PAN Germany
Pestizid Aktions-Netzwerk e.V.

Exports of EU-banned pesticides from EU countries to South Africa

Results of a research carried out by PAN Germany
for Women on Farms Project (WFP) South Africa

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1. About this Report

This report is the result of a research commissioned by the Women on Farms Project (WFP) South Africa, carried out by PAN Germany in August and September 2022.

The goals and leading questions[1] for this research were to:

- provide a brief overview which of the 193 pesticides (active substances) listed by the European Chemicals Agency (ECHA) as banned are used in which of the 7 countries identified by WFP and which companies (in which countries) manufacture / export these pesticides;
- identify the health impacts/effects of these pesticides and why they were banned in the European Union (EU);
- provide a short description of the legal bases / strategies and pathways of three countries (viz. Mexico, Tunisia, Palestine) which allows banning the import of Highly Hazardous Pesticides (HHPs)[2];
- identify future possible joint research and advocacy for WFP and PAN.

2. Executive summary

Using three different sources, the export of 24 pesticide active substances not having marketing approval in the European Union were identified to have been exported to the Republic of South Africa between 2018 and 2021. The common names of these 24 pesticides and additional information are listed in the table below.

The reasons / circumstances for a ban or non-approval listed in this table can be summarised as follows (Note: in case of several concerns, only one was selected):

- Insufficient data or application retracted: **11** (1,3-chlorothalonil, butralin, carbosulfan, chloropicrin, fenpropathrin, imidacloprid, picoxystrobin, propargite, thiram, zineb)
- Carc 1B[3]: **1** (chlorothalonil)
- Repro 1B[4]: **3** (amitrole, carbendazim, glufosinate)
- WHO 1B: **3** (azinphos-methyl, carbofuran, cyfluthrin)
- EDC: **2** (cyanamide, propineb)
- Ground water contamination: **2** (atrazine, fipronil)
- Exceedance of Acceptable Operator Exposure Level (AOEL): **1** (alachlor)
- Parkinson's disease: **1** (paraquat)

As it can be seen, the most frequent reason (11 cases) was "insufficient data" to complete the risk assessment. This is a serious issue, because it represents the situation where industry obtained marketing authorisation in the past, subsequently exposing humans and the environment for many years, but did not provide sufficient information according to contemporary standards of toxicology. By doing this, the producers of these pesticides possibly avoided a cut-off criterion classification. While these pesticide active substances are listed in the EU PIC-list, the missing hazard classification due to insufficient data may become an obstacle concerning future legislation to ban the export of HHPs.

[1] According to mid-term review, the original question of residues in commodities had been dropped.
[2] https://pan-international.org/wp-content/uploads/PAN_HHP_List.pdf; http://apps.who.int/iris/bitstream/10665/205561/1/9789241510417_eng.pdf
[3] classified or proposed by authority
[4] classified or proposed by authority

Table 1: Banned / not approved pesticides exported from EU countries to South Africa in 2018/19 - Overview

Pesticide ingredient	Date of ban or expiration of approval	Remarks from EU review reports and/or scientific assessment	Use	Listed by PAN as HHP[5] Y/N
1,3-dichloropro-pene	Sep 2007	Insufficient data for a proper risk assessment (consumers, operators, bystanders, groundwater) in particular for up to 11 manufacturing impurities	Soil fumigant	Y
Alachlor	Dec 2006	Likely human carcinogen (EPA); possible exceedance of AOEL	Herbicide	Y
Amitrole	June 2016	Repro 2, proposed in peer review as Repro 1B; suspected EDC; exceeding 0,1 µg/l drinking water limit	Herbicide	Y
Atrazine	Oct 2003	Permanent exceedance of 0,1 µg/l drinking water limit	Herbicide	N
Azinphos-methyl	Jan 2007	High acute toxicity (WHO 1B); reports on genotoxic effects	Insecticide	Y
Butralin	Oct 2008	insufficient data for appropriate risk assessment	Herbicide	N
Carbendazim	Nov 2014	Muta 1B and Repro 1B	Fungicide	Y
Carbofuran	June 2007	High acute toxicity (WHO 1B) (high acute toxicity); Insufficient information for ground water risk assessment	Insecticide	Y
Carbosulfan	June 2007	Insufficient information to complete the risk assessment for operators, consumers and the environment	Insecticide	Y
Chloropicrin	Oct 2011	Insufficient information to complete the risk assessment for operators, groundwater, long-range atmospheric transport and environmental aspects	Soil fumigant	Y
Chlorothalonil	May 2019	Carc 1B according to EFSA conclusion, although still listed as Carc 2 in EU Pesticides Database	Fungicide	Y
Cyanamide	Sept 2018	Carc 2; Repro 2; EDC; according to EU clear indications of harmful effects on human health (operators)	Pesticide	Y
Cyfluthrin	April 2014	High acute toxicity (WHO 1B)	Pesticide	Y
Fenpropathrin	July 2013	Insufficient information to complete risk assessment	Insecticide	Y
Fipronil	Sept 2017	Insufficient information to complete the risk assessment for bees; Classified (EU) as very toxic to aquatic organisms; increased potential for groundwater contamination	Insecticide	Y
Glufosinate	July 2018	Repro 1B	Herbicide	Y
Imidacloprid	Dec 2020	Lacking submission for renewal;	Insecticide	Y

[5] According to PAN International list of highly hazardous pesticides (HHPs) edition from March 2021 https://pan-international.org/wp-content/uploads/PAN_HHP_List.pdf

Pesticide ingredient	Date of ban or expiration of approval	Remarks from EU review reports and/or scientific assessment	Use	Listed by PAN as HHP[5] Y/N
		highly toxic to bees; potential for developmental neurotoxicity		
Paraquat	July 2007	Link between paraquat exposure and Parkinson's disease	Herbicide	Y
Picoxystrobin	Oct 2017	Insufficient data to eliminate concerns about genotoxicity	Fungicide	Y
Procymidone	June 2008	Insufficient information to complete the risk assessment. Potential EDC, supported by a number of scientific publications	Fungicide	Y
Propargite	Dec 2011	Insufficient information to complete the risk assessments for consumers, operators, workers and bystanders, and environmental aspects; classified as Carc 2; concerns about potential genotoxic effects of impurities	Acaricide	Y
Propineb	Mar 2018	Main metabolite (4methylimidazolidine-2-thione, PTU) classified as EDC and Repro 2	Fungicide	Y
Thiram	Spray: Apr 2019 Seeds: Feb 2020	Carc 2; Carc 1B for metabolite; insufficient data to complete EDC assessment; concerns regarding drinking water contamination	Fungicide	(N)
Zineb	March 2001	Industry retracted application for market approval; known teratogen (reproductive toxin) and suspected carcinogen	Fungicide	N

3. Background

The export of pesticides, that are prohibited for use in the EU for environmental and/or health reasons, but are being exported from corporations in EU member states to third countries, represents a double standard in pesticide trade. In the view of many civil society organisations and UN human rights experts[6], this double standard needs to be abolished urgently. Currently, in the EU 193 pesticide active substances that have lost their approval are listed under EU-PIC-Regulation as "banned" (as of August 2022)[7]. Despite the fact, that these pesticides (mostly HHPs) are regarded as too dangerous for EU citizens or for the environment in the EU, they are being exported – some of them in large quantities – to third countries. Corporations from Germany play a relevant role in these toxic exports. The Pesticide Action Network is committed to reducing/abolishing the use of this double standard in order to contribute to greater health and environmental justice worldwide.

For many years the Pesticide Action Network is campaigning for a global phase-out of HHPs and their replacement by sustainable, non-chemical alternatives, including agroecology. This campaign gained

[6] https://www.ohchr.org/en/press-releases/2020/07/states-must-stop-exporting-unwanted-toxic-chemicals-poorer-countries-says-un?LangID=E&NewsID=26063

[7] https://echa.europa.eu/de/information-on-chemicals/pic/chemicals?p_p_id=chemicals_WAR_echapicportlet&p_p_lifecycle=1&p_p_state=normal&p_p_mode=view&_chemicals_WAR_echapicportlet_javax.portlet.action=searchForChemicals

support from more than 570 organisations from 112 countries which signed a respective appeal[8]. Even though the devastating effects of HHPs, especially on rural communities, is widely known, the leading corporations continue to produce and market HHPs, especially in the global south. An official commitment made by BASF, Bayer Cropscience and Syngenta to phase out voluntarily pesticides of high acute toxicity – those that are classified as category 1A or 1B according the WHO[9] - made in 2013, was not fulfilled. Research conducted by PAN Germany in 2015[10] revealed that Bayer CropScience and Syngenta only partially lived-up to their commitment. It should be noted that even in 2021 Bayer CropScience continued to export the WHO 1B-compound Fenamiphos, e.g. to Brazil. The results of the research at hand provide further proof.

The introduction of so-called cut-off criteria in the European Commission's Directive 1107/2009 for active substances which are "probably for humans" mutagenic, carcinogenic, reprotoxic or endocrine disrupting was an important step of pesticide regulation in the European Union which would not have happened without pressure from civil society. The cut-off is defined as EU (GHS) category 1A or 1B for mutagenicity, carcinogenicity or reproductive toxicity. According to European legislation (Directive 1107/2009), endocrine disruption belongs to this too, but no categories (1A/1B) have yet been allocated. Active substances classified as hazard of one of these categories – in principle – are banned from marketing in the European Union.

4. Overview on pesticides listed by ECHA as banned in the EU which had been exported to South Africa

There were 24 pesticide active substances without EU approval, which have been exported at least once from the EU to South Africa between 2018 and 2021. This finding was derived from three different sources. Data for 2018 and 2019 came from a database of the Swiss NGO Public Eye[11] which contains detailed information extracted from the official export notifications on the amounts of the active substances exported (as single substance or as mixture), the country of origin, the target country, and the exporting company/-ies (Table 1). Public Eye received this information by individual freedom-of-information requests for each and every export notification. The identified pesticides from this resource are: 1,3-dichloropropene, alachlor, amitrole, atrazine, azinphos-methyl, butralin, carbendazim, chloropicrin, cyanamide, cyfluthrin, fenpropathrin, fipronil, paraquat, picoxystrobin, procymidone, and propargite.

[8] https://pan-germany.org/download/appeal-for-a-ban-of-highly-hazardous-pesticides/?wpdmdl=1444&refresh=6331888f258611664190607&ind=1617786612663&filename=HHP-Appeal_with_signatures_EN_2020.pdf

[9] WHO (World Health Organisation) https://www.who.int/publications-detail-redirect/9789240005662

[10] PAN Germany (2015): Überprüfung der Einhaltung der Selbstverpflichtung von BASF, Bayer und Syngenta von 2013 bezüglich des Verzichts auf die Vermarktung von Pestiziden der WHO-Klasse 1a und 1b

[11] https://www.publiceye.ch/fileadmin/doc/Pestizide/EU-banned-pesticide-exports_dataset.xlsx

Table 2: Exports of EU-banned pesticides to South Africa in 2018 and 2019[12]

Banned pesticide ingredient (s)	Year of planned export	Exports notifications, confirmed (kg/l per year)	Foreseen use in importing country	Exporting company	Exporting country
1,3-dichloropropene	2018	100,000	Soil fumigant plant protection product, Registered for use in South Africa (Registration number L5223)	Corteva	Spain
1,3-dichloropropene /Chloropicrin	2018	19,200	Soil disinfection for vegetables and flowers	Agroquimicos de Levante SA	Spain
1,3-dichloropropene /Chloropicrin	2018	19,200	Soil disinfection for vegetables and flowers	Agroquimicos de Levante SA	Spain
1,3-dichloropropene /Chloropicrin	2018	96,000	Soil fumigant	Corteva	Spain
Alachlor	2018	220,000	Agriculture use	SIPCAM OXON SPA	Italy
Alachlor	2019	100,000	Herbicide	SIPCAM OXON SPA	Italy
Amitrole	2019	5,000	herbicide	Nufarm	France
Atrazine	2019	23,000	Active ingredient for the herbicide product	Syngenta	France
Atrazine	2018	50,000	Herbicide	SIPCAM OXON SPA	Italy
Atrazine	2019	60,000	Herbicide	SIPCAM OXON SPA	Italy
Azinphos-methyl	2019	40,000	Control and treatment of several crops	General Quimica S.A.U.	Spain
Butralin	2019	10,000	Herbicide, plant growth regulator	Nufarm	France
Butralin	2018	10,000	Herbicide, plant growth regulator	Nufarm	France
Butralin	2018	10,000	Herbicide, plant growth regulator	Nufarm	France
Carbendazim	2019	16,320	Fungicide	ARYSTA	Belgium
Carbendazim	2018	16,320	Fungicide	ARYSTA	Belgium
Carbofuran/ carbosulfan	2019	10,160	Insecticide	Cheminova	Denmark
Cyanamide	2018	900,000	Pesticide	AlzChem AG	Germany
Cyfluthrin	2018	90	Pesticide	Bayer	Germany
Cyfluthrin	2019	100	Pesticide	Bayer	Germany
Fenpropathrin	2019	9,000	Insecticide	Sumitomo	France

[12] Extracted from the PublicEye full datasheet: https://www.publiceye.ch/fileadmin/doc/Pestizide/EU-banned-pesticide-exports_dataset.xlsx

Banned pesticide ingredient (s)	Year of planned export	Exports notifications, confirmed (kg/l per year)	Foreseen use in importing country	Exporting company	Exporting country
Fenpropathrin	2019	4,000	Insecticide	Sumitomo	France
Fenpropathrin	2018	2,000	Insecticide	Sumitomo	France
Fipronil	2019	20,000	Pesticide for crop protection	BASF	France
Paraquat	2018	240,000	Herbicide	Syngenta	United Kingdom
Paraquat	2019	500,000	Herbicide	Syngenta	United Kingdom
Picoxystrobin	2019	20,000	Fungicide	Corteva	France
Picoxystrobin	2019	10,000	Fungicide	Corteva	France
Procymidone	2018	4,620	Fungicide	Sumitomo	France
Procymidone	2019	9,000	Fungicide	Sumitomo	France
Propargite	2018	3,500	Acaricide	ARYSTA	Netherlands
Propargite	2019	4,164	Acaricide	ARYSTA	Netherlands

Three additional active substances were identified when consulting the PIC-list of ECHA as being exported to South Africa in 2020 and/or 2021. The ECHA PIC-list[13] contains all chemicals that fall under the EU PIC Regulation[14], but it contains only the name of the pesticide, the country of origin and the country of destination. It neither provides amounts nor the name of the exporting company /-ies. Also, the ECHA notifications do not indicate the intended use (plant protection/pesticide, veterinary use, others). In our review of the 2020/21 export notifications we took only substances into account that had not yet been identified in 2018/19 and that were without doubt and deeper research, being identified as substances used for plant protection products (and not e.g. as biocides). In this, way, four additional pesticides with export notifications to South Africa in 2020/21 were detected: chlorothalonil, propineb, triflumuron and zineb. Chlorothalonil, propineb and zineb are discussed in detail in Section 4 (Health effects). As triflumuron lost its approval only on 31/03/2021, it was not further considered, as exports in 2020 for sure and in 2021 possibly happened, while the substance was still approved for use in the EU and, thus, the export at this time cannot be regarded as a "double standard".

One additional source of information was available for 2021: a list of pesticides exported from Germany to South Africa, including the exported amounts, disclosed be the German government's response to a parliamentary inquiry[15]. From this list three additional active substances were identified which did neither appear in the Public Eye database of 2018/19 nor in the 2021 EU-PIC list. At this time, it remains unclear why the EU-PIC list of 2021 does not contain these German exports to South Africa. Specifically, these 2021 German exports were (exported amount in parentheses): glufosinate (11,467 kg), imidacloprid (28,128 kg),

[13] https://echa.europa.eu/information-on-chemicals/pic/chemicals

[14] REGULATION (EU) No 649/2012 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 4 July 2012 concerning the export and import of hazardous chemicals

[15] https://dserver.bundestag.de/btd/19/275/1927578.pdf

thiram (75 kg). These pesticides too are discussed in Section 4 (Health effects). Similar to triflumuron mentioned above, clothianidin was excluded, because it lost its approval in the EU in May 2022. In other words, the export from Germany in 2021 did not qualify as a "double standard".

According to the sources described above, no export notifications of active substances were detected for the other six countries WFP is working with, namely Mozambique, Namibia, Swaziland, Tanzania, Zambia or Zimbabwe.

5. Health effects of these pesticides and reasons why they were banned in Europe

In this section, the 24 pesticides identified above are briefly characterized regarding the time point and reason for not approving them for (further) marketing in the EU. If applicable this included the so-called cut-off criteria, i.e. EU (GHS) hazard category 1A or 1B for mutagenicity, carcinogenicity or reproductive toxicity or as an endocrine disruptor. Furthermore, all pesticides classified as WHO category 1A and almost all pesticides classified as WHO category 1B (for their acute toxicity) have no market approval in the EU. When available, the review reports for the active substances were analysed, in addition to the EU pesticide database. Not for all substances, the reason for the non-approval could be identified, due to deficits in the EU database. Were it is known, the reason for non-approval (e.g. bee toxicity or exceedance of the parametric EU limit for groundwater contamination) has been added in the profile below. In case of a banned active substance were no reason for non-approval could be found, a search of the scientific literature was performed and the toxicological profile of the compound according to these academic papers was summarised.

1,3-Dichloropropene

Applications for marketing approval of 1,3-Dichloropropene (1,3-D) were denied in September 2007 and in July 2010.[16] Both times the authorities concluded that information made available by the applicant was insufficient for a proper risk assessment. According to the review report of 2010, there were concerns "with regard to

- the potential contamination of groundwater in relation to 1,3-D, its relevant toxic breakdown product (EZ)-3-chloroacrylic acid and 11 unidentified manufacturing impurities;
- the consumer exposure in relation to 11 unidentified manufacturing impurities;
- the potential for long-range transport through the atmosphere of 10 manufacturing impurities."

In 2015 two chemical companies, namely Dow AgroSciences and Kanesho Soil Treatment SPRL/BVBA, again submitted their marketing application. The authorities recognised similar problems as during the earlier applications. The risk assessment for consumers, operators, workers, bystanders and residents could not be finalised due to insufficient data. The potential for groundwater contamination was identified. Further concerns related to non-target arthropods (including bees), birds and mammals, and soil organisms. Finally, on 19 January 2022, the applicants withdrew their application for the approval of 1,3-D.[17]

The International Agency for Research on Cancer (IARC) classified 1,3-D as "possibly carcinogenic to humans" (IARC 1999). Not surprisingly, in a recent industry-sponsored review (financed by Dow Agrosciences) it was concluded that 1,3-D is "not likely to be carcinogenic to humans" (Hays et al. 2020).

[16] The review reports leading to the denial of marketing approval can be downloaded here: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/active-substances/details/384

[17] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0740&from=EN

However, US EPA as well classified 1,3-D as "likely to be carcinogenic to humans" via both oral administration and inhalation (US EPA 1998).

References:

- Hays, S.M. et al. (2020): Peer review of a cancer weight of evidence assessment based on updated toxicokinetics, genotoxicity, and carcinogenicity data for 1,3-dichloropropene using a blinded, virtual panel of experts. Critical Reviews in Toxicology 50: 861-884; doi:10.1080/10408444.2020.1854680.
- IARC (1999): Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 71. https://publications.iarc.fr/_publications/media/download/2279/d7e4bcce9c42cec078b965c33b0298cf0a3aff3d.pdf.
- US EPA (1998): Registration eligibility decision (RED) 1,3-dichloropropene. Washington (DC): Office of Prevention, Pesticides and Toxic Substances; cited in Heys et al. (2020).

Alachlor

Alachlor lost its market approval in the EU in December 2006[18], because a carcinogenic potential of the compound could not be excluded, resulting in an increased safety factor for the acceptable operator exposure level (AOEL). The authorities concluded that exposure in reality would exceed the AOEL posing an unacceptable risk for operators. In addition, genotoxic potential of one of the alachlor metabolites could not be excluded, and other metabolites appeared in ground water exceeding the parametric EU-limit for pesticides of 0.1 µg/L. Consequently, the European Commission decided to not approve this pesticide.

Amitrole

EU authorities were concerned about "a high risk to operators, workers and bystanders from the use of amitrole"[19], obviously related to its effects on the endocrine and reproductive system. In the same document it is pointed out that amitrole is classified as "as toxic for reproduction category 2" and that it has toxic effects on endocrine organs. During the peer review of the assessment report it was proposed that amitrole should be re-classified as toxic for reproduction category 1B. Probably even more decisive for the ban was the high potential groundwater contamination above the parametric drinking water limit of 0,1 µg/lConsequently, in June 2016, the European Commission decided the non-renewal of the pesticide.

Atrazine

In 2003 the European Commission concluded with regard to atrazine that "the available monitoring data were insufficient to demonstrate that in large areas concentrations of the active substance and its breakdown products will not exceed 0.1 µg/l in groundwater. Moreover, it cannot be assured that the continued use in other areas will permit a satisfactory recovery of groundwater quality where concentrations already exceed 0.1 µg/l in groundwater."[20] This was the ultimate reason for its ban in the EU.

[18] Commission Decision 2006/966/EC, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006D0966&from=EN

[19] Commission Implementing Regulation (EU) 2016/871, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0871&from=EN

[20] http://www.pic.int/Portals/5/download.aspx?d=European%20Community-SD-Commission%20Decision%20on%20Atrazine%202004.pdf

In addition, a critical assessment commissioned by Public Eye indicated the potential of atrazine for serious adverse effects on human health, including endocrine and reproductive effects and potential cancer risks (Clausing 2020). This report, endorsed by 33 scientists from Canada, New Zealand, South Africa, Spain and the USA, was sent to Bruce Gordon, Unit Coordinator of the Water, Sanitation, Hygiene and Health Unit at the WHO.

Reference:

- Clausing, P. (2020): WHO Guideline Value for Atrazine in Drinking Water. A Critical Review. Public Eye, 40 p. https://www.publiceye.ch/fileadmin/doc/Pestizide/2020_PublicEye_WHO_Guideline_Value_for_Atrazine_in_Drinking_Water_Report.pdf

Azinphos-methyl

Authorisations for Azinphos-methyl had been withdrawn in the EU by 01 January 2007.
Azinphos-methyl has a high acute toxicity being classified as 1B by WHO (2019). Genotoxicity has been described in the scientific literature, including dose-dependent effects in a novel *in vitro Echerichia coli*-test system (Yuan et al. 2019), genotoxic damage shown in a comet assay using the NL-20 and the HACAT cell-lines (Arteaga-Gómez et al. 2016), and an up to 22-fold increase in the number of DNA-adducts of azinphos-methyl-exposed calf-thymus *in vitro* (Shah et al. 1997).
In an assessment of occupational exposure "some percentage of workers were predicted to exceed the level of concern" (Pouzou et al. 2018), and an epidemiological study revealed "a positive correlation between urinary organophosphate metabolite levels", including those of azinphos-methyl, "and poorer performance of some neurobehavioral tests of agricultural workers (Rothlein et al. 2006).

References:

- Arteaga-Gómez, E. et al (2016): Cytogenotoxicity of selected organophosphate insecticides on HaCaT keratinocytes and NL-20 human bronchial cells. Chemosphere 145: 174-184; doi: 10.1016/j.chemosphere.2015.11.043.
- Pouzou, J.G. et al. (2018): Comparative Probabilistic Assessment of Occupational Pesticide Exposures Based on Regulatory Assessments. Risk Analysis 38: 1223-1238; doi: 10.1111/risa.12936.
- Rothlein, J. et al. (2006): Organophosphate Pesticide Exposure and Neurobehavioral Performance in Agricultural and Nonagricultural Hispanic Workers. Environmental Health Perspectives 114:691–696; doi: 10.1289/ehp.8182.
- Shah, R.G. et al. (1997): Determination of genotoxicity of the metabolites of the pesticides Guthion, Sencor, Lorox, Reglone, Daconil and Admire by 32P-postlabeling. Molecular and Cellular Biochemistry 169: 177–184; doi: 10.1023/a:1006861621031.
- WHO (2019): The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification. https://apps.who.int/iris/rest/bitstreams/1278712/retrieve.
- Yuan, P. et al. (2019): Qualitative and quantitative assessment of genotoxins using SRRz lysis reporter under the control of a newly designed SOS responsive promoter in Escherichia coli. Royal Society of Chemistry Advances 9: 35662-35670; doi: 10.1039/c9ra06202e.

Butralin
Butralin lost its EU-marketing approval on 20 April 2009 based on a Commission Decision of 20 October 2008.[21] In the Review Report dated 25 April 2008[22], it was concluded that the information provided by the applicant (the company Nufarm) was insufficient to satisfy the needs for an appropriate risk assessment. Very few scientific studies on butralin from the academia exist. These included an epidemiological study in tobacco farmers in Malaysia showing a reduced velocity of nerve transmission after they had been using the herbicide Tamex with butralin as the active ingredient (Kimura et al. 2005).
Two recent studies described DNA damage and/or oxidative stress – both effects being known possible mechanisms for carcinogenicity in female rats (Refaie et al. 2020, Refaie et al. 2021).

References:

- Kimura, K. et al. (2005): Effects of pesticides on the peripheral and central nervous system in tobacco farmers in Malaysia: Studies on peripheral nerve conduction, brain-evoked potentials and computerized posturography. Industrial Health 43: 285-294; doi: 10.2486/indhealth.43.285.
- Refaie, A.A. et al. (2020): Over-gene expression in the apoptotic, oxidative damage and liver injure in female rats exposed to butralin. Environmental Science and Pollution Research 27: 31383-31393; doi: 10.1007/s11356-020-09416-6.
- Refaie, A.A. et al. (2021): DNA Damage and Expression Profile of Genes Associated with Nephrotoxicity Induced by Butralin and Ameliorating Effect of Arabic Gum in Female Rats. Applied Biochemistry and Biotechnology 193: 3454-3468; doi: 10.1007/s12010-021-03607-8.

Carbendazim
EFSA (2010) concluded that according to available studies Carbendazim caused numerical chromosome aberrations both *in vitro* and *in vivo*. Furthermore, reproduction toxicity studies in rats showed that carbendazim produces infertility in males, decreased sperm counts, testicular atrophy and absence of spermatogenesis. Studies on developmental toxicity by oral gavage in rats and rabbits demonstrated that carbendazim is a developmental toxicant and teratogen. Consequently, it was classified as Muta 1B and Repro 1B. It lost its market approval on 30 November 2014.[23]
In addition, carbendazim lost its approval as a biocidal product in the EU in November 2019[24], based on the Opinion of ECHA's Biocidal Product Committee.[25]

Reference:

- EFSA (2010): Conclusion on the peer review of the pesticide risk assessment of the active substance carbendazim. EFSA Journal 2010; 8(5):1598. [76 pp.]; doi:10.2903/j.efsa.2010.1598.

Carbofuran
Carbofuran lost its EU-approval in June 2007.[26] The main reasons were the following: The risk assessment for ground water contamination could not be concluded, because the applicant (for authorization) "did not provide sufficient information about a number of metabolites which have a hazardous profile". Also, concerns were raised about the acute exposure of vulnerable groups of consumers, in particular children,

[21] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008D0819&from=EN
[22] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/backend/api/active_substance/download/1051
[23] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/active-substances/details/506
[24] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019D1942&from=EN
[25] https://echa.europa.eu/documents/10162/4230c62d-7422-4c3d-a1e2-38a7f2dd2067
[26] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32007D0416&from=en

which could not be dispelled due to lack of information. In addition, data to assess ecotoxicological effects of carbofuran were insufficient.

Carbofuran is labelled with the highest hazard categories for acute toxicity ("fatal if …") for swallowing (H300) and inhaling (H330)[27], and is listed as a 1B compound according to WHO (2019). Several scientific papers describe cases of unintended human poisoning in China (Zhang et al. 2013), South Korea (Moon et al. 2016), Sri Lanka (Van der Hoek and Konradsen 2006), and Turkey (Daglioglu et al. 2011).

References:

- Daglioglu, N. et al. (2011): Pesticide intoxications in Cukurova, Turkey: three years analysis. Human and Experimental Toxicology 30: 1892–1895; doi:10.1177/0960327111402241.
- Moon J.M. et al. (2016): The characteristics of emergency department presentations related to acute herbicide or insecticide poisoning in South Korea between 2011 and 2014. Journal of Toxicology and Environmental Health, Part A, 79: 466-476; doi: 10.1080/15287394.2016.1172529.
- Van der Hoek and Konradsen (2006): Analysis of 8000 Hospital Admissions for Acute Poisoning in a Rural Area of Sri Lanka. Clinical Toxicology, 44:225–231; doi:10.1080/15563650600584246.
- WHO (2019): The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification; https://apps.who.int/iris/rest/bitstreams/1278712/retrieve.
- Zhang, M. et al. (2013): Pesticide poisoning in Zhejiang, China: a retrospective analysis of adult cases registration by occupational disease surveillance and reporting systems from 2006 to 2010. BMJ Open 3: e003510; doi:10.1136/bmjopen-2013-003510.

Carbosulfan

Carbosulfan lost its EU-approval in June 2007, because the applicant did not provide adequate information to dispel concerns regarding risks for operators, consumers and the environment. The European Commission observed that the "use of carbosulfan leads to the appearance of metabolites which have a hazardous profile", leading to "concerns about the exposure of consumers and the possible risk of ground water contamination".[28] In addition, the technical product, i.e. carbofuran active substance as it is marketed, contains a carcinogenic impurity (N-nitrosodibutylamine).

Chloropicrin

In their Review Report of 2011 the European Authorities[29] assessing chloropicrin stated that the information submitted by the applicant was insufficient to perform a risk assessment. Concerns related to risk to operators, risk for groundwater contamination, risk for long-range atmospheric transport, risk to aquatic organisms, and risk to birds and mammals. The responsible committee concluded that chloropicrin should not be approved according to EU Regulation 1107/2009.

[27] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=as.details&as_id=508

[28] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32007D0415&from=EN

[29] European Commission (2011): Review report for the active substance chloropicrin. SANCO/11440/2011 rev.4, 11 October 2011, download at https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/backend/api/active_substance/download/47

In December 2014 the "European Chloropicrin Group", an industry consortium working on the approval of chloropicrin submitted a new application. Once again, due to insufficient data, the Authority „could not finalise the risk assessment for consumers, operators, workers, bystanders and residents and identified potential concerns for groundwater, soil macro-organisms and micro-organisms and soil dwelling non-target arthropods".[30]

Besides other concerns, according to EFSA, it was not possible to draw a conclusion on the genotoxic potential of chloropicrin due to data gaps (EFSA 2020). In January 2022, the applicant withdrew its application for the approval of chloropicrin[31]. Therefore, chloropicrin continues to be not approved in the European Union.

Reference:

- EFSA (2020): Conclusion on the peer review of the pesticide risk assessment of the active substance chloropicrin. EFSA Journal 2020;18(3):6028, doi: 10.2903/j.efsa.2020.6028.

Chlorothalonil

The compound lost its market approval in the EU in May 2019. While chlorothalonil is listed as a Carc 2 chemical in the EU Pesticides Database, the regulatory document on its ban[32] points out that EFSA concluded that it should be classified as carcinogen category 1B (EFSA 2018). This conclusion was based on the observation of kidney tumours observed in studies with both rats and mice considered of relevance for humans.

In addition, concerns were raised with regard to groundwater contamination by metabolites of chlorthalonil being predicted to occur above the parametric value of 0.1 µg/L in all scenarios, and remaining concerns with regard to genotoxicity for residues to which consumers would be exposed (see link to non-renewal document in EU Pesticide Database[33])

Reference:

- EFSA (2018): Conclusion on the peer review of the peer review of the pesticide risk assessment of the active substance chlorothalonil. EFSA Journal 2018;16(1):5126, https://doi.org/10.2903/j.efsa.2018.5126.

Cyanamide

On 18 September 2008 the European Commission decided to exclude Cyanamide from market approval, because of "clear indications that it may be expected that it has harmful effects on human health and in particular on operators".[34] In EFSA's conclusion of 2010, the experts agreed to propose hazard categories corresponding to an EU (GHS) classification of Carc 2 and Repro 2 (EFSA 2010, p. 7-8). More specifically, the experts proposed

- limited evidence of a carcinogenic effect (old hazard category R40), mainly because of tumours seen in mouse studies (granulosa-theca cell tumours seen in female mice and heamangiosarcomas seen in male mice);

[30] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0751&from=EN
[31] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0751&from=EN
[32] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0677&from=EN
[33] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/backend/api/active_substance/download/393
[34] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008D0745&from=EN

- possible risk of impaired fertility (old hazard category R62), because of effects on testis development and reduced fertility in a rat study, and
- possible risk of harm to the unborn child (old hazard category R63), because of malformations seen after prenatal exposure in another rat study.

Cyanamide was labelled by ECHA as STOT-RE Category 2 (presumed toxic to humans following repeated exposure on the basis of evidence from studies in experimental animals) because of effects on the thyroid.[35] Recently the Biocidal Products Committee assessed cyanamide as a "Product Type 18" which covers "insecticides, acaricides and products to control other arthropods", and concluded that cyanamide is an endocrine disruptor (ECHA 2021)

References:

- ECHA (2021): Opinion on the application for approval of the active substance: Cyanamide Product type: 18 ECHA/BPC/302/2021, Adopted 30 November 2021.
- EFSA (2010): Conclusion on the peer review of the pesticide risk assessment of the active substance cyanamide. EFSA Journal 2010;8(11):1873. [61 pp.] doi:10.2903/j.efsa.2010.1873.

Cyfluthrin

Cyfluthrin's approval expired on 30 April 2014. It is a compound of high acute toxicity, classified as WHO category 1B. It lost its market approval as one of the 68 active substances for which "applications for renewal were either not submitted or were submitted but withdrawn".[36] Cyfluthrin is listed as highly toxic to bees in the PAN List of Highly Hazardous Pesticides.[37]

Fenpropathrin

The compound lost its marked approval on 25 July 2003 (except for certain uses in the UK where market approval continued until 20 June 2007). It belonged to the active substances "for which a commitment to further prepare the necessary dossier has not been notified" which, therefore, were excluded from marketing after the aforementioned grace periods.[38] According to ECHA, fenpropathrin is labelled as "fatal if inhaled" (GHS-Code H330).[39]

Fipronil

Fipronil lost its marketing approval in the EU on 30 September 2017 because it had expired.[40] Apparently, the applicant did not submit the required supplementary dossier. Restrictions on the use of fipronil were already in place from 01 March 2014. In particular, the use as a seed treatment of maize was no longer permitted.[41] The authorisation of fipronil-containing pesticides was restricted to seeds used in the greenhouse and for seeds of vegetables grown in the open that are harvested before flowering. Specifically, this concerned the various types of cabbage, onions and leeks.

[35] https://echa.europa.eu/da/information-on-chemicals/cl-inventory-database/-/discli/details/124450
[36] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0801&qid=1662708002715&from=en
[37] https://www.pan-uk.org/site/wp-content/uploads/PAN-HHP-List-2021.pdf
[38] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32002R2076&from=EN
[39] https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/details/29984
[40] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R1792&from=EN
[41] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0781&from=EN

Fipronil was classified by ECHA as very toxic to aquatic organisms both after acute and chronic exposure (GHS categories H400, H410). Furthermore, there is an increased potential for groundwater contamination, "in particular by metabolites that are more persistent than fipronil itself"[42].

EFSA's concerns were summarised in a Conclusion specifically dedicated to bees (EFSA 2013). In this document, EFSA highlights that the bee hazard assessment could not be completed due to data gaps, among others in the following areas:

- exposure of honey bees to dust and to guttation fluid (water excreted by plants);
- exposure through consumption of contaminated nectar and pollen;
- exposure to residues in succeeding crops or wild herbs;
- risk to pollinators other than honey bees.

The reason for not completing the bee hazard assessment was missing or insufficient data that should have been submitted by the applicant.

Fipronil was also given the label "STOT RE1" for specific organ toxicity. This provides the context for the extremely low threshold values:

- ADI value (Acceptable Daily Intake per kg body weight): 0.0002 mg/kg
- AOEL (Acceptable Operator Exposure Level): 0.0035 mg/kg

There is ample evidence in the scientific literature that fipronil induces oxidative stress - a mechanism known to be involved in the development of genetic damage, cancer and neurotoxicity. A 2016 review summarises the state of knowledge at that time (Wang et al. 2016). The authors point out that oxidative stress caused by fipronil has been demonstrated in numerous animal species (rats, mice, cattle, birds, tadpoles, fish, honeybees). They cite work demonstrating the dose-dependent occurrence of neurotoxic effects following oral administration to rats and mice. This review describes reproductive toxic effects (sperm damage) as well as impairment of liver, thyroid and kidney function.

References:

- EFSA (2013): Conclusion on the peer review of the pesticide risk assessment for bees for the active substance fipronil. EFSA Journal 2013;11(5):3158. [51 pp.] doi:10.2903/j.efsa.2013.3158.
- Wang et al. (2016): Fipronil insecticide toxicology: oxidative stress and metabolism. Critical Reviews in Toxicology; doi:10.1080/10408444.2016.1223014.

Glufosinate

According to the EU Pesticides Database, glufosinate lost its marketing approval on 31 July 2018. With Commission Implementing Regulation (EU) 2022/801 of 20 May 2022 it was officially deleted from Annex I – the list of approved active substances,[43] after being declared a "candidate for substitution.[44] According to the EU Pesticide Database glufosinate is classified as Repro 1B.

[42] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0781&from=EN
[43] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0801&from=EN
[44] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015R0408&from=EN

Imidacloprid
Imidacloprid lost its market authorisation in the EU on 01 December 2020 because it had expired.

In 2013, the manufacturer was requested to provide additional information on bee and pollinator toxicity, [45] which was submitted in December 2014. It took the EU Commission until April 2018 to determine that this December 2014 submission did not provide the requested "additional confirmatory information". [46] Therefore, since 19 December 2018, seeds treated with imidacloprid may only be used in permanently constructed greenhouses, and the resulting plant crops must also remain in permanently constructed greenhouses. [47] This restrictive imidacloprid authorisation expired on 01 December 2020, because no application for renewal was submitted.

The risks to honey bees and other pollinators are described in detail in two EFSA documents (EFSA 2016, EFSA 2018). In another document, EFSA dealt with the risk assessment of imidacloprid for aquatic organisms, which was less critical (EFSA 2014).

Interestingly, EFSA issued a scientific opinion in 2013 on the potential of the neonicotinoids acetamiprid and imidacloprid to cause damage to the nervous system of developing organisms (developmental neurotoxicity, DNT). The preparation of this scientific opinion was triggered by an *in vitro* study on cell cultures obtained from the cerebellum of newborn rats (Kimura-Kuroda et al. 2012). After evaluating the available literature, the EFSA Panel concluded that

- both substances may affect neuronal development and function;
- despite the available (regulatory) DNT studies, important uncertainties remain, so that further *in vivo* studies based on the OECD Test Guideline 426 are needed to robustly characterise the DNT potential and the dose-response relationships
- the current ARfDs for DNT of imidacloprid may be insufficient.

Reports on the further *in vivo* studies considered necessary above could not be found. Presumably they were not conducted.

Imidacloprid is no longer approved in the EU for the reasons described above, but acetamiprid remains on the market.

A number of studies have been published since EFSA's scientific opinion on DNT (EFSA 2013), including an industry review article (Sheets 2016) which, as expected, concludes that "no consistent nicotine-associated" DNT effects were found for the neonicotinoids.

A recent paper summarises the knowledge on the human health risks associated with neonicotinoids (Zhang an Lu 2022). Its analysis included data from 25 publications on urine concentrations of acetamiprid, imidacloprid, clothianidin, thiacloprid, dinotefuran and thiamethoxam or their metabolites. In addition, there were (less comprehensive) studies on residues in blood, hair and breast milk. The residue spectrum differed between countries. Globally, imidacloprid had the largest share of neonicotinoid residues detected in human urine. From the measured urine concentrations, the authors drew conclusions about the actual exposure or the ingested amount of neonicotinoids. These were two to five orders of magnitude lower than

[45] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0485&from=EN
[46] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R0783&from=DE
[47] Ibidem

the available reference values such as the ADI. According to the authors, it is all the more remarkable that despite the exposure being significantly below the reference values, epidemiological studies found a connection between these low concentrations in urine or other body fluids and increased health risks.

For example, Li et al. (2020) described significant positive relationships[48] between the concentrations of imidacloprid (and other neonicotinoids) and marker substances (parameters) for oxidative stress, e.g. 8-OHdG. Importantly, numerous animal studies (14 studies in rats and mice) have also demonstrated that imidacloprid can induce oxidative stress (Wang et al. 2017).

In a study on Thai farm workers, a correlation between urine concentrations of imidacloprid and parameters of testosterone metabolism was demonstrated. In another study, a negative correlation was found between sperm quality and the concentration of the metabolite imidacloprid olefin (Wang et al. 2022).

In a recently published paper, an increased risk of liver cancer was found in southern China with exposure to neonicotinoids and its metabolites, measured in blood samples (Zhang and Lu 2022). One hundred healthy volunteers were compared with 274 cancer patients. A total of six neonicotinoids and five metabolites were analytically recorded. The concentrations were 0.19 - 1.28 ng/mL in healthy volunteers and 0.20 - 2.03 ng/mL in the cancer patients. The increased risk of liver cancer was described with statistically significant odds ratios ranging from 2.33 to 9.02.

The particular value of these epidemiological studies lies in the direct evidence of exposure and its relationship to the measured parameters of human health (or disease).

References:

- EFSA (2013): Scientific Opinion on the developmental neurotoxicity potential of acetamiprid and imidacloprid. EFSA Journal 2013;11(12):3471, 47 pp.; doi:10.2903/j.efsa.2013.3471.
- EFSA (2014): Conclusion on the peer review of the pesticide risk assessment for aquatic organisms for the active substance imidacloprid. EFSA Journal 2014;12(10):3835, 49 pp.; doi:10.2903/j.efsa.2014.3835.
- EFSA (2016): Conclusion on the peer review of the pesticide risk assessment for the active substance imidacloprid in light of confirmatory data submitted. EFSA Journal 2016;14(11):4607, 39 pp.; doi:10.2903/j.efsa.2016.4607.
- EFSA (2018): imidacloprid considering the uses as seed treatments and granules. EFSA Journal 2018;16(2):5178, 113 pp.; doi:10.2903/j.efsa.2018.5178.
- Kimura-Kuroda, J. et al. (2012): Nicotine-Like Effects of the Neonicotinoid Insecticides Acetamiprid and Imidacloprid on Cerebellar Neurons from Neonatal Rats. PLoS ONE 7(2): e32432.; doi:10.1371/journal.pone.0032432.
- Li, A.J. et al. (2020): Variability in urinary neonicotinoid concentrations in single-spot and first morning void and its association with oxidative stress markers. Environment International 135: 105415; doi:10.1016/j.envint.2019.105415.
- Sheets, L.P. et al. (2016): A critical review of neonicotinoid insecticides for developmental neurotoxicity. Critical Reviews in Toxicology, 46: 153-190; doi:10.3109/10408444.2015.1090948.
- Suwannarin et al. (2021): Exposure to Organophosphate and Neonicotinoid Insecticides and Its Association with Steroid Hormones among Male Reproductive-Age Farmworkers in Northern Thailand. Int. J. Environ. Res. Public Health 2021, 18, 5599; doi:10.3390/ijerph18115599.

[48] i.e. the increase of measured biomarkers in parallel to urinary concentrations of neonicotinoids

- Wang, X. et al. (2017): Mechanism of Neonicotinoid Toxicity: Impact on Oxidative Stress and Metabolism. Annual Review of Pharmacology and Toxicology 58:471–507; doi:10.1146/annurev-pharmtox-010617-052429.
- Wang, A. et al. (2022): Neonicotinoid insecticide metabolites in seminal plasma: Associations with semen quality. Science of The Total Environment 811, 10 March 2022, 151407; doi:10.1016/j.scitotenv.2021.151407.
- Zhang and Lu (2022): Human exposure to neonicotinoids and the associated health risks: A review. Environment International 163: 107201; doi:10.1016/j.envint.2022.107201.

Paraquat

On 07 July 2007, the "Court of First Instance of the European Communities" (since 01 December 2009 called the European General Court) in its judgment on Case T-229/04[49] annulled the Commission Directive 2003/112/EC[50] authorising paraquat as an active plant protection substance. The case was brought to court by the governments of Sweden, Denmark, Finland and Austria. The court noted that "although there are studies on the link between paraquat and Parkinson's disease, that issue was never referred to by the notifier. Moreover, the Commission's reports did not contain any assessment of the literature relating to possible links between paraquat and Parkinson's disease." In addition, according to the court, the Commission omitted an important French study showing that the operators' acceptable exposure level was exceeded. The court concluded that Directive 2003/112/EC failed to satisfy the requirement of protection of human health. Subsequently, paraquat lost its market approval in the EU. Besides others, it is currently labelled as STOT RE1 – H372 ("causes damage to organs through prolonged or repeated exposure") according to the EU Pesticide Database.

Picoxystrobin

Picoxystrobin's EU-approval expired on 31 Oct 2017.[51] Besides other concerns, EFSA (2016) identified genotoxic potential of metabolite IN-H8612 formed as a residue, and a high risk for aquatic organisms and earthworms from exposure to picoxystrobin.

The compound was positive in an *in vitro* mammalian gene mutation assay, and the EFSA experts considered it necessary to perform genotoxicity *in vivo* tests. Obviously, these tests were not conducted, because it was not "possible to complete the assessment of genotoxicity for picoxystrobin". Likewise, "(t)he absence of endocrine-mediated effects caused by picoxystrobin could also not be concluded" (EFSA 2016). Instead of providing study results the applicant provided comments on the regulator's evaluation which were considered insufficient to eliminate the concerns.

In addition, the EFSA experts proposed to classify picoxystrobin as a Category 2 carcinogen because of testicular tumours observed in a rat study (EFSA 2016).

Due to data gaps it was not possible to finalise the risk assessment and consequently no hazard classification is indicated in the EU Pesticide Database, neither for carcinogenicity nor for genotoxicity.

Reference:

- EFSA (2016): Conclusion on the peer review of the pesticide risk assessment of the active substance picoxystrobin. EFSA Journal 2016;14(6):4515, 26 pp. doi:10.2903/j.efsa.2016.4515.

[49] https://curia.europa.eu/en/actu/communiques/cp07/aff/cp070045en.pdf
[50] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:321:0032:0035:EN:PDF
[51] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R1455&from=EN

Procymidone

In 2006, the authorities identified potential endocrine-disrupting properties of procymidone,[52] and, as a precautionary measure, limited its market approval to 18 months (instead of the seven years originally proposed). On 30 June 2008 procymidone's market approval expired.

While the anti-androgenic effects after oral exposure to procymidone in rats were known to some degree since years (Ostby et al. 1999, Christiansen et al. 2008), it is meanwhile considered a model anti-androgenic compound (Christiansen et al. 2020, Scholze et al. 2020, Boberg et al. 2021).

References:

- Boberg, J. et al. (2021): Perinatal exposure to known endocrine disrupters alters ovarian development and systemic steroid hormone profile in rats. Toxicology 458:152821; doi: 10.1016/j.tox.2021.152821.
- Christiansen, S. et al. (2008) Combined exposure to anti-androgens causes markedly increased frequencies of hypospadias in the rat. International Journal of Andrology 31:241-248; doi: 10.1111/j.1365-2605.2008.00866.x.
- Christiansen, S. et al. (2020): Grouping of endocrine disrupting chemicals for mixture risk assessment - Evidence from a rat study. Environment International. 2020 142:105870; doi: 10.1016/j.envint.2020.105870.
- Ostby, J. et al. (1999): The fungicide procymidone alters sexual differentiation in the male rat by acting as an androgen-receptor antagonist in vivo and in vitro. Toxicology and Industrial Health 15:80-93; doi: 10.1177/074823379901500108.
- Scholze, M. et al. (2020): Quantitative *in Vitro* to *in Vivo* Extrapolation (QIVIVE) for Predicting Reduced Anogenital Distance Produced by Anti-Androgenic Pesticides in a Rodent Model for Male Reproductive Disorders. 128:117005; doi: 10.1289/EHP6774.

Propargite

Propargite lost its market approval by end of 2011, because it was neither possible to perform reliable risk assessments for consumers, operators, workers and bystanders nor to finalise the ecotoxicological risk assessment.[53] EFSA was concerned about potential genotoxic effects of impurities generated during the chemical synthesis of propargite which could not be adequately assessed (EFSA 2011). In addition, a carcinogenic potential was identified, based studies in two strains of rats. Namely, intestinal tumours were observed in both studies and mammary tumours in one study. Furthermore, developmental toxicity (skeletal abnormalities in fetuses) was detected in the study with rabbits. Consequently, EFSA concluded that propargite should be labelled with a "possible risk of harm to the unborn child" and "Limited evidence of a carcinogenic effect" (EFSA 2011). According to the EU Pesticide Database, propargite is currently labelled as Carc 2.

Reference:

- EFSA (2011): Conclusion on the peer review of the pesticide risk assessment of the active substance propargite. EFSA Journal 2011; 9(5):.2087 [70 pp.]; doi:10.2903/j.efsa.2011.2087.

[52] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006L0132&from=EN

[53] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011R0943&from=EN

Propineb

Propineb lost its market approval in the EU in March 2018, mainly because of concerns "related to the endocrine-disrupting properties of the relevant metabolite 4-methylimidazolidine-2-thione (PTU) which is classified as toxic for reproduction category 2 and has the thyroid as a target organ for toxicity".[54] These concerns are described in more detail in the EFSA conclusion on Propineb (EFSA 2016).
In addition, the authorities were unable to conduct a consumer risk assessment addressing the toxicity of the propineb metabolite propane - 1,2 - diamine (PDA) due to lack of data (see link to non-renewal report 2018 in EU Pesticide Database[55]).

Reference:

- EFSA (2016): Conclusion on the peer review of the pesticide risk assessment of the active substance propineb. EFSA Journal 2016;14(11):4605, 26 pp. doi:10.2903/j.efsa.2016.4605.

Thiram

Thiram lost its approval to for spraying ("foliar application") in the EU on 30 April 2019. This was due to a withdrawal of the renewal application concerning foliar spraying sent to the European Commission by the applicant on 18 May 2018. This withdrawal came after EFSA published its peer review of the thiram risk assessment in January 2017 (EFSA 2017). In addition, seeds treated with thiram are no longer allowed in the EU since 01 February 2020.[56] EFSA (2017) classified thiram as a category 2 carcinogen because of hepatocellular adenoma and C-cell adenoma in a 2-year rat study. In addition, the authorities identified a groundwater contaminant: DMCS (Dimethylamino)(oxo)methanesulfonic acid). From residues of both thiram and DMCS a category 1B carcinogen molecule (N,N-dimethylnitrous Amide) can be formed which raised concerns regarding drinking water contamination. Furthermore, due to a data gap in the documents submitted by the applicant, it was not possible to assess potential endocrine disruptive properties of thiram. With regard to ecotoxicology, a high risk for birds and mammals was identified for all "representative uses", i.e. the thiram formulations tested.
Reference:
EFSA (2017) Conclusion on the peer review of the pesticide risk assessment of the active substance thiram. EFSA Journal 2017;15(7):4700, 29 pp. https://doi.org/10.2903/j.efsa.2017.4700

Zineb

In March 2001 the applicants retracted their application for market authorization of Zineb in the EU.[57] Thereby the industry prevented a hazard classification. The retraction needs to be seen in relation to the fact that zineb's major metabolite, ethylenethiourea (ETU), is a known teratogen and a suspected human carcinogen (see e.g. Houeto et al. 1995 for review). In addition it is known since many years that zineb and/or ETU are affecting the thyroid (e.g. Nebbia et al. 1995; and Fink-Gremmels 1996 see references below) which nowadays would qualify this fungicide a an endocrine disruptor.

References:

- Houeto et al. (1995): Ethylenebisdithiocarbamates and ethylenethiourea: possible human health hazards. Environmental Health Perspectives 103: 568-573; doi: 10.1289/ehp.95103568.

[54] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R0309&from=EN
[55] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/backend/api/active_substance/download/584
[56] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R1500&from=EN
[57] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32001D0245&from=EN

- Nebbia, C. et al. (1995): Effects of the subchronic administration of zinc ethylene-bis-dithiocarbamate (zineb) to rabbits. Veterinary and Human Toxicology 37:137-142.
- Nebbia, C. and Fink-Gremmels, F. (1996): Acute effects of low doses of zineb and ethylenethiourea on thyroid function in the male rat. Bulletin of Environmental Contamination and Toxicology 56:847-852; doi: 10.1007/s001289900123.

6. Description of the legal bases / strategies and pathways of three countries which allows banning the import of HHPs

One possibility to reduce double standards in pesticide trade is to introduce export bans in exporting countries. The European Union itself has set the goal of banning the export of hazardous chemicals banned in the EU[58]. France is the first EU member state that forbids the production, storage and export of pesticide formulations containing pesticide active substances, that are not approved in the EU for health or environmental reasons, although the implementation of the law which became effective on 01 Jan 2022 is on hold[59]. Germany made a commitment to legally ban the export of certain pesticides[60]. In a recent statement, German agricultural minister, Cem Oezdemir, announced that he wants to introduce an executive order for such a ban in 2023.[61]

Double standards can also be tackled by restricting pesticide imports. Examples of Tunis, Palestine and Mexico show that there are already importing countries, that have established the legal obligation to ban the import of pesticides that are not allowed for use, produced or banned in the country of origin. The overview shows, that legal bans or options to ban certain imports alone does not prevent those imports. The laws must be enforced to be effective. Strong civil society engagement for a legal ban of "banned pesticides" is known e.g. from Nigeria, Kenia and South Africa.

Tunisia

In Tunisia, a legal provision forbids the import of pesticides that are not in use or registered at the country of origin. However, the law is clearly not implemented.

In Tunisia the legal decree No. 2010-2973 of 15 November 2010[62] is regulating and determining the modalities and conditions for obtaining approval and provisional authorisations for the sale of pesticides for agricultural use, as well as the conditions for their manufacture, import, formulation, packaging, storage, sale, distribution and conditions of use for highly hazardous pesticides. Article 5 of the Decree makes it a condition for importing that the pesticide is registered and used in the country of origin:

[58] https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf
[59] https://www.legifrance.gouv.fr/dossierlegislatif/JORFDOLE000036562265/
[60] https://www.bundesregierung.de/resource/blob/974430/1990812/04221173eef9a6720059cc353d759a2b/2021-12-10-koav2021-data.pdf?download=1
[61] https://www.bmel.de/SharedDocs/Pressemitteilungen/DE/2022/119-vo-exportverbot-pestizide.html
[62] Decree no 2010-2973 of 15 November 2010, modifying and completing decree n° 92-2246 of 28 December 1992, determining the modalities and conditions for obtaining approval, provisional authorisations for the sale of pesticides for agricultural use, as well as the conditions for their manufacture, import, formulation, packaging, storage, sale, distribution and conditions of use of conditions for the use of severely hazardous agricultural agricultural use.

Article 5 (2) "For imported pesticides, the original of the registration certificate of the pesticide issued by the official authorities of the country of origin or a copy certified true to the original by the embassy of Tunisia in the country of origin valid and mentioning that the pesticide to be registered is used and in use in the country of origin on the date of submission of the application"[63].

Imports of pesticides play an important role in Tunisia. According to FAO Tunisia imported 9,753 tons of pesticides in 2019, while the use is indicated with 3,511 tons the same year.[64] Although the legal basis for excluding certain pesticide imports exists, import of pesticides banned in the country of origin is common practice (see Table 1)

In 2020 AEEFG and IPEN published the "National Report on the Situation of Highly Hazardous Pesticides (HHPs)"[65] revealing the use of Highly Hazardous Pesticides (HHPs) in Tunisia and with this exposing double standards and pushing the Ministry of Agriculture to take action.

Table 3: Exports of pesticides banned in the EU from EU countries to Tunisia in 2018 and 2019[66].

Banned pesticide ingredient (s)	Year of planned export	Exports notifications, confirmed (kg/l per year)	Foreseen use in importing country	Exporting company	Exporting country
Cyanamide	2018	35,000	Pesticide	AlzChem AG	Germany
Iprodione	2019	5,000	Fungicide	ARYSTA	France
Linuron	2019	2,000	herbicide	ARYSTA	France
Maneb	2019	5,000	Agricultural uses	Industrial Quimica Key SA	Spain
Simazine	2018	60,000	Agriculture uses	Industrial Quimica Key SA	Spain
Simazine	2019	80,000	Agriculture uses	Industrial Quimica Key SA	Spain
Thiocyclam	2018	6,000	insecticide	ARYSTA	France
Thiocyclam	2019	6,480	insecticide	ARYSTA	France
Triasulfuron	2019	5,000	Pesticide	Pergande	Germany
Trifluralin	2018	35,000	Agricultural uses	Industrial Quimica Key SA	Spain

FAO Statistics: Tunisia: import of pesticides in 2019: 9,753 tonnes. Pesticide use: 3,511 tons[67]

[63] The original text reads as follows: *"2 - Pour les pesticides importés, l'original de l'attestation d'homologation du pesticide délivrée par les autorités officielles du pays d'origine ou une copie certifiée conforme à l'original par l'ambassade de Tunisie du pays d'origine valide et mentionnant que le pesticide à homologuer est utilisé et en cours d'utilisation dans le pays d'origine à la date du dépôt de la demande."*

[64] https://www.fao.org/faostat/en/#data/RT

[65] AEEFGIPEN (2020): Tunisia: National Report on the Situation of Highly Hazardous Pesticides (HHPs). April, 2020. https://ipen.org/sites/default/files/documents/final_2july2020_tunisia_national_report_hhps.pdf

[66] Source: PublicEye Database based on EU export notification and responses from countries/companies.

[67] https://www.fao.org/faostat/en/#data/RP

Palestine

Palestine has a regulation in place, which forbids the import of pesticides that are banned in the country of origin for health or environmental reasons. Although border controls take place, pesticides prohibited by law are nevertheless imported.

The Regulation "Council of Ministers Resolution No. 9 of 2012 on the system of agricultural pesticides"[68] aims at issuing a strict pesticides management system in the territory of Palestinian Authority setting rules on pesticides in terms of import, export, and registration processes. Article 4 prohibits the use of pesticides that are (i) banned for use in the Occupied West Bank; (ii) banned for use in their country of origin for health or environmental reasons; (iii) classified by the World Health Organization or the US Environmental Protection Agency as causing cancer or birth defects or genetic mutations, or severe toxicity to humans or animals; and (iv) being groundwater pollutants.

Palestinian officials endeavour to run a process of strict control over pesticide importation. Because of the political situation, the effectiveness is limited.[69] If the authorities detect pesticides falling under Article 4 at border control, they are confiscated. During their visit to the Occupied West Bank in Palestine in 2016, the Arab Group for the Protection of Nature (APN) and PAN Asia Pacific (PANAP), assessed human rights and environmental implications of the manufacture and illicit trade of pesticides. Assessing import of pesticides banned at the country of origin was not the focus of their visits. However, the NGOs reported of Dukatalon, a paraquat and diquat mixture manufactured by Syngenta, Switzerland, that had been confiscated by the border control. Paraquat is banned in Switzerland since 1989.[70]

Even though, the Palestine law forbids their import, exports of banned pesticides from EU countries to Palestine took place (see Table 2).

Table 4: Exports of pesticides banned in the EU from EU countries to Palestine in 2018 and 2019[71].

Banned pesticide ingredient (s)	Year of planned export	Exports notifications, confirmed (kg/l per year)	Foreseen use in importing country	Exporting company	Exporting country
1,3-dichloropropene	2018	19,200	Soil disinfection for vegetables and flowers	Agroquimicos de Levante SA	Spain
Iprodione	2019	2,016	fungicide	ARYSTA	Belgium
Propargite	2019	850	Acaricide for fruits, vegetables and others	ARYSTA	Netherlands

FAO Statistics: use in 2019: 1,348 tons. No figures available for pesticide trade (imports/exports).

[68] https://leap.unep.org/countries/national-legislation/council-ministers-resolution-no-9-2012-system-agricultural
[69] AEP/PANAP (2016): Pesticides and Agroecology in the Occupied West Bank. Conclusions from a Joint APN-PANAP Mission in Palestine, May 2016. https://www.apnature.org/sites/default/files/2019-12/pestiagroeco-palest-web.pdf
[70] https://www.swissinfo.ch/eng/business/swiss-ban-export-of-highly-dangerous-pesticides/46099090
[71] Source: PublicEye Database based on EU export notification and responses from countries/companies.

Mexico

In Mexico, a law is in place that forbids the import of pesticides, which are not permitted in the producing country. According to Mexican NGOs, so far, this law has never applied. Research indicates that such imports still take place.

More specifically, the import of pesticides is restricted according to article 144 of the *Environmental protection and ecological equilibrium general law*[72]. The article says: No authorisations may be granted for the importation of pesticides, fertilisers and other hazardous materials, when their use is not permitted in the country in which they have been developed or manufactured [73].

Table 5: Exports of pesticides banned in the EU from EU countries to Mexico in 2018 and 2019[74]

Banned pesticide ingredient (s)	Year of planned export	Exports notifications, confirmed (kg/l per year)	Foreseen use in importing country	Exporting company	Exporting country
Ametryn	2018	100,000	Herbicide	SIPCAM OXON SPA	Italy
Ametryn	2019	50,000	Herbicide	SIPCAM OXON SPA	Italy
Atrazine	2019	50,000	Herbicide	SIPCAM OXON SPA	Italy
Cyanamide	2018	700,000	Pesticide	AlzChem AG	Germany
Cyfluthrin	2018	300	Pesticide	Bayer	Germany
Cyfluthrin	2019	300	Pesticide	Bayer	Germany
Flufenoxuron	2019	4,000	Agriculture insecticide	BASF	France
Flufenoxuron	2018	3,000	AGRICULTURE USE	BASF	France
Paraquat	2018	2,500,000	Herbicide to be used for further formulation	Syngenta	United Kingdom
Paraquat	2019	1,472,000	Herbicide to be used for further formulation	Syngenta	United Kingdom
Propisochlor	2018	30,000	herbicide	ARYSTA	France
Propisochlor	2019	10,000	herbicide	ARYSTA	France
Thiodicarb	2018	100	Use as Insecticide	Bayer	Germany
Zineb	2018	40,000	Plant protection product	Agria	Bulgaria

[72] *Ley General del equilibrio ecológico y la protección al ambiente.* https://biblioteca.semarnat.gob.mx/janium/Documentos/Ciga/agenda/DOFsr/148.pdf

[73] The spanish original text is: *No podrán otorgarse autorizaciones para la importación de plaguicidas, fertilizantes y demás materiales peligrosos, cuando su uso no esté permitido en el país en el que se hayan elaborado o fabricado.*

[74] Source: PublicEye Database based on EU export notification and responses from countries/companies.

Though it is difficult to gain information about whether the pesticides being exported are also produced in the country, the information given at https://www.alzchem.com/de/unternehmen/ stands to reason that for example cyanamide is produced in Germany. Syngenta manufactures the weedkiller paraquat under the brand name Gramoxone in its Huddersfield plant and exports it across the world, even though paraquat has been banned in the UK and the European Union since 2007. These are two examples where the Mexican import ban obviously had been ignored.

FAO Statistics: pesticide use in Mexico 2019: 48,989 tonnes, and imported in 2018: 136,519 tonnes (not data for 2019 available)

7. Glossary

EU GHS category 1A or 1B for mutagenicity, carcinogenicity or reproductive toxicity: The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) is an international standard of classification for identifying long term health effects. GHS carc (1A, 1B) = Known or presumed human carcinogens; GHS muta (1A, 1B) = Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans. Substances known to induce heritable mutations in the germ cells of humans'; GHS repro (1A, 1B) = Known or presumed human reproductive toxicant.

EU-PIC list: The so-called PIC-list lists chemicals (here pesticides) that are listed in Annex I of the EU-PIC-Regulation (Regulation (EU) No 649/2012 concerning the export and import of hazardous chemicals). The "EU-PIC list" is managed by the European Chemical Agency (ECHA) https://echa.europa.eu/en/home. Pesticides listed are not / no longer approved in the EU and have to be notified prior to their export to third countries (Prior Informed Consent – PIC).

HHPs: Highly Hazardous Pesticides are defined by FAO / WHO as "*Pesticides that are acknowledged to present particularly high levels of acute or chronic hazards to health or environment according to internationally accepted classification systems such as the World Health Organization (WHO) or the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) or their listing in relevant binding international agreements or conventions. In addition, pesticides that appear to cause severe or irreversible harm to health or the environment under conditions of use in a country may be considered to be and treated as highly hazardous".*[75]

WHO category 1a and 1b: WHO classification for acute toxicity. According to WHO (United Nations World Health Organisation) Recommended Classification of Pesticides by Hazards, WHO Class 1a indicates the highest toxicity 'Extremely hazardous', Class 1b the second highest Classification of a substance.

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75 http://apps.who.int/iris/bitstream/handle/10665/205561/9789241510417_eng.pdf;jsessionid=461152C67E3F50F4E723482ED0311B72?sequence=1