

## ECPA position on SDHI fungicides

In 2018 and 2019, a group of French scientists published results of experiments with cell cultures treated with SDHI (succinate dehydrogenase inhibitor) fungicides. This group of scientists, along with certain NGOs, claimed that SDHIs are toxic for humans and have been calling for an immediate ban of this family of fungicides. In 2019, the French competent authority carried out an independent expert appraisal that thoroughly reviewed the results of these *in vitro* studies as well as the relevant regulatory studies, monitoring data, international literature and relevant databases and concluded that there are no reasons for concern. In 2020 Belgian Authorities determined from the 2018/19 studies that “*There is no new evidence whatsoever to support the claim that it makes the population ill.*” And, like France, state “*...that there is no reason to withdraw or restrict the approval of these active substances.*”<sup>1</sup>

SDH inhibitors are well researched, strictly regulated and have been approved as safe for use in the EU and around the world for many years. Regulatory approvals have been delivered following thorough assessment of comprehensive toxicological studies carried out to the highest scientific standard. These studies are more reliable and suitable for human risk assessment than those conducted using cell cultures by the group of French scientists.

Succinate dehydrogenase (SDH) is a specific enzyme which plays a critical role in the cellular energy household of all living beings. An SDHI fungicide is a substance that has been designed to protect crops from fungal diseases by preventing the enzyme from working in the fungus. The energy supply of the fungus is blocked and essential life processes of fungal pathogens are stopped. To date, 12 active substances of the SDHI family have been authorized at EU level<sup>2</sup>.

In 2018, a group of French scientists raised awareness in the press about SDHIs used for the protection of agricultural crops, alleging potential risks on human and animal health. On 7 November 2019, the same scientists (Rustin *et al*, 2019<sup>3</sup>) published results of cell culture experiments (*in vitro*), in which the potential for SDH inhibition by SDHI fungicides was investigated in different species. A pronounced inhibition of fungal SDH was demonstrated, along with an inhibition of SDH to some extent of earthworms, bees and of human cells under the chosen study conditions. In additional investigations, cell growth was impacted in cultures of human cells exposed to SDHI test substances, but only when these cells were additionally deprived of glucose. In basic terms, the cells died as they had no food not because of SDH inhibition. Based on these investigations, this group of French scientists claimed that SDHIs can affect organisms other than fungi.

Ensuring safety of crop protection products is our number one priority and we have thorough screening and testing procedures in place, based on the highest standards and sound science, to ensure that our products can be used safely. Pesticides are only placed on the market following independent expert assessment by public authorities around the world. In the EU pesticides may only be approved if the active ingredient “*shall have no immediate or delayed harmful effect on human health, including that of vulnerable groups...*”<sup>4</sup>.

<sup>1</sup> <https://fytoweb.be/en/plant-protection-products/use/whats-sdhis>

<sup>2</sup> benzovindiflupyr, bixafen, boscalid, carboxin, fluopyram, flutolanil, fluxapyroxad, isofetamide, isopyrazam, penflufen, penthiopyrad and sedaxane.

<sup>3</sup> PLOS ONE | <https://doi.org/10.1371/journal.pone.0224132> November 7, 2019

<sup>4</sup> <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:309:0001:0050:EN:PDF>

As scientific knowledge is constantly evolving, ECPA welcomes new research investigating pesticide risks for human and animal health and the environment. In this instance, we have responded to the publication of the authors by raising scientific questions on the study methods to better understand how the conclusions were reached<sup>5</sup>. For example, we have asked why the cultured cells used were grown without an energy source, as it prevents them from surviving for a long period and call into question the interpretation of results.

Based on our current understanding and assessment of the data published by this group of French scientists, **we fundamentally disagree with their conclusions.**

- Whilst we understand the thinking of the group of scientists, in our view their findings are a form of correlation not causation<sup>6</sup>.
- The hundreds of studies assessed at European level by the European Food Safety Authority (EFSA) and reviewed by Member State authorities, demonstrated that no adverse effects of SDHIs are to be expected in humans under approved conditions of use. This is also confirmed by many regulatory reviews in non-EU countries.
- There is no evidence to support claims that SDHIs would cause diseases to humans.
- The overall dietary exposure level to these substances is low and the resulting safety level is high, as confirmed by EFSA (2019)<sup>7</sup>.
- In addition, it is worth noting that EU approval for pesticide active ingredients also require that to be approved "*it shall have no unacceptable effects on the environment.*"<sup>4</sup> Pollinator and bee health is always considered during the risk assessment process. SDHIs have been extensively tested according to legal requirements in Europe. The currently approved SDHI active substances do not show any unacceptable risks to adult bees and larvae both on an individual and colony level.
- Active substances used as plant protection products can be reviewed by regulatory authorities at any time if there are safety concerns. For the time being, there are no studies that support claims from this group of French scientists, and we are actively following any new research in this field. If we believe there are valid reasons to reassess safety, member companies will take swift and appropriate action accordingly.

**ECPA and its member companies will continue to engage constructively with the scientific community and follow new research and publications with great interest. Based on the current scientific knowledge and the stringent approval process, we stand behind the safe uses of authorised SDHI fungicides in Europe.**

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<sup>5</sup> <https://journals.plos.org/plosone/article/comment?id=10.1371/annotation/37f69efc-49f9-4d7f-ab64-8f01ed5cff4b>

<sup>6</sup> This concept is explained here: <https://hbr.org/2015/06/beware-spurious-correlations>

<sup>7</sup> <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2019.5743>