Expert Elicitation on Neurodevelopmental Implications of CPF

Policy context

- Chlorpyrifos (CPF) is an organophosphate pesticide used in Europe for outdoor and indoor pest control. A ban on residential use of CPF has been in effect in the US since 2001 but the EU has no such restrictions.
- In 2003 organophosphates accounted for over 59% of insecticide sales in the EU, with CPF the top selling insecticide.
- Organophosphate compounds act by inhibiting acetylcholinesterase (AChE), which affects nerve function in insects, humans and other animals.
- There are concerns about the safety of CPF in indoor settings. While previous studies have shown levels of CPF that are safe in adults, recent animal studies show the young may be more sensitive to toxicity. It affects synaptic transmission in neurons, which can lead to developmental and behavioural problems. It may affect children on a large scale and may be a contributing factor related to the large scale of emotional and behavioural diagnoses in Europe.
- Such effects, combined with those of other neurotoxic industrial chemicals, could lead to a ‘silent pandemic’ of pervasive, nonspecific developmental disorders that might affect a large proportion of the population.

Policy options

The prior consideration and rejection of an indoor use ban for CPF twice before, in 2002 and 2008, raises the question of what impact current knowledge assessment may have on future policy options.

More data and better understanding were indicated as tasks for science to address in the next five years. Funding for fundamental science focussing on population behaviour and physical processes is of high importance. For applied science, developing interventions in these areas was favoured.

EU-level monitoring of population behaviour, physical processes, dispersion and transfer is supported by scientists. Awareness raising of possible risks due to population behaviour was also indicated. One of the experts felt strongly that there is enough information available to enact prohibitory policies immediately with an eye towards altering usage of the products in homes, with a ban on home use considered to have the most direct effect on outcomes. Once this was in place it was then suggested that science and policy might then turn to the question of whether agricultural applications were also safe.

Confidence that these suggestions could be achieved in the scientific realm over the next five years were medium and high. Confidence that policy could achieve these in the next five years ranged between low and very high.
Executive summary

Preventing potential adverse effects on human health caused by CPF is a task for authorities around the world. Taking appropriate political actions requires knowledge on the outcome of indoor exposure. How much is needed to support policy measures is open for debate amongst experts, policymakers and stakeholders.

Two questionnaires were distributed for input from published experts in this field. An initial expert questionnaire was deployed in order to evaluate the state of the current scientific knowledge and highlight important policy considerations. Of 35 potential contributors identified, 8 were able to complete the online questionnaire.

- In light of current, albeit limited, knowledge available on the risks of CPF, most favour a precautionary ban or restrictions on its use.
- Most agree more research and monitoring is needed to develop better understanding of the risks involved in the use of CPF.

Respondents were asked to complete a second questionnaire and take part in an expert panel workshop where the results were discussed. Of the 8, two were available for the workshop. Priorities for further action were identified.

First Questionnaire

A causal diagram illustrating scientists’ current understanding of the cause-effect relationship between use of CPF and its impact on health was made. The diagram was based on the latest review articles and reports available. Experts have all published research studies on the subject. They were asked to express their confidence in the current knowledge by completing an online questionnaire.

Questions related both to specific areas of the diagram and to the structure of the diagram overall. In addition, experts were asked to assess their feelings regarding whether there was enough scientific knowledge to justify a restriction on uses of CPF.

The following shows example questions where there were high levels of disagreement between experts:

- When asked if CPF should be banned due to specific neurodevelopmental effects, again the majority agreed.

None of the experts chose the ‘No, and more work needs to be done’ or ‘No, and there is sufficient evidence’ options. When asked if CPF should be banned due to specific neurodevelopmental effects, again the majority agreed.

Response Scale

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<th>Very High</th>
<th>Medium</th>
<th>Low</th>
<th>Very Low</th>
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- What is your level of confidence in:
  - the ability to predict sex-specific health effects in experimental animals?
  - the ability to predict CPF has the potential to cause detrimental health effects?
  - the knowledge of the mechanism(s) of action of CPF and its metabolites?

There were also areas of high agreement. Experts considered the quality of evidence for a clear risk, results of which varied from very high confidence to very low. Many felt more research was necessary to quantify the risk. However, when asked whether CPF should be banned from home use, the majority agreed.

The results for the question whether CPF should be banned from home use.

The results for the question whether CPF should be banned due to specific neurodevelopmental effects.
Second Questionnaire and Workshop

An expert consultation and second questionnaire on policy action followed the first questionnaire. Two respondents attended the workshop along with a social scientist and a consortium moderator. The participants represented the farthest ends of the continuum from the first questionnaire. The depth of examination in such a group can help to identify areas of concern where perhaps a larger group would not be able to explore such issues.

Experts agree that the three priority areas to investigate are:

- Population behaviour, including occupation, diet, and at-home use,
- Physical processes, such as uptake or absorption, since these determine exposure, and
- Pathophysiological processes, like enzyme function, which determine exposure outcome

Pre- and post-natal exposures were considered important. Specific questioning for more detail revealed:

- ‘Frequency and duration of exposure... affects health risks’
- ‘Age and genetic polymorphisms influence toxicity’
- ‘More research needed... in low doses of chlorpyrifos.’

More research was recommended regarding specific EU indoor exposures to CPF. It was also discussed whether CPF is the causal toxin or if it is a proxy in studies for some other exposure or behaviour. Merits of particular study designs were discussed.

It was felt both research and policy action can contribute to reducing problems. One scientist commented changes in policy were “feasible immediately”. More data about exposure, better scientific understanding, and CPF monitoring were supported.

Further comments included ‘I think CPF is fine for outdoor use... indoor use is of concern.’ Another suggested ‘strict evaluation of current use in... domestic settings.’

Recommendations

Areas of concern: Population behaviour and physical processes were considered the most important factors in toxicological outcome.

The arguments: There are limited data on effect at low, sub-toxic levels but also a request for more epidemiological evaluation of the risk issue. More focus in the future should be addressed on design of studies being appropriate to realistic exposures in the home that are suitable to the EU.

Type of action: Experts suggested more scientific research with focus on more data and better understanding of fundamental science. Also a request for policy action, especially more monitoring activities, but also some restricting and prohibiting activities.

Form of action: Research to determine whether factors influencing use of CPF in North America are applicable here, and whether exposure at a sub-clinical level has a measurable effect. Use policy to decrease or stop this exposure by raising awareness and restricting certain activities.

Confidence in science: Most experts have some confidence in science coming up with usable or decisive knowledge within the next five years.

Confidence in policy action: As indoor usage restrictions for CPF have been considered and rejected in the EU before, there were questions of whether policy makers could be motivated to examine the area further, but most felt policy could have a significant impact.
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