

Forskningsprogram			
SNAP	<input checked="" type="checkbox"/>	REPROSAFE	<input type="checkbox"/>
FLIPP	<input type="checkbox"/>	Inriktning: Ekonomiska styrmedel	<input type="checkbox"/>
		Inriktning: Informationssystem och indikatorer IPP	<input type="checkbox"/>
Projekttitel (svensk): Ozonexponering och påverkan på inflammation och koagulation			
Projekttitel (engelsk): Ozone exposure, inflammation and coagulation			
Huvudsökande	Efternamn: Sjögren	Förnamn: Bengt	Födelseår: 1946
			Kvinna <input type="checkbox"/> Man <input checked="" type="checkbox"/>
	Organisation: Karolinska Institutet		Institution: Institutet för miljömedicin
	Adress: Nobels väg 13	Postnr: 171 77	Ort: Stockholm
Telefon: 08/524 822 29	E-post: bengt.sjogren@imm.ki.se	Tjänst: Forskare	
Medsökande	Efternamn, förnamn, tjänst, organisation, institution: Johanson Gunnar, professor, Karolinska Institutet, Institutet för miljömedicin		
	Telefon: 08/524 877 52	E-post: gunnar.johanson@imm.ki.se	Kvinna <input type="checkbox"/> Man <input checked="" type="checkbox"/>
1) Projektets betydelse för programmet			
Ozon är en betydande luftförorening i utomhusmiljön och en kraftig oxidant. Flera epidemiologiska studier har observerat en ökad dödlighet och sjuklighet vid lätt förhöjda ozonhalter. En meta-analys av flera korttidsstudier har visat att en ökning av ozonhalten med 10 µg/m ³ (5 ppb) innebar ökad dödlighet i samtliga sjukdomsorsaker utom olycksfall med 0,2 till 0,6%. I flera Nordamerikanska städer har man iakttagit en ökad förekomst av hjärtsjukdom som associerats med exponering för ozon. I vilken grad ozon bidrar till hjärtsjukdom och verkningsmekanismen för detta är fortfarande oklart.			
2) Miljörelevans och förväntad betydelse för miljöpolitiken			
En större förståelse för mekanismerna bakom sambandet mellan exponering för ozon och hjärtsjukdom kan förbättra riskbedömningen av ozon och därmed ge ett bättre underlag för miljöpolitiska åtgärder.			
3) Mål och hypotes			
Syftet är att studera doseffekts sambandet mellan exponering för ozon och koncentrationerna av olika biomarkörer för inflammation och koagulation samt hjärtfrekvensvariabilitet.			
Hypotesen är att ozon skapar en låggradig inflammation i lungorna som ökar plasmahalten av etablerade riskfaktorer för hjärtinfarkt. Dessa riskfaktorer är bl a fibrinogen och C-reaktivt protein (CRP).			
4) Metodik och genomförande			
Friska icke-rökande försökspersoner (10 kvinnor och 10 män) kommer att delta i undersökningen. Försökspersonerna kommer att exponeras vid fyra olika tillfällen för 0, 100, 200 och 400 µg/m ³ (0, 50, 100 och 200 ppb) under 2 timmar med intermittent lätt arbete i vår försökskammare. Exponeringen kommer att ske under tiden september – mars då utomhushalterna av ozon är låga. Historiska data har visat att halterna är omkring 20 µg/m ³ (10 ppb) och nästan aldrig överskrider 80 µg/m ³ (40 ppb) i Stockholm. Flera biomarkörer i plasma eller serum kommer att bestämmas såsom interleukin-6, CRP, fibrinogen, fibrin D-dimer och Claracellprotein. Blodgrupperna kommer att bestämmas eftersom blodgrupp O förknippats med en högre risk för hjärtinfarkt vid exponering för luftföroreningar. Lungfunktionen undersöks också. Ett godkännande av den regionala etiska kommittén vid Karolinska Institutet krävs innan studien påbörjas.			
5) Kommunikationsinsatser i relation till programmet			
Resultaten kommer att presenteras vid nationella och internationella vetenskapliga konferenser och i internationella vetenskapliga tidskrifter. Resultaten kommer också att presenteras på svenska för allmänheten och för myndigheter för att utgöra underlag för riskbedömning.			
		År 2004	År 2005
Summa sökta medel per år i kr:		939 438	840 510

Miljöforskningsnämnden
Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram

Sökta projektmedel fördelade på kostnadslag	År 2004 (kr)	År 2005 (kr)
Personalkostnad inkl. soc. avgifter* Bengt Sjögren, forskare, 25% under 2 år, 0,25 x 2 x 12 x 1,6 x 40 000 Lena Ernstgård, biomedicinsk analytiker, 25% under 2 år, 0,25 x 2 x 12 x 1,6 x 22 000 Susanna Höglund-Lenninger, forskningsingenjör, 25% under 2 år, 0,25 x 2 x 12 x 1,6 x 20 000	192 000 105 600 96 000	192 000 105 600 96 000
Övriga omkostn exkl moms (förbrukningsmtrl, analyser, resor etc)** Ozongenerator, ozonlogger 2 telemetriutrustningar à 13 970 2 programlicenser för ekg-utrustningar Installation av program och utrustningar Redigering av EKG-registreringar Ersättning till försökspersoner Analys av prover 240 prover à 600 Förbrukningsmaterial	141 000 27 940 63 340 5 000 40 000 25 000	20 000 40 000 144 000 25 000
Delsumma av ovanstående poster:	695 880	622 600
Förvaltningspåslag: 35 %	243 558	217 910
Totalsumma per år: (införs sid. 1):	939 438	840 510

*) Specificera namn, tjänst **) Specificera

Samtliga övriga miljörelaterade projekt för vilka de sökande har beviljats anslag eller söker anslag för 2004-2006. OBS Även EU-finansiering.

Projekttitel	Finansiär	Tidsperiod	Sökt kr	Beviljat kr
Kontrollerad exponering för ozon – påverkan på hjärtfrekvensvariabilitet och biomarkörer för oxidativ stress, inflammation och koagulation	FORMAS	2004-2005	1 510 480	-
Kan cyanid i utandningsluft användas för att påvisa cyanidförgiftning?	Carnegie	2004	247 000	-

**Miljörelaterade projekt för vilka sökande har beviljats anslag för 2000-2003
OBS Även EU-finansiering**

Projekttitel	Finansiär	Tidsperiod	Beviljat Kr
Förbättrat underlag för bedömningsfaktorer genom toxikokinetisk modellering	FAS	2002-2003	1 125 000

Datum och sökandes underskrift, vilken samtidigt ger Naturvårdsverket tillåtelse att publicera sökandes namn på sin webbplats:	Datum och underskrift av prefekt eller motsvarande med namnförtydligande: Göran Pershagen
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Ansökan skall bestå av detta formulär jämte högst sex sidor lång projektbeskrivning på **engelska** (strukturerad som den svenska sammanfattningen samt en redovisning av kunskapsläget). Referenser till egna publikationer ges med sifferhänvisning till CV. Andra referenser ges i löpande text. Sökandes och eventuell medsökandes CV får omfatta högst två sidor. Inga bilagor kommer att beaktas vid bedömningen. Ansökan (max 10 A4-sidor, 12 punkters teckenstorlek) skall inlämnas i **original + 15 kopior samt elektroniskt** till ansok@naturvardsverket.se. Häfta ihop ansökan och använd hålat papper. Ansökan skall ha inkommit senast den 15 oktober 2003 till Naturvårdsverket, Forskningssektariatet, 106 48 STOCKHOLM.

Ozone exposure, inflammation and coagulation

Background

Inflammatory disorders and ischemic heart disease

Several disorders associated with inflammation have been linked with the occurrence of ischemic heart disease (IHD). Some of these diseases are periodontitis (*Beck et al, Annals Periodontol 1998;3:127-41*), rheumatoid arthritis (*Wällberg-Jonsson et al, J Rheumatol 1997;24:445-51*), systemic lupus erythematosus (*Manzi et al, Am J Epidemiol 1997;145:408-15*), psoriasis (*Mallbris et al, Euro J Epidemiol, accepted*), and chronic bronchitis (*Haider et al, Am J Med 1999;106:279-84*). These inflammations show changes of several markers of inflammation and coagulation. Thus the concentrations in plasma of C-reactive protein (CRP) and fibrinogen increase at inflammations. Concentrations of circulating fibrin D-dimer reflect the extent of fibrin turnover in the circulation, as this antigen is present in several degradation products from the cleavage of cross-linked fibrin by plasmin. Meta-analyses have shown CRP, fibrinogen, and D-dimer to be risk factors for IHD, table 1. During the 1990s a theory was launched which linked inhalation of air pollutants to the occurrence of IHD (*Seaton et al, Lancet 1995;345:176-8; 2*). Inhaled air pollutants are assumed to evoke a low grade inflammation in the lungs, which increases the level of fibrinogen and other coagulation factors in the plasma. This idea has been called the Seaton-Sjögren hypothesis (*Kristensen, Scand J Work Environ 1999;25:550-7*). We have observed an increase of plasma fibrinogen among volunteers weighing pigs (4) and a slightly increased risk for IHD among livestock agricultural workers (13). Several occupations with known air pollutant exposure have been associated with an increased occurrence of IHD such as welders (10), miners (11), and female cleaners (12).

Table 1. Relative risk for ischemic heart disease between subjects with high and low levels of some markers of inflammation and coagulation (*Danesh et al, JAMA 1998;279:1477-82; Danesh et al, Circulation 2001;103:2323-7*).

Marker	High mean concentration	Low mean concentration	Relative risk and 95% confidence interval
C-reactive protein (CRP)	2.4 mg/l	1.0 mg/l	1.7 1.4-2.1
Fibrinogen	3.5 g/l	2.5 g/l	1.8 1.6-2.0
D-dimer	126 µg/l	50 µg/l	1.7 1.3-2.1

Role and significance for the SNAP programme

Ozone is an important part of outdoor air pollution and a potent oxidant. During the latest decade the levels of ozone have increased by 5-10% in the Stockholm area.

Ozone inhalation causes an increase in free radicals, oxidative stress and an inflammatory response. These effects include changes in lung capacity, flow resistance, epithelial permeability, and reactivity to bronchoactive challenges. After exposure of humans to 100 ppb ozone for 6.6 hours with moderate exercise the number of neutrophils and interleukin-6 increased in the bronchoalveolar lavage as an expression of inflammation (*Devlin et al, Am J Respir Cell Mol Biol 1991;4:72-81*). Interleukin-6 is known to increase the production of fibrinogen in the liver (*Akira & Kishimoto, Immunol Rev 1992;127:25-50*) and increased

fibrinogen concentration in plasma is an established risk indicator for ischemic heart disease (*Danesh et al, JAMA 1998;279:1477-82*). At an ozone exposure of 350 ppb the concentration of fibrinogen increased in bronchoalveolar lavage (*Weinmann et al, Am J Respir Crit Care Med 1995;152:1175-82*), but this increase may have been caused by an increased vascular permeability and is not necessarily associated with an increased plasma concentration.

Heart rate variation reflects the balance between the sympathetic and parasympathetic nervous system. The interest in this balance increased after the observation of the link between low heart rate variability and an increased cardiovascular mortality (*Tsuji et al, Circulation 1994;90:878-83*). In a study of 21 (53 to 87-year-old) active Boston residents a low heart rate variability was associated with higher concentrations of ozone or particles in ambient air (*Gold et al, Circulation 2000;101:1267-73*).

A well-controlled investigation of biomarkers and heart rate variability are needed in order to understand more of the mechanisms of ozone toxicity. Demonstration of an exposure-dependent increase of markers of inflammation and coagulation would add further support to the link between inflammation and IHD. Validated biomarkers are expected to improve the quality and reduce the uncertainty in risk estimates and may thus play an important role in the Swedish National Air Pollution and Health Effects Programme.

Environmental relevance and significance for environmental policy

Ambient ozone exposures have in numerous publications been shown to cause measurable decrements in lung function and airway antioxidant concentrations (*Lippmann & Schlesinger, Annu Rev Public Health 2000;21:309-33*). Epidemiological studies indicate increases in human mortality and morbidity at slightly elevated ambient concentrations (*Mudway & Kelly, Molecular Aspects Med 2000;21:1-48*). Respiratory and cardiac hospitalization have been associated with ambient levels of ozone in several North American cities (*Burnett et al, Environ Health Perspect 1997;105:614-20*) and in ten large European cities (*Zmirou et al, Epidemiol 1998;9:495-503*). Meta-analysis of studies published between 1996 and 2001 on short-term effects of ozone on all non-accidental causes of death showed a significantly increased mortality between 0.2% and 0.6% per 5 ppb of ozone increase (*WHO Working Group, 2003, www.who.dk*). A recently published study observed an increased mortality related to ozone concentrations in the summer in Vancouver, British Columbia, despite rather low levels of ozone (90 percentile 39 ppb) (*Vedal et al, Environ Health Perspect 2003;111:45-51*). In Sweden a total of about 1730 deaths per year are calculated to occur earlier than expected as a cause of ozone exposure (*Forsberg et al, Hälsokonsekvenser av ozon, Institutionen för folkhälsa och klinisk medicin, Umeå 2003*).

Information of the behaviour of biomarkers of IHD among healthy subjects after experimental ozone exposure is one important step for improving the data base on effects by ozone exposure. Future steps (not included in the present study) include investigations on persons with risk factors for IHD during summer days with high concentrations of ozone. The results may improve risk assessment of ozone exposure.

Objective and hypothesis

The information necessary to fully assess the health significance of ozone is not currently available. The primary aim of the present study is to establish a dose-effect relationship between ozone exposure and some non-invasive biomarkers of inflammation and coagulation as well as heart rate variability. A dose-effect relationship will also address the issue of thresholds.

Methods and implementation

Healthy, non-smoking, non-asthmatic volunteers (10 females and 10 males) will participate in the study. All volunteers should be younger than 45 years of age and they will have a medical check prior to participation. Persons with asthma or other airway diseases will be excluded. Exposures to ozone will be carried out in our in-house dynamic exposure chamber designed for exposure of volunteers to vapors and gases (*Ernstgård et al, Occup Environ Med 2002; 59:759-67*). Up to four individuals at a time will be exposed to 0, 50, 100 or 200 ppb ozone for 2 h during intermittent light exercise. The participants will be exposed to all levels and the order of exposures will be balanced. The exercise will be performed on an ergometer bicycle within the chamber during two periods of 30 minutes with 50 W workload. The period between two exposures will be at least 2 weeks. The volume of the chamber is 20 m³. Ozone will be generated in the inflowing air using an AM 3000 instrument (Ozone Technology, Sweden). Ozone will be measured inside the chamber. The days of exposure data from local environmental authorities will be used to survey outdoor ozone concentrations. All exposures will be performed between September and March when outdoor concentrations of ozone are low. Historical data show that during this period the average level is around 10 ppb and almost never exceeds 40 ppb in Stockholm.

The study presumes an approval from the Regional Ethical Committee at Karolinska Institutet. Exposures will only be performed after informed consent by the participants.

Several biomarkers in plasma or serum will be measured such as interleukin-6 (IL-6), C-reactive protein (CRP), fibrinogen, fibrin D-dimer, myeloperoxidase, and Claracell protein (CC16). These markers of inflammation and coagulation will be measured before and after; 2 h, 5 h and 25 h after the beginning of exposure. The blood groups (ABO) of the participants will be determined as subjects with blood group O were reported to have a higher risk for IHD when exposed to occupational air pollutants (*Suadicani et al, J Cardiovasc Risk 2002;9:191-8*).

It is well documented that ozone exposure affects lung function. Non-smokers had a more pronounced response than smokers when exposed to 220 ppb for 4 hours with intermittent moderate work (*Frampton et al, Am J Respir Crit Care Med 1997; 155:116-21*). Lung function tests will be performed in order to correlate possible changes with the levels of biomarkers. The following parameters will be measured before and after exposure: VC, FVC, PEF, FEV1, FEF25, FEF50, and FEF75.

The participants will rate perceived irritation and symptoms from the central nervous system in a questionnaire before, during, and after ozone exposure.

Electrocardiogram (ECG) will be monitored during the exposure to assure that adverse health effects do not occur. The heart rate variability will be studied with Holter ECG registration during the exposure period and two hours after exposure.

The genotype for the quinone-metabolizing enzymes NQO1 and GSTM1 will be determined as they were recently reported to influence the degree of ozone-induced acute effects on the lung.

Ozone generates oxidative stress and blood samples will be collected and stored in *RNA Later* (Ambion Austin, TX) at -20°C for future analyses of gene expression that reflect oxidative stress in another study.

Time plan

Before summer 2004 the ozone generator and complimentary ECG equipment will be installed and volunteers recruited.

Between September 2004 and March 2005 the exposure will take place.

April 2005- August 2005 analyses of blood samples.

Autumn 2005 analyses of data and in December presentation of results to SNAP.

Costs

Salaries

Project leader and physician 25% for 2 years, 2 x 0.25 x 12 x 1.6 x 40 000	384 000
Med. lab. techn. 25% % for 2 years, 2 x 0.25 x 12 x 1.6 x 22 000	211 200
Research engineer 25% for 2 years, 2 x 0.25 x 12 x 1.6 x 20 000	192 000

Technical equipment

Ozone generator and ozone logger	141 000
2 equipments for telemetric surveillance à 13 970	27 940
2 licences for ECG registration programs à 31 670	63 340
Installation of equipments and programs	5 000

Further expenses

Compensation to participants 4 exposures x 20 subjects x 1000	80 000
Analyses of blood samples 240 samples à 600	144 000
Editing ECG recordings	20 000
Consumable articles	50 000

Overhead costs for Karolinska Institutet 35%	461 468
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Total: 1 779 948 SEK

Competence

The unit of Work Environment Toxicology at the Institute of Environmental Medicine was previously the Program for Toxicology and Risk Assessment at the National Institute for Working Life. This unit has long experience of experimental studies on humans from e.g. solvents. Co-applicants are professor Gunnar Johanson, with long experience of human

exposure chamber studies, and associate professors Agneta Rannug and Margareta Warholm, both with long experience of studies of biomarkers.

The contribution from Bengt Sjögren will be 25% which is included in the application. The contributions from Gunnar Johanson, Agneta Rannug and Margareta Warholm will be approximately 10% during two years and this will be covered from other sources. Professor Björn Wiman at the Department of Clinical Chemistry and Blood Coagulation at the Karolinska Hospital will analyse most of the markers of inflammation and coagulation.

Dissemination of results

The results will be presented at national and international conferences and will be published in international scientific journals in the field of environmental medicine. The results will also be presented in Swedish reports to the general public and to public agencies for use in risk assessment.

Curriculum Vitae

Bengt W Sjögren

Date of birth: March 21, 1946

Affiliation: Institute of Environmental Medicine, IMM
Karolinska Institutet, SE-171 77 Stockholm

Education: M.D. 1972, Karolinska Institutet, Stockholm
1978 specialist in Occupational Medicine
Ph.D. 1985, Karolinska Institutet, Stockholm
Title of thesis: *Respiratory disorders and biological monitoring among electric-arc welders and brazers.*

Present position:

Senior Researcher, Institute of Environmental Medicine, Karolinska Institutet,
From January 2002.

Previous positions:

Research Physician, National Board of Occupational Safety and Health (1974-1987).
Research Physician, National Institute of Occupational Health (1987-1995).
Senior Researcher, National Institute for Working Life (1995-2001).

Appointments:

Secretary in the Programme for Research and Development in Occupational Health Services at the National Institute of Occupational Health, (1989-1990).
Chairman, Working Group for Health and Safety, Swedish Institute of Welding (1991-present).
Member of the Swedish Criteria Group for Occupational Standards (1993 – present).

Assistant Course Leader, Course for Occupational Health Physicians, (1990-2002).

Member of Course Faculty, Course for Occupational Health Nurses, (1990-2001).

Member of Course Faculty, Occupational Safety and Health in Practice. Eastern and Central Europe, 1995-1996 and 1997-1998. Asia 1997-1998.

Member of Course Faculty, NIVA Baltic Course on Planning and Reporting of Research in Occupational Safety and Health, Tallinn, Estonia 1996.

Member of Course Faculty, Occupational Safety and Health & Development, Latin America and the Caribbean, 1998-2000.

Expert tasks regarding risk assessment:

WHO Task Group on Environmental Health Criteria for Aluminium.
Environmental Health Criteria 194. *Aluminium*. WHO Geneva 1997.
Criteria Documents from the Nordic Expert Group, *Ethyleneglycol*, 1980,
Welding gases and fumes, 1990, and *Aluminium*, 1992.

Publications and reports:

Author or co-author of 34 published original scientific papers, 6 book chapters, and more than 50 popular scientific articles, scientific reports, including letters to the editor.

Some publications regarding the association between occupational exposures, inflammation and coronary heart disease:

1. Sjögren B. Symptoms of chronic bronchitis and the risk of coronary disease. Letter to the editor. *Lancet* 1996; 348: 1389.
2. Sjögren B. Occupational exposure to dust: inflammation and ischaemic heart disease. *Occup Environ Med* 1997; 54: 466-469.
3. Sjögren B. Mortality of Dutch coal miners in relation to pneumoconiosis, chronic obstructive pulmonary disease, and lung function. Letter to the editor. *Occup Environ Med* 1998; 55: 503.
4. Sjögren B, Wang Z, Larsson B-M, Larsson K, Larsson PH, Westerholm P. Increase in interleukin-6 and fibrinogen in peripheral blood after swine dust inhalation. *Scand J Work Environ Health* 1999; 25: 39-41.
5. Sjögren B. Lung cancer among industrial sand workers exposed to crystalline silica. Letter to the editor. *Am J Epidemiol* 2001; 154: 785.
6. Sjögren B. Association between pleural plaques and coronary heart disease. Letter to the editor. *Scand J Work Environ Health* 2001; 27: 420-421.
7. Sjögren B. Ta hänsyn till influensavaccinering vid studier av hjärtsjukdom, Korrespondens. *Läkartidningen* 2001; 98: 1717.
8. Sjögren B, Gunnare S, Sandler H. Inhalation of decomposed freon and myocardial infarction. *Scand J Work Environ Health* 2002; 28: 205-207.
9. Sjögren B, Knutsson A, Bergström H, Fellenius E, Fernström B, Isling D, Söderholm M. Fibrinogen concentrations in aluminium smelter workers. *C Eur J Occup Environ Med* 2002; 8: 49-54.
10. Sjögren B, Fossum T, Lindh T, Weiner J. Welding and ischemic heart disease. *Int J Occup Environ Health* 2002, 8: 309-311.
11. Sjögren B, Barlow L, Weiner J. Ischemic heart disease among miners and other quartz-exposed workers. *La Medicina del Lavoro* 2002; 93 suppl: S34-S35.
12. Sjögren B, Fredlund P, Lundberg I, Weiner J. Ischemic heart disease in female cleaners. *Int J Occup Environ Health* 2003, 9: 134-137.
13. Sjögren B, Weiner J, Larsson K. Ischaemic heart disease among livestock and agricultural workers. *Occup Environ Med* 2003; 60:e1.

Curriculum Vitae for Gunnar Johanson

Date of birth 26 March 1951
Nationality Swedish
Current position Head of Division and Professor of Occupational Toxicology and Risk Assessment
Division Work Environment Toxicology,
Institute of Environmental Medicine (IMM), Karolinska Institutet (KI)
Address Division f Work Environment Toxicology, IMM, KI, SE-171 77 Stockholm, Sweden
Phone +46 8 5248 7752
Fax +46 8 314124
Email Gunnar.Johanson@imm.ki.se

Academic degrees

1988 Doctor of Medical Sciences (equivalent to Ph.D.) in toxicology, KI
Thesis title: Toxicokinetics of 2-butoxyethanol. Uptake, distribution, metabolism, and excretion in man and laboratory animals
1984 Master of Science in toxicology, KI
1973 Bachelor of Science in chemistry and biology, Uppsala University

Previous positions

2000 - 2001 Professor of occupational toxicology/risk assessment, National Institute for Working Life (NIWL)
1999 - 2002 Adjunct professor of occupational toxicology, Dept. of Medical Sciences, Uppsala University
1999 - 2001 Program Director, Toxicology and Risk Assessment, NIWL
1991 - 1999 Associate professor of occupational and environmental medicine, Dept. of Medical Sciences, Uppsala university
1989 - 1990 Occupational hygienist/toxicologist, Dept. of occupational and environmental medicine, Uppsala university hospital
1988 - 1997 Senior researcher, NIWL
1984 - 1988 Research engineer, NIWL
1982 Toxicologist, Dept. of Toxicology, Swedish National Food Administration
1979 - 1982 Teacher in mathematics and biology, Escola Agrária de Namachaa, and councillor in mathematics, Ministry of Education, Moçambique
1974 - 1979 Research assistant, Dept. of Animal Physiology, Swedish University of Agriculture

Expert tasks

2003 - Scientific Advisory Panel, Swedish National Board of Health and Welfare
2003 - Steering Group, Knowledge Center in Emergency Toxicology, Swedish National Board of Health and Welfare
2001 - Advisory Expert Group for Cancer, Swedish Chemicals Inspectorate
1999 - Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (chairman)
1999 - Scientific Committee on Occupational Exposure limits, DG Employment, European Commission
1998 Expert, health risk assessment of dichloromethane, IMM, KI
1993 - Expert and vice chairman, Swedish Criteria Group for Occupational Exposure Limits, NIWL
1993 - 1995 Scientific secretary of the Toxicological Council, Swedish Chemicals Inspectorate, Stockholm

Membership in scientific societies

American Conference of Governmental Industrial Hygienists (ACGIH)
International Commission on Occupational Health (ICOH) + Scientific Committee on Occupational Toxicology
International Society of Exposure Analysis (ISEA)
International Society for the Study of Xenobiotics (ISSX)
Swedish Academy of Pharmaceutical Sciences
Swedish Medical Association
Swedish Occupational and Environmental Hygiene Association
Swedish Society of Toxicology
U.S. Society of Toxicology (SOT) + Biological Modeling and Risk Assessment Specialty Sections

Supervision of PhD students

Presently supervising: BSc Lena Ernstgård, MSc Sara Gunnare, MSc Tina Isaksson, MSc Matias Rauma

PhD degrees completed:

- 2001 Fredrik Jonsson: "Physiologically based pharmacokinetic modeling in risk assessment. Development of Bayesian population methods"
- 2000 Annsofi Nihlén: "Ethers as Gasoline Additives: Toxicokinetics and Acute Effects in Humans"
- 1998 Jill Järnberg: "Toxicokinetics of Inhaled Trimethylbenzenes in Man"
- 1995 Agneta Falk Filipsson: "Toxicokinetics and acute effects of inhalation exposure to monoterpenes in man"

Publications and presentations

Author or coauthor of over 70 internationally published peer-reviewed scientific papers, 8 edited books and book chapters, 12 risk assessment reports and criteria documents, over 140 conference presentations (whereof over 20 as invited or keynote speaker), and about 40 popular scientific articles and other scientific reports.

Awards

- 2001 Recipient of the Herbert E. Stokinger Award for outstanding achievement in industrial toxicology by the American Conference for Industrial Governmental Hygienists
- 1992 Best presentation award, 10th Scandinavian Cell Toxicology Congress

Fellowships

- 1994 Visiting scientist (1 mo), Dept of Environmental Health, Medical University of Yamanashi, funded by the Japanese Science Foundation
- 1991 Visiting scientist (3 mo), Institute of Toxicology, GSF, Munchen, funded by the Swedish Work Life Fund
- 1989 Popular science writing (1 mo), Forskning och Framsteg magazine, funded by the popular scientific journal Forskning och Framsteg
- 1988 Visiting scientist (3 wk), Dept of Environmental Health, Medical University of Yamanashi, funded by the Swedish Work Life Fund