CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Comments by the National Health Federation

The National Health Federation (NHF) respectfully submits the following comments noted below for this Committee's consideration in establishing the Maximum Levels for the specified pesticide residues in food and feed (**CX/PR 19/51/5)**.

Introductory Statement

There are 336 scientific articles on PubMed alone showing a correlation between exposure to **endocrine active pesticides (endocrine disruptors)** and illnesses and conditions mediated by pesticide-residue-induced inflammation: congenital anomalies, developmental and cognitive/neurodegenerative disorders, DNA and genetic damage, oxidative stress, carcinogenic effects, reproductive disorders in both man, bees, aquatic, and terrestrial species, soil and much more. Additionally, risk of miscarriage, low birth weight, hypospadias, cryptorchidism, and micropenis were significantly greater in areas with higher use of pesticides in relation to those with lower use. **It is well established that pesticide residues constitute a significant source of contamination of environmental factors such as air, water, and soil, thereby creating a continuous threat to the co-existence of plant and animal communities of the ecosystem, let alone the knock-on effects upon human health.**

A study by Pimentel (1995) showed that only a small percentage (0.3%) of applied pesticides go into the target pest while 99.7% go into the environment. **With losses due to pests leading to one-third of the World's agricultural production being lost annually juxtaposed against the degradation of entire global ecosystems by 99.7% with those pesticide residues, many of which remain in the soils years after the initial exposure, entering the environment, it is clear that this is neither wise nor sustainable,** particularly when building soils would strengthen plants so they wouldn't require the synthetic chemicals or at least not at the current usage rates. Indeed, communities have begun bans on glyphosate and other synthetic chemicals in order to preserve life and avoid the lawsuits currently underway against Bayer (and thousands more are lined up behind the first precedent-setting cases against glyphosate).

A 2015 study titled "Assessment of three approaches for regulatory decision making on pesticides with endocrine disrupting properties," noted that no specific science-based approach for the assessment of substances with endocrine disrupting properties had been agreed upon.[i] It doesn't appear that since that time, a decision has been reached either.

Moreover, antifungals are applied to prevent agricultural plants from rotting. Some scientists cite evidence that rampant use of fungicides on crops is contributing to the surge in drug-resistant fungi infecting humans[ii]. "It's an enormous problem," said Matthew Fisher, a professor of fungal epidemiology at Imperial College London, who was a co-author of a recent scientific review on the rise of resistant fungi. "We depend on being able to treat those patients with antifungals."

In fact, Dr. Lynn Sosa, Connecticut's deputy state epidemiologist states that the urgent threat of fungal infection C. auris is "the top" threat among resistant infections and that "it's pretty much unbeatable and difficult to identify." Like antibiotic resistance, resistance to antifungal drugs and other such products is now becoming prevalent and antifungal-product overuse in farming is being blamed.

In short, the National Health Federation retains its position stated in the past, that is, that the pesticide MRLs are too high, there have been no studies of cumulative and varied/synergistic pesticide, herbicide, and chemical exposures, and therefore neither this Committee nor the Codex Alimentarius Commission can suggest with any degree of confidence any safe level of exposure of pesticide residues. Below are studies proving our stance is responsible and respectful of the World and not merely protecting food production for humans and animals in light of a one-third potential loss, particularly when reducing waste and building soils is our ready answer to a growing global degradation problem.

Specific Substances

Chlorfenapyr (254). Chlorfenapyr is a widely used, moderately hazardous pesticide.[iii] Previous reports have indicated that chlorfenapyr intoxication **can be fatal in humans**. A study reported the first non-fatal case of chlorfenapyr-induced toxic leukoencephalopathy in a 44-year-old female with resolution of extensive and abnormal signal intensities in white matter tracts throughout the brain, brain stem, and spinal cord on serial magnetic resonance imaging. This compound must be studied more before any MRLs for its use may be approved.

Cyantraniliprole (263). Cyantraniliprole, a diamide, is one of the most promising new classes of insecticides. Yet studies indicate **even low levels of diamides can pose ecological risks to aquatic ecosystems.**[iv] Currently, a catastrophic fungus disease is killing frogs everywhere, linked to impending "'mass extinction" of an entire species.[v] By continuing to poison aquatic species' habitats with pesticide residues upsetting the natural environment, fungi become opportunistic and are now quite presumably leading to extinction of frogs globally. Again, this compound's ill-effects must be studied more before any MRLs for its use may be approved.

Cyprodinil (207). In a 2015 study, the effects of cyprodinil on cancer-cell proliferation and metastasis were examined. In a xenograft mouse model with transplanted BG-1 cells, **cyprodinil significantly increased tumor mass formation** about 2 times as did E2 (6 times) compared to the vehicle (0.1% DMSO) over an 80-day period.[vi] Cyprodinil also induced cell proliferation along with the expression of proliferating cell nuclear antigen (PCNA) and cathepsin D in tumor tissues similar to E2. Taken together, these results imply that **cyprodinil may have disruptive effects on ER-expressing cancer** by altering the cell-cycle and metastasis-related gene expression via an ER-dependent pathway. This compound must be studied more before any MRLs for its use may be approved.

Diquat (031) Inflammation generated by environmental toxicants including pesticides could be one of the factors underlying neuronal cell damage in neurodegenerative diseases**.** A 2018 study found that **diquat induced apoptosis**, as demonstrated by the activation of caspases and nuclear condensation, inhibition of mitochondrial complex I activity, and decreased ATP level in PC12 cells.[vii] **Diquat also reduced the dopamine level**, indicating that cell death induced by diquat is due to cytotoxicity of dopaminergic neuronal components in these cells. The study results demonstrate that **diquat induces cell damage and may lead to Parkinson's and other neurological diseases.** This particularly nasty compound merits more study before any MRLs for it are approved.

Ethiprole (304). A 2017 study by researchers studying birth defects found **exposure to ethiprole produced several adverse effects in neurobehavioral parameters** in mice.[viii] "Movement time increased with a significant dose-related trend, and frequencies of mice with urination increased in the high-dose group of adult males in the F0 generation. The average body weight of male and female offspring increased significantly in treatment groups at postnatal days (PNDs) 7, 14, and 21. Surface righting on PND 7 of male offspring was accelerated in a significant dose-related trend. In female offspring, olfactory orientation on PND 14 was accelerated significantly on the route of higher-dose groups, and time of all treatment groups. Total distance, movement time, average speed, and average time of movement significantly decreased, and frequencies of mice with urination increased in a significant dose-related trend in male offspring in the F1 generation. Longitudinal patterns of spontaneous behavior differed in the number of horizontal activities, movement time, and average speed in treatment groups in males. The number of horizontal activities of females decreased in a significant dose-related trend through 120 min." These study outcomes support further review of this compound before MRLs for it may be approved.

Fenpicoxamid (305). While an EFSA study implied relative safety of this compound, **thyroid effects were observed** in ***all*** treatment groups of the two-year rat study.[ix] As discussed in the experts' meeting, these effects cannot be attributed definitively to the presence of iodine in the test material and **they may be related to endocrine disruption**. No carcinogenic potential was observed in this study however **some increases in the liver adenomas and carcinomas incidences were observed** but as being inside the range of the historical control values they were not considered as treatment related or biologically relevant. **With these discoveries, implied safety must be challenged.**

Fenpyroximate (193). Acute neurotoxicity was reported in a 2018 study[x] and in a 2012 study[xi] evaluating the potential risk of 45 chemicals to soil invertebrates. In fact, Fenpyroximate was listed as "super toxic." These uses, particularly when less-toxic chemicals are available, contribute to the destruction of soils negatively impacting immunity and soil health, thus leading to a viscous cycle of more pesticide use.

Fluazinam (306) is toxic and induces **contact dermatitis** in some individuals, with symptoms ranging from mildly itchy, papular rash to a painful, weeping and blistering dermatitis.[xii]

Fludioxonil (211) is toxic. Information from effects of pesticides in sediments at an ecosystem level, to validate current and proposed risk assessment procedures, is scarce. Exposure and effects of sediment-spiked fludioxonil on macroinvertebrates and zooplankton in outdoor aquatic microcosms and **Fludioxonil persisted in the sediment** and mean measured concentrations were 53–82% of the initial concentration after 84 days.[xiii] This compound must be studied more before any MRLs for its use may be approved.

Fluopyram (243) is carcinogenic and induces threshold dependent liver tumors in rats and increased hepatocellular proliferation due to CAR/PXR activation was demonstrated with exposure to Fluopyram.[xiv] Carcinogenic compounds such as this one should not have any approved MRLs.

Fluxapyroxad (256). The dissipation of fluxapyroxad is painfully slow in soil, and the degradation half-lives varied from 158 to 385 days depending on the concentration tested.[xv] Fluxapyroxad treatment significantly **shifted the microbial community structure,** thus impacting innate soil integrity. When soil biome is out of balance, more pesticides are needed as plants are weak. And when more pesticides are needed, then human health is adversely affected.

Imazalil (1108) is an **endocrine disruptor.**[xvi] Studies show Imazalil exposure damaged the testicular structure and impaired spermatogenesis in the F_1 generation male mice. Data suggests that maternal Imazalil exposure could induce endocrine disruption in the next generation of mice. Imazalil exposure decreased serum TC, HDL-C and LDL-C levels in the F_0 generation and increased them in F_1 generation mice. Imazalil exposure affected the serum estrogen and androgen levels as well as the activity of aromatase. Imazalil exposure affected the genes expression involved in sex hormone receptors, cholesterol synthesis and T synthesis. Imazalil had binding characteristics with AR protein. This pesticide is a particularly nasty piece of work that, in the interests of human health, should be kept away from human or animal use.

Isofetamid (290) is known to cause a problem with reproduction and developmental defects as an **endocrine disruptor.**[xvii] Isofetamid is noted for being moderately persisting in the soil and moderately impacting birds, fish, aquatic species, and sediment dwelling organisms, which in turn impacts human health.

Kresoxim-methyl (199) is **carcinogenic.** Occupational exposure to kresoxim-methyl may occur through inhalation of dust and dermal contact with this compound at workplaces where kresoxim-methyl is produced or used as a fungicide.[xviii] Mild-to-moderate toxicity typically consists of mild dermal and mucous membrane irritation. Burning of mucous membranes may occur with ingestion as well as gastrointestinal upset. Report of respiratory tract pain, eye pain, pruritus, skin redness, weakness, headache and dizziness occurred following an inhalational exposure after an aerial application as well as mild cases of eye pain and conjunctivitis. More study is required of this compound.

Lambda-cyhalothrin (146). The symptoms and signs of acute poisoning resulting from exposure to different pyrethroids are similar. Clinical analysis of 573 cases of acute pyrethroid poisoning due to occupational or accidental exposure revealed symptoms including burning, itching, and tingling sensations of the skin, which resolved after several hours. Washing was not an effective treatment. The systemic symptoms included dizziness, headache, nausea, anorexia, and fatigue; vomiting was most common in cases due to ingestion of pyrethroids. Although less frequently reported, tightness of the chest, paresthesia, palpitation, blurred vision, and increased sweating were observed in some cases. Coarse muscular fasciculations were observed in more serious cases. While not likely to be carcinogenic, convulsions and coma can also result from acute poisoning with pyrethroids**.**[xix] More study of this compound is required.

Lufenuron (286). While Diflubenzuron is apparently neither a skin irritant nor a skin sensitizer, it is marginally irritant to the eyes. More seriously, however, for populations at special risk, the diflubenzuron metabolite, 4-chloroaniline, has been reported to cause methemoglobinemia in exposed workers and in neonates inadvertently exposed.[xx] Further, the same study reported that some individuals who are deficient in NADH-methemoglobin reductase may be particularly sensitive to 4-chloroaniline and, hence, to diflubenzuron exposure. More study of this compound is required before any MRLs for it may be approved.

Mandestrobin (307) has moderate toxicity on fish, soil, and aquatic plants.[xxi] More study of this compound is required.

Profenofos (171) is an environmental pollutant that is genotoxic to aquatic species, mutating their DNA. Fish exposed to Profenofos showed significantly ($p < .05$) higher level of erythrocytic nuclear abnormalities (ENA) such as micronuclei, bi-nuclei, degenerated nuclei, notched nuclei, nuclear bridge and nuclear buds, as well as erythrocytic cellular abnormalities (ECA) such as echinocytic, elongated, fusion, spindle, tear-drop and twin shaped cells.[xxii] Once again, more study of this toxic compound is required before any MRLs for it may be approved.

Propiconazole (160) is a fungicide and an **endocrine disruptor**. It is listed as a possible human carcinogen displaying an increased incidence of benign and malignant liver cell tumors among male laboratory rats and mice. Additionally, it is a skin and gastric mucosa irritant and highly toxic to aquatic species. Propiconazole degrades into triazole compounds, which can then be toxic to terrestrial and avian organisms.[xxiii] This highly toxic compound most definitely should not have any MRLs approved for it by Codex.

Pydiflumetofen (309) is a fungicide with **moderate toxicity** to mammals,[xxiv] aquatic species, invertebrates, and plants, sediment dwelling organisms, and remains currently undetermined as an endocrine disruptor. Further study, however, is necessary.

Pyraclostrobin (210) is a fungicide with **high levels of toxicity to fish and aquatic invertebrates**. Pyraclostrobin exhibits moderate toxicity to sediment-dwelling organisms, bees, aquatic plants and species, earthworms and remains currently undetermined as an endocrine disruptor. It is noted as having concern for its bio-concentration factor.[xxv]

Pyriofenone (310) is a fungicide listed as an environmental hazard that is **toxic to aquatic life** with long lasting effects.[xxvi] And it may cause an allergic skin reaction. Further study is necessary.

Pyriproxyfen (200). The substance may have **effects on the blood and liver**. This may result in **anemia, impaired functions, and tissue lesions**. Pyriproxyfen remains an undetermined endocrine disruptor; however, a study evaluated the potential of pyriproxyfen to activate the ER by using an estrogen-responsive luciferase reporter gene in human ovarian carcinoma cells (E-CALUX assay system). Pyriproxyfen was reported to have some **estrogenic activity** with an EC10 of 2.9 x 10-5 M.[xxvii] This compound requires further study because of these probable endocrine-disrupting effects upon humans.

Sulfoxaflor (252) is an environmental toxin and has been found to reduce bee colonies by half. This is highly significant. Sulfoxaflor has a high potential to bioaccumulate, is generally moderately toxic to birds and mammals but with a low toxicity to most aquatic species. It is toxic to honeybees and earthworms. No serious direct human health risks have yet been identified.[xxviii] Still, its highly toxic effects upon bee populations – an important measure f human health and viability – indicate that this compound merits further study before any approval of MRLs here.

Tioxazafen (311). Human health-risk information indicates that this chemical has a low acute toxicity profile for all major routes of exposure.[xxix] It is a mild eye irritant, but a non-irritant to the skin. Chronic toxicity study with mice indicated liver tumors occur. Based on the available data, tioxazafen was classified as "likely to be **carcinogenic** to humans," thereby warranting further study and review before any MRLs for it may be approved by Codex.

Final Comments

In light of the damage from the overuse, unregulated, and irresponsible use of pesticides, herbicides, fungicides, and chemicals, the National Health Federation respectfully but firmly submits that this Codex Committee on Pesticide Residues (CCPR) has been lagging in solid science and is becoming increasingly out of touch with consumer demands and the marketplace. When entire American counties are banning the use of glyphosate, when it is being banned from major retailers, when Bayer lost the first lawsuit regarding cancer formation due to glyphosate use (and hundreds more lawsuits lined up behind the first with the same probable outcome of payouts to victims of pesticide poisoning in the millions of dollars), Codex must not continue along with disregard of the major health dangers posed by a multitude of pesticides, not even to mention the deadly synergistic effect of such compounds upon human and animal health. This last concern has ***never*** been studied and is a clear and present danger.

Entire communities are banning not only glyphosate but all synthetic chemicals unless a waiver is obtained due to an "emergency need."[xxx] If CCPR continues to set maximum residue levels on pesticides that man, animals, and the environment will be exposed to, community leaders simply bypass CCPR's decisions and act responsibly for the Planet and all affected and discontinue using killer products. Codex will be proven as completely irrelevant when these actions occur. This is not an outcome that any of us should want as Codex must remain strong and relevant in world health matters.

People realize that each of us must demand the creation of health and safety, educate others, support transition to natural products and building a healthy soil through natural means. Bowing to corporate sponsor demands at Codex is bringing about the destruction of the Earth and the health of us all. The U.S. State of Maine is setting a precedent in opposing this.[xxxi] Others will demand the same in their locality now. The ones who do not will face the same fate as Bayer, that is with multiple lawsuits to pay for bad decisions.

The endocrine-disruption effects, due to not only massive glyphosate use but to most pesticides, herbicides, and chemicals that are reviewed and approved in CCPR, have impacted aquatic species globally and reduced sperm counts, caused hermaphrodites, and forever damaged the soils around the World. Frogs are threatened with extinction, pollinators such as the bees face the same fate, and birth rates around the World are down. Yet, Codex goes along with utter disregard as though these glaring problems and threats to the World and all it holds didn't exist. The departure from the stated goal of Codex is so far lost now that it needs a complete revamp. Codex has served corporations and the bottom line of industry. That is the stated goal in all reality. With a reckless and utter disregard for the health of mankind, the animal and insect world, and the environment, that is the unfortunate outcome of a governing body that is too reliant upon bought-and-paid-for science. This must change.

Now, antibiotic resistance is well-established globally. We have nearly arrived at the point where there are no antibiotics we can turn to in the event of an emergency or crisis. While not directly an issue here in CCPR, this issue does march hand-in-glove with the rampant overuse of pesticides in world agriculture. The irresponsible use of antibiotics, which should have been reserved for human and special animal use alone, have been casually and very unwisely allowed to be used universally in animal feed. Pesticides and veterinary drugs for compounds with dual uses as pesticides and veterinary drugs for use have contaminated the food supply and increased antibiotic resistance in man and beast. Coupled with factory farming and heavy antibiotic use in food production animals, now the problem has reached such a crisis that an emergency meeting of the WHO was even held. Yet, they came away with no firm policy.

The major problems with the Planet and tainted food supply stem from poor decisions made in this CCPR committee, and the lack of current science and data gaps as excuses are completely unacceptable from those in global leadership. To only now, at this late date and under dire circumstances, come to the conclusion that "closer cooperation between CCPR and CCRVDF on issues of mutual interest for compounds used as pesticides and veterinary drugs and exploration of innovative ways to foster such collaboration as well as the discussions and decisions of CCPR50 and CCRVDF24 in this regard is needed" is sadly late.

The National Health Federation asks this Committee to respect the global nature of decisions made here and to stop acting solely in the interest of corporations and pesticide sponsors intent on just improving their financial bottom line. Instead, NHF asks that this Committee protect and preserve the Planet for the sake of Mankind and all that exists on it.

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