INTERNATIONAL COHORT STUDY OF CANCER MORTALITY AMONG EUROPEAN ASPHALT WORKERS
CASE-CONTROL STUDY OF LUNG CANCER

A Short Project Description

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Summary

Background and purpose of study
In 2001, the International Agency for Research on Cancer (IARC) reported that the relative risk for lung cancer was slightly increased in the total asphalt worker population and in pavers. However, the authors concluded that the data are insufficient to determine a causative link to any specific agent. The Phase II IARC study, funded by industry, is a case control study nested within the cohort study (NCC). A feasibility study showed that a case-control study is not feasible in Sweden, because of lack of information on companies in which cohort members were employed and ethical constraints in acquiring additional data. A case-control study of lung cancer is feasible in all other countries. The NCC is designed to clarify prior results by controlling the effect of confounding factors, i.e. coal tar and tobacco smoke. Results should be published in 2007.

Organisation
IARC is scientifically responsible for the study. To support the study, a Steering Committee, a Liaison Committee and a Scientific Advisory Committee have been established.

Cost and Funding
Total cost of study is 2.196.590.00 Euros, including 54.400.00 Euros for the Dermal Exposure Assessment. The project is funded by organisations representing producers and users of bitumen in Europe and USA.

Schedule and milestones
The case-control study commenced 1st June 2004 and is expected to last 36 months according to the following timetable:

<table>
<thead>
<tr>
<th>IARC NCC Study Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
</tr>
<tr>
<td>Selection of participants, identification of NOK</td>
</tr>
<tr>
<td>Dermal exposure database and evaluation of model</td>
</tr>
<tr>
<td>Interviews of subjects, NOK, fellow workers</td>
</tr>
<tr>
<td>Exposure assessment</td>
</tr>
<tr>
<td>Management of common database</td>
</tr>
<tr>
<td>Data analysis</td>
</tr>
<tr>
<td>Report writing</td>
</tr>
<tr>
<td>Meetings of steering committee</td>
</tr>
<tr>
<td>Meetings of Liaison Committee</td>
</tr>
</tbody>
</table>

Nomenclature:
- Activity
- Decision
- Meeting
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EUROPEAN ASPHALT WORKERS
CASE-CONTROL STUDY OF LUNG CANCER

A Short Project Description

Background and purpose of study
In 2001, the International Agency for Research on Cancer (IARC) reported that the relative risk for lung cancer was slightly increased in the total asphalt worker population and in pavers. However, there were also possible confounding exposures, i.e., coal tar and tobacco smoke, and the authors concluded that the data are insufficient to determine a causative link to any specific agent. The Phase II IARC study, funded by industry, was designed to clarify prior results by controlling the effect of confounding factors. Results should be published in 2007.

The main hypothesis to be tested in the case-control study will be whether the risk of lung cancer is increased according to estimated exposure (both by inhalation and dermal uptake) to bitumen fume, coal tar, total PAHs or other agents occurring in the asphalt industry, while adjusting for the estimated carcinogenic effect of tobacco smoking and exposure to other known and suspected lung carcinogens.

Description
The study is a Nested Case Control Study designed to investigate better the causes of mortality from lung cancer among cohort members in Phase I. This will be achieved by collecting more detailed information on occupational and non-occupational factors for all cohort members who died from (or were diagnosed with) lung cancer (cases) and a sample of cohort members free from lung cancer (controls).

Improvements in the assessment of confounding exposures and exposures to bitumen and bitumen fumes will be achieved by pursuing the following specific objectives:

i. Improving job histories within the asphalt companies via interviews to NOK and fellow workers;

ii. Improving inhalation exposure estimates (ROCEM) for bitumen fume and coal tar;

iii. Obtaining better information on significant potential confounding exposures, in particular smoking habits

iv. Obtaining better information on exposures of cases and controls in asphalt companies not included in the cohort;

v. Obtaining information on jobs held by cases and controls in non-asphalt companies;

vi. Deriving dermal exposure estimates for bitumen condensate and coal tar (feasibility evaluation of the dermal assessment model to be done after about 6 months)

Schedule and milestones
The case-control study is expected to last 36 months from signature of contract, according to the following timetable:
<table>
<thead>
<tr>
<th>Task</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection of potential participants</td>
<td>1</td>
</tr>
<tr>
<td>First meeting of the steering committee</td>
<td>1</td>
</tr>
<tr>
<td>Training of interviewers</td>
<td>1-2</td>
</tr>
<tr>
<td>Elaboration of dermal exposure database</td>
<td>1-3</td>
</tr>
<tr>
<td>Development and evaluation of dermal exposure model</td>
<td>2-6</td>
</tr>
<tr>
<td>Identification of NOK</td>
<td>2-8</td>
</tr>
<tr>
<td>Interviews to subjects and NOK</td>
<td>3-22</td>
</tr>
<tr>
<td>Interviews to fellow workers</td>
<td>3-22</td>
</tr>
<tr>
<td>Second meeting of the steering committee</td>
<td>12</td>
</tr>
<tr>
<td>Exposure assessment</td>
<td>13-24</td>
</tr>
<tr>
<td>Third meeting of the steering committee</td>
<td>24</td>
</tr>
<tr>
<td>Management of common database</td>
<td>13-27</td>
</tr>
<tr>
<td>Data analysis</td>
<td>25-30</td>
</tr>
<tr>
<td>Preparation of report</td>
<td>31-33</td>
</tr>
<tr>
<td>Finalization of report</td>
<td>34-36</td>
</tr>
<tr>
<td>Fourth meeting of steering committee</td>
<td>35</td>
</tr>
</tbody>
</table>

**Organisation**

IARC is scientifically responsible for the study.

Eurobitume is designated by the co-funders of the study to implement their financial and administrative contractual obligations on behalf of the Industry Group.

To execute, support and communicate the project, the following committees have been established:

1. The study Steering Committee: IARC, under the supervision of its Director, will carry out and supervise the study based on a protocol agreed to by all parties. IARC has established 9 collaborating centres, including the coordinating centre, which collectively form the study team. The principal investigators of each centre will form the Study Steering Committee, which is responsible for the conduct of all aspects of the study.

2. The Liaison Committee: The members are representatives of IARC and its collaborators on the one hand and representatives of Industry Group and its partner institutions on the other hand. The committee will meet as appropriate, but at least two times per year, to discuss the progress of the case-control study. The Industry Group is prepared to support the study with technical and scientific advice and information on industry practices or information on particular study cases. The Industry Group has designated a pool of experts and resources for this purpose, and its co-operation with the research team and input to the study will be coordinated through the Liaison Committee.

3. Scientific Advisory Committee (SAC): In order to facilitate the resolution of methodological, procedural and data quality issues the study team and the sponsors agreed to create a Scientific Advisory Committee (SAC), comprising independent experts:
   - J. Gamble
   - T. Sorahan
   - H. Roos
   - J. Melius

The SAC’s joint expertise covers both the conduct of nested case control studies including retrospective exposure assessment, as well as knowledge of the asphalt industry.

The SAC will support the study team with:
- Advice on the relevance and limitations of data obtained from non-peer reviewed studies, in particular where these have been obtained using non-standardised approaches;
• Review of the proposed study protocol, including the outcome of feasibility assessments of elements of the study;
• Review of feasibility of dermal exposure assessment;
• Advice throughout the study on request;
• Advice on data analysis;
• Peer-review of draft papers;
• Audits (to be agreed with study team and liaison group).

The SAC reports to the Liaison Committee

**Cost and funding**

Total cost of study is 2,196,590,- Euros, including 54,400,-Euros for the Dermal Exposure Assessment. The project is funded by organisations representing producers and users of bitumen in Europe and USA:

- CONCAWE : 549,147,50 Euro
- Eurobitume : 549,147,50 Euro
- EAPA : 549,147,50 Euro
- NAPA : 250,000,00 USD
- ARMA : 175,000,00 USD
- NRCA : 75,000,00 USD
- Eurobitume guarantee : Balance, limited upwards to 200,000,00 Euro

**SUM** : 2,196,590,00 Euro

It is understood that the Eurobitume Guarantee has been established for the outstanding funding in order to enable the Industry Group to sign the contracts without delay and start the IARC NCC study whilst the funding is continued to be worked in order to achieve a 50/50 user/producer balance

**Contractual relationships**

A contract for undertaking the study is entered between IARC and Eurobitume (the “IARC Agreement”), Eurobitume acting for itself and on behalf of the members of an Industry Group. The Study Technical protocol is included as Annex I in the IARC Agreement. The Industry Group consists of the funders of the study, ref the Cost and Funding section above. A separate agreement is entered between the members of the Industry Group regulating their commitments and interaction (“The Industry Agreement”)
IARC NCC Project Organisation
16th June 2004

Industry Liaison Committee
Purpose: Sponsors communication with the Study Steering Committee
• IARC/P. Boffetta
• CONCAWE/J Urbanus
• EAPA/N. Remmer
• Eurobitume/K Soraas
• ARMA/R. Snyder
• NRCA/T. Shanahan
• NAPA/G. Fore

Supported by their respective collaborators and organisations technical experts.

Scientific Advisory Committee
Purpose: Support the Study Team with advice
• J. Gamble
• T. Sorahan
• H. Roos
• J. Melius

Study Steering Committee
• P Boffetta
• Lead Collaborators (7 Ntl, 1 Exposure Assessment)

Coordinating Centre
• P. Boffetta

Collaborator Centers
• 7 National
• 1 Exposure Assessment Ctr.