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Abstract: Urease and nitrification inhibitors for climate and environmental protection: opportunity or risk?

Urease and nitrification inhibitors are increasingly being used in agriculture to reduce fertilization derived ammonia, nitrous oxide emissions and the leaching of nitrate. Their use is expected to become even more important after 2030, when the agricultural sector will be obliged to make a significant contribution to the ambitious European and national climate targets. Our estimates for extensive usage of inhibitors in the EU show that their use could reduce agricultural ammonia emissions by up to nine per cent and greenhouse gas emissions by up to five per cent.

However, the potential risks of large-scale application of inhibitors to human health and the environment have not yet been sufficiently investigated and understood. The specific efficacy of different urease and nitrification inhibitors, for example at different sites or over longer periods of time, has also not yet been sufficiently clarified. In addition, the data on the fate of the substances in the environment is patchy and sometimes contradictory. These uncertainties have so far only been partially taken into account in the legal regulations at EU and national level. This can be seen, for example, by the fact that five of the eleven inhibitor compounds available on the German market would, due to their toxicity, very probably not be approvable under the EU Plant Protection Products Regulation. This points to a regulation gap, as the method of application in the open environment, the quantities used and, in some cases, the target effect are identical for inhibitors and plant protection products. In addition, the inhibitors can be approved for the market via two different and sometimes non-transparent legal regulations. This makes it difficult for the public to understand the risk of using inhibitors.

Large-scale use of inhibitors can therefore by the German Environment Agency (UBA) only be recommended if a standardised European regulation on authorisation ensures that the protection of human health and the environment is ensured in the long run and that the precautionary principle specified in the Treaty on the Functioning of the European Union is thus fulfilled. An obvious solution would be the creation of an EU regulation with an authorisation and approval procedure similar to that of the EU Plant Protection Regulation or the integration of inhibitors into the EU Plant Protection Regulation.

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1 Objective

Nitrous oxide and ammonia are emitted as a consequence of the use of mineral nitrogen fertilisers and organic fertilisers such as liquid manure, solid manure and anaerobic digestates, as well as during the storage of organic fertilisers, in animal houses and from faeces and urine deposited on pasture land (LfU 2018, UBA 2023a). Agriculture currently contributes to 75 per cent of EU-wide and 78 per cent of German nitrous oxide emissions[1] (EEA 2023, UBA 2023b, UBA 2023c) as well as 90 per cent of European and 95 per cent of German ammonia emissions (EEA 2019, UBA 2023a). High nitrate concentrations in ground and surface waters are mainly a result of fertiliser-related, high nitrogen surpluses. Neither the EU nor Germany meet the target of the EU Nitrates Directive (EU Directive 91/676/EEC) to reduce nitrate levels in groundwater to below 50 milligrams per litre.

A significant reduction in nitrous oxide and ammonia emissions, nitrate leaching and nitrogen surpluses is urgently needed in order to achieve European and national climate and environmental targets. This need will become even more pressing by the year 2030 and beyond, when the ambitious long-term European and national environmental and climate protection targets, such as those enshrined in climate protection legislation (EU Regulation 2021/1119, KSG 2019) or in the NEC Directive (reduction of national emissions of transboundary air pollutants, EU Directive 2016/2284), have to be implemented. The use of urease and nitrification inhibitors has the potential to reduce the release of ammonia and nitrous oxide into the atmosphere and nitrate into groundwater and surface water, thereby contributing to the achievement of current and future environmental and climate protection goals. When considering the use of inhibitors in this paper and in the current discussion, the focus is on the reduction of trace gas emissions. The possible reduction of nitrate leaching and a potential increase in nitrogen efficiency are therefore only considered indirectly in relation to these emissions.

To ensure that the use of inhibitors[2] in agriculture can significantly contribute to achieving these targets, the inhibitors would have to be applied together with mineral and organic nitrogen fertilisers to a large part of conventionally[3] farmed agricultural land in the EU and Germany. This would correspond to 45 per cent of the total land surface in Germany (UBA 2023d and UBA 2023e) and to around 35 per cent in the EU (Eurostat 2024). Assuming the minimum quantities prescribed in the German Fertiliser Ordinance (DüVM 2012) are added to mineral fertilisers and that only one active ingredient is added to all relevant fertilizers (no mix of UI or NI active ingredients) either 63,000 tonnes of the nitrification inhibitor DCD (dicyandiamide) or 5,100 tonnes of the nitrification inhibitor DMPP (3,4-dimethylpyrazole phosphate) or 100 tonnes of the urease inhibitor 2-NPT (N-(2- nitrophenyl)phosphoric acid triamide) would have to be applied annually in Germany[4]. In the EU, this would be 123,000 tonnes of the nitrification

[1] For the EU, the greenhouse gas figures for 2020 are given here, for Germany figures from the previous year's estimates for 2022.

[2] Inhibitors can be used in many areas, for example in medicine. In this article, however, the term inhibitor is only used for urease and nitrification inhibitors that are applied together with nitrogen fertilisers.

[3] According to the EU Organic Regulation (EU Regulation 2018/848), the use of chemically synthesised products and substances is strictly limited to cases in which the use of external inputs would contribute to unacceptable environmental impacts. According to paragraph 5 of the Regulation, external inputs are the non-chemical synthetic inputs that are to be used in organic farming. This paragraph could theoretically apply to the use of inhibitors, as the non-use of inhibitors could lead to unacceptable effects on the environment. However, this is currently not the case in practice.

[4] The International Fertilisation Organisation estimates domestic sales of 1,034,000 tonnes of mineral nitrogen for Germany in 2022. The Fertiliser Ordinance (DüMV) specifies minimum levels for almost all nitrification inhibitors in relation to the ammoniacal nitrogen content (ammonium and urea). These minimum contents range from 0.05 to 10 per cent. DCD has a minimum content of 10 per cent and DMPP a minimum content of 0.8 per cent. In the EU, according to the old fertiliser regulation (Regulation (EC) 2003/2003), the minimum application rate for DCD was 2.25 percent. The urease inhibitor 2-NPT is added with a minimum application rate of 0.04 percent of the urea content. The total quantity of sold nitrogen multiplied by the minimum content indicates the minimum quantity of nitrification and urease inhibitors that would be applied if inhibitors were added to the entire ammoniacal

inhibitor DCD, 43,800 tonnes of the nitrification inhibitor DMPP or 1,000 tonnes of the urease inhibitor 2-NPT[5,6].

The release of chemicals into the environment on this scale, whose risks to human health and the environment[7] have not yet been comprehensively analysed and determined, should be particularly well regulated by the legislator. The precautionary principle specified in Article 191 of the Treaty on the Functioning of the European Union (TFEU) also stipulates that a policy or measure may not be implemented if it may cause harm to the general public or the environment, i.e. if there is a potential risk and there is still no scientific consensus regarding that risk (EUR-Lex 2023)[8].

However, not only is there a need to fully understand the effects of the use of inhibitors on health and the environment, but also the efficacy of the inhibitors must be assured. This is the only way to balance the economic costs of use, any unavoidable risk to the environment and human health with the overall benefits of use.

This paper aims to contribute to answering the question of whether inhibitors should be used in agriculture to achieve environmental and climate targets and, if so, under what conditions. To this end, the following decision-relevant points are analysed:

1. What technical potential does the use of inhibitors have for achieving environmental and climate targets? (Chapter 2)
2. How do nitrification and urease inhibitors work? (Chapter 3)
3. What are the open questions on effect sizes? (Chapter 4)
4. Which active ingredients and what quantities of inhibitors are currently used in the EU and Germany? (Chapter 5)
5. What are the legal regulations for market access and to what extent can they effectively limit risks to human health and the environment? (Chapter 6)
6. What is the fate of the inhibitors and their degradation products in soil and water? (Chapter 7)
7. What risks do the use of inhibitors harbour for human health and the environment? (Chapter 8)

Finally, the paper makes recommendations for improving existing legal regulations and closing relevant knowledge gaps (Chapter 9).

nitrogen. This does not include organic fertilisers. An ammonium content of 50% is conservatively assumed for all synthetic fertilisers except urea (100% content) and UAN. For UAN, a urea content of 50% (urease inhibitor) and 75% ammoniacal N (nitrification inhibitor) is assumed.

[5] The International Fertilisation Organisation states sales of 10.58 million tonnes (IFA 2023) for the EU.

[6] These figures are only a rough estimate. On the one hand, it is uncertain whether inhibitors will really be added to all mineral fertilisers in the future. On the other hand, nitrification inhibitors can also be added to organic fertilisers, which we have not taken into account in our estimate.

[7] Here and in the following, we refer to the protection of human health and the risk to the environment. By this we mean abiotic protected goods (soil, water, air/climate) and biotic protected goods (humans, plants, animals, biotopes and biocenoses). This wording is also used in the objective of the REACH Regulation: "is a regulation of the European Union adopted to improve the protection of human health and the environment from the risks that can arise from chemicals" (EC Regulation 1907/2006).

[8] This concept of precaution was concretised in a Commission Communication of 2000 as follows: "Thus, it (the precautionary principle) is applicable in specific cases where scientific evidence is insufficient, inconclusive or unclear, but where there are reasonable grounds for concern, based on a preliminary and objective scientific risk assessment, that the potentially dangerous effects on the environment and human, animal and plant health may be incompatible with the Community's high level of protection" (EU COM 2020).

2 Relevance and technical potential of the use of inhibitors for achieving environmental and climate targets

Numerous scientific publications and agriculture-related statements recommend the use of nitrification and urease inhibitors as a contribution to achieving environmental and climate targets. The sixth assessment report of the Intergovernmental Panel on Climate Change (IPCC), for example, recommends nitrification inhibitors as an additive to fertilisers to reduce nitrous oxide emissions and urease inhibitors as an additive for farm manure, in stables and during storage to reduce ammonia emissions (IPCC 2022). A report published by the EU Commission on the integration of agriculture into European emissions trading lists the use of nitrification inhibitors as an important low-cost measure to reduce greenhouse gases (Trinomics, 2023). The current guideline for the Geneva Convention on long-range transboundary air pollution (CLRTAP) recommends the use of inhibitors to reduce nitrogen emissions (especially ammonia) into the environment (Sutton et al., 2022). Scientists advocate the addition of urease inhibitors to urea and urea-based fertilisers in order to reduce ammonia emissions across the EU and comply with reduction commitments (Hu and Schmidhalter, 2021, 2024) or call for the use of inhibitors as a globally applicable strategy to reduce emissions (Kanter and Searchinger, 2018). In its "Twelve tips for more efficient fertilisation", the Federal Office for Agriculture and Food recommends the use of nitrification inhibitors in liquid manure and mineral fertilisers (Klages et al. 2018). Lam et al. (2022) see fertilisers with added inhibitors as an effective measure to reduce the input of harmful nitrogen surpluses into the environment. The German Academy of Science and Engineering considers the overall effect of nitrification inhibitors on the environment to be fundamentally positive and recommends including nitrification inhibitors in the catalogue of eligible eco-schemes[9] of the Common Agricultural Policy (Acatech 2023). The German Commission on the Future of Agriculture (ZKL) also sees the use of urease and nitrification inhibitors as a way of conserving natural resources in crop cultivation, reducing emissions of ammonia and nitrous oxide, and thus making a significant contribution to "reducing greenhouse gas and nutrient emissions" in agriculture (ZKL 2021). In 2016, Corteva was awarded an environmental prize by the US Environmental Protection Agency for the fact that the use of the nitrification inhibitor sold by the company has led to a reduction in nitrate leaching and atmospheric nitrous oxide emissions in the United States (EPA 2023). In Switzerland, the use of a tested fertiliser product with nitrification inhibitor has been accepted as a compensation mechanism of the Swiss CO_2 Act and has been applied in this way since 2016 (Swiss Ordinance on the Reduction of CO_2 Emissions, Chapter 1, Section 5, First Climate 2024).

In Germany, the use of urease inhibitors in urea fertilisers is already integrated into legislation. Since the beginning of 2020, urease inhibitors must either be added when fertilising with urea or urea fertilisers must be incorporated within four hours after application onto the soil (Section 6 (2), DüV). The German Academy of Science and Engineering recommends extending the current regulations of the German Fertiliser Ordinance on the use of urease inhibitors and also applying them to fertiliser mixtures with a urea content of less than 44% (Acatech 2023).

To be able to assess whether the extensive use of nitrification and urease inhibitors can actually make a significant contribution to achieving environmental and climate protection targets, it is necessary to know their technical reduction potential. In the following, a rough estimate of the technical reduction potential is made on the basis of mitigation potentials from previously published review articles. Aspects of economic efficiency, the range and uncertainty of effectiveness and possible application restrictions in practical implementation have not been

[9] Organic schemes are part of direct payments and aim to improve agriculture's contribution to environmental, nature and climate protection, even when applied for one year.

taken into account. The calculations also did not take into account any indirect mitigation effects resulting from an increase in fertiliser efficiency (increase in yields or reduced fertiliser use for the same yields).

It is not yet clear to what extent the use of inhibitors in the European context can actually lead to reduced fertiliser use (Fan et al. 2022, Lit et al. 2018). The reduction of indirect nitrous oxide emissions both through the reduction of nitrogen deposition through the use of urease inhibitors and through a possible reduction in nitrate leaching through nitrification inhibitors was also not taken into account in this estimate of potential.

According to the EU Fertiliser Products Regulation (EU Regulation 2019/1009), nitrification inhibitors may only be used if the nitrogen fertiliser used has an ammonium or urea content of at least 50 per cent of the mineral nitrogen content[10]. This is the case in Germany and in the EU for almost all fertilisers used in arable farming. However, a stable and applicable inhibitor does not exist for every form of nitrogen fertiliser. While the use of nitrification inhibitors is technically feasible for all mineral fertilisers and liquid manure, nitrification inhibitors are not used for the application of other organic fertilisers, such as solid manure or compost. Therefore, the simplifying assumption was made that nitrification inhibitors are added to mineral and liquid organic fertilisers only. A value of 40 per cent was assumed as the reduction effect for nitrous oxide emissions (see chapter 4 for explanations on the derivation of this value). The calculations of the potential in Germany were based on the amount of nitrogen applied in 2021, 2,367 kilotonnes[11] (Rösemann et al. 2023), and the resulting calculated nitrous oxide emissions of 6.11 million tonnes of CO_2 equivalents[12]. By applying a reduction effect of 40 per cent, this results in a potential emission reduction of 2.44 million tonnes CO_2 equivalents or 4.5 per cent of the German agricultural greenhouse gas emissions.

The calculation of the reduction potential of nitrification inhibitors in the EU and the UK was based on the fertiliser quantities used in 2017[13] and information from the literature on the share of slurry nitrogen (50 per cent) in organic fertiliser nitrogen in the EU (IFA 2023, Köninger et al. 2021, Oenema et al. 2007). The IPCC default emission factor of 0.01 was used as the emission factor (IPCC 2019). For the EU and the UK, this results in potential greenhouse gas savings of 26.9 million tonnes of CO_2 equivalents, which corresponds to 5.2 per cent of total agricultural emissions (EEA 2023).

Urease inhibitors are used to reduce ammonia emissions from the application of urea and urea-containing fertilisers. As described above, this is already enshrined in the German Fertiliser Ordinance, and in practice, urea in Germany is almost unavailable for practical farmers without urease inhibitor (see also chapter 5). Since the introduction of the corresponding regulations, ammonia emissions from the use of mineral nitrogen fertilisers have fallen from 90 kilotonnes in 2017 to 35 kilotonnes in 2021 according to the emissions inventory (Rösemann et al. 2023). This results in a reduction in agricultural ammonia emissions of 9.5 per cent over this period. However, this reduction was not only achieved through the use of urease inhibitors, but also by halving the use of urea.

[10] EU Fertiliser Product Regulation, Part II.

[11] Fertiliser quantity of 1,301 kilotonnes of mineral nitrogen, 767 kilotonnes of nitrogen from liquid manure and 299 kilotonnes of nitrogen from the vegetable portion of fermentation residues.

[12] The nitrous oxide emissions were calculated using the Germany-specific emission factor of 0.0062, which is also used in the National Emissions Inventory (Mathivanan et al. 2021).

[13] Fertiliser quantity of 10,896 kilotonnes of mineral nitrogen and 5,250 kilotonnes of liquid manure nitrogen (50 per cent of the nitrogen produced from organic fertilisers).

In 2017, 1,500 kilotonnes of nitrogen were applied as ammonium nitrate urea solution (AHL) and 2,500 kilotonnes as urea in the EU and the UK. Assuming that the reduction potential of urease inhibitors for ammonia is 60 per cent[14] (see chapter 4 for the derivation of this potential), the theoretical reduction potential in the EU is 325 kilotonnes of ammonia or 8.9 per cent of total ammonia emissions.

[14] The valid EMEP emission factors (European Monitoring and Evaluation Programme; EEA 2013) for the relevant mineral fertilisers and the relevant reference year were used for the calculation.

3 Mode of action of urease and nitrification inhibitors

Both urease and nitrification inhibitors are generally applied to the soil together with the fertilisers. In the case of mineral fertilisers, the inhibitor is usually added to the fertiliser before they are sold. For liquid organic fertilisers, there are formulations of nitrification inhibitors that are added directly to the slurry immediately before application. Separate application of the active ingredient, i.e. the specific inhibitory chemical compound, completely without fertiliser is not permitted in Germany or the EU. Nitrification of the ammonium contained in the fertiliser and the associated nitrous oxide emissions and nitrate leaching (area of application of nitrification inhibitors) take place over several weeks after fertilisation, while ammonia emissions (area of application of urease inhibitors) generally occur within a few days to weeks after fertilisation. Accordingly, nitrification inhibitors must remain in the soil significantly longer than urease inhibitors in order to achieve a relevant effect.

Urease and nitrification inhibitors have fundamentally different modes of action. Soil-borne nitrous oxide emissions occur primarily during the conversion of ammonium to nitrate (nitrification) and the conversion of nitrate to elemental atmospheric nitrogen (denitrification). The use of nitrification inhibitors can slow down these processes by inactivating the enzyme responsible for bacterial ammonia oxidation. The lower nitrification rates lead to lower nitrate concentrations in soil and thus to reduced nitrous oxide emissions from microbial denitrification. This reduces direct and indirect nitrous oxide emissions. By stabilising nitrogen in the ammonium form, nitrification inhibitors can also reduce the discharge of nitrate with leaching water (Figure 1). The reason for this is that ammonium is bound to clay minerals and humus in the soil and is therefore transported in a much smaller degree as nitrate with the seepage water into deeper soil layers towards the groundwater. In addition, the lower nitrate quantities in the soil and the resulting reduction in nitrate leaching reduce the indirect formation of nitrous oxide emissions. As the stabilisation of the ammonium form leads to a longer retention of the fertilised ammonium nitrogen in the uppermost centimetres of the soil, the use of nitrification inhibitors can increase ammonia emissions (see chapter 4).

While the effect of nitrification inhibitors is based on the inhibition of nitrifying soil bacteria, urease inhibitors act indirectly via several biochemical factors. During the conversion of urea to plant-available ammonium by the enzyme urease in soil, the pH value in the vicinity of the fertiliser is increased. The higher pH value leads to a higher gaseous emission of ammonia. The urease inhibitor blocks urease, thereby reducing the increase in pH and thus the release of ammonia from urea derived ammonium (Figure 1). In addition, the slower conversion of urea to ammonium means that less ammonia is emitted because urea has more time to be distributed in the soil and the risk of pH is thereby decreased. Urease inhibitors can reduce ammonia emissions, especially when applied with mineral urea. They are also effective as an additive to urea-containing animal excrements in stables or in the storage of liquid manure, and since autumn 2024 a product has been authorised for practical use[15]. As ammonia emissions lead to increased indirect nitrous oxide emissions via nitrogen deposition, reducing ammonia emissions also reduces nitrous oxide emissions into the atmosphere.

Nitrification and urease inhibitors not only have the potential to reduce emissions, but can also lead to increased fertiliser efficiency, as nitrogen remains available to the plants for a longer period.

[15] https://atmowell.de/en/

Figure 1: Concept of the mode of action of urease and nitrification inhibitors in soil

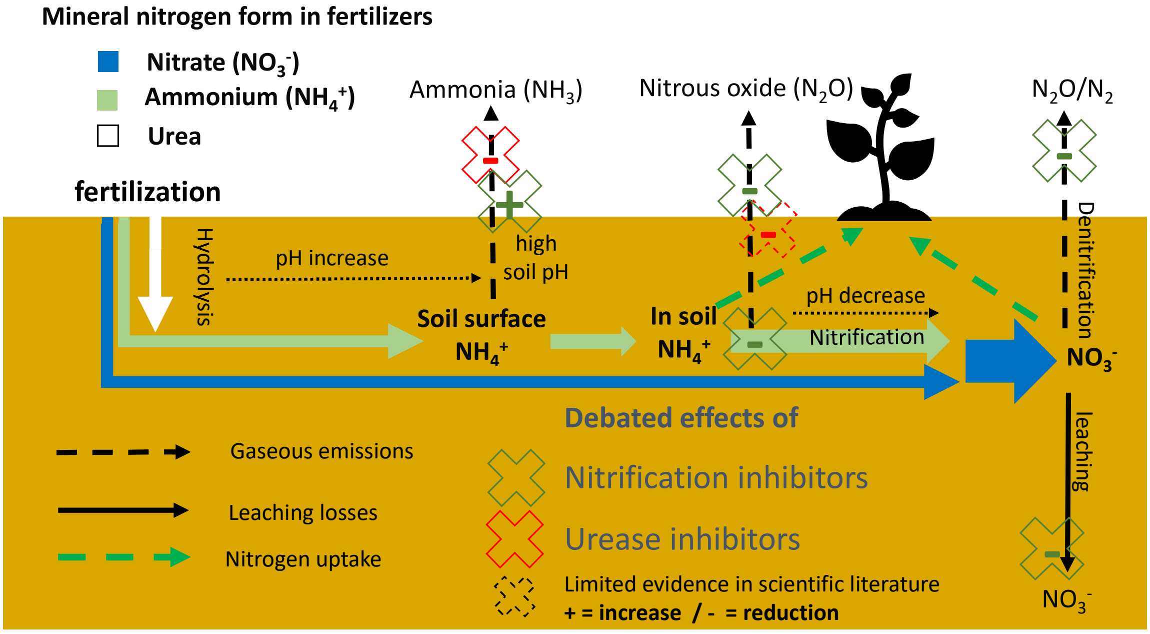

Illustration 1: Concept of the mode of action of urease and nitrification inhibitors in soil. Cross symbols indicate which processes and emissions are influenced or reduced by the inhibitors. Urease inhibitors influence the conversion of urea and downstream processes; nitrification inhibitors influence the conversion of ammonium (NH4+) and downstream processes. The mineral nitrogen form ammonium is also contained in organic fertilisers (e.g. slurry and manure), while urea is also contained in animal excrement in stables and - to a very small extent - in the slurry store. (Source: own illustration)

4 Current state of knowledge on the efficacy of inhibitors

The reduction of ammonia emissions through urease inhibitors has been demonstrated in various studies. The addition of the urease inhibitor NBPT[16] to urea-containing fertilisers reduced ammonia emissions by around 60 per cent on average (Pan et al. 2016, Li et al. 2018, Fan et al. 2022). Across studies, there is a 95 per cent probability that the mean value of the reduction effect lies within a range of 55 to 65 per cent. (Fan et al. 2022).

Review studies based on globally collected data (e.g. Akiyama et al. 2010, Abalos et al. 2014, Ruser et al. 2015, Gilsanz et al. 2016, Li et al. 2018, Kanter and Searchinger 2018) show that fertilisers with added nitrification inhibitors can reduce fertiliser-related nitrous oxide emissions by an average of 40 percent[17] under the conditions of the cited studies (including measurement of emission reduction only in the vegetation period). The use of nitrification inhibitors is described by Grados et al. (2022) as a measure with comparatively safe efficacy for reducing nitrous oxide emissions, even if the range of emission reduction potentials determined in the various studies was very wide. Important here, however, is that the review studies show a mean emission reduction of 35 to 45 percent estimated with a confidence level of 95 percent (95 percent confidence interval). The range of predicted emission reductions lies within 27 to 63 percent with 95 percent probability (Grados et al. 2022) (95 percent prediction interval).

The extent to which plant yields can be increased by the use of inhibitors is still uncertain and depends on the inhibitor type (Fan et al. 2022) and location (yield advantage on sandy soils, Pasda et al 2001). However, studies show that yield increases of around five per cent are possible (Abalos et al. 2014, Yang et al. 2016, Li et al. 2018, Fan et al. 2022). With an increased fertiliser efficiency, fertiliser quantities can be reduced and thus result in lower nitrogen surpluses as well as lower nitrous oxide and ammonia emissions.

In addition, various scientific studies have shown that the use of nitrification inhibitors can also lead to a direct reduction in nitrate leaching (Li et al. 2018). However, the data available from field trials in this review is uncertain and the number of studies and the variation in experimental conditions[18] is lower than that for gaseous losses and yield effects.

However, the scientific studies published to date, are not sufficient for a sound scientific understanding of the efficacy of inhibitors. There are various reasons for this, which we explain below.

Review studies on the effect of nitrification inhibitors on the reduction of nitrous oxide emissions (e.g. Akiyama et al. 2010, Ruser and Schulz 2015) analyse primarily publications that only reported emissions during the vegetation period, i.e. only in a period of around 160 days. However, this measurement period is too short as a significant proportion of annual nitrous oxide emissions is emitted outside the growing season. In Germany, for example, that on average 50 per cent of annual nitrous oxide emmisions are emitted outside the growing season (Flessa et al. 1995, Kaiser and Ruser 2000). A recent study, based on an analysis of globally available data sets, shows that nitrous oxide emission in the non-growing season account for 10-20 per cent of annual emissions depending on the crop grown and climate conditions (Shang et al. 2020). Scientific studies therefore recommend, for the measurement of the efficacy of inhibitors, a measurement period of at least one year (Shang et al. 2020, IPCC 2019, Hutchings et al. 2024). If

[16] We only use the short forms of the active ingredients in the text. In Table 1 all active ingredients are listed with their full chemical names.

[17] This figure is averaged over various inhibitor products and globally available studies.

[18] 80 per cent of the studies were carried out on grassland.

emissions outside the growing season would have been taken into account in these studies, the nitrification inhibitor efficacy would probably be smaller.

The mean effects of emission reduction observed in individual studies cannot simply be transferred to other locations, as the efficacy of urease and nitrification inhibitors depends on soil (texture, carbon content, pH values) and weather conditions (temperature, precipitation) (Li et al. 2018, Fan et al. 2022). A reduction in emissions by the use of an inhibitor in a specific study may therefore be higher or lower at other locations, but also in other years, or may not occur at all. The study results to date are not sufficient to differentiate the effects regionally depending on soil properties, weather conditions, fertiliser form, application technique and inhibitor formulation.

The use of nitrification and urease inhibitors to reduce nitrous oxide emissions is only useful if the reduction in emissions is also stable over several years of application at the same location and with a comparable efficacy. Therefore, it needs to be ensured that an adaptation of soil organisms to the inhibitors' mechanisms of action does not reduce the effectiveness of the active substances through a build up of resistance. However, the durability of the effect over several years has hardly been considered to date (exceptions to this are Dong et al. 2013 and Duff et al. 2022, who did not observe a decreasing effect over time, see also chapter 8 on this).

Studies often only analyse the direct reduction effect of nitrification inhibitors on nitrous oxide emissions. However, some more comprehensive studies have shown that although the use of nitrification inhibitors reduces nitrous oxide emissions, it can, at the same time, also increase ammonia emissions, particularly in the case of slurry or urea fertilisation. This effect is also known as "pollution swapping". As some of the emitted ammonia isconverted into nitrous oxide, this effect can reduce or, in extreme cases, cancel out the positive climate effects (Di et al. 2021, Lam et al. 2017).

In order to correctly determine the effect of nitrification inhibitors on nitrous oxide emissions[19], it is important to also measure emissions from reference areas that have not been fertilised (IPCC 2019, Hutchings et al. 2024). This is the only way to distinguish between nitrous oxide emissions that originate from unfertilised soil in the accounting year and emissions that originate from fertilisation. The subtraction of natural soil emissions from those of fertilised areas has not been carried out in many of the studies used in the meta-analyses, which may lead to an underestimation of the reduction in fertiliser-related emissions due to nitrification inhibitors.

In addition, only the nitrification inhibitors DMPP, DCD, nitrapyrin and the urease inhibitor NBPT have mainly been investigated in the international scientific literature. There are, however, other active substances in use, particularly in Germany, such as the nitrification inhibitors 3-MP, MPA and DMPSA or the urease inhibitors 2-NPT and the mixture NBPT/NPPT. There are far fewer published studies on these (see also Kübeck et al. 2022, as of January 2024, Matse et al 2024)[20].

Another weakness of previously published studies is the fact that they do not take into account dose-response relationships. In most studies, commercial fertiliser products are used in which active ingredient quantities are added in accordance with inhibitor limits prescribed in regulations and the company's own formulation. However, these quantities are not declared on the packaging and are therefore often unknown to the study authors. If active ingredient dosages

[19] This approach is also relevant for urease inhibitors, but is also implemented accordingly in most studies.

[20] Kübeck et al. 2022 provide an overview of relevant active substances and the frequency with which they are analysed in scientific studies in Table 6, p.18.

are changed in the future due to the new EU Fertiliser Regulation (see chapter 6) it is possible that already published evaluations of inhibitors cannot be further applied for efficacy assesments of new formulations.

Conclusion

The scientific literature does currently not suffice to conclusively assess the efficacy of the inhibitors investigated. This applies regardless of the fact that the findings on the individual urease inhibitors are more reliable than those on nitrification inhibitors, and that the target effects of inhibitors (such as the reduction of nitrous oxide emissions and nitrate leaching in the case of nitrification inhibitors) have been investigated to varying degrees. In addition only a few of the inhibitor substances available on the market have been extensively analysed in internationally published studies. But most importantly the above-mentioned scientific evaluation standards have only partially been taken into account in the literature. In particular, the efficacy of inhibitors under different conditions and over longer periods of time has not yet been sufficiently investigated.

Against the background of the interrelationships described, it is clear that it is not appropriate or expedient to identify an average environmental protection efficacy for all active substances and all sites. Therefore, assessments need to be specific for an active substance or a mixture of active substances and also take into account site characteristics such as weather or soil and fertiliser type to which it is added. The efficacy reported in future studies will also be subject to uncertainties. However, by standardising the measurement protocols and increasing the number of active sub-stances tested, the uncertainties in the efficacies of the individual active substances determined, according to their different modes of action, can be tackeled.

5 Active substances and quantities used in the EU and in Germany

Urease and nitrification inhibitors have been applied for several decades as substances that prolong nitrogen availability to plants. Subbarao et al. (2006) list 64 known nitrification inhibitors. However, only some of these substances have been scientifically studied in depth and an even smaller number of those are used on a larger scale. Since the 1990s, the nitrification inhibitor nitrapyrin has been used on a larger scale in the USA and DCD and DMPP in Europe and Asia/Pacific (Subbarao 2006, Singh and Verma 2007, Woodward et al. 2021). Their main purpose is to reduce nitrate leaching and increase fertiliser efficiency. In India, it is a legal requirement that the relatively weak urease inhibitor neem oil is added to urea fertiliser (Ramappa et al. 2022). However, this measure primarily ensures that the urea, which is heavily subsidised by the Indian government, is not used outside the agricultural sector.

According to the German Fertiliser Ordinance (DüMV), eleven inhibitors or inhibitor mixtures are approved; two are urease inhibitors and nine nitrification inhibitors (Table 1). Since 2015, four new active substances have been added. There is no explicit list of individual inhibitors in the EU Fertiliser Regulation, which has been in force since 2022, as active substances must be re-approved here[21].

Table 1: Active substances authorised in Germany according to DüMV (source: DüMV and Beisecker et al. 2023)

	Active ingredient	Short form[22]	Authorisation according to DüMV
	Nitrification inhibitors		
1.	Dicyandiamide	DCD	before 2003
2.	Mixture of dicyandiamide and ammonium thiosulphate	-	2003
3.	Mixture of dicyandiamide and 3-methylpyrazole	DCD, 3-MP	before 2003
4.	Mixture of dicyandiamide and 1H-1,2,4-triazole	DCD, Triazole	2003
5.	3,4-Dimethyl pyrazole phosphate	DMPP	2003
6.	Mixture of 1H-1,2,4-triazole and 3-methylpyrazole	Triazole, 3-MP	2003
7.	N-((3(5)-methyl-1H-pyrazol-1-yl)methyl)acetamide	MPA	2015
8.	Nitrapyrin [2-chloro-6-(trichloromethyl)pyridine]	Nitrapyrin	2015
9.	Isomer mixture of 2-(4,5-dimethyl-1H-pyrazol-1-yl) succinic acid and 2-(3,4-dimethyl-1H-pyrazol-1-yl) succinic acid	DMPSA	2019
	Urease inhibitors		

[21] In contrast to the currently valid EU Regulation No. 2019/1009 , there was a list of authorised substances in EU Regulation EC No. 2003/2003, which was valid until 2022. This did not include the active substances MPA, nitrapyrin and mixtures of DCD and 3-MP or DCD approved under the German Fertiliser Ordinance. The inhibitor NPBT was only explicitly authorised in the EU Regulation and in the DüMV only as a mixture with NPPT.

[22] In the following text, we use these abbreviated forms of the active ingredients to refer to the substances in this table. Triazole, for example, always refers to 1,2,4-triazole.

	Active ingredient	Short form[22]	Authorisation according to DüMV
10.	N-(2-nitrophenyl)phosphoric acid triamide	2-NPT	2008
11.	Mixture of N-butyl thiophosphorus triamide and N-propylthiophosphorus triamide	NBPT, NPPT	2015

An official register for the production quantities or quantities of inhibitors (such as for plant products) does not exist in either Germany or for the EU. Also, the manufacturers themselves do not publish their production quantitiesBut a search revealed that all inhibitors approved in Germany and the EU are currently used in various products and are available on the EU market, albeit to very different extents (Table 4 in chapter 8).

Table 2: Quantities of mineral nitrogen fertilisers with urease (UI) and nitrification inhibitors (NI) sold from 2016 to 2021 in Western Europe (source: IFA (2023)). Double inhibition means that urease and nitrification inhibitors are added to the fertiliser together.

Fertiliser type	2016	2017	2018	2019	2020	2021
	In 1,000 tonnes of nitrogen fertiliser per year					
Nitrogen fertilisers with added UI and double-inhibited fertilisers with UI and NI	482	n.a.	560	548	814	811[23]
Nitrogen fertiliser only with added NI	437	n.a.	469	483	461	484
Total amount of nitrogen fertiliser with added inhibitors	919	n.a.	1.029	1.031	1.275	1.295
	In per cent					
Proportion of fertilisers with added inhibitors in all pure nitrogen fertilisers	9	n.a.	11	11	14	n/a
Percentage of fertilisers with added inhibitors in all fertilisers (pure nitrogen and compound fertilisers)[24]	8	n.a.	9	9	12	n/a

Data from the International Fertiliser Association (IFA) for Western and Central Europe (corresponding to the EU, UK, Switzerland and Balkan countries) shows that in 2020, 14 per cent of straight nitrogen fertilisers sold (without the addition of other nutrients) contained inhibitors. Looking at the entire amount of fertilisers, e.g. straight nitrogen fertilisers and compound fertilisers together, twelve percent of fertilisers had inhibitors added. The total quantity of fertilisers with urease inhibitors added was almost twice as high as the quantity of fertilisers with nitrification inhibitors (see Table 2). The increase in fertilisers with urease inhibitors since 2020 can largely be attributed to the new regulations of the German Fertiliser Ordinance and the requirement to add urea with urease inhibitors (personal communication IFA, see also chapter 2). There are no market figures for organic fertilisers such as liquid manure to which nitrification inhibitors are added.

[23] Of these, 200,000 - 250,000 tonnes per year are double-inhibited.

[24] Complex fertilisers are fertilisers that contain other important plant nutrients in addition to nitrogen, for example phosphorus and potassium.

The use of inhibitors is more widespread in the USA than in Europe. According to estimates, efficiency-enhancing additives such as inhibitors or similar substances were added to almost a quarter of all fertilisers in 2017 (Woodward et al. 2021).

Conclusion

The lack of data on the quantities of active substances produced or used and the corresponding application areas at the EU level and in Germany make it difficult to assess the risk to human health and the environment. Without knowing where and in what quantities these substances are applied, targeted environmental monitoring is not possible. However, it is also not without hurdles for companies to provide information on sales volumes, as it must be ensured that the trade secrets of the manufacturing companies are not jeopardised. But the legally binding provision of fertiliser sales data (albeit without the exact proportion of inhibited fertilisers) to the Federal Statistical Office for the estimation of emissions by the German Federal Thünen Institute shows that it is possible to pass product information when the data are anonymised (Rösemann et al. 2021, p.342). Also for plant protection products, manufacturers pass on product information to the Federal Office of Consumer Protection and Food Safety, which is only published in aggregated and anonymised form.

6 Legal regulations for placing on the market in the EU and in Germany

There is no specific legal framework for approving urease and nitrification inhibitors either at national or EU level, which only regulates inhibitors in a general sense. The inhibitors are regulated as components of mineral fertilisers or additives to organic fertilisers according to general regulations. Manufacturers can decide whether to have their products approved nationally or via the EU Fertiliser Products Regulation as part of a conformity assessment.

Every chemical that is manufactured or imported in the EU in quantities of more than one tonne per year and that is not regulated by any other legislation must be registered at the European Chemicals Agency (ECHA)[25])and evaluated in accordance with the REACH Regulation (EC Regulation 1907/2006)[26]. This also applies to the inhibitors discussed here. In the following, we take a closer look at registration under REACH, the conformity assessment under the EU Fertiliser Products Regulation and the national German authorisation procedure.

Registration under REACH

Manufacturers and importers of chemicals in the EU are required to gather information on the properties of their chemical substances and prepare a chemical safety assessment. The scope of these tests depends on the quantity of the substance that an individual company imports into the European Economic Area or manufactures in the EU.

According to the EU Fertiliser Products Regulation, all inhibitors must at least meet the REACH data requirements for produced or imported quantities in the category 10 to 100 tonnes per year, even if the substance is produced or imported in a lower quantity[27]. Substances in higher tonnage categories must fulfil the testing requirements of the corresponding category. The following tests are required in the categories relevant for the inhibitors:

1. In the quantity category 10-100 tonnes per year, basic information for the assessment of chemical safety is mandatory. This includes the physical and chemical properties of the substance as well as tests that enable an assessment of the harmful effects on human health and the aquatic environment at screening level.
2. In the quantity category 100-1,000 tonnes, simple ecotoxicological tests for the effect on terrestrial soil organisms are also provided for non-critical substances. For substances with critical substance properties[28], at least one of the acute terrestrial tests possible under REACH (on invertebrates or plants) and a microorganism toxicity test must be carried out (Table 5 in the appendix for the mandatory test requirements according to the substance properties).
3. From 1,000 tonnes per year, longer-term tests are required for soil ecosystems (invertebrates and plants). Here, too, the testing requirements depend on the Table 5 (Appendix).

Table 3 shows for each inhibitor in which quantity category it is registered under REACH and which test results for terrestrial organisms are available in the ECHA database. As manufacturers and importers are obliged under the REACH Regulation to submit all information

[25] https://echa.europa.eu/de/about-us

[26] REACH stands for Registration, Evaluation, Authorisation and Restriction of Chemicals.

[27] EU Fertiliser Products Regulation, Annex II, Part II, CMC 1 (1.b) and Preamble (26).

[28] This means that the substances in soil, water and air are probably (very) adsorptive, (very) persistent or toxic to organisms.

available to them on the properties of the substances to ECHA[29], there might be more test results in the database than required. One reason for the existence of these additional test results could be higher testing requirements in national authorisation procedures.

A summary of the information used for the evaluation of certain substance properties is published in the ECHA database[30] (ECHA 2023). However, the extent to which the assessments published in the ECHA database comply with the legal requirements is only controlled on a random basis. In the period from 2009 to 2023, ECHA only carried out a review of the formal data requirements of the REACH annexes for around twenty per cent of the substances submitted for registration (ECHA 2024). Accordingly, a study commissioned by the German Federal Environmental Agency concluded that a quarter of REACH registration dossiers were incomplete and did not comply with the legally required information (Oertel et al. 2020).

For some of the registered substances, there is an obligation to carry out an exposure and risk assessment. This is a further very important assessment step. Here, the risk to human health and the environment resulting from the life cycle of the substances is determined. Specifically, the concentration-dependent toxic effect of the substance is compared with the expected concentration of the substances in soil and water. For human health, the expected concentration is estimated by taking into account the extent to which people come into contact with the substance. For the risk assessment, only substance concentrations resulting from the manufacture or intended use of the substance are taken into account. Neither misuse of the substance nor the waste phase of the substance or a release as a result of incidents is part of the risk assessment.

An obligation for exposure and risk assessment[31] exists for substances that either have a certain critical substance property[32] or are classified in a hazard class according to the Classification and Labelling Regulation CLP (EU Regulation 1272/2008)[33]. However, there is no hazard class in the Classification and Labelling Regulation that reflects a hazard to soil ecosystems, even if the soil is most affected by the application of inhibitors (Karges et al. 2023, p.25). Table 3 provides an overview of the substances for which a risk assessment is available. However, the results of the risk assessment are not public and can therefore not be analysed here.

Table 3: Overview of the REACH tonnage categories, the terrestrial test results available in REACH and the risk assessments available in REACH for the currently authorised inhibitors (source: ECHA 2023)

The study results available in the ECHA database may differ from the obligations arising from the REACH Regulation and the EU Fertiliser Products Regulation. DMPSA and triazole are registered with less than 10 tonnes, but as inhibitors they must at least meet the test requirements of the 10-100 tonne category according to the EU Fertiliser Products Regulation.

[29] REACH Regulation, Article 12, paragraph 1

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

[31] The term "risk" comprises the product of the extent and probability of occurrence of damage. Exposure data form the basis for determining the probability of occurrence." (BfR 2010). This definition therefore differs from the colloquial understanding of risk.

[32] Specifically, the risk assessment is mandatory for PBT/vPvB substances. This means for substances that are persistent (P), bioaccumulative (B), toxic (T), very persistent (vP) or very bioaccumulative (vB).

[33] REACH Regulation, Article 14 (4).

Active ingredient[34]	Quantity registered with ECHA in tonnes	Tests available in the ECHA database for testing the harmfulness to terrestrial organisms	Risk assessment available[35]
DCD	Over 1,000	Acute earthworm test, plant test, soil microorganism toxicity test	No (no critical substance property)
3-MP	100-1,000	Acute earthworm test, plant test, soil microorganism toxicity test	Yes
Triazole	Under 10	Acute and long-term earthworm test, soil microorganism toxicity test	Yes
DMPP	100-1,000	Acute earthworm and plant test	Yes
MPA	100-1,000	Acute and long-term earthworm test, plant test, soil microorganism toxicity test	Yes
Nitrapyrin	100-1,000	Long-term earthworm test, plant test, soil microorganism toxicity test and tests on birds (from publications)	Yes
DMPSA	100-1,000	Two longer-term tests on soil organisms (earthworm and collembolans), soil microorganism toxicity test	Yes
2-NPT	100-1,000	Long-term test on soil organisms (plants), acute earthworm test, soil microorganism toxicity test	Yes
NBPT	over 1,000	Two longer-term tests on soil organisms (invertebrates and plants), soil microorganism toxicity test	Yes
NPPT	100-1,000	Two longer-term tests on soil organisms (invertebrates and plants), soil microorganism toxicity test	Yes

Comparison of REACH registration and authorisation under the Plant Protection Products Regulation

The REACH Regulation does not (or only partially) apply to chemicals that are regulated in other regulations such as the EU Plant Protection Products Regulation (EU Regulation 1107/2009) or the EU Biocides Regulation (EU Regulation 528/2012). Instead of being registered in REACH, these substances must be approved in accordance with the respective EU regulation and comprehensively tested and authorised by the authorities as part of a national authorisation procedure.

The product groups regulated in the Plant Protection Products Regulation are applied on a large scale to the open environment. This is also true for urease and nitrification inhibitors which are applied on large agricultural areas in combination with fertilisers. Nitrification inhibitors also have target effects, similar to plant protection products, as active substances are used to kill

[34] CAS and EC number and link to the ECHA factsheet see Table 6 in the Appendix

[35] Results not publicly accessible.

unwanted organisms, specifically ammonia oxidising prokaryotes (see chapter 8). For this reason, a comparison of the REACH tests required under the EU Fertiliser Products Regulation with the requirements of the EU Plant Protection Products Regulation can help to understand the extent to which the REACH assessment of inhibitors ensures adequate protection of human health and the environment.

According to the EU Plant Protection Products Regulation, and in contrast to REACH, all active substances submitted for approval must fulfil the same data requirements[36], regardless of production or import quantities.

Under the Plant Protection Products Regulation there are high testing requirements on the risk to living organisms. As part of the approval of plant protection products, each active substance must be tested for its effect on bees and arthropods and chronic and acute tests must be carried out on birds. These types of tests are not required under REACH. Under REACH, the mandatory testing of the long-term effects of plant protection product active substances on the representative soil organisms (earthworms, springtails and mites as well as on plants) is only required for substances in the quantity category of 1,000 tonnes or more and for critical substances (Table 5) in the quantity categories 100 - 1,000 tonnes. Karges et al. (2023, p.26) reached the conclusion that particularly the testing requirements in REACH for substances in the 100-1,000 tonne and 10-100 tonne quantity categories are far below the testing requirements of the Plant Protection Products Regulation.

Another important difference between the Plant Protection Products Regulation and the registration under REACH is the risk assessment described above. A risk assessment must always be carried out for plant protection products. Under REACH, an assessment only has to be carried out under certain conditions[37,38]. In addition, the risk assessment of the EU Plant Protection Products Regulation is more meaningful than the risk assessment under REACH. This is due to the fact that the concept for determining the expected concentrations under REACH is not intended to analyse substances that are deliberately released into the environment. For this reason, the data requirements standards for estimating the effects of substances in the Plant Protection Products Regulation are much higher. Furthermore, in REACH the concentration of the substances needed for the risk assessment is calculated under the assumption that the substance is applied at locations that are connected to collection systems for rainwater or wastewater. For this reason, the amount of substances entering the soil is assumed to be lower in the risk assessment according to REACH. The basis for calculating the risk assessment under REACH also assumes that the use of the respective substance in industrial plants is evenly distributed over the entire year. However, this assumption is incorrect for inhibitors, as they are only applied during certain periods of the vegetation period. As plant protection products are not applied evenly over the year, the Plant Protection Products Regulation takes into account targeted application on a few days of the year. This means that in a comparable application case, the expected calculated concentration of a substance would be significantly higher according to the Plant Protection Products Regulation than in the calculation under REACH.

Also the publication processes for the risk assessments between REACH and the EU Plant Protection Regulation differ significantly. Under REACH, neither the estimated quantities of substances released in the environment nor the results of the associated risk assessment are made publicly available. Only the measures required for "safe" use must be communicated along

[36] These tests are required under plant protection legislation in accordance with the data requirements of EU Regulation 283/2013 and 284/2013.

[37] See Article 14 (4) of the REACH Regulation

[38] The assessments for the substances in Table 3 were largely carried out even though there was no corresponding obligation.

the supply chain. In the case of plant protection products, the risk assessment report of the active substances is made available to the public as part of an EU-wide authorisation process and there is the possibilitiy for the public to comment. The final test result is then published. When plant protection prod-ucts are authorised at national level, the entire comprehensive assessment reports are published.

Plant protection active substances - and the products made from them - are generally re-evaluated ten years after the first authorisation and then every 15 years after the renewal of the authorisation. A substance under REACH only needs to be registered once.

Furthermore, the approval of plant protection products is dependent on EU climate zones because climatic conditions influence the effect of the substances. REACH does not provide for this test in any category, although the efficacy of inhibitors depends strongly on location and climate zones.

Under REACH, there are no structured requirements for the testing of degradation products, of chemicals. However, this is important because degradation products of inhibitors can be just as, or even more, problematic than the active substance itself (see chapter 8). The Plant Protection Products Regulation therefore stipulates that the effect of degradation products must also be tested when the formation of the degradation products exceeds a certain threshold[39].

Another decisive difference between the two regulations are the consequences that follow from the evaluation of the substances. In the Plant Protection Products Regulation, a substance with very problematic properties is generally not approved[40] (see also the section on the comparison of active substances under different regulations in this chapter), whereas in REACH the evidence of problematic substance properties established via the regulatory procedure[41] only leads to the exclusion of uses if a responsible authority takes action.

EU Fertiliser Products Regulation

The approval of fertilisers at EU level has since 2019 been regulated in the EU Fertiliser Products Regulation (which came into force in 2022 after a 3-year transitional period). Inhibitors are defined here as fertiliser products, as they can improve the nutrition efficiency of plants. The regulation stipulates that EU fertiliser products must be sufficiently effective and must not pose a risk to human, animal or plant health, safety or the environment[42]. The regulation formulates uniform requirements for the component material categories and product function categories[43] of fertiliser products:

1. The safety requirements include regulatory thresholds for pathogens and harmful heavy metals[44]. In addition, information has to be available for tests carried out in accordance with the REACH Regulation corresponding at least to the quantity category of 10 - 100 tonnes per year (see above).

[39] Degradation products must be examined more closely if one of the following three criteria applies: Degradation product accounts at at least one measurement time point for more than 10 per centof the amount of active substance, degradation products account at two consecutive measurement time points for more or 5 per cent of the amount of active substance, maximum of formation is not yet reached at the end of the study.

[40] Plant Protection Products Ordinance Annex II.

[41] Defined in Article 57, REACH Regulation, e.g. persistent (P), bioaccumulative (B), toxic (T); very persistent (vP) or very bioaccumulative (vB).

[42] EU Fertiliser Products Regulation, Preamble (53).

[43] This means that the substances are categorised according to their starting materials or product properties.

[44] Cadmium, chromium, mercury, nickel, lead and arsenic.

2. The minimum efficacy of the substances is regulated in the quality requirements. In the case of nitrification inhibitors, this means that they must reduce the nitrification process by at least 20 per cent even after a period of 14 days. In the case of urease inhibitors, the rate of urea hydrolysis must be reduced by at least 20 per cent after the same period of time. The efficacy of the inhibitors must be determined in laboratory tests. The standardisation of these laboratory tests (CEN[45] tests) is currently still under development (as of 2024).
3. With regard to labelling requirements, the regulation stipulates the kind of information that must be placed on the packaging.

However, new problems may arise when implementing the minimum efficacy requirement. If the active ingredient dosage of current products is changed to meet the new requirements, the known effects on gaseous emissions and the fertiliser efficacy of these products may not apply to the new products.

The fulfilment of the above mentioned requirements is checked in a so-called conformity assessment. In 2023, there were five conformity assessment bodies in the EU that specifically assessed inhibitors, none of which were in Germany. The implementation of the requirements for the assessment is defined in various modules in the Appendix to the EU Fertiliser Products Regulation[46]. If the corresponding conformity test is successful, the inhibitor can be sold as an EU fertiliser product on the EU internal market and the manufacturer is entitled to affix a CE mark[47] to the product.

However, the modules do not specify exactly how the conformity assessment must be implemented. For example, there are no specifications in the regulation on the "appropriate risk analysis and assessment" prescribed in Module B (technical documentation). It is therefore not clear whether the risk assessment from REACH must be implemented here or whether a risk analysis and assessment is mandatory at all. Neither does the regulation define whether - and if so, how - the conformity assessment body should check whether the classification of the substances in the corresponding hazard classes is correct. Nor does it specify how and whether to check if the data requirements under REACH are fulfilled and if the REACH tests carried out are complete. In these and other cases, the conformity assessment bodies have room to manoeuvre in terms of implementation. This is problematic because, due to the likely differences in the testing process between different assessment bodies, there may be an incentive for manufacturers of inhibitor substances to have the substances assessed at the body and in the country where the requirements and costs for the conformity assessment are particularly low. However, the testing practice of the conformity assessment bodies is still under development, as the EU Fertiliser Product Regulation has only come into force in 2022.

Products are authorised via the conformity assessment. Under the REACH Regulation, however, only the individual substances are tested. This means that the effect of productformulations on human health and the environment, for example in the case of double-inhibited fertilisers, is not examined under REACH. This is problematic because combined active substances can have different and also worse effects than the individual active substances. For this reason, not only the active substance but also the product is tested in the case of plant protection products.

[45] The abbreviation stands for European Committee for Standardisation.

[46] Modules B followed by C and D 1 are relevant for the inhibitors, as they are assigned to the product function category PFC 5 and the component material category CMC 1 (Appendix EU Fertiliser Product Regulation).

[47] With the CE mark, the manufacturer declares that the product has been tested by the manufacturer and that it fulfils all EU-wide requirements for safety, health protection and environmental protection.

German Fertiliser Ordinance

As an alternative to the EU Fertiliser Products Regulation, fertiliser products can also be approved via the German Fertiliser Ordinance (DüMV). Here, not the products are approved, but the individual components of the fertiliser product. Fertilisers with added inhibitors or inhibitor products are automatically approved if they are listed in the ordinance[48] (DüMV, LfU 2023). If a manufacturer wants to bring a product with a new inhibitor active ingredient to the market, an enquiry must be submitted to the Federal Ministry of Food and Agriculture (BMEL 2023b, Bundestag 2017). The ministry asks for advice from the Scientific Advisory Board on Fertilisation Issues for the assessment of this enquiry. The members of the advisory board are interdisciplinary, work on a voluntary basis and are appointed by the ministry (BMEL 2023a). In addition to advising on inhibitors, the Advisory Board also has other tasks, such as preparing statements on regulatory projects relating to fertiliser law at national and European levels. If the active substance is recommended for inclusion in the German Fertiliser Ordinance by the Advisory Board and the ministry agrees, the ordinance is amended accordingly.

The national Fertiliser Ordinance also stipulates that approved fertilisers "shall not present a risk to human, animals or plant health or the environment"[49]. The basis for assessing the hygienic, toxicological and ecotoxicological safety of the substances is the manufacturer's data submitted to the Advisory Board in accordance with REACH registration. However, the minimum requirements for REACH testing that apply under the EU Fertiliser Regulation (see above) do not apply to authorisation at the national level. If, in the view of the Advisory Board, the review of the manufacturer's data reveals gaps in the assessment that are relevant to the approval, the applicants are requested to submit further information.

Environmental impacts have to be systematically considered in the German fertiliser ordinance assessment since 2008 (Beisecker et al. 2023). This means that inhibitors that were included in the German Fertiliser Ordinance before this date can be placed on the market even if they would not be approved under the current regulations (see also Beisecker et al. 2023). This concerns six of the nine nitrification inhibitors approved under the German Fertiliser Ordinance (Table 1). It is also problematic that the substances in the German Fertiliser Ordinance are approved without a timely limit. This is in contrast to the authorisation practice for pesticide active substances. Here, the authorisation for each active substance must be renewed regularly, taking into account the current state of science and technology.

As the advisory board has requested tests in addition to the REACH registration requirements in the past, it can be assumed that the tests are more detailed. Nevertheless, the list of inhibitor substances approved in Germany includes three active substances and one substance mixture that are not included in the list of EU Regulation EC No. 2003/2003, which were valid until 2022. The reason for this is possibly that these substances were only intended for the German market.

In any case, it can be criticised that the tests required by the advisory board to ensure the safety of environments and ecosystems are not published and are not standardised. (Karges et al. 2023, p. 21). This means that it is not possible for the public to understand which criteria were used for testing.

[48] The fertiliser type must be listed in Annex 1, Section 1 and the inhibitor (application aid) in Annex 2, Table 2 of the DüMV.

[49] Paragraph 3 Fertiliser Ordinance.

Comparison of active ingredients under different regulations

Some of the substances that are approved as inhibitors in the EU would very probably not be approved under the EU Plant Protection Products Regulation. This applies to the substances triazole, 2-NPT, MPA and 3-MP[50] . According to the CLP Regulation (EU Regulation 1272/2008), these active substances are classified as probably harmful to fertility and the unborn child (toxic for reproduction, category 1B). They would therefore not fulfil the criteria of the EU Plant Protection Products Regulation, which states that "an active substance ... shall only be approved if it ... is not or is not to be classified as toxic for reproduction, category 1A or 1B"[51]. The regulation does allow for exemptions if the "exposure of humans to this active substance ... is negligible under realistic conditions of use, i.e. the product is used in closed systems or under other conditions where contact with humans is excluded ..."[52]. However, this exemption would not apply to the large-scale application of inhibitors at field scales. In addition, the exemption in the EU Plant Protection Products Regulation is very strictly applied. An exemption would still be possible if the substance is "necessary to combat a serious danger to plant health which cannot be averted by other available means"[53]. Here too, it is clear that the criterion would not be met by certain inhibitor substances.

It can also be assumed that the nitrification inhibitor nitrapyrin would not be authorised under the current Plant Protection Products Regulation. Nitrapyrin works simultaneously as a plant protection product and nitrification inhibitor, but is currently not authorised as a plant protection product in the EU (EU-KOM 2023). An indication that nitrapyrin would not be approved is the fact that prior to the EU-wide harmonisation of the approval of plant protection product active substances, nitrapyrin was actively banned as a plant protection product in Austria in the "Legal regulation for the prohibition of certain hazardous plant protection products" (RIS 1992). The basis for this ban was paragraph 14 of the Austrian Federal Chemicals Act, which regulates bans and restrictions on chemicals where this is necessary to prevent risks to human life or health or to the environment (Austrian Chemicals Act 1987).

The nitrification inhibitor triazole is also an example of a substance that is subject to differing regulatory requirements, although the applications are comparable in terms of their impact on the environment. Triazole is not only an active substance, it is also formed during the degradation of various plant protection products from the azole fungicide group. For plant protection products containing triazole-forming azole fungicides, groundwater monitoring is required in Germany for limited periods of time. This is based on the regulations in the Plant Protection Products Regulation, which demands the clarification of risks in "post-approval-monitoring" (König et al., 2020; Banning et al. 2022). Furthermore, the Drinking Water Ordinance[54] specifies threshold values of 0.1 micrograms per litre for pesticides and toxicologically relevant metabolites (individual substance) and 0.5 micrograms per litre for the sum of the individual pesticides detected and quantified in the corresponding analysis. That threshold values are not exceeded lies in the responsibility of the approval process of the Plant Protection Products Regulation. In the case of triazole, the manufacturers of the corresponding plant protection products are obliged to measure triazole in the groundwater as part of a monitoring programme under realistic application conditions (e.g. crop and spraying sequences of various azole fungicides). The goal of the monitoring obligation is to rule out any risk from the

[50] Authorised as a mixture in the German DüMV.

[51] EC Regulation 1107/2009, Annex II, 3.6.4.

[52] EC Regulation 1107/2009, Annex II, 3.6.4.

[53] EC Regulation 1107/2009, Article 4(7).

[54] Ordinance on the Quality of Water for Human Consumption (Drinking Water Ordinance of 20 June 2023 (Federal Law Gazette 2023 I No. 159)

entry of the degradation product triazole into the groundwater. There are no such requirements for fertilisers containing triazole as a nitrification inhibitor. However, internal calculations indicate that the potentially realistic application quantities of the use of triazole as a nitrification inhibitor exceed the formation potential of triazole from plant protection products.

Labelling of the quantities added to the product

Both the EU Fertiliser Products Regulation and the German Fertiliser Ordinance stipulate that the active ingredients of the product must be indicated on the product packaging. However, there is no obligation for manufacturers to indicate the quantities of the active substances used or the upper or lower limits of the active substances. For the German approval regulation, the minimum amount of nitrification inhibitors used in a fertiliszer product can be derived from the requirements of the German ordinance, as this stipulates a minimum content (in relation to the fertiliser quantity). For urease inhibitors, the German Fertiliser Ordinance specifies ranges with minimum and maximum contents. However, the EU Fertiliser Products Regulation does not provide for such specifications. The lack of mandatory labelling makes environmental monitoring more difficult, as it is not possible to estimate the actual quantities of active substances used in a specific product and therefore its overall application amount. However, it is also difficult for users to assess the effect of the product, especially if the composition of a product changes. Additionally, due to the instability of some active ingredients, it is not possible to state the exact content of the inhibitor in the product. In principle, however, the amount of active ingredient added during the production process could be indicated on the packaging.

It is also problematic that German legislation allows manufacturers to change the active ingredient and substance quantities of a product while retaining the name of the product. This makes it difficult to assess the environmental risks of the product and creates a lack of transparency and uncertainty for consumers. In the context of the INHIBIT research project, such an approach was noted for several products (Kübeck et al. 2022). This problem does not exist under the EU Fertiliser Products Regulation, as not substances but rather fertiliser products are approved here.

Information for the public

As described under 6.a, importers and manufacturers must submit study summaries[55] when registering under REACH. These are publicly available on the ECHA website (ECHA 2023), but the test reports on which the summaries are based are not. The data required from the conformity assessment bodies under the EU Fertiliser Regulation, the results of the assessments and the type of tests required under the German approval procedure are also not publicly available.

The given reason for not publishing the evaluation data is product protection. Internal company information about the products and their composition could be made public from the reports and thus reach competitors. However, it would be helpful for the evaluation of individual active substances if information on the evaluation of the substances were made available. This would eliminate uncertainties in the evaluation of active substances and avoid duplication of testing. European case law (e.g. European Court of Justice 2016) and national case law (VG Köln, 13.07.2023 - 13 K 5068/18) on the broad interpretation of the undefined legal term "information on emissions into the environment" within the meaning of the Environmental

[55] In English study summary.

Information Regulation (Regulation (EC) 1367/2006), the Environmental Information Directive (Directive 2003/4/EC) and the Environmental Information Act (UIG) has established for plant protection and human medicinal products that not only the study summaries, but also the complete study reports must be made available to any person upon request, even if this would compromise the manufacturer's trade and business secrets. This assessment of the legal situation should also apply to inhibitors that are deliberately and intentionally released into the environment during fertilisation.

In addition to information on the evaluation of active substances, it is also relevant for the public where and to what extent active substances are applied. In Germany, users must document their pesticide applications, but there is no public register of these applications (Umweltinstitut München 2022). In Denmark, Lithuania, Spain and Croatia, such a digital register is already kept (Wissenschaftlicher Dienst des Bundestages 2021). In order to be able to scientifically analyse the environmental impact of the large-scale use of inhibitors, it would be useful if users were obliged to document their use of inhibitors in a public register.

Parallel legal regulations

If a manufacturer or importer decides to have their inhibitor-product approved via a national procedure, they have the possibility to sell it throughout the EU on the basis of the EU regulations on the mutual recognition of goods (EU Regulation 2019/515)[56]. As the testing standards and approval requirements differ in the national regulations as well as between national and EU-regulations, there is a risk that manufacturers will choose the national procedure with the lowest testing requirements. On the other hand, the various approval options for inhibitor products (both EU and national) lead also to intransparency for the users. Beissecker et al. (2023) therefore concluded as well that the parallel regulations lead to a "lack of transparency of the fertiliser products and active substances available and used on the market".

Examination of effectiveness in the context of legal obligations

In the future, inhibitors could play an important role for farmers in realising farm-specific environmental goals. The use of nitrification inhibitors could, for example, reduce the need for farms to purchase emission-certificates as part of a possible future European agricultural emissions trading scheme or, in the case of a climate tax on agricultural emissions, reduce costs. In such a case, however, the legislator must ensure that the effect of the inhibitors also fulfils the promised reduction in situ so that environmental and climate targets are actually achieved. Currently, the efficacy is not guaranteed as the current authorisation procedures do not aim for a specific reduction effect on gaseous losses or leachate discharges in their regulatory focus. If, in future, inhibitors are used to implement legal requirements, official certification standards must be established to guarantee that the promised reduction performance is actually realised. These standards could, for example, be analogous to the standards of the EU framework for the certification of carbon removal (European Council 2024).

[56] However, there are exceptions here. In France, only inhibitors that are regulated by national or EU regulations can be placed on the market.

Conclusions

The legal regulations for bringing nitrification and urease inhibitors to the market are inconsistent and considered inadequate by the authors. Adequate protection of human health and the environment as well as the compliance with the EU precautionary principle are currently not ensured.

The reasons for this are:

1. **Deficits in the information requirements:**

The information on environmental behaviour and ecotoxicology of inhibitors required by the EU Fertiliser Regulation does not allow a sufficient assessment of the risks to human health and the environment. Special attention must here be given to new active substances that are initially only manufactured or imported in small quantities and for which no substance properties are yet known. Under REACH, these fall into the category with the lowest testing requirements.

Information that must be made available by the inhibitor manufacturers under the German Fertiliser Ordinance as a basis for approval is generally more comprehensive. However, the assessment of the substances is not standardised and neither the test requirements nor the results are publicly accessible.

2. **Deficits in the approval regulations:**

There are currently regulatory gaps in the approval procedures for inhibitors at EU and national level. Substances that are classified as hazardous to human health and the environment under the CLP Regulation which would not be approved under the Plant Protection Products Regulation are approved as inhibitors. The EU Fertiliser Products Regulation contradicts its own declared aim as the preamble states that the safety of the intended uses of the fertiliser products should be demonstrated in a comparable manner to that specified in the Plant Protection Products Regulation[57]. The ECHA also considers the EU Fertiliser Products Regulation to be insufficient to address the risks of using inhibitors on humans and the environment. Specifically, they state in a document on the assessment of regulatory requirements that "the EU Regulation does not contain a paragraph that prevents substances that are toxic for reproduction, endocrine disruptors, persistent or highly mobile from being used in fertilisers" (ECHA 2021).

[57] "Where an EU fertilising product contains a substance or mixture within the meaning of Regulation (EC) No 1907/2006, the safety of its constituent substances for the intended use should be established through regis-tration pursuant to that Regulation. The information requirements should ensure that the safety of the intend-ed use of the EU fertilising product is demonstrated in a manner comparable to that achieved through other regulatory regimes for products intended for use on arable soil or crops, notably Member States' national fertiliser legislation and Regulation (EC) No 1107/2009 (Plant Protection Products Regulations)." (EU Fertilising Products Regulation, preamble).

7 Mobility and persistence in air, surface water and groundwater

When nitrification and urease inhibitors are applied via fertilisers to the soil, there is a possibility that inhibitors and their degradation products may enter surface waters (e.g. through water and wind erosion or dust drift) and groundwater. Besides, they may remain in the soil longer than their intended lifetime. In order to be effective, nitrification inhibitors need to be stable in their active form in the soil for several weeks, i.e. they must be persistent[58]. However, if the substances are highly persistent, the residence time in soil can increase and with it the risk of active substances entering ground- or surface water. This risk is further increased by low sorption, i.e. low attachment of the substances to the soil. Marsden et al. (2016) showed through small-scale laboratory translocation experiments that the nitrification inhibitors DCD and DMPP have the ability to reach deeper soil layers and may thus potentially reach groundwater. As microbial activity in saturated groundwater is significantly lower than in topsoil, inhibitors will presumably degrade there very slowly or not at all[59]. It cannot be ruled out that nitrification inhibitors will remain in groundwater for longer time periods, even if there are currently no published studies on this.

Very volatile substances can also enrich in the air as pollutants. Nitrapyrin, for example, must be incorporated into the soil or injected due to its volatility (Flessa et al. 2014; Trenkel, 2010; Scheurer et al. 2014). Accordingly, in an Austrian study that aimed to measure air pollutants, nitrapyrin was one of the most frequently found substances in the air (Zaller et al. 2022).

Little is known about the resulting degradation products of nitrification inhibitors. Redeman et al. (1964) showed that nitrapyrin is degraded in the soil to 6-chloropicolinic acid (6-CPA). This degradation product is more water-soluble than nitrapyrin (Woodward et al. 2019) and significantly more mobile than nitrapyrin in both mineral and organic soils (US EPA 2005). An increased leaching potential of 6-CPA from soils must therefore be expected. The nitrification inhibitor MPA forms the degradation product 3-MP during degradation processes in the soil (ECHA, 2020), which also acts as a nitrification inhibitor.

Urease inhibitors are intended to work directly after application. For this reason, a low stability of the substances in the soil for only a few days is sufficient and the risk of the urease inhibitors being transferred to groundwater and surface water is lower in comparison to nitrification inhibitors. However, it is unclear whether all urease inhibitors decompose quickly enough to rule out any groundwater hazard. For the urease inhibitor NBPT, Peters and Thiele-Bruhn (2022) showed that it converts to various substances in the soil after three days, which were no longer detectable after one week. On the other hand, half-lives between 26 and 30 days were determined for NBPT in soil in standardised degradation tests for REACH registration (ECHA 2023). One reason for the different results could be that the rate of degradation in soil depends on weather conditions (temperature and soil moisture) and soil properties. Reliable statements on the degradation behaviour of the inhibitors and their degradation products therefore require tests on soils with different soil properties and under standardised temperature and moisture conditions.

[58] Persistence in the sense of this paper is not identical to the persistence criterion according to the REACH Regulation (EC Regulation 1907/2006). In our paper we define as persistent if a substance is not degraded by UV radiation or by reaction with water and is also not or only very slowly degraded by microorganisms. The degradation rate of active substances can vary greatly in the different media of water and soil. The different environmental conditions such as temperature, the presence or absence of oxygen or the composition of the microbial community also play a decisive role.

[59] However, chemical degradation by hydrolysis is still possible. This is dependent on the pH value.

Surface waters

Woodward et al. (2016) have shown that surface run-off caused by rain after the application of nitrapyrin-containing fertilisers led to increased concentrations of nitrapyrin in rivers. In another study, this was also observed for 6-CPA, the degradation product of nitrapyrin, although the concentrations were significantly lower than those of nitrapyrin (Woodward et al. 2019). In Germany, Scheurer et al. (2016) detected triazole and DCD in surface waters, with DCD being found in almost all water samples. However, other investigated inhibitors (3-MP, DMPP[60] , NBPT and 2-NPT) were not found in this study. An investigation by the Lower Saxony State Agency for Water Management, Coastal Protection and Nature Conservation revealed that DCD and triazole already occur extensively in surface waters in Lower Saxony (Schaffer and Schmid 2019). As the inhibitors DCD and triazole also have numerous applications in industry and pharmacy, there is also the possibility that they have entered the water bodies from industrial emissions and wastewater treatment plants. Triazole is also a degradation product of some fungicides that are frequently used in agriculture (Kübeck et al. 2022). DCD is formed in the soil during the degradation of calcium cyanamide, which is used as a fertiliser in agriculture (SCHER 2016).

In laboratory tests with various nitrification inhibitors (triazole, 3-MP, DCD and DMPP[60]) and urease inhibitors (NBPT, 2-NPT) in surface water, all the inhibitors tested for (except NBPT) proved to be persistent over the five-day test period (Zeeshan et al. 2023). Even if no statement can be made about a longer period on the basis of these tests, it can be assumed that the probability of a high degradation rate is rather low. The REACH registration data for the substances mentioned by Zeeshan et al. (2023) attest that the substances are "not readily biodegradable". According to the new criteria of the CLP Regulation, DCD would even be "very persistent" (EU Regulation 1272/2008, Annex I, 4.4.2.1 and Table 4). The aforementioned nitrification inhibitor nitrapyrin was also found to be persistent in rivers during a study period of five weeks (Woodward et al. 2016). In REACH, the half-life of nitrapyrin in freshwater sediments is even estimated at 2.7 years (ECHA 2020). Overall, there are hardly any studies that systematically investigate the degradation rate of inhibitors in surface waters, especially over a longer period of several weeks.

Groundwater and bank filtrate

There are currently only few studies on the occurrence of inhibitors in groundwater (Kübeck et al. 2022). However, Scheurer et al. (2014) reported findings of triazole and DCD in 2.5 per cent of groundwater samples in a monitoring study in Southwestern Germany, whereby an agricultural influence on the monitoring sites could be largely ruled out. In Denmark, triazole was increasingly found in the monitoring sites that were part of a groundwater monitoring programme (GEUS 2019). Teuner et al. (2019) assumed that the limit value for triazole of 0.1 micrograms per litre in groundwater [as required by the European Ordinance on Plant Protection Product] could be exceeded, particularly in agricultural catchment areas, due to the different entry paths of triazole (e.g. from forest soils, agriculture, industry, pharmaceuticals).

In another publication, Scheurer et al. (2016) also detected triazole in the bank filtrate[61] of the Rhine. As approximately the same concentrations of triazole were found in the bank filtrate and in the river (Scheurer et al. 2016), it can be concluded that no attenuation effect was achieved

[60] In this case, the analyte 3,4-dimethylpyrazole (DMP), which is the active component of DMPP, was actually detected.

[61] Bank filtrate refers to water from surface waters that penetrates into groundwater close to the banks and is extracted after underground passage.

during bank passage. It can therefore be concluded that triazole behaves persistently under these conditions and is highly mobile.

The fate of triazole, 3-MP, DCD, DMPP[60], NBPT and 2-NPT during bank filtration in sandy subsurface was investigated in semi-technial scale (i.e. under near-natural conditions). It was found that sorption played no role for the substances analysed and therefore did not contribute to the removal of the substances from water. After a flow distance of 1.5 metres and a residence time of around five days, the substance concentration was reduced by around 50 percent for triazole and DCD due to degradation (Zeeshan et al. 2023). For 3-MP, DMPP and 2-NPT, however, the elimination was lower (approx. 30 per cent for 3-MP and approx. 20 per cent for DMPP[60] and 2-NPT), which indicates poor degradability of the substances under these environmental conditions. NBPT, on the other hand, was almost completely eliminated. These non-sorptive substances are therefore considered highly mobile under these conditions, which is also consistent with the test results of REACH (Table 4). As the degradation of the respective active substances is usually particularly high at the beginning of a natural flow path, it must be assumed that the degradation rate per metre for longer flow paths is lower than in the first metre and therefore lower than in the described experiment.

Conclusions

The results presented here show that some of the inhibitors are problematic due to their persistence and mobility, as these properties can lead to distribution in the water cycle and possibly also to accumulation in it (e.g. 3-MP, DMPP, 2-NPT, nitrapyrin). To date, only few scientific studies have been published on the fate of inhibitors in water and soil. In particular, there is a lack of studies on the fate in various environmental media, taking into account different environmental conditions. Publicly available data on the fate of inhibitors are patchy and sometimes contradictory (Kübeck et al. 2022). In addition, little is known about the formation and fate of degradation products. This means there is no meaningful basis for both a comprehensive assessment of the risks to the environment and for risk assessment with regard to the protection of drinking water resources.

8 Risks to human health and the environment

The following chapter provides an overview of the findings of relevant scientific studies and the results of the tests available in the ECHA database on the question of whether the use of inhibitors is problematic for the environment and human health.

Soil organisms

Most nitrification inhibitors act by blocking enzymes in the respiration of ammonium-oxidising bacteria (Subbarao 2006). This means that microorganisms that are affected can no longer generate energy and therefore cease their activity. Inactive bacteria are a readily available source of carbon for other organisms. In other words, they will be “eaten” by other organisms. While most inhibitors will not kill ammonium-oxidising bacteria directly, the inactivation results in the degradation of parts of the population over the intended effective period. According to several studies, the effect of nitrapyrin is based on its toxicity to soil organisms (e.g. Scheurer et al. 2014, Woodward et al. 2016), whereby enzyme inhibition comparable to other nitrification inhibitors is also described in some cases (Woodward et al. 2021).

Both the killing and blocking of relevant bacteria by nitrification inhibitors can lead to a change in the composition of the microbial community (e.g. Nguyen 2017; Luchibia 2020; Corrochano-Monsalve 2021; Schmidt 2022). Corrochano-Monsalve et al. (2021) and Luchibia et al. (2020) have shown that the application of DMPP and DMPSA changes the bacterial diversity in the soil and that bacteria that were not part of target organisms were also affected by nitrification inhibitors. Tao et al. (2021) also demonstrated similar effects for nitrapyrin and NBPT. Schmidt et al. 2022 found "widespread effects of nitrapyrin on soil and wheat rhizosphere microbial communities across different sampling dates”. The observed effects of the inhibitors on the soil microbiome depend strongly on soil properties such as organic matter content, soil moisture, pH value and observation period. Some of the studies lack fertilizer-free controls. Therefore, the results of the studies are not generally transferable. It is important to note that fertilisation without added inhibitors also has a significant effect on the composition of the soil microbiome. In this context, studies show that nitrogen fertilisation using urea or ammonium fertilisers leads to a strong increase in nitrifying bacteria, including a shift in the microbial community from ammonia oxidizing archea to bacteria and that inhibitors can reduce this effect (Luchibia 2020; Corrochano-Monsalve 2021; Tao 2021). However, repeated application of inhibitors to the soil has been shown to reduce microbial diversity (Corrochano-Monsalve 2021). These opposing findings make it difficult to assess the change in the soil microbiome caused by the application of inhibitors.

In addition to studies that show significant effects of the use of inhibitors on soil organisms, there are also publications that demonstrate no or only minor effects on the occurrence of soil organisms (Kong et al. 2016; Callaghan et al. 2010; Dong 2021, Fan et al. 2023). The interpretation of the long-term impact and potential harmfulness of the measured effects on non-target organisms is the subject of controversial scientific debate. Knowledge gaps exist even in long-term studies with multiple fertiliser/inhibitor applications and correctly conducted controls.

When inhibitors are used several times a year and over several years at the same location, there is also a risk that microorganisms will develop resistance to the active substances and that these will subsequently be less effective or no longer effective at all. The development of resistance to certain active substances after frequent use is also known, for example, in connection with the use of plant protection products or antibiotics in agriculture. In the case of inhibitors, however, this development of resistance has not yet been proven (Dong et al. 2013; Duff et al. 2022).

As both the fertility of soils and their function as a filter to protect groundwater are based on a healthy microbial community, interventions in the soil microbiome can also affect these functions, for example because certain environmental chemicals can no longer be degraded.

The majority of existing studies on effects onto the microbial community used the inhibitors DCD, DMPP, DMPSA and nitrapyrin. This means that no statement can be made about other frequently used inhibitors due to a lack of scientific publications. The existing studies are also individual publications; a comprehensive review on the matter does not exist (as of 2024).

Investigations of the effect of various inhibitors on other soil organisms such as springtails, mites, worms, arthropods or smaller vertebrates have hardly been addressed in scientific studies to date. An exception is the publication by Kong et al. (2016), who investigated the effect of DMPP on earthworms and found no effects. However, ecotoxicity tests with earthworms are available as part of the REACH registrations (ECHA 2023). Nitrapyrin and MPA have long-term effects on earthworms and NBPT/NPPT and 3-MP are moderately toxic to earthworms. DCD and nitrapyrin have a long-term effect on soil organisms (see also Table 4).

Aquatic organisms and plants

For some of the most frequently used nitrification inhibitors, scientific studies exist that go beyond the tests carried out using standard test systems in the ECHA database. These studies show that the substances tested can have a harmful effect on animals and plants. Kösler et al. (2021) conclude that the fertiliser products Piadin and Vizura containing the inhibitors 3-MP and DMPP have ecotoxicological effects on the humpback duckweed (*Lemna gibba*) and the Red List species corn cockle (*Agrostemma githago*). However, in the study on the effect of Vizura, higher quantities of the inhibitor were used than recommended by the manufacturerand in standard practice (Pasda and Schmid 2020). Salis et al. (2019) investigated the effects of the inhibitor DCD on river ecosystems in two experiments and came to the conclusion that it has negative effects on algal communities, especially if the algae are already exposed to other stressors. Phytotoxic effects of DCD on clover were demonstrated in a study by Macadam et al. (2003). Several studies show that nitrapyrin exhibits phytotoxicity, which manifests itself, for example, in reduced root length or reduced dry weight (Scheurer et al. 2014).

Based on the results of the tests carried out for registration under REACH, almost all inhibitors are assessed as either non-toxic or moderately toxic (DMPP, DMPSA) to aquatic organisms. Exceptions are nitrapyrin and 2-NPT, which are classified as toxic to aquatic organisms with long lasting effects under the CLP Regulation (Table 4). Some of the active substances are classified as moderately toxic to plants, only DCD is toxic with long term effects.

Human health

The question of the harmfulness of inhibitors to human health was first raised when the nitrification inhibitor DCD was found in imported dairy products in China in 2013. The inhibitor probably ended up in the milk powder because large quantities of DCD were sprayed directly onto pastureland in New Zealand with the aim of reducing nitrate leaching and nitrous oxide emissions (Byrne et al. 2020). Even though this type of application of inhibitors is not permitted under the legal regulations in the EU and Germany and is not directly comparable with the application of a fertiliser-bound inhibitor, the example shows that DCD can possibly enter food and thus the human body via ingestion by animals. However, current studies show that the risk of DCD to human health is rather low (Ray et al. 2023). Even if DCD is not very toxic, it is very persistent (Table 3). This means that an accumulation of the substance can be problematic in the long term.

The potential risks that could arise from the use of inhibitors and their degradation products for the water supply have also not been sufficiently analysed. The toxicologically relevant triazole, for example, is considered by the German Technical and Scientific Association for Gas and Water (DVGW) to be a substance that can jeopardise drinking water resources (DVGW, 2023). There is a need for research in this field, particularly in the topic of drinking water resource protection. Investigations into the fate of the substances in soil and water as well as a possible translocation into groundwater are necessary.

The frequent use of fungicides with the degradation product triazole in agriculture has led to the selection of resistant mould fungi. The problem here is that fungi that are responsible for fatal or serious respiratory infections (aspergillosis) can thus become resistant. Hence, drugs for humans similar in composition to triazole then no longer work or work less effectively. People can be exposed to these moulds via air as well as directly via treated products, for example via cut flowers (Dunne et al. 2017; Rybak et al. 2019).

In a study from Austria, which examined the concentration of various chemicals in air, the volatile nitrapyrin was not only the most frequently found substance, but also the one with the greatest potential negative health effects (carcinogenic, acute toxicity, specific target organ toxicity, skin irritation and sensitisation as well as eye irritation; Zaller et al. 2023). The authors therefore conclude that caution is required when using nitrapyrin in the future. Zerulla et al. (2001) come to the same conclusion pointing out that nitrapyrin is a chlorine compound that is corrosive and can pose toxicological problems. Indications that the use of nitrapyrin can be problematic for the environment and human health are also derived from the fact that it was banned as a plant protection product in Austria in 1992 (RIS 1992, see chapter 6).

In addition to the potential risk from contaminated food, an assessment should also take into account risks from direct contact with users. This is important because the active substances (together with the fertiliser) are applied in the open environment and therefore contact cannot be ruled out. With the exception of DCD, all inhibitor active substances are subject to at least one or more of the following CLP classifications: harmful to eyes, harmful to organs or toxic if swallowed (Table 4). However, it is important to bear in mind that many substances used in everyday life are also problematic in direct contact. This applies, for example, to acetic acid, which can cause severe skin burns and serious eye damage according to the classification of the CLP Regulation (ECHA 2023).

More seriously, the substances 3-MP, triazole, DMPP, MPA, 2-NPT, NBPT and NPPT are suspected of damaging fertility or the unborn child according to the classification of the CLP Regulation, i.e. they are toxic to reproduction. The substances 3-MP, triazole, MPA and 2-NPT are categorised as category 1B, i.e. they are classified as "may damage the unborn child ". The other substances are categorised as category 2 ("suspected of damaging fertility or the unborn child", Table 4). 3-MP is also suspected of impairing the endocrine system.

Table 4: Overview of the products available in the EU, their active ingredients and substance properties: Column 1: Active substance. Column 2: Available products according to an internet research as of 2023; Columns 3 and 4: Compilation of the substance properties from the REACH registration dossiers. Statements on environmental behaviour and ecotoxicological effects are based on the information in the dossiers. Column 5: Classification and Labelling Regulation (CLP, EU Regulation 1272/2008). If a classification is available, the CLP hazard categories are indicated (according to CLP Regulation or Annex VI of the CLP Regulation). The hazard of a substance is highest in category 1 and decreases with increasing numbers (ECHA 2023). The CAS[62] and EC[63] numbers, the exact tests carried out under REACH and the links to the registration dossiers can be found in the Annex, Table 6.

Active ingredient	**Product containing the active substance (manufacturer)**[64]	**Substance properties according to REACH/CLP and classification according to CLP**		
		Environmental behaviour (persistence and mobility)	*Ecotoxicological effect*	*Human health (Hazard classes according to CLP)*
		Nitrification inhibitors		
DCD	Ensin PLUS (Duslo)	REACH/CLP: Hydrolytically stable Very persistent Very mobile	REACH: Non-toxic to aquatic organisms Long-term toxic effect on soil microorganisms and plants	No harmonised classification according to CLP
		CLP: No environmental classification		
3- MP	Piadin (SKW, after 2017)	REACH/CLP: Hydrolytically stable No ready biodegradability in screening test s[65] Very mobile	REACH: Non-toxic to aquatic organisms Toxic to plants and moderately toxic to earthworms	Harmonised classification: May damage the unborn child (Repr. 1B) Harmful if swallowed (Acute Tox. 4) Causes severe skin burns and eye damage (Skin Corr. 1)

[62] International labelling standard for chemical substances (CAS = Chemical Abstracts Service).

[63] EC numbers are a classification category under European chemicals legislation. EC stands for European Community and EC for European Community.

[64] As far as is known at the time of research for this article.

[65] Screening tests to determine the potential for biodegradation usually utilise microorganisms that originate from sewage sludge from municipal sewage treatment plants.

Active ingredient	Product containing the active substance (manufacturer)[64]	Substance properties according to REACH/CLP and classification according to CLP		
				Causes serious eye damage (Eye Dam. 1) May cause damage to lung through prolonged or repeated exposure (STOT RE 2)
		CLP: No environmental classification		
Triazole	Piadin (SKW, before 2017) Ensin PLUS (Duslo)[66]	REACH/CLP: Hydrolytically stable No ready biodegradability in screening tests Indications of biodegradation in soil Very mobile	REACH: Moderately toxic to algae	Harmonised classification: May damage the unborn child (Repr. 1B) Harmful if swallowed (Acute Tox. 4) Causes serious eye damage (Eye Irrit. 2)
		CLP: No environmental classification		
DMPP	Entec (EuroChem) Vizura (BASF) NovaTec (COMBO EXPERT)	REACH/CLP: Hydrolytically stable No ready biodegradability in screening tests Indications of persistence[36] in water/sediment test (OECD 308) and soil Very mobile	REACH: Moderately toxic to aquatic organisms and plants	Harmonised classification: Harmful if swallowed (Acute Tox. 4) Causes serious eye irritation (Eye Dam. 1) Self-classification: May cause damage to organs – olfactory (STOT RE 2) Suspected of damaging fertility or the unborn child (Repr. 2)
		CLP: Harmful to aquatic life with long lasting effects (Aquatic Chronic 3)		

[66] According to the manufacturer's website, ENSIN Plus 4-amino uses 1,2,4 triazole and not 1,2,4 triazole. However, we assume that the compounds are similar in their intended and unintended effects. The active ingredient was probably approved for the European market in Slovakia, as the manufacturer DUSLO is based in Slovakia.

Active ingredient	**Product containing the active substance (manufacturer)[64]**	**Substance properties according to REACH/CLP and classification according to CLP**		
MPA	Piadin, Alzon neo-N (SKW)	REACH/CLP: Hydrolytically stable No ready biodegradability in screening tests Indications of biodegradation in soil under aerobic conditions (degradation product: 3-methylpyrazoles) Very mobile	REACH: No acute aquatic toxicity Long-term toxic to earthworms and springtails	Self-classification: May damage fertility or the unborn child (Repr. 1B) Causes serious eye irritation (Eye Irrit. 2)
		CLP: No environmental classification		
Nitrapyrin	Instinct, N-Lock (CORTEVA agriscience)	REACH/CLP: Slow hydrolysis[67] No ready biodegradability in screening tests Indications of biodegradation in soil and sediment/water system under aerobic conditions (degradation products 6-CPA, 2-chloro-6-(dichloromethyl)pyridine (DCMP)) Mobile	REACH: Toxic to aquatic organisms with long lasting effects Long-term toxic to earthworms and soil microorganisms Non-toxic to plants	Harmonised classification: Harmful if swallowed (Acute Tox. 4) Self-classification: Causes serious eye iritiation (Eye Irrit. 2) May cause allergic skin reaction (Skin Sens. 1)
		CLP: Toxic to aqutic life with long lasting effects. (Aquatic Chronic 2)		
DMPSA	Entec (EuroChem)	REACH/CLP: Hydrolytically stable No ready biodegradability in screening tests Indications of biodegradation in soil Very mobile	REACH: No acute aquatic toxicity Long-term low toxicity for aquatic invertebrates Non-toxic to soil organisms	Self-classification: Causes serious eye damage (Eye Dam. 1)
		CLP: no environmental classification		
Urease inhibitors				

[67] Half of the substance is broken down to the degradation product 6-CPA in 129 to 233 days at 25 degrees Celsius and a pH value of 7 to 9 under the influence of water.

Active ingredient	**Product containing the active substance (manufacturer)[64]**	**Substance properties according to REACH/CLP and classification according to CLP**		
2-NPT	PIAGRAN (SKW) Alzon neo-N (SKW)	Slow hydrolysis[68] No ready biodegradability in screening tests Indications of biodegradation in soil Very mobile	No acute toxicity for aquatic organisms and soil organisms Moderately toxic to algae	Harmonised classification: May damage fertility. Suspected of damaging the unborn child (Repr. 1B) May cause damage to organs – kidney – through prolonged or repeated exposure (STOT RE 2)
		Self-classification: Harmful to aquatic life with long lasting effects (Aquatic Chronic 3)		
NBPT	This substance is used in several products, e.g: Limus (BASF) UTEC (EuroChem)	REACH/CLP: Slow hydrolysis[69] No ready biodegradability in screening tests Indications of biodegradation in soil Very mobile CLP: no environmental classification	REACH: Acutely non-toxic to aquatic life Moderately toxic to earthworms and plants	Self-classification: Suspected of damaging fertility or the unborn child (Repr. 2) Causes serious eye damage (Eye Dam. 1)
NPPT	Evaluation as for NBPT, as substances are structurally similar.			

[68] Half of the substance is broken down in 148 days at 25 degrees Celsius and a pH value of 7 under the influence of water.

[69] Half of the substance is broken down in 92 days at 25 degrees Celsius and a pH value of 7 under the influence of water.

Conclusions

At the time of publication of this article, the number of scientific publications on the effects of inhibitors on terrestrial and aquatic organisms, biotic communities and human health is small. The REACH database (ECHA 2024b) and the US-EPA database "CompTox Chemicals Dashboard" (US-EPA 2024) contain studies with animal experiments for all of the inhibitors, which are primarily used to derive human toxicological parameters. Ecotoxicological effects are only partially addressed, whereas integrative effects on biotic communities are not considered in these toxicity/ecotoxicity studies, which are usually prepared according to OECD or based on OECD protocols. Woodward et al. (2021) conclude for nitrapyrin that despite 50 years of use, many questions about direct and indirect environmental effects remain unanswered. As most of the other inhibitors have been studied much less, the number of unanswered questions is probably even higher.

The data from REACH registration is also not sufficient to fully understand the risks to human health and the environment. This is because the planned tests are not intended for substances that are released into the environment on a large scale (see chapter 6). The substance with the most serious negative effects on soil organisms and aquatic organisms is nitrapyrin. In terms of effects on human health, the four substances of concern are 3-MP, triazole, MPA and 2-NPT, which are classified as "hazardous" due to reproductive toxicity in accordance with the CLP Regulation.

Overall, it should be emphasised that the substances currently approved as inhibitors are very different in terms of their undesirable effects. All of the inhibitor substances considered here either have problematic environmental behaviour, are hazardous to soil and aquatic organisms or pose a risk to human health (see chapter 7 and 8). However, none of the substances combines problematic properties in all areas.

9 Recommendations

The last few decades have shown that achieving European and national climate and environmental targets is a huge task. All environmentally compatible measures that can make a contribution should be considered. The use of urease and nitrification inhibitors can be a building block for achieving these goals in the agricultural sector.

It is important to make a precise assessment of each individual inhibitor rather than giving general recommendations for or against the use of inhibitors or inhibitor groups. The effect of nitrification inhibitors with regard to the level and permanence of the emission reduction, for example, is rather uncertain according to the current state of research. However, it has been relatively robustly scientifically quantified for the commercially available active substances of the urease inhibitors. The substance groups also differ in terms of their fate in the environment. While some of the nitrification inhibitors currently used remain in the environment longer than necessary, the most relevant urease inhibitor NBPT decomposes quickly in the soil. In both groups of urease and nitrification inhibitors, there are substances that may be toxic to specific organisms or to human health, while other substances have not yet been sufficiently analysed to provide a conclusive assessment. Concerning the risk to the environment no conclusive assessment is possible for any of the substances. The various inhibitors have a very wide range of environmental effects and efficacies and must therefore be assessed individually.

Another aspect is the high cost of developing and authorising products for manufacturers and the additional costs of using inhibitors for agricultural purposes. It can be assumed that particularly environmentally friendly new active substances and products will initially be more expensive than products that have already been developed and tested. Politicians must take this aspect into account if they want to promote the use of environmentally friendly inhibitors. An additional incentive for farmers to use inhibitors could be the reduction of costs within a framework of environmental economic instruments for the implementation of environmental goals (for example, in the case of a tax on agricultural greenhouse gas emissions).

At present, the German Environment Agency does not recommend the general use of all currently authorised inhibitors for climate, air pollution control and water protection measures for the following reasons:

1. Relevant risks of inhibitors for human health and the environment as well as their long-term behaviour in the environment have not yet been sufficiently researched. However, the knowledge available to date suggests problematic properties.
2. The current legal regulations for placing inhibitors on the market do not ensure the long-term protection of human health and the environment and do not fulfil the precautionary principle as a guideline for environmental policy.
3. A safe, relevant and long-term effectiveness with repeated use with regard to the reduction of nitrous oxide and ammonia emissions as well as nitrate leaching is not sufficiently proven in the scientific literature.

Ultimately, the decisive factor is to use inhibitors which have been proven to contribute to achieving environmental and climate protection goals and have no negative impact on human health and the environment.

If the following recommendations for the legislative process and for research and development are implemented, the use of urease and nitrification inhibitors could become a building block for achieving EU environmental and climate protection targets in the future:

Proposals for legal regulations at EU level

1. Inhibitors are active substances and should therefore be brought to the market via an approval procedure similar to that of the EU Plant Protection Products Regulation or integrated into the existing EU Plant Protection Products Regulation.
2. Parallel national authorisation procedures should be abolished.
3. The EU regulation should contain scientifically based minimum testing requirements with regard to the efficacy of the inhibitors and the effect on human health and the environment and ensure adequate protection of soil and water resources. This must also be ensured for combinations of active substances.
4. The mandatory study summaries for approval should, in accordance with the OECD Harmonised Templates (OECD 2024), be made available to the public in accordance with the requirements of the EU Environmental Information Directive.
5. The use of active substances should be authorised according to the current and general state of science and technology and only for a limited period of time.
6. Relevant data from other areas of application, for example the approval of plant protection products, should be taken into account when approving inhibitors.
7. National authorities should be involved in the development of efficacy and environmental and human health impact assessments under EU legislation.
8. If the inhibitors are used within the framework of regulations (as it is currently the case in the Fertiliser Ordinance or will be possibly within the framework of the integration of agriculture into European emissions trading) to achieve environmental and climate targets, it must be ensured that the assumed effectiveness corresponds to a real reduction.
9. The sales volumes of each active substance should be reported at EU level and made available in national public registers.
10. Users should be obliged to report the area-related application quantities to the authorities.
11. The manufacturer or importer of a fertiliser product should be obliged to make the maximum active ingredient content traceable at the time of packaging. One possibility for this would be a database in which the active ingredient quantities in grams per kilogramme fertiliser are stored and can be retrieved batch by batch. For this purpose, the packaging must be labelled accordingly, for example with a barcode.
12. The inhibitor active substances should be taken into account as part of the existing EU processes for monitoring water quality (EU COM 2022) and, where critical or frequent detection occurs, integrated into existing government monitoring programmes for soils and waters.
13. It should be examined whether inhibitors should not be approved in general, but rather depending on soil and climate zones, analogous to the already established procedure for plant protection products.
14. As long as a uniform EU regulation does not yet exist, national authorisation procedures should fulfil the criteria required above.

Recommendations for German legislation

Even if a standardised EU regulation on the use of inhibitors must be the goal, German legislation should be adapted as long as no regulation on EU level exists:

1. In the German Fertiliser Ordinance, a mandatory periodic review of active substances should be introduced. Active substances that have been authorised without environmental testing must undergo such testing.

2. Substances that are proven to be toxic to reproduction (category 1B) should no longer be approved.
3. When selecting members for the Scientific Advisory Board on Fertilisation Issues, all relevant aspects of the approval of inhibitors, including human and ecotoxicological aspects, must be taken into account.
4. The tests required by the Scientific Advisory Board on Fertilisation Issues should be standardised. Testing requirements should be made public.
5. The relevant evaluations for the approval of fertiliser additives should be transferred to the established substance enforcement bodies. If the evaluation is not transferred to the enforcement bodies, it should be ensured that the Scientific Advisory Board cooperates with the substance enforcement bodies to guarantee that the risk assessment of active substances and degradation products in different applications is harmonised.
6. Risk assessments must be mandatory and published in accordance with the Environmental Information Act (German abbreviation "UIG"). There must be scientifically sound and publicly accessible criteria for the authorisation of a substance.
7. The general obligation to use urease inhibitors, regardless of the specific active ingredients, their efficacy and effects on the environment and human health, should be comprehensively re-examined within the framework of the German Fertiliser Ordinance.

In order to be able to make well-founded recommendations for the use of inhibitors as an environmental and climate protection measure, the critical aspects of the use of inhibitors must be much better researched. Recommendations are given below. However, the effectiveness and risks to the environment and human health are already being researched in numerous projects. Box 1 provides an overview of relevant research projects in Germany.

Recommendations for research and development

1. The potential of using inhibitors to achieve statutory climate and environmental protection targets should be scientifically comprehensively analysed.
2. More public research funding should be made available for projects to investigate risks to the environment and human health. Research results found in this context should also be published, especially if they show that the active substances are unproblematic.
3. Public funding should also be made available for research aimed at developing effective inhibitors that are harmless to the environment and human health.
4. Scientific recommendations regarding measurement protocols should be developed and implemented for testing the effectiveness of inhibitors in scientific studies that are used to demonstrate emission reductions.

Selected ongoing and completed research projects on the use of urease and nitrification inhibitors in Germany

Güllebest (Funding: Agency for Renewable Resources):

Investigation of slurry application techniques to reduce ammonia emissions. Examination of the use of nitrification inhibitors (active ingredient DMPP) to reduce potential nitrous oxide emissions after slurry injection. The use of inhibitors showed no significant effect on ammonia and nitrous oxide emissions after slurry application.

(Duration: 2018-2022; www.guellebest.de)

NH3 -Min (Funding: Landwirtschaftliche Rentenbank/Federal Office for Agriculture and Food):

Analysis of the efficiency of various measures to reduce ammonia emissions after the application of mineral nitrogen fertilisers. These include the use of urease inhibitors in urea fertilisation (active ingredient 2-NPT) and fertilisation with ammonium nitrate urea solution (AHL, active ingredient NBPT/NPPT). Double-inhibited urea fertilisers with urease (2-NPT) and nitrification inhibitor (MPA) are also being investigated. In addition to the reduction effect on ammonia emissions, the focus is on the effects on fertiliser effectiveness (yield, nitrogen efficiency).

(Duration: 2020-2024; https://www.nh3min.de/en/)

Win-N (Funding: Agency for Renewable Resources):

Investigation of the effect of a urease (2-NPT) and a nitrification inhibitor (MPA) in single and combined application on ammonia and nitrous oxide emissions as well as yield effects. In addition, the fate of the active substances in a test facility with the possibility of recording the leachate discharge with subsequent discharge simulation (PELMO) and the ecotoxicological effects on the soil fauna (nematodes + enchytraeids) are considered.

(term: 2021-2024; https://www.thuenen.de/en/institutes/agricultural-technology/projects/products-from-renewables)

NitriKlim (Funding: Federal Office for Agriculture and Food):

Research into the effect of nitrification inhibitors (especially DMPP) on nitrous oxide emissions in crop production at various German locations. In addition, the multi-year efficacy stability of the use of inhibitors is being investigated for all nitrification inhibitors registered in Germany. In addition to the field trials, various inhibitors and the effectiveness of the active substances are analysed in soil samples from sites with decades of continuous use of nitrification inhibitors. In addition, the effect of nitrification inhibitors on the soil microbiome and on the leaching of active substances will be analysed. Last but not least, an agronomic and agro-economic analysis of the use of inhibitors will be carried out.

(Duration: 2022-2026; https://www.nitriklim.de/en/)

INHBIT (Funding: German Technical and Scientific Association for Gas and Water):

The project looks at the behaviour of these substances in the environment. In order to assess the risks with regard to groundwater protection and the interests of the water supply industry, possible entry pathways via the (unsaturated) soil zone and saturated bank filtration were primarily investigated experimentally. In addition to creating a uniform and consistent database to describe the initial situation and the state of knowledge based on available literature, the methodological basis for investigating the substances in soil leachates was further developed to enable a more detailed assessment of the translocation of active substances. (Duration: 2020 - 2022; https://www.dvgw.de/themen/forschung-und-innovation/forschungsprojekte/dvgw-forschungsprojekt-inhibit)

DüBoWa (Funding: Federal Ministry for the Environment, Nature Conservation and Nuclear Safety/German Environment Agency):

The project generates findings on an experimental basis (laboratory and lysimeter tests) on the fate, degradation and migration of additives in soil, leachate and groundwater and evaluates these from the perspective of soil and groundwater protection (duration: 2023 - 2026).

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11 Appendix

Table 5: Overview of test requirements for effects on terrestrial organisms under REACH according to substance properties (Source: ECHA 2015)

Property of the substance		Test requirements
Very toxic to aquatic organisms	**Indication of high adsorption or high persistence in the soil**	
Not fulfilled	Not fulfilled	Calculation of terrestrial toxicity based on existing aquatic toxicity values
Fulfilled	Not fulfilled	Calculation of terrestrial toxicity based on existing aquatic toxicity values as well as an acute terrestrial test and a microorganism toxicity test
Not fulfilled	One or both of these properties are fulfilled.	
Fulfilled	One or both of these properties are fulfilled.	Several long-term terrestrial tests (invertebrates and plants) and a microorganism toxicity test

Table 6: Detailed chemical name and EC and CAS numbers for clear identification of the substances and summary of existing terrestrial tests (Source: ECHA 2023)

Abbreviation	Full chemical name according to ECHA website (IUPAC names)	EC and CAS numbers	Links to the ECHA registration dossiers (as at 17 April 2024)
DCD	N-cyanoguanidine	EC: 207-312-8 CAS: 461-58-5	https://chem.echa.europa.eu/100.006.649/dossier-list/reach/dossiers/active?searchText=207-312-8
3- MP	3-methylpyrazoles	EC: 215-925-7 CAS: 1453-58-3	https://chem.echa.europa.eu/100.014.478/dossier-list/reach/dossiers/active?searchText=215-925-7
Triazole	1,2,4-triazoles	EC: 206-022-9 CAS: 288-88-0	https://chem.echa.europa.eu/100.005.476/dossier-list/reach/dossiers/active?searchText=206-022-9
DMPP	3,4-dimethyl-1H-pyrazol-1-ium dihydrogen phosphate --------------------- 3,4-dimethyl-1H-pyrazole	CAS: 202842-98-6 EC: 424-640-9 CAS: 2820-37-3 EC: 429-130-1	https://chem.echa.europa.eu/100.102.315/dossier-list/reach/dossiers/active?searchText=202842-98-6
MPA	Reaction mass of N-[(5-methyl-1H-pyrazol-1-yl)methyl]acetamide AND N-[(3-methyl-1H-pyrazol-1-yl)methyl]acetamide	EC: 700-208-8 CAS: -	https://chem.echa.europa.eu/100.224.950/dossier-list/reach/dossiers/active?searchText=%20700-208-8
Nitrapyrin	2-chloro-6-(trichloromethyl)pyridine	EC: 217-682-2 CAS: 1929-82-4	https://chem.echa.europa.eu/100.016.076/dossier-list/reach/dossiers/active?searchText=1929-82-4
DMPSA	Reaction mass of 2-(3,4-dimethyl-1H-pyrazol-1-yl)succinic acid and 2-(4,5-dimethyl-1H-pyrazol-1-yl)succinic acid	EC 940-877-5	https://chem.echa.europa.eu/100.233.693/dossier-list/reach/dossiers/active?searchText=940-877-5
2-NPT	N-(diaminophosphoryl)-2-nitroaniline	EC: 618-024-0 or 477-690-9 CAS: 874819-71-3	https://chem.echa.europa.eu/100.105.163/dossier-list/reach/dossiers/active?searchText=618-024-0
NBPT	butyl[diamino(sulfanylidene)-λ^5-phosphanyl]amine	EC: 435-740-7 CAS: 94317-64-3	https://chem.echa.europa.eu/100.103.392/dossier-list/reach/dossiers/active?searchText=435-740-7

Abbreviation	Full chemical name according to ECHA website (IUPAC names)	EC and CAS numbers	Links to the ECHA registration dossiers (as at 17 April 2024)
NPPT	[diamino(sulfanylidene)-λ^5-phosphanyl](propyl)amine	EC: 618-780-1 CAS: 916809-14-8	https://chem.echa.europa.eu/100.127.866/dossier-list/reach/dossiers/active?searchText=618-780-1