved	Not found
ACRINATHRIN	Acaricide	Not approved	Not found	Approved
ALACHLOR	Herbicide	Not approved	Not approved	Approved
ALANYCARB	Inseticide	Not approved	Not found	Not found
ALLETHRIN	Inseticide	Not approved	Not approved	Not approved
ALPHA-CYPERMETHRIN	Inseticide	Not approved	Approved	Approved
AMETRYN	Herbicide	Not approved	Approved	Approved
AMICARBAZONE	Herbicide	Not approved	Approved	Approved
AMITRAZ	Acaricide and inseticide	Not approved	Approved	Approved
ASULAM	Herbicide	Not approved	Not approved	Not approved
ATRAZINE	Herbicide	Not approved	Approved	Approved
AVIGLYCINE	Growth regulator	Not approved	Not found	Not found
AVIGLYCINE HYDROCHLORIDE	Growth regulator	Not approved	Approved	Not found
AZAMETHIPHOS	Inseticide	Not approved	Not approved	Approved
AZIMSULFURON	Herbicide	Not approved	Not approved	Not approved
BENALAXYL	Fungicide	Not approved	Not approved	Not approved
BENDIOCARB	Inseticide	Not approved	Not approved	Approved
BENFURACARB	Inseticide and nematicide	Not approved	Not approved	Approved
BENTHIAVALICARB ISOPROPYL	Fungicide	Approved	Not approved	Not found
BENZALKONIUM CHLORIDE	Fungicide and bactericide	Not approved	Approved	Not found
BETA-CYFLUTHRIN	Inseticide	Not approved	Approved	Approved
BETA-CYPERMETHRIN	Inseticide	Not approved	Not found	Approved
BIFENTHRIN	Insecticide, formicide and acaricide	Not approved	Approved	Approved
BIOALLETHRIN	Inseticide	Not approved	Not approved	Approved
BORIC ACID	Inseticide	Not approved	Approved	Approved
BRODIFACOUM	Raticide	Not approved	Approved	Approved
BROMACIL	Herbicide	Not approved	Approved	Approved
BROMOXYNIL	Herbicide	Not approved	Approved	Approved
CADUSAFOS	Inseticide and nematicide	Not approved	Not approved	Not approved
CARBARYL	Inseticide	Not approved	Approved	Approved
CARBENDAZIM	Fungicide	Not approved	Approved	Approved
CARBOSULFAN	Insecticide, acaricide and nematicide	Not approved	Not approved	Approved
CARBOXIN	Fungicide	Not approved	Approved	Approved
CARTAP	Inseticide and fungicide	Not approved	Not found	Approved
CARTAPE HYDROCHLORIDE	Inseticide and fungicide	Not approved	Not approved	Not found
CHLORFENAPYR	Inseticide and acaricide	Not approved	Approved	Approved
CHLORFLUAZURON	Inseticide	Not approved	Not approved	Approved
CHLORIMURON	Herbicide	Not approved	Approved	Not found

CHLOROTHALONIL	Fungicide	Not approved	Approved	Approved
CHLORPYRIFOS	Insecticide, formicide and acaricide	Not approved	Approved	Approved
CHOLECALCIFEROL	Rodenticide	Not approved	Approved	Approved
CLOTHIANIDIN	Inseticide	Not approved	Approved	Approved
COUMATETRALYL	Raticide	Not approved	Not approved	Approved
CYANAMIDE	Growth regulator	Not approved	Approved	Approved
CYCLANILIDE	Growth regulator	Not approved	Approved	Not found
CYCLANILIPROLE	Inseticide	Not approved	Approved	Not found
CYFLUTHRIN	Inseticide	Not approved	Approved	Approved
CYPROCONAZOLE	Fungicide	Not approved	Approved	Approved
CYROMAZINE	Inseticide	Not approved	Approved	Approved
D-ALLETHRIN	Inseticide	Not approved	Approved	Not approved
DIAFENTHIURON	Acaricide and inseticide	Not approved	Not approved	Approved
DIAZINON	Inseticide and acaricide	Not approved	Approved	Approved
DICHLORVOS	Inseticide	Not approved	Approved	Approved
DICLORAN	Fungicide	Not approved	Approved	Not found
DIFENACOUM	Raticide	Not approved	Approved	Not found
DIFETHIALONE	Raticide	Not approved	Approved	Not found
DIFLUBENZURON	Inseticide and acaricide	Not approved	Approved	Approved
DIFLUFENICAN	Herbicide	Approved	Not approved	Approved
DIMETHENAMID	Herbicide	Not approved	Approved	Not found
DIMETHOATE	Inseticide and acaricide	Not approved	Approved	Approved
DINOTEFURAN	Inseticide	Not approved	Approved	Approved
DIPHACINONE	Rodenticide	Not approved	Approved	Not found
DIQUAT	Herbicide	Not approved	Not approved	Approved
DIQUAT DIBROMIDE	Herbicide	Not approved	Approved	Not found
DITHIANON	Fungicide	Approved	Not approved	Approved
DIURON	Herbicide	Not approved	Approved	Approved
D-TETRAMETHRIN	Inseticide	Not approved	Approved	Not approved
EPOXICONAZOLE	Fungicide	Not approved	Not found	Approved
ESBIOL	Inseticide	Not approved	Not approved	Not found
ESBIOTHRIN	Inseticide	Not approved	Not approved	Approved
ETHIPROLE	Inseticide	Not approved	Not approved	Approved
ETHOPROPHOS	Nematicide and inseticide	Not approved	Approved	Approved
ETHOXYSULFURON	Herbicide	Not approved	Not found	Approved
ETHYL CHLORIMURON	Herbicide	Not approved	Approved	Approved
ETRIDIAZOLE	Fungicide	Not approved	Approved	Not approved
FAMOXADONE	Fungicide	Not approved	Approved	Approved
FENAMIDONE	Fungicide	Not approved	Approved	Not found
FENAMIPHOS	Nematicide	Not approved	Not approved	Not approved
FENARIMOL	Fungicide	Not approved	Not approved	Not approved
FENBUTATIN OXIDE	Acaricide	Not approved	Approved	Approved
FENITROTHION	Inseticide and formicide	Not approved	Not approved	Approved
FENPROPATHRIN	Inseticide and acaricide	Not approved	Approved	Approved
FENPROPIMORPH	Fungicide	Not approved	Approved	Not found
FENTIN	Fungicide	Not approved	Not found	Not found
FENTIN HYDROXIDE	Fungicide	Not approved	Approved	Not approved
FENVALERATE	Inseticide and acaricide	Not approved	Not approved	Approved

FIPRONIL	Insecticide, formicide and cupinicide	Not approved	Approved	Not approved
FLOCOUMAFEN	Raticide	Not approved	Not found	Approved
FLUBENDIAMIDE	Inseticide	Approved	Not approved	Approved
FLUFENOXURON	Acaricide and inseticide	Not approved	Not approved	Approved
FLUMETSULAM	Herbicide	Not approved	Approved	Approved
FLUMICLORAC-PENTYL	Herbicide	Not approved	Approved	Not approved
FLUQUINCONAZOLE	Fungicide	Not approved	Not found	Not found
FLURIDONE	Herbicide	Not approved	Approved	Approved
FLUROXYPYR	Herbicide	Not approved	Approved	Approved
FLUTRIAFOL	Fungicide	Not approved	Approved	Approved
FLUVALINATE	Inseticide and acaricide	Approved	Approved	Not approved
FOMESAFEN	Herbicide	Not approved	Approved	Approved
GLUFOSINATE	Herbicide and growth regulator	Not approved	Approved	Not found
GLUFOSINATE-AMMONIUM	Herbicide and growth regulator	Not approved	Approved	Approved
HALOXYFOP-P	Herbicide	Not approved	Not found	Not found
HALOXYFOP-P-METHYL	Herbicide	Not approved	Not found	Approved
HEXAFLUMURON	Inseticide and growth regulator	Not approved	Approved	Approved
HEXAZINONE	Herbicide	Not approved	Approved	Approved
HYDRAMETHYLNON	Inseticide	Not approved	Approved	Approved
IMAZAPIC	Herbicide	Not approved	Approved	Approved
IMAZAPYR	Herbicide	Not approved	Approved	Approved
IMAZAQUIN	Herbicide	Not approved	Approved	Approved
IMAZETHAPYR	Herbicide	Not approved	Approved	Approved
IMIDACLOPRID	Inseticide	Not approved	Approved	Approved
INDOXACARB	Insecticide, cupinicide and formicide	Not approved	Approved	Approved
IOXYNIL OCTANOATE	Herbicide	Not approved	Not approved	Approved
IPBC - IODOPROPYNYL BUTYL-CARBAMATE	Fungicide	Not found	Not approved	Not found
IPRODIONE	Fungicide	Not approved	Approved	Approved
IPROVALICARB	Fungicide	Approved	Not approved	Approved
KASUGAMYCIN	Fungicide and bactericide	Not approved	Approved	Approved
LACTOFEN	Herbicide	Not approved	Approved	Approved
LINURON	Herbicide	Not approved	Approved	Approved
LUFENURON	Inseticide and acaricide	Not approved	Approved	Approved
MANCOZEB	Fungicide and acaricide	Not approved	Approved	Approved
METHIDATHION	Inseticide and acaricide	Not approved	Not approved	Approved
METHIOCARB	Inseticide	Not approved	Approved	Not found
METHOMYL	Inseticide and acaricide	Not approved	Approved	Approved
METHOPRENE	Inseticide	Not approved	Approved	Not approved
METHYL BROMIDE	Insecticide, formicide, fungicide, herbicide and nematicide	Not approved	Approved	Approved
MILBEMECTIN	Inseticide and acaricide	Approved	Not approved	Not found
MSMA	Herbicide	Not approved	Approved	Not found
MYCLOBUTANIL	Fungicide	Not approved	Approved	Approved
NOVALURON	Inseticide	Not approved	Approved	Approved
OLEIC ACID	Formicide	Approved	Not approved	Not approved
ORTHOSULFAMURON	Herbicide	Not approved	Approved	Approved
OXADIAZON	Herbicide	Not approved	Approved	Approved

OXYCARBOXIN	Fungicide	Not approved	Approved	Not found
PENCYCURON	Fungicide	Not approved	Not approved	Not approved
PERMETHRIN	Inseticide and formicide	Not approved	Approved	Approved
PHENOTHRIN	Inseticide	Not approved	Approved	Approved
PHOSPHINE	Inseticide, formicide and cupinicide	Approved	Approved	Not approved
PHOXIM	Inseticide	Not approved	Not approved	Approved
PHTHALIDE	Fungicide	Not approved	Not found	Not approved
PICOXYSTROBIN	Fungicide	Not approved	Approved	Approved
PIRIMICARB	Inseticide	Approved	Not approved	Approved
PROCYMIDONE	Fungicide	Not approved	Not approved	Approved
PROFENOFOS	Inseticide and acaricide	Not approved	Not approved	Approved
PROFOXYDIM	Herbicide	Not approved	Not approved	Not found
PROMETRYN	Herbicide	Not approved	Approved	Approved
PROPANIL	Herbicide	Not approved	Approved	Approved
PROPARGITE	Acaricide	Not approved	Approved	Approved
PROPICONAZOLE	Fungicide	Not approved	Approved	Not found
PROPINEB	Fungicide	Not approved	Not found	Approved
PROPOXUR	Inseticide	Not approved	Approved	Approved
PYMETROZINE	Inseticide	Not approved	Approved	Approved
PYRITHIOBAC	Herbicide	Not approved	Not found	Not found
PYRITHIOBAC-SODIUM	Herbicide	Not approved	Approved	Not found
PYROXASULFONE	Herbicide	Not approved	Approved	Not found
QUINCLORAC	Herbicide	Not approved	Approved	Approved
QUINTOZENE	Fungicide	Not approved	Approved	Approved
SETHOXYDIM	Herbicide	Not approved	Approved	Approved
SIMAZINE	Herbicide	Not approved	Approved	Approved
SPIRODICLOFEN	Acaricide	Not approved	Approved	Approved
SULFENTRAZONE	Herbicide	Not approved	Approved	Approved
SULFLURAMID	Inseticide and formicide	Not approved	Not approved	Not approved
SUMITHRIN	Inseticide	Not approved	Approved	Approved
TANNINS	Fungicide	Not found	Not approved	Not found
TEBUTHIURON	Herbicide	Not approved	Approved	Approved
TEFLUBENZURON	Inseticide	Not approved	Not approved	Not found
TEMEPHOS	Inseticide and larvicide	Not approved	Not approved	Approved
TEPRALOXYDIM	Herbicide	Not approved	Not approved	Not approved
TERBUFOS	Inseticide and nematicide	Not approved	Approved	Not approved
TETRAMETHRIN	Inseticide	Not approved	Approved	Not approved
THIACLOPRID	Inseticide	Not approved	Not approved	Approved
THIAMETHOXAM	Inseticide	Not approved	Approved	Approved
THIAZOPYR	Herbicide	Not approved	Not approved	Not found
THIDIAZURON	Herbicide and growth regulator	Not approved	Approved	Approved
THIOBENCARB	Herbicide	Not approved	Approved	Approved
THIODICARB	Inseticide	Not approved	Approved	Approved
THIOPHANATE-METHYL	Fungicide	Not approved	Approved	Approved
THIRAM	Fungicide	Not approved	Approved	Approved
TOLFENPYRAD	Inseticide and acaricide	Not approved	Approved	Approved
TRIADIMEFON	Fungicide	Not approved	Approved	Approved
TRIADIMENOL	Fungicide	Not approved	Not approved	Approved

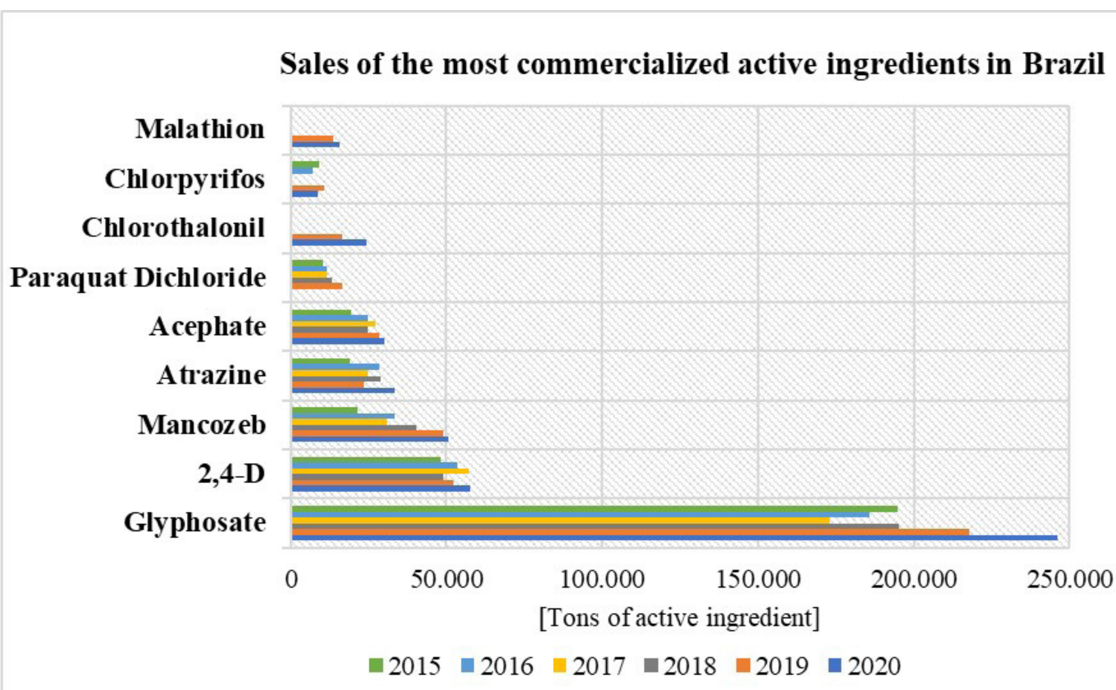
TRIAZOPHOS	Inseticide and acaricide and nematicide	Not approved	Not approved	Approved
TRICYCLAZOLE	Fungicide	Not approved	Not approved	Approved
TRIFLOXYSULFURON	Herbicide	Not approved	Not found	Not found
TRIFLUMIZOLE	Fungicide	Not approved	Approved	Approved
TRIFLUMURON	Inseticide	Not approved	Not approved	Approved
TRIFLURALIN	Herbicide	Not approved	Approved	Approved
ZETA-CYPERMETHRIN	Inseticide	Not approved	Approved	Approved

Supplementary material 2: Tons of active ingredients per year marketed between 2015 and 2020 in Brazil.

Sales of the most commercialized active ingredients in Brazil (tons)							
Active ingredient	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**	**TOTAL**
Glyphosate	246.018	217.592	195.056	173.151	185.602	194.940	1.212.358
2,4-D	57.598	52.427	48.921	57.389	53.374	48.013	317.723
Mancozeb	50.527	49.163	40.550	30.815	33.233	21.574	225.862
Atrazine	33.321	23.429	28.799	24.731	28.616	18.869	157.766
Acephate	29.982	28.433	24.657	27.058	24.859	19.325	154.313
Paraquat Dichloride	*	16.398	13.200	11.756	11.638	10.537	63.529
Chlorothalonil	24.191	16.653	*	*	*	*	40.844
Chlorpyrifos	8.865	10.828	*	*	7.271	9.187	36.151
Malathion	15.702	13.576	*	*	*	*	29.279

Source: http://www.ibama.gov.br/relatorios/quimicos-e-biologicos/relatorios-de-comercializacao-de-agrotoxicos

*Active ingredients that were not in the top ten this year



Source: http://www.ibama.gov.br/relatorios/quimicos-e-biologicos/relatorios-de-comercializacao-de-agrotoxicos *Active ingredients that were not in the top ten this year