Across the fields and far away: Adverse health effects due to spray drift from plant protection products are unlikely

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When a plant protection product is applied it is virtually unavoidable that some of this product will not end up where it should. This is particularly the case for spray applications in fields where some of the product will be subject to drift into the surroundings. There are various reasons for this. During spraying, the wind and other influencing factors can cause the product to drift away from the field where it is applied. Also, the product may vaporise during or after application or might be subject to subsequent drift while attached to dust.

Sprayed plant protection products can be absorbed through the skin or breathed in by agricultural workers or other people passing by. Do these products pose a hazard to humans? This question and others are part of the BfR's health risk assessment of substances used in plant protection products.

Processes such as spray drift and the evaporation of plant protection products are considered during risk assessment by means of mathematical models. In each case a worst-case scenario is assumed. The outcome, together with measured values is then used to answer the question of whether adverse effects on health can arise for workers and passers-by up to ten metres from the field's edge. The respective concentrations of these active substances are inherently higher near the field than at greater distance. Moreover, plant protection products are licensed for use only if no harmful effects on health are to be expected in the immediate vicinity of the agricultural land being treated. Therefore, health risks caused by spray drift from plant protection products are not to be expected if the product is used correctly and as authorised.

Strict rules for plant protection product testing ensure a high level of safety

In the EU, plant protection products are subjected to stringent testing according to a uniform set of safety legislation in order to protect consumers and the environment. These laws apply to products approved for conventional agriculture as well as those used in organic farming. Both of these sectors depend on the use plant protection products. In terms of test specifications and the data required, EU regulations are among the most comprehensive anywhere in the world. Together with the assessments based on these, this provides a level of protection for health that is considered a global gold standard.

Unlike other chemicals, both the active substances used for plant protection and the product formulations themselves are subjected to approval and authorisation procedures, respectively. This includes strict requirements concerning toxicology (assessment of the toxicity) and application (i.e. use). This legal framework ensures safe use of plant protection products, when used correctly and as intended. It also ensures approval and use of plant protection products to be in accordance with the latest scientific and technical standards and in strict observance of the need to protect human health. In line with the principles of consumer protection, the assumptions and safety factors applied in the assessments are always conservative, i.e. chosen to offer the highest level of protection for health and to avoid any possibility of underestimating risk.

The intake of small quantities of plant protection products during use is unavoidable and thus explicitly envisaged by the relevant legislation. The respective uptake is subject to comprehensive toxicological risk assessments and limited to amounts where health effects are considered

unlikely from a toxicological perspective. The mere detection of a substance therefore does not imply a health risk or a toxicological risk.

There is an intrinsic and unavoidable societal conflict of interest whenever it comes to acceptable risk, but this cannot and should not be resolved as a question of science. Instead, governments around the world have passed laws stating that the authorisation process for plant protection products must account for and uphold the core aspects and tenets of health protection. This applies in particular to the handling of plant protection product residues. These are not 'contaminants' in the conventional sense, but an expectable and tolerated consequence of the authorised use of plant protection products under conditions considered toxicologically safe. .

Toxicological evaluation of plant protection products routinely includes assessment of long-term effects due to potential inhalative exposure of active substances

As part of the approval process for active substances intended for use in plant protection products, a comprehensive toxicological analysis based on data from animal studies is always performed and required by law. This analysis also considers potential long-term effects resulting from inhalation (after breathing in the substance).

Based on the properties of the substances, the level of toxicity and the expected intake (exposure), is determined either by studies that have looked directly at exposure by inhalation or by extrapolation (estimation) based on the available data for acute and long-term toxicity, metabolism and kinetics.

Explanation:

Regulation (EU) No 283/2013, which sets out the data requirements for active substances used in plant protection products, stipulates that, wherever practicable, the oral route (intake via the mouth) should be chosen for toxicity testing, unless exposure in humans mainly takes place via the gas phase, in which case experiments based on exposure via inhalation instead of oral exposure may be more appropriate.

In the majority of toxicological studies, the test substance is therefore initially administered via the gastrointestinal tract, i.e. orally (since this is typically the most relevant route of exposure). The data obtained by these tests permit the determination of relevant toxic effects and the derivation of systemic reference values for the overall assessment. Following their scientific validation, these values then form the basis for the first partial assessment of the potential consequences of exposure via inhalation. This extrapolation from the oral route to inhalation uses a precautionary and conservative approach by setting respiratory uptake at 100 %. In practical terms, this amounts to a significant overestimation, since some of the inhaled gas or aerosol will be exhaled, and some of the substance particles deposited in the respiratory tract will be moved upwards by the lung's natural cleaning mechanisms and then swallowed (where they are then covered by the oral assessment).

A situation may also arise where an active substance, once inhaled, is capable of triggering an adverse effect at lower concentrations than the same substance when ingested (absorbed by the gut), either as a result of its toxicokinetics (metabolism in the organism) or its metabolism in the lung itself. Both of these situations are covered by statutory testing regimens on metabolism, toxicokinetics and acute (i.e. occurring immediately) inhalation toxicity and thus are accounted for appropriately.

If there is reason to believe that repeated inhalation exposure would lead to a greater stress on the organism than the more persistent and uniform internal exposure resulting from oral absorption (intake via the mouth), the assessing agency will request appropriate tests to be carried out pursuant to Regulation (EU) No 283/2013. The same applies if other concerns should arise. Ultimately, such *ad hoc* study requests are also in line with animal protection law, since unnecessary studies are avoided without impairing the required level of safety for humans.

Risk assessment of potential drift of active substances in plant protection products, including long-range transport

Concerns have also been raised that plant protection product active substances can spread over a wide area, for example via soil particles. The potential health risks of this 'long-distance transport' are typically accounted for during the scientific risk assessment of standard drift due to the worst-case assumptions used in these assessments. Models and measured values are applied to answer the question whether adverse effects on health can arise if active substances in pesticides are present nearby, that is up to a distance of up to 10 metres from the field's edge. This also conservatively covers distances further afar as local spray concentrations are inherently higher than concentrations expectably caused by long-range drift.

Plant protection products are authorised for use only if no harmful effects on health are to be expected in the immediate vicinity of the agricultural land being treated. The scientific assessment made considers exposure both via the skin (transdermal route) and via the lungs (inhalation).

Scientific standards for the assessment of long-range drift

The Acceptable Daily Intake (ADI) is a value that specifies the quantity of a substance that can be consumed orally on a daily basis over an entire lifetime without posing a risk to health. Consequently, this value is exclusively envisaged for use in the assessment of potential health risks arising from the residues of a substance taken up in some form by consumers from food and drink. In cases where long-distance drift involving active substances in pesticides results in this kind of oral intake of residues their potential effects on human health are also accounted for by the ADI.

The value relevant for inhalation is the Acceptable (Acute) (Operator) Exposure Level (A(A)(O)EL). Unlike the ADI the A(A)(O)EL accounts for the total absorbed dose over all uptake pathways (exposure routes). During active substance approval and plant protection product authorisation the A(A)(O)EL is therefore used for the assessment of spray drift and volatilisation of active substance. It is also used to assess the potential effects on human health resulting from exposure to respective airborne drift residues.

Explanation:

In addition to an appraisal of the potential health risks resulting from residues in food and drinking water, the authorisation process for a plant protection product also assesses the immediate risks to health that result from the use and application of the product for bystanders (e.g. local residents, people walking, etc.).

An overview of the basic elements of this evaluation can be found by consulting the relevant

harmonised EU Guideline from EFSA (EFSA Journal 2014;12(10):3874). Exposure is estimated by using mathematical models that are based on experimental data[1]. Properties of the active substances and details of the application are taken into consideration, so as to arrive at a prediction of the potential maximum exposure of local and neighbouring populations.

This procedure considers the potential volatilisation of the active substance (inhalation of the evaporated portion), direct exposure of bystanders to drift from spray mist (inhalation of spray mist and skin contact with spray mist), deposition on neighbouring areas (e.g. a garden adjacent to the field) and the potential entry of persons to treated (agricultural) land. Persistent (i.e. recurring on a daily basis) exposure to the active substance(s) in the plant protection product is assumed in each case as a conservative estimate.

As part of the risk assessment required for authorisation, the maximum amount of an active substance that could be taken up by an exposed person via the aforementioned routes is likewise predicted, i.e. the quantities that are then present in the body and circulatory system, and therefore relevant in terms of effects. The corresponding amount of the active substance taken up must not exceed the A(O)EL derived from animal experiments. The same applies for the acute reference value also derived from animal experiments and the Acceptable Acute Operator Exposure Level (AA(O)EL) when assessing acute effects on health.

For a better understanding is worth noting that the reference values (A(O)EL, AA(O)EL), i.e. the quantity of an active substances for which an intake at this level is considered without risk to human health, is typically around 0.01 to 1 mg/kg body weight per day for the majority of substances. These values are usually at least 100 times lower than the levels at which no harmful effects were observed in animal experiments.

A plant protection product is granted authorisation only if the sum total of all levels of maximum exposure from the above-mentioned routes via the skin and airways is lower than the health based reference value. One can put this into picture by as follows. When assuming a reference value of 1 mg/kg body weight the maximum sum total of exposure via the skin and airways for an adult weighing 60 kg would be 60 mg. This is a quantity only slightly larger than a single drop of water (0.05 ml, approx. 50 mg), applied daily and over a life-time.

Acceptable Daily Intake and inhalation exposure to active substances in plant protection products

The Acceptable Daily Intake (ADI) is not a suitable metric for assessing exposure to active substances in plant protection products via inhalation. The ADI is solely intended for use in the assessment of potential health risks arising from residues taken up in via food and drink.

If a person is exposed to a plant protection product active substance via multiple routes, e.g. the skin (dermal), the gastrointestinal tract and/or the airways (inhalation), the risk assessment is therefore carried out using a reference value that enables an aggregated of these routes. The systemic reference value applied in such cases is the A(O)EL mentioned above.

The A(O)EL relates to internal exposure in humans, and not only considers the quantity of a substance that enters via the skin or the lungs, but also the proportion of the substance actually taken in by the body. This methodology is applied to all uptake and exposure routes, and the sum total amount is used as input for the risk assessment.

[1] Details of models and data can be found by consulting the EU Guideline from EFSA mentioned above and the Guideline's bibliography.

The A(O)EL value is typically derived by looking at findings for the most sensitive animal species and the most sensitive study with repeated administration. The possibility of increased sensitivity following inhalation or dermal exposure is also taken into account. If doubts exist, regulators may also request further information or tests for clarification as per the EU plant protection product regulations.

Pesticide aerosols and the human lung

Depending on their aerodynamic properties, particle size and density in particular, aerosols are either deposited in the upper or lower airways, or breathed out again. These processes have been widely researched, and can now also be modelled for laboratory animals and humans. Particles present in the respiratory tract are transported by mucus to the stomach. Release of the active substance before this happens, combined with uptake by the mucous membranes, is, however, also possible. Substances transported as far as the alveoli pass into lung tissue and the circulatory system by diffusion, unless they are subsequently breathed out or removed together with their transporting particles by the immune system. In pesticide risk assessments, these processes are typically accounted for by the conservative assumptions made for the worst-case scenario. It is assumed that all of the active substance is passing into the circulatory system.

Plant protection products are authorised only if the maximum possible level of exposure is lower than the corresponding health based reference values and given the very conservative (i.e. cautious) assumptions, no impairment to health is to be expected.

For further information, please visit the BfR website:

https://www.bfr.bund.de/en/a-z_index/pesticides-130187.html

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. The BfR advises the Federal Government and the States (‘Laender’) on questions of food, chemical and product safety. The BfR conducts its own research on topics that are closely linked to its assessment tasks.

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