“Absence of evidence is not evidence of absence” – the case of glyphosate

--Fred Pearce

Our knowledge of the impacts on human health and ecology of the world’s most used herbicide – and Britain’s number one, too – is a shambles. Despite many individual studies, there is no settled view on the dangers posed by glyphosate, whose main brand name is Roundup. Evidence of its toxicity or otherwise is patchy at best, and interpretation of the available evidence is often contradictory.

Glyphosate has been in widespread use across hundreds of millions of hectares for half a century – longer than climate change has been a live public issue. But while the basic science of how we are changing the climate has been clear for a long time, we are nowhere near that with glyphosate.

Opinion is polarized and entangled with wider political and economic debates about the virtues and dangers of GM crops, the power of the agrochemicals industry and accusations that some environmental activists are indulging in scaremongering.

For some, the absence of conclusive evidence of damaging impacts is seen as evidence of the herbicide’s safety. They would agree with the senior writer at *New Scientist*, Michael le Page, who argued a decade ago that a “ban on weedkiller glyphosate won't save anyone from cancer.” Well, maybe so. But others point to a scientific nostrum first popularized by the late Carl Sagan, that “absence of evidence is not evidence of absence”.

Meanwhile, farmers and other stewards of the land are caught amid a maelstrom of contradictory views, trying to balance their desire to care for the land, soils, nature and the health of their families with the practical realities of farming. On the eve of the completion this year of a new assessment of glyphosate by Britain’s chemicals licensing authority, the Health and Safety Executive, the saga is a textbook example of the failure of science to effectively inform policymaking.

Better than Agent Orange

Glyphosate, N-(phosphonomethyl)glycine, was first synthesized in the 1950s, initially as a water softener. Then, researchers at the American agrochemicals company Monsanto (now part of German chemicals giant Bayer) discovered its herbicidal properties. Monsanto first marketed it under the brand name Roundup in 1974, as a safe alternative to other non-selective herbicides such as paraquat, diquat and 2,4-D, a notoriously toxic component of Agent Orange, the defoliant widely used by US armed forces during the Vietnam War.

Farmers first used glyphosate primarily to clear fields of weed before planting crops such as soybeans, maize, wheat and cotton. From around 1980, it was also applied to grown cereal crops. By killing the plant while leaving the mature grain intact, it speeded up drying prior to harvest – a technique known as pre-harvest desiccation.

Glyphosate's popularity surged again in the 1990s, when Monsanto began marketing soybeans, maize and other crops genetically modified to be resistant to the herbicide, allowing it to be sprayed onto fields as the crops grew – thought not in most of Europe and the UK, where GM crops remain banned.

Today, glyphosate is applied to more than 80 percent of GM crops worldwide, making around half of all sales. It is by a large margin the world's most popular herbicide. More than 700,000 tonnes of active ingredient are sprayed each year onto more than 600 million hectares of fields – an area roughly twice the size of India.

Even in countries where GM crops are not grown, it has become the go-to herbicide. Analysing government data, the Pesticide Action Network estimates that in 2024, some 2200 tonnes were applied to some 2.6 million hectares of mostly arable fields in Britain, an area larger than Wales.

Glyphosate's environmental credentials have been helped by its widespread use among farmers practicing regenerative agriculture. It eliminates weeds while avoiding the soil disturbance caused by ploughing. Helen Metcalfe, an ecologist at Rothamsted Research, a largely government-funded agricultural research agency, says it "currently provides the most effective substitute for the mechanical destruction of weed seedlings that tillage achieves."

Georgie Bray, manager of the RSPB's Hope Farm in Cambridgeshire, which aims to demonstrate methods of nature-friendly farming using regenerative methods, told this year's Oxford Real Farming Conference that glyphosate is vital for her in combating the virulent weed black-grass.

Glyphosate is also seen as a weapon against climate change, since ploughing is a major source of carbon dioxide in the atmosphere, releasing the greenhouse gas at rates of up to 3 tonnes per hectare, though its total contribution to global CO2 emissions is not clear.

Away from farms, many local authorities and other land managers use glyphosate as a cheap and effective way to control weeds in public spaces such as pavements, cemeteries, roadside verges and, most controversially, school yards and playgrounds. Meanwhile, conservationists deploy it widely in the countryside to remove plants often considered "alien" and "invasive", such as Himalayan balsam, giant knotweed, rhododendrons and Japanese knotweed.

With many other competing herbicides, such as paraquat, diquat and glufosinate, banned in the UK and the EU (though not in the US) because they are considered too toxic, glyphosate has often had a clear commercial run for a variety of uses. But recently, its environmental credentials have been increasingly questioned. Sporadic reports of its toxicity have combined with the discovery of traces of glyphosate in our food to raise public concern. More than half of non-organic bread in Britain is reported to contain traces of the chemical. Faced with public hostility, some local authorities have ended its use in public spaces. (A search of the BBC news web site found that almost all references to glyphosate in the past five years have been on this topic.)

These changes in perceptions have come against a backdrop of an increasingly fractious public debate, in which scientific evidence has often become a sideshow, and malign corporate influence is often accused of polluting the discourse.

The Ohio-based Genetic Literacy Project, a web site ostensibly devoted to public education but formerly funded by Monsanto, regularly hosts vitriolic attacks on those who question the safety of glyphosate. One recent post from David Zurak -- whose CV includes public affairs director at controversial corporate reputations consultants Burson-Masteller and work for the European Chemical Industry Council, a trade association -- recently called glyphosate "the poster-boy of hate in the front line in the war against chemicals, conventional farming and capitalism." Castigating "opportunistic activist scientists", he opined that "if you torture the data long enough, it will confess to anything."

Truth to tell, however, there is an underlying point behind such language, says Toby Bruce, professor of insect chemical ecology at Keele University. "Glyphosate has been demonized by pressure groups... regardless of evidence," he says.

Opponents of glyphosate regularly use phrases such as "linked to" and "associated with" as synonyms to suggest causality with cancers and other diseases, when none can be rigorously demonstrated. "Glyphosate is a dangerous chemical which has proven links with leukaemia and other cancers," the Pesticide Action Network's Josie Cohen told *Farmers Weekly* last December. But what constitutes a "proven link"?

And while in Europe opposition to glyphosate has been largely led by left-leaning and green voices, the most vocal opposition in the US centres around the populist right-wing Make America Healthy Again movement, led by supporters of Trump's health secretary and anti-vaxxer Robert F. Kennedy Jr., who, as the *New York Times* has noted, "once served as co-counsel in a lawsuit against Monsanto over exposure to Roundup".

Bad science

Perceptions among both the public and regulators have been strongly influenced by two widely cited – and widely divergent -- reviews of research findings. Both have been

shrouded in controversy over their conclusions and questions about the integrity of their authorship.

The first study, completed in 2000 and widely cited ever since by regulators approving glyphosate's use, gave the chemical and its formulations an almost unqualified clean bill of health. It stated, without qualification, that Roundup "does not result in adverse effects on development, reproduction, or endocrine systems in humans and other mammals" and is "non-carcinogenic". It was, in other words, assuredly safe. Fifteen years on, the study helped the EU to conclude, following a review by the European Food Safety Agency, that glyphosate was "unlikely to pose a cancer risk for man."

But that assurance was thrown into serious doubt last December when, a quarter of a century after its publication, the article was abruptly retracted by *Regulatory Toxicology and Pharmacology*, the journal that first published it. The retraction was a belated recognition of internal Monsanto documents discovered during American litigation proceedings in 2017. The documents showed that parts of the paper were, in the words of a Monsanto memo at the time, "ghost-written" by company scientists who were not listed as co-authors, and that many of the findings relied on unpublished company data.

Another contemporary company memo expressed the hope that the study would become "the reference on Roundup and glyphosate safety." Which it undoubtedly did for many years.

In retracting the paper, journal editor Martin van den Berg, a toxicologist at Utrecht University, said he "had lost confidence in the results and conclusions of this article," because of "serious ethical concerns regarding the independence and accountability of the authors... and the academic integrity of the carcinogenicity studies presented."

A review of the affair by Sasha Kaurov and Naomi Oreskes, a leading Harvard science historian, found that the ghost-written paper was in the top 0.1 percent of cited academic literature on glyphosate. "Corporate authorship shaped two decades of glyphosate safety discourse," they concluded.

Philip Landrigan, an epidemiologist and paediatrician at Boston College who has campaigned against pesticides, agreed, telling the *New York Times* that the retraction was "a seismic, long-awaited correction of the scientific record [that] pulls the veil off decades of industry efforts to create a false narrative that glyphosate is safe... People have developed cancers, and people have died because of this scientific fraud."

But even before the belated retraction, a new appraisal was gaining attention – a 2015 review by the World Health Organization's International Agency for Research on Cancer (IARC). It concluded that, far from being safe, glyphosate was "probably carcinogenic" for humans. Among other things, it reported, based largely on experiments on rats, a

“positive association” between glyphosate and a form of blood cancer called non-Hodgkin lymphoma.

Just as the 2000 study was endlessly cited by those convinced that glyphosate was safe, so the 2015 study has become a go-to source for those convinced of its toxicity. But it too has come under critical scrutiny. Critics say it assessed theoretical hazard rather than real-world risk, an approach that had previously resulted in the IARC giving the same carcinogenic status to red meat and very hot beverages.

And questions have arisen about the authors’ probity and candour. *Reuters* reported that the head of the IARC evaluation group, epidemiologist Aaron Blair, had, prior to the evaluation, been involved in a separate unpublished large-scale study by his employer, the US government’s National Cancer Institute. The study of American agricultural workers and their families had found no association between exposure to glyphosate and non-Hodgkin lymphoma. Blair later agreed under oath that, if those findings had been assessed by the IARC working group, this would have made the “probably carcinogenic” conclusion less likely.

Reuters also discovered that three weeks after its publication, a key instigator of the report, IARC statistician Christopher Portier, had signed up to advise lawyers representing people suing Monsanto in California. Whether or not that represented a conflict of interest, it is clear that the IARC conclusion triggered an upsurge in litigation against Monsanto, and after the 2018 takeover, against Bayer.

The first case was brought by Dewayne “Lee” Johnson, who developed non-Hodgkin lymphoma at the age of 42 after regularly spraying Roundup during his work as a school groundsman. Jurors found that Monsanto had acted with “malice” in not warning him about the risks. Since then, Bayer, while firmly denying blame, has settled a slew of other cases with payouts so far amounting to some $10 billion.

Many would conclude that neither the 2000 nor the 2015 reviews could fully justify their very different conclusions. But while the Monsanto ghost-written study all but shut down research and detailed regulatory scrutiny for many years, the IARC study reignited it -- resulting in a range of findings that, at the least, call the original sanguine ruling of the regulatory agencies into doubt.

Worrying signs

So where does the science stand today? On human health, toxicologists have in the past decade found plausible routes by which glyphosate could deliver damaging outcomes, even at doses currently regarded as safe. These findings have sometimes contradicted past assumptions.

For instance, proponents of glyphosate have long argued that the herbicide is intrinsically safe for humans because it kills weeds by impacting the shikimate pathway,

a metabolic process that manufactures amino acids in plants, fungi and bacteria, but which isn't present in animals. True enough, but the pathway IS present in our gut bacteria, says Michael Antoniou, a molecular geneticist at Kings College London. And gut bacteria matter greatly for our health.

A 2023 *Lancet* article tentatively linked glyphosate to an upsurge in Parkinson's disease - through its potential impacts on gut bacteria, which are thought to influence neurodegenerative conditions. "The evidence is inconclusive," the authors admitted, but suggest "a biologically plausible link" that is "a serious cause for concern". Other recent epidemiological research raises similar concerns. A California study found an increased risk of fatty liver disease and cardiometabolic disorders such as heart attacks, strokes and diabetes among people exposed to glyphosate.

But many studies use animal surrogates, and not all pass statistical muster. Last year, scientists at the Ramazzini Institute in Bologna, Italy, published an investigation into cancer links. It claimed to provide "robust evidence supporting the IARC conclusion", showing "increased incidences of benign and malignant tumours at multiple sites ... at doses that are currently considered safe," according to author Daniele Mandrioli.

But Will Summers, a molecular plant biologist who has investigated the toxicology of glyphosate as part of work on regenerative agriculture at Deep Science Ventures, a group of science entrepreneurs, is not so sure. He says that while the findings are suggestive, the statistical methods were sometimes dubious. So many separate tests were done in the study that the researchers "should adjust for the risk of significant results [arising] purely by chance, but they didn't. There seems to be a combination of both bad statistical practice and confirmation bias going on."

Statisticians have yet to find persuasive and consistent evidence of real-world effects of glyphosate on humans. Too many of the apparent associations could arise without any causal connection. But that doesn't mean the associations ARE caused by chance. At the least, such findings call into question the past bland assertions of an absence of risk. And the very large number of people exposed to some amounts of the herbicide mean that even ultra-low levels of risk could deliver serious numbers of victims.

Summers concludes that: "The way we assess toxicity risks often has limitations. Funding is limited and we miss factors such as the toxicity-enhancing effects of adjuvants [chemicals added to help the herbicide spray and stick better], mixtures with other agrochemicals and low-dose chronic effects caused by exposure through the human lifespan."

Much more research, including large-scale epidemiological studies of humans -- perhaps using the giant UK Biobank, which has biological samples and health data on half a million people -- are needed, he says. Meanwhile, "I do believe there is sufficient

smoke around glyphosate that we should be concerned about the health risks, even if the magnitude remains challenging to judge."

What of threats to nature, ecosystems and biodiversity? Here too the evidence is thin on the ground, fragmented and contested, but worrying because of the sheer scale of glyphosate's use.

The Glyphosate Renewal Group, an industry group lobbying European regulators for the herbicide's use, claims scientific backing for its view that the compound has "a strong safety record", and that banning it would "harm biodiversity". This latter claim is seemingly based on glyphosate's widespread use to get rid of virulent species often regarded as invasive threats to native ecosystems.

Others contest that there can be any overall biodiversity benefit, since the chemical kills many plants and changes soil ecosystems. But both the extent of the impacts, which may be subtle and sub-lethal, and how they compare with other methods of weed management, are less clearly understood.

Some studies have looked specifically at soil ecosystems, including soil bacteria. They suggest glyphosate may reduce beneficial bacteria while increasing pathogenic fungi. One, published this year, warned that glyphosate acts as an antibiotic for soil bacteria, through its impact on the shikimate pathway, and that this could spread to clinical pathogens, potentially helping to generate hospital "superbugs".

While readily binding to soil, glyphosate and its breakdown products do leach into water, where they may cause ecological changes among algae, releasing phosphorus that causes eutrophication, so messing widely with aquatic ecosystems. But, again, detailed findings on real-world effects are lacking.

Precaution or pragmatism?

How should policymakers, farmers and land managers respond to these competing and sometimes contradictory research findings? Should a precautionary approach prevail, or is greater pragmatism required?

Toxicologists, understandably given their discipline, mostly confine themselves to assessing any potential toxic risk from a chemical such as glyphosate. They operate a *de facto* precautionary approach. Any risk is bad. The implied policy default is that risky substances should be banned, or their risks tightly managed.

But in the real world, we run risks all the time. Competing risks need to be compared. One risk should not be allowed to trump another without proper evaluation. In this context, those working on the land may not see a simple choice between using glyphosate and not using glyphosate. Rather, their choice is between using the herbicide and finding an alternative means of weed control. And any alternatives may

also have downsides, whether toxicological, logistical, financial, ecological or even, in the case of ploughing, through contributing to CO2 emissions.

These “real world” dilemmas are not reflected in reductionist toxicology. But some researchers take up the challenge. Few would disagree with Melanie Kah, an environment professor at the University of Auckland, that “there is a scientific consensus that glyphosate is less toxic than many of the other agricultural compounds currently in use.” Many would also agree with her that “phasing it out would result in other herbicides being used instead, which would probably have more impact on human and environmental health.”

That is already happening. Such is the opprobrium -- and litigation -- that has surrounded glyphosate that in some markets it has been replaced in Roundup formulations with likely more toxic alternatives, such as diquat.

But while other chemical herbicides may be more harmful, they are not the only item in the toolbox. Many will agree with Antoniou that “we need to get away from pesticides in farming and move to agroecology.” That involves a more fundamental rethink about how we do farming, embracing diversity of crops and ways of managing weeds, and doing the necessary research to underpin this more diversified approach.

One route is organic farming, which prohibits the use of all chemical herbicides, and sees the plough as vital to return crop residues to the soil, and bury weeds and their seeds. But this puts organic farmers at odds with regenerative farmers, who see ploughing as part of the problem, but as a result are frequently dependent on herbicides to remove weeds. So, can farmers avoid both the plough and the use of glyphosate?

Martin Lines, who farms in Cambridgeshire and is CEO of the Nature Friendly Farming Network, advocates using cover crops that are crushed using crimper rollers. The flattened plants form a mulch on the soil that suppresses weeds while allowing seeds to be drilled.

Alternatively, farmers can plant cereal crops in permanent swards of clover, or adopt relay cropping, in which a second commercial crop is planted into an existing standing crop. An example might be introducing soybeans into a wheat crop. But Lines says such methods may not be foolproof and he does not call for an outright glyphosate ban.

Another approach is to use natural organisms to get rid of weeds. They might be insects that consume the target weeds, or extracts from plants, fungi or other microorganisms that release weed-killing compounds. But in practice, these too often fail to provide the secure and simple solution that farmers can achieve by spraying herbicides.

Summers says the ultimate answer may be bioherbicides of the kind currently being developed using technologies such as Ribonucleic Acid Interference (RNAi). RNA molecules are messengers that play a crucial role in controlling the function of genes.

RNAi-based products can turn off essential genes in chosen weed species, leading to the death of the weed while surrounding species, including crops and wildlife, are left unharmed. This remains research work in progress, however.

End of the road

Even among those who regard glyphosate as essentially benign, there are growing concerns about its future agricultural utility. Any agrochemical encourages the development of resistance among its targets, and the more that is applied the more likely resistance is to develop. That creates a paradox, says Summers. "Glyphosate is probably better than any chemical herbicide that came before in terms of both toxicity and function. But as a result, its use is an order of magnitude more than any other – and this pervasiveness becomes a problem."

Resistance to glyphosate has now been identified in around sixty target species worldwide, most frequently in Italian ryegrass, a widely used cover crop. Weed resistance is, unsurprisingly, most marked in countries such as the US, Argentina and Australia which spray glyphosate liberally onto crops genetically modified to be resistant to it. But increasingly it is showing up in countries that have never done this. UK resistance was first reported in 2025 in Italian ryegrass in Kent, Gloucestershire, North Yorkshire and Essex.

This discovery "serves as a serious warning sign," says Metcalfe at Rothamsted. "When resistance evolves in a key herbicide, the tool can become ineffective." Especially when the immediate response of farmers to a herbicide losing its efficacy is to spray more.

The right response, Metcalfe says, "is reducing overall glyphosate use to essential-use cases" within broader systems for managing weeds. "The priority must be to preserve its long-term efficacy." Otherwise, it may become all but useless.

So how can regulators reduce its use? Top of the list for urgent curtailment in Britain is deploying glyphosate as a pre-harvest desiccant. It is responsible for about a third of all use on cereal crops, most notably in the wetter north of the country. This use was banned in the European Union in 2023. And there is growing pressure for the British government's chemicals regulator the Health and Safety Executive to follow this lead during its current reassessment of the permitted uses for the product.

Farmers and manufacturers have been lobbying heavily – in the latter case through the Glyphosate Renewal Group -- to maintain the existing licence. Until recently, a government post-Brexit drive towards US-style deregulation of the economy seemed likely to support the industry approach. But the mood may be changing.

A wide range of experts favour outlawing pre-harvest desiccation. And the HSE review comes as the UK negotiates with the EU on aligning food product rules to reduce trade barriers on food and agriculture, including pesticides regulation through the Sanitary

and Phytosanitary Agreement. So, it may now be both scientifically and politically attractive for Britain to align with the EU ban.

Lines and his Nature Friendly Farming Network, who opposes an outright ban on glyphosate as impractical, nonetheless says pre-harvest desiccation is “bad practice” and ought to be prohibited. “If it’s being applied days before harvest and then going straight into milling, that’s difficult to justify,” he says. “Glyphosate still has a role, but… there’s a real concern about reliance on a single, cheap product, both in terms of resistance and wider soil health and public trust… Farming systems shouldn’t depend on it.”

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