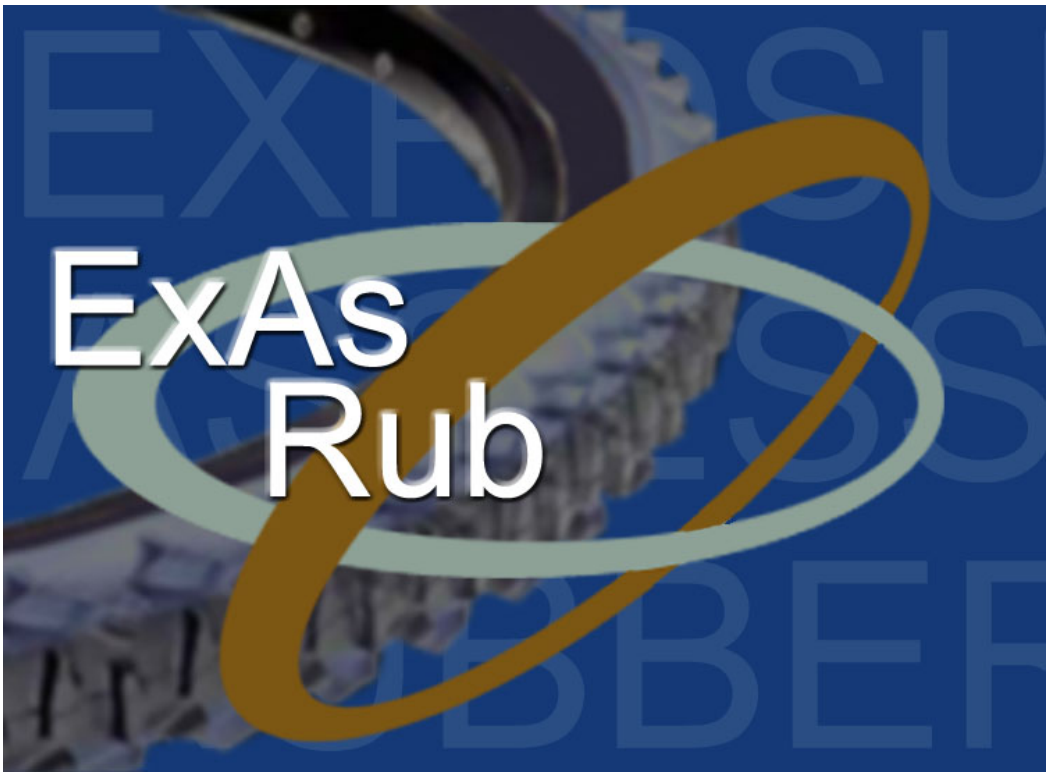
Final Report

Improved Exposure Assessment for Prospective Cohort Studies and Exposure Control in the Rubber Manufacturing Industry

(Jan 2002 - June 2004)



QLK4-CT-2001-00160
QLK4-CT-2002-02786

Utrecht, August 2004

PREFACE

The rubber manufacturing industry has come a long way to show that chemical exposures have decreased considerably over the last two decades. The 1982 and 1987 IARC reviews of carcinogenic risks in this industry came with a strong verdict declaring that working in this industry *entails exposures that are carcinogenic to humans (Group 1)*. A more recent review evaluating evidence coming from epidemiological studies carried out since the IARC evaluations, still indicated presence of a widespread moderate increased cancer risk among rubber workers. The most consistent results were for bladder, laryngeal, and lung cancer and for leukaemia. The authors stated that preventive measures taken in the industry may have decreased risks, but this was not documented yet in epidemiological studies and only to a very limited extent in industry-wide exposure surveys.

This EU-funded Concerted Action took up all these challenges and tried to improve exposure assessment for current epidemiological studies in this industry together with an evaluation of trends in exposures in this industry. In a very short time period a pan-European database was created consisting of ten-thousands of measurements of occupational exposures. The consequent statistical analyses of the compiled exposure data enabled the reproduction of the history of occupational exposures to rubber process dust and fumes, solvents and N-nitrosamines covering more than three decades. Not all challenges could be met due to for instance lack of detailed information relevant for exposure control. Nevertheless with the cooperation and support of the industry a unique industry-specific occupational exposure database was created that is now available for stakeholders in this industry and the public at large via the ExAsRub website. The analyses have shown that harmonised exposure assessment can be achieved in the ongoing epidemiological evaluation of cancer and other health risks and even pooled studies to increase the statistical power could be considered in the near future.

Working with a dedicated consortium was very efficient, but also very rewarding.

Hans Kromhout, coordinator EXASRUB
August, 2004

EXECUTIVE SUMMARY

<table>
<tr><td colspan="3">Section 1: PROJECT IDENTIFICATION
EXASRUB
QLK4-CT-2001-00160
QLK4-CT-2002-02786 (NAS extension)</td><td>NOT CONFIDENTIAL</td></tr>
<tr><td colspan="4">Title of the project
Improved Exposure Assessment for Prospective Cohort Studies and Exposure Control in the Rubber Manufacturing Industry</td></tr>
<tr><td colspan="4">Acronym of the contract
EXASRUB</td></tr>
<tr><td colspan="3">Type of contract
Concerted Action</td><td>Total project cost
€ 262,113</td></tr>
<tr><td>Contract number
QLK4-CT-2001-00160
(including amendment no (2)
QLK4-CT-2002-02786</td><td colspan="2">Duration (in months)
30 months</td><td>EU contribution
€ 262,113</td></tr>
<tr><td colspan="2">Commencement date
January 1, 2002</td><td colspan="2">Period covered by the final report
January 1 2002 - June 30, 2004</td></tr>
<tr><td colspan="4">PROJECT COORDINATOR</td></tr>
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<tr><td colspan="4">Key words
Exposure database, rubber manufacturing, exposure modelling, occupational hygiene, occupational epidemiology,</td></tr>
<tr><td colspan="4">World wide web address
http://exasrub.iras.uu.nl</td></tr>
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Section 2: PROJECT SUMMARY NOT CONFIDENTIAL

Objectives

To facilitate occupational exposure data exchange among stakeholders in health effects of employment in rubber manufacturing industry by creating a database of relevant chemical exposures in the industry.
In addition, to develop (via statistical modelling of the contents of the database):
- A scientific framework for creating a common exposure matrix for studies of health effects of exposures among workers in European rubber manufacturing industry, either through pooled analysis, meta-analysis or comparable national analyses
- Priorities for reducing personal occupational exposures in rubber manufacturing industry- Mechanisms for dissemination of current efforts to control exposures
- New ideas for effective exposure control measures in the industry

Results and Milestones

In the first year, Phase 1 consisting of work packages 1 to 3 was completed. The statistical analyses (Phase 2 covering work packages 4 to 6) took more time than anticipated and the granted extension of six months of the duration of the project was highly appreciated.
In ***work package 1*** partners 1, 3, 5, 7 and 9 identified and described data sets of occupational exposure measurements available to them. This work package resulted in a description of available exposure data in the European rubber manufacturing industry. Each of the 5 participants supplied to the co-ordinating centre a detailed description of occupational exposure data from the rubber manufacturing industry that they later made available for incorporation into a centralised database. The co-ordinating centre provided the participants with a database management system to facilitate standardised collection and reporting of the data. ***Deliverable 1*** summarises the findings of work package 1.
In ***work package 2***, the co-ordinating centre developed a database management system (DBMS) for exposure measurements collected in the European rubber manufacturing industry in order to facilitate efficient and effective amalgamation of the previously identified data sets. The structure of the DBMS depended on the outcome of work package 1. The DBMS comprises ***deliverable 2***. A training session with a first version of the DBMS was held during the second meeting of the Concerted Action in Lund (Sweden) to familiarise partners with use of the DBMS and to consult partners on how to improve the DBMS.
In ***work package 3***, all exposure information identified by the national partners was assembled into a common database using the DBMS developed at the co-ordinating centre. Data was either added to the database manually at each national centre, using a data entry interface that is an integral part of the DBMS, or (if data existed in electronic format) computer algorithms to import data were implemented.
Data gathered into the database were checked for errors using validation rules built into the data entry interface. We assessed the reproducibility of the coding and data entry procedures by re-entering a stratified random sample (1% from each country) of original records into the database. The EXASRUB database (DBMS, deliverable 2, with data) was produced that contains exposure measurements in the European rubber manufacturing industry; it constituted ***deliverable 3***. The EXASRUB database contains 27,095 measurements comprising 59,609 individual concentrations alongside auxiliary information, which puts the measurements into appropriate context. The time period covered in the database is from 1965 to 2003, with the majority of data from the last two decades. Before commencing statistical analyses of the data, additional checks for logical consistency of the information in the database took place. An add-on study comprising an international comparison of aerosol sampling heads, with fieldwork in four of the five participating counties, yielded very valuable data that allowed better calibration of dust measurements.
For ***work packages 4*** and ***5***, centralised statistical analysis of inhalable and respirable dust (rubber process dusts) and rubber fumes measurements revealed clear downward time trends as well as differences between countries, sectors within the industry and jobs. The elaborated statistical models were used to build historical job exposure matrices that could be used in

epidemiological research. These analyses were also done for exposure to solvents and n-nitrosamines. However limitations of the available data (e.g. different solvents were analysed in each survey, n-nitrosamines were almost exclusively measured in Germany) restricted the analyses to the solvents toluene and n-heptane and the n-nitrosamines NDMA and Nmor. Overexposure (long term exposure above occupational exposure limits) to rubber process dusts and rubber fumes was estimated and trends in exposure "hot spots" were visualised. We showed that average exposure to rubber process dusts and rubber fumes has dropped below existing occupational exposure limits for most countries since the beginning of the 1990s. As ***deliverables 4*** and ***5***, numerous statistical models were built and these are presented in this report. Information on control measures appeared to be less valid and reproducible or was often unavailable. Especially when data was entered from existing computerised databases, like the German MEGA-database and the British NEDB-database, detailed information on control measures was not available. This precluded the development of new ideas for effective measures to reduce exposure levels.
In ***work package 6***, the results of the Concerted Action were presented in a final report (***deliverable 6***). In addition a brochure (***deliverable 7***) was created in which the main results of the Concerted Action and the EXASRUB database are summarised. 1500 copies of the brochure were produced and have been disseminated through national and international associations of the rubber industry. In this folder the EXASRUB website (http://exasrub.iras.uu.nl) is brought to the attention to the stakeholders in the rubber industry. Through this website, the EXASRUB database is accessible via a web-based application that allows selection of agent, time period, type of industry, department, type of measurement, and measurement strategy, returning a graphical representation of the exposure data by country and year together with descriptive statistics (***deliverable 8***).
The results of this project will be published in peer-reviewed scientific journals. Several papers are in preparation. Results of the Concerted Action have already been presented at national and international scientific conferences.
A short delay occurred partly due to the extension of the project with (data from) the Polish partner. The Commission granted extension of the duration of the project with 6 months.

Benefits and Beneficiaries

The scope of the Concerted Action has exceeded our expectations. The sheer amount of measurement data that became available in a relatively short time was much greater than originally anticipated. With measurement data covering an almost 40 year period (1965-2003), the EXASRUB database will prove to be the major source for information on occupational exposures in the European rubber manufacturing industry. With the inclusion of Polish data, via a successful proposal for an extension of the consortium under NAS partnership, the database also covers working conditions that no longer exist. This should be especially valuable to scientists investigating chronic health risks due to exposures in the industry.
Through membership of representatives of the rubber manufacturing industry and their trade associations, the Concerted Action has been brought to the attention of the industry, as well as to the attention of individual companies and has also attracted interest from the USA. In addition, the two EXASRUB brochures were widely distributed to individual rubber companies in participating countries and rubber trade organisations. The most significant beneficiaries of the overall project will of course be persons employed in rubber manufacturing industry and communities where they reside. By using knowledge gained from analyses of the EXASRUB database and prior knowledge about important exposure determinants, further improvements in working conditions via reduction of exposures to potentially toxic substances, and through better epidemiological research can be expected. Such activities should lead to lowering the community burden of diseases attributable to occupation in rubber manufacturing.

Future Actions

The EXASRUB consortium has indicated that cooperation among its members will continue after the end of the Concerted Action. The prolonged existence of the EXASRUB website will be of great help in this regard. The website is accessible for the public at large, but has in addition a restricted area for the consortium members to monitor the progress of continued data analysis. Interest from rubber companies from the USA might lead to extensions of the database outside its current pan-European nature. Funding possibilities for pooling of ongoing European epidemiological studies are being explored. The ongoing studies in Germany, Poland, United Kingdom and Sweden will in any case apply the exposure estimates generated from the EXASRUB project.

LIST OF PARTICIPANTS

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