BACKGROUND

1. In 1999, the COT published a report on organophosphates which considered whether prolonged or repeated low level exposure to organophosphates, or acute exposures to organophosphates at levels insufficient to cause overt toxicity, can cause long-term adverse health effects. In the report, COT had drawn conclusions from the available data and made recommendations for further research to address outstanding issues (Annex 3) and the research has been funded jointly by a number of Government Departments. In 2007, COT considered a review of the Government funded research reports available at the time (Annex 4).

2. This update to the 2007 COT review of Government funded organophosphate research focuses on the outstanding final research report for the prospective cohort study of sheep dip exposure and ‘dipper’s flu’ funded by the Health and Safety Executive (HSE).

INTRODUCTION TO THE OUTSTANDING GOVERNMENT RESEARCH

3. The research recommendations from the 1999 COT review (Annex 3) were grouped around the following questions:

   i. What are the most common patterns of exposure, clinical presentation and subsequent clinical course among people in the United Kingdom with chronic illnesses that they attribute to organophosphates?
   ii. How common is ‘dipper’s flu’, and what causes it?
   iii. Does low-level exposure to organophosphates cause disabling neurological or psychiatric disease in a small subgroup of exposed persons?
   iv. Do people with chronic disabling illness that is suspected of being related to organophosphates differ metabolically from the general population?
   v. Other than acetylcholinesterase inhibition, what mechanisms play an important role in the causation of adverse health effects by organophosphates?

4. Six research projects were commissioned to address the five COT research recommendations (Table 1):
Table 1. Government commissioned research projects

<table>
<thead>
<tr>
<th>Research Project Number</th>
<th>Title</th>
<th>COT research recommendation number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SHAPE: Survey of Health and Pesticide Exposure</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Prospective Cohort Study of Sheep Dip Exposure and ‘Dipper’s Flu’</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Disabling neuropsychiatric disease in farmers exposed to organophosphates</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Genetic variation in susceptibility to chronic effects of organophosphate exposure</td>
<td>4</td>
</tr>
<tr>
<td>5i</td>
<td>Investigation of possible autoimmune responses induced by organophosphate exposure</td>
<td>5</td>
</tr>
<tr>
<td>5ii</td>
<td>Characterisation of non-acetylcholinesterase actions of organophosphates by identification of novel protein targets</td>
<td>5</td>
</tr>
</tbody>
</table>

5. The final report of the outstanding Government funded research project on a ‘Prospective cohort study of sheep dip exposure and ‘dipper’s flu’ has recently been finalised. The interim report on the study was reviewed by COT in September 2007, and the final report is now being presented to the Committee in-confidence for review.

6. A summary of this Government funded research project is given in Annex 1 (In confidence - Members only). and the full research report is provided in Annex 2 (In confidence - Members only).

OVERVIEW OF COT CONCLUSIONS REACHED IN 2007

7. At its meeting in September 2007, the Committee considered an interim report on this research project and Members’ comments relevant to this project have been extracted from the minutes (Annex 4) and given below for information.

Research Project 2. Prospective cohort study of sheep dip exposure and ‘dipper’s flu’. HSE Project R51.242. (Povey et al.)

8. A limitation of this prospective cohort study of sheep dip exposure and ‘dipper’s flu’ was that it did not include ex-farmers, who might include a disproportionate number of susceptible individuals if there were variations in susceptibility from person to person. The recruitment rate was low; however, this was of less concern with respect to recruitment bias since this was a prospective study. It was noted that ‘dipper’s flu’ was not an established occupational hazard, but a phenomenon talked about by those involved in sheep-dipping. If a
toxicologically mediated effect, it would be of interest since it could be an indicator of high exposure to organophosphates. However, the study did not provide evidence for a flu-like condition related to sheep dipping or of acute organophosphate exposure being a cause of ‘dipper’s flu’. A Member advised that the results were consistent with other research which had not indicated any unusual clustering of flu-like symptoms following sheep dipping (Solomon et al. Occup. Med. 2007 Oct;57(7):505-11).

9. An increase in endotoxin levels in sheep dip was observed after dipping, and it was noted that very high endotoxin levels could cause respiratory effects. Organophosphate exposure in the sheep dippers appeared to be low; only three farmers showed a decrease in plasma cholinesterase activity following dipping, and this was unlikely to have been sufficient to result in ill health. This low exposure contrasted to the reports of high acute exposures in research project 1.

DISCUSSION

10. The Committee is asked to consider the research report and advise on the significance of the results.

QUESTIONS FOR THE COMMITTEE

1. What is the significance of the findings of the research project in relation to the question of possible effects of chronic or acute low dose exposure to organophosphates?
2. To what extent have the research recommendations made by the COT been addressed?
3. How does this project contribute to understanding the effects of organophosphates on human health?

HPA COT Secretariat

November 2009

REFERENCES

ANNEXES

Annex 1  SUMMARY OF RESEARCH PROJECT 2. 
PROSPECTIVE COHORT STUDY OF SHEEP DIP EXPOSURE AND 

In confidence - Members only.

Annex 2  FINAL PROJECT REPORT.
Prospective cohort study of sheep dip exposure and ‘dipper’s flu’.
HSE Project R51.242. (Povey et al.)

When published, the report will be available online at:

In confidence - Members only.


http://cot.food.gov.uk/cotreports/cotwgreports/organophosphates

Annex 4  Minutes of the COT meeting held 4 September 2007.
TOX/MIN/2007/05.