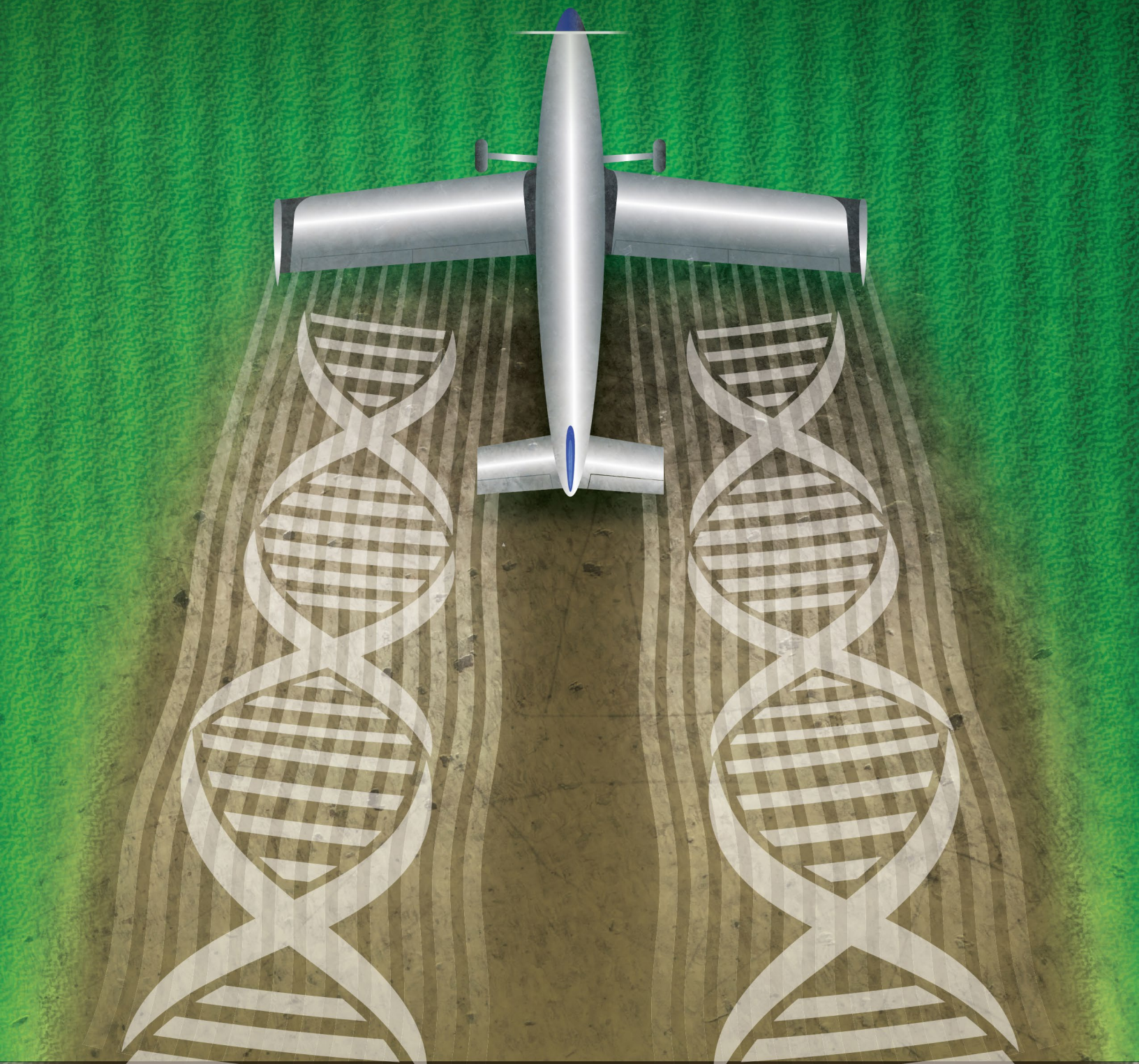
Friends of the Earth

Gene-Silencing Pesticides

Risks and Concerns



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Friends of the Earth

About Friends of the Earth:

Friends of the Earth fights to protect our environment and create a healthy and just world. We are more than one million members and activists across all 50 states working to make this vision a reality. We are part of the Friends of the Earth International Federation, a network in 74 countries working for social and environmental justice.

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Executive Summary

Gene-Silencing Pesticides

Risks and Concerns

Introduction

Pesticides have been linked to a range of significant unintended consequences, including harming our health, decimating biodiversity, and damaging the soil and water resources that we need to produce food now and into the future.[1] Now, the pesticide industry is developing a new wave of products using genetic engineering techniques, raising a novel set of risks and concerns.

Pesticide companies, including Bayer, BASF, and Syngenta, are developing "gene-silencing pesticides" that exploit a cellular process called RNA interference (RNAi). These pesticides are intended to switch off or "silence" genes that are essential for survival in pests, thus killing them. [i]

Rather than these technologies themselves being a genetically modified organism (GMO), gene-silencing pesticides are designed to be applied as an external product that will modify exposed organisms in the open environment. Organisms may start out their life as non-GMO and be modified partway through their life, constituting a vast, open-air genetic experiment.[2,3]

Gene-silencing RNAi pesticides would be applied to entire fields, and any exposed organism with a matching or similar gene sequence may potentially become genetically modified, whether it is a target or non-target organism.

Gene-silencing RNAi pesticides are virtually unregulated, both domestically and internationally, and therefore are on track to be commercialized without proper risk assessments or precautions. Given the enormous potential risks and major gaps in knowledge surrounding RNAi pesticides, it is imperative that civil society, farmers, and concerned scientists push for strong regulations and proper risk assessments before this technology is commercialized.

Gene-silencing RNAi pesticides constitute an open-air genetic experiment. Unintended genetic consequences could be inherited and persist in the environment for generations.

i RNA (ribonucleic acid) is a molecule essential in various biological roles in coding, decoding, regulation, and expression of genes. RNA and DNA arze nucleic acids. Along with lipids, proteins, and carbohydrates, nucleic acids constitute one of the four major macromolecules essential for all known forms of life. Some RNA molecules play an active role within cells by catalyzing biological reactions, controlling gene expression, or sensing and communicating responses to cellular signals. RNA interference is one essential regulatory process that uses certain types of "interfering" RNAs to control gene expression, by silencing or switching off genes.

How gene-silencing RNAi pesticides work

RNA interference (RNAi) is a naturally occurring cellular process in plants, fungi, and animals, including insects. The RNAi pathway controls whether a gene is turned off or not. Genetic engineers have figured out how to activate this process in organisms by using synthetic interfering RNA molecules produced in the laboratories. The resulting RNAi pesticides can kill a pest by triggering a process in the organism that turns off genes that are essential for survival.

For example, RNAi could be applied as a foliar spray on leaves. After the pest eats the leaves, interfering RNA enters the insect's stomach and silences a gene that is essential for cell division, following which the pest cannot make functioning new cells, and dies.

Gene-silencing RNAi pesticides can be applied to plants or insects directly in agricultural fields or other open-air settings via sprays, root soaks, or trunk injections.

RNAi applications could also be designed for various other functions, including as growth enhancers or as agents to reverse herbicide resistance, to modify post-harvest traits such as ripening, to initiate resistance to disease in target crops or animals, and more.

Risks, concerns, and knowledge gaps

The limitations of our knowledge and ability to predict or control the outcomes of this novel technology are profound and varied.

Environmental concerns

- **Open-air experimentation:** Genetically modifying organisms in the open environment makes controlling exposure difficult or impossible. Entire agroecosystems could be affected, and unintended genetic consequences could be inherited by plants and insects and may persist in the environment for generations.
- **Unintended silencing of genes:** RNAi technologies are widely associated with off-target activity – the silencing of genes that weren't intended to be silenced, both within the genome of target organisms as well as in related non-target species.[4,5]
- **Effects on non-target organisms, including bees and beetles:** Interfering RNA targeting a specific pest's genes may bind to and shut down genes in other organisms as well. This off-target effect may extend beyond closely related species to potentially thousands of different species.[6,7] Research already demonstrates the potential to harm beneficial insects, including honeybees[8,] and beetles.[5]
- **Entrenching the pesticide treadmill:** There is evidence suggesting that, as with other pesticides, targeted pests will rapidly develop resistance to RNAi pesticides.[9,10]

Unintended consequences could include killing beneficial insects or creating public health risks.

Human health concerns

- **Inhalation of synthetic interfering RNAs:** Farmers, farmworkers, and rural communities may be exposed to synthetic interfering RNAs via spray drift. The risks pertaining to inhalation exposure are completely unknown.
- **Altering crops' genetic composition:** Unwanted gene silencing could occur in target crops as the result of exposure to RNAi pesticides. This could alter the crops' genetic composition in a way that raises safety concerns, such as altering levels of toxins or allergens.[11]
- **Dietary consumption of synthetic interfering RNAs:** Preliminary research suggests that naturally occurring interfering RNAs in our diet play a role in regulating physiological or pathological conditions in our bodies.[12,13] This suggests that synthetic RNAi products may also interfere with human gene regulation, with unforeseen health implications. Further investigation is needed to fully understand the safety implications of consuming synthetic interfering RNAs.
- **Medical research on interfering RNAs suggesting potential for toxicity:** Research investigating therapeutic uses of interfering RNAs has been hampered by the observation that they can cause an immune reaction in the body, triggering an unwanted inflammatory response.[14,15]

HOW THEY WORK

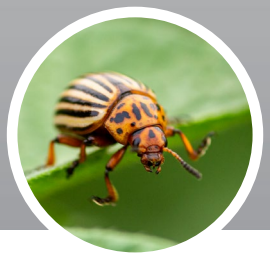
Interfering RNAs genetically modify organisms mid-life. They can kill pests or other insects by silencing genes needed for survival.

The technology is imprecise. Unwanted silencing of genes can occur both in the genome of the target organism as well as in non-target species. Unintended genetic consequences could be inherited and persist in the environment for generations.

Corporations developing RNAi pesticides are applying for patents that would give them ownership of exposed organisms. This would result in a massive expansion of property rights over nature and would threaten farmers' rights.

Many significant knowledge gaps—from the genome to organism to ecosystem level—limit our ability to adequately understand and assess the potential impacts of RNAi pesticides.

Farmworkers and rural communities may be exposed to interfering RNAs via spray drift. The health risks of inhalation exposure are completely unknown.



How it works: When applied to a crop, RNAi pesticides could kill pests by direct contact, when an organism eats a pesticide-covered plant, or when the pesticide is taken up by the plant, which is then eaten by an organism.

RNAi pesticides may contaminate neighboring fields and ecosystems where there is a vast genetic diversity of organisms.

Any exposed organism with a matching or similar gene sequence may potentially be genetically modified and killed, including beneficial insects.

Socioeconomic concerns

Biotech companies are filing patents for RNAi pesticide products that include claims of property rights to exposed organisms and their offspring, regardless of whether the exposure was intentional.[16] Such patents would make owners of RNAi sprays also the owners of exposed organisms, "potentially including entire fields of conventional crops or long-lived trees and their seeds."[3] This would constitute a massive expansion of property rights over nature, ever more deeply entrenching the power of biotech and agribusiness companies over the food system, farmers and the natural world itself.

RNAi pesticide patents would constitute a massive expansion of corporate property rights over nature.

Knowledge gaps

Many significant knowledge gaps – from the genome to organism to ecosystem level—limit our ability to adequately assess the potential impacts of RNAi pesticides.

- RNAi pathways are not currently fully understood and are more complex than the simplistic, linear theory that is exploited by developers.
- It is not currently possible to predict off-target effects within organisms' genomes for a variety of reasons: target gene expression is not always static, but mediated by physiological and environmental factors, some interfering RNAs have hundreds of DNA targets, additional processes can extend the effect of the RNAi pathway across time and space once activated, and sequence-independent factors can influence off-target binding to genes.[2,17,18,19]
- It is not currently possible to design adequate bioinformatics tools that could improve our understanding of off-target effects.[17]
- We currently lack the ability to answer fundamental questions such as which species could be exposed, what their genome sequences are, or how similar the genomes of non-target organisms are to those of target organisms.
- Research conducted to date on RNAi mechanisms has primarily been in model organisms, not in the diversity of species that exist in the wild, seriously limiting our understanding of how certain species may respond to being exposed to RNAi pesticides.
- The concentration level of interfering RNAs in a product that result in a modified effect may vary between species and individual RNAs, further complicating exposure and risk assessment.

RNAi technologies are widely associated with off-target activity – the unwanted silencing of genes that weren't intended to be silenced.

Responding to industry's false claims

The biotech and agribusiness companies developing gene-silencing products are creating false distinctions between RNAi and other genetic engineering technologies and are downplaying potential risks in order to avoid regulation and achieve rapid commercialization of RNAi products.

- **Effects of RNAi pesticides are not "transient" and sometimes can be inherited across generations.** Research demonstrates that RNAi pesticides can result in heritable modifications that last up to 80 generations.[3,20] Industry patent applications for RNAi products have claimed heritability.[3]
- **RNAi pesticides are not "natural."** RNAi pesticide formulations are based on synthetically derived interfering RNA molecules. Developers may add chemicals, nanoparticles and other synthetic materials to RNAi products to enhance their function – for example, to make them degrade more slowly.
- **RNAi pesticides are not "precise."** There are significant gaps in our scientific understanding of the underlying mechanisms of the RNAi pathway, and research suggests a host of potential unintended effects from the genome to organism to ecosystem level.

Federal regulations and international guidelines

RNAi pesticide technology presents challenges for regulatory systems that were not originally designed to address the development of genetic modification agents being released into the environment. RNAi pesticides currently fall outside of existing domestic and international regulatory structures and therefore have yet to be regulated in most parts of the world.

Based on the evidence detailed in this report, RNAi pesticides should be regulated as a form of genetic engineering. RNAi processes can result in genetic changes in exposed organisms as well as altered traits that can be passed down to offspring. This has been raised by U.N. delegates at the United Nations Convention on Biological Diversity (CBD), in particular under the Cartagena Protocol on Biosafety (CPB).[21,22]

To date, country-level regulations have failed to acknowledge RNAi pesticides as a form of genetic engineering and have therefore failed to enact proper assessments or precautions for this novel technology. In the U.S. and EU, it is expected that RNAi pesticides will be regulated under existing pesticide regulations. Such regulations are inadequate to address the novel biosafety and environmental challenges of RNAi pesticides and products.

RNAi pesticides should be regulated as a form of genetic modification. RNAi processes can result in genetic changes in exposed organisms that can be passed down to offspring.

Conclusion

Gene-silencing RNAi pesticides represent both an extension of an old, failed paradigm of pesticide-intensive agriculture, as well as a completely novel set of potential harms. Based on evidence from available scientific assessments, it is not possible to assure the safe use of RNAi products, designed to induce genetic modifications in organisms in the open environment.

The pesticide industry is pitching RNAi pesticides as a solution to a problem the industry itself created: weed and pest emergence and resistance.[23] Despite drastic and costly increases in pesticide use, some analyses show that farmers are losing more of their crops to pests today than they did in the 1940s.[24,25]

Rather than continue on a pesticide treadmill in which farmers use new formulations of toxic pesticides to deal with resistant pests, ecological farming methods offer a true solution.[26] A growing body of science shows that farmers who rely on ecological methods for pest management instead of pesticides can meet or outperform their conventional counterparts in terms of yield and profits.[27,28,29,30] Ecological farming techniques build healthy soils that confer greater pest immunity to plants and increase biodiversity in farming systems to disrupt the growth of pests and to foster natural predators. This includes crop rotations, cover cropping, composting, reducing tillage, and planting habitat for beneficial insects.

Over the past decade, a series of expert consensus reports have called for a rapid shift from input-intensive industrial agriculture to agroecological farming methods.[31,32] Business as usual is not an option. Our ability to continue to feed ourselves and future generations is at stake.

For more information and to read the full report:
foe.org/RNAI-report

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