



SIKKER-MOTOR

# Sikker-Motor

Sundhedsskadelige effekter af rense- og smøremidler – bedre risikovurdering på virksomheder der vedligeholder motorer og maskiner

Projektnr.: 29-2019-09



Niels Hadrup, Seniorforsker

Jorid B. Sørli, Seniorforsker

Marie Frederiksen, Senioforsker

3. Maj 2023

# Formål

Afdække i hvilket omfang motorrense og smøremidler på sprayform udgør et sundhedsproblem på danske arbejdspladser

- *autobranchen, maskiner i landbruget og entreprenørbranchen samt i skibes maskinrum.*

Bidrage til en bedre risikovurdering ved at kortlægge produkternes indholdsstoffer samt udføre toksikologiske analyser

*Vi fik ideen til projektet fordi branchen efterspurgte flere data på området*

# Trin 1: Database over indholdsstoffer i 82 produkter

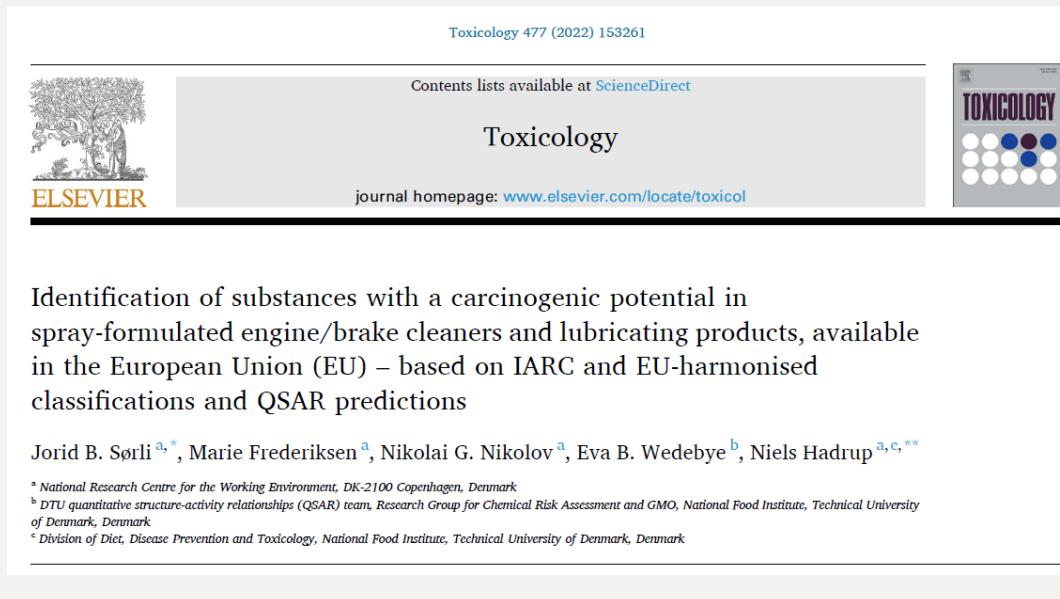
- A) Prioritering af stoffer til testning
- B) Klarlægning af genotokskisk (DNA-skadende) effekt samt kræftpotentialet
- Metode: IARC klassificering
- EU harmoniseret klassifikation
- Quantitative structure activity relationship (QSAR) computermodeller
- Database: 376 indholdsstoffer

82 produkter

43	Producer 2							
44	3	Engine cleaner	Mechanical spray	Potassium hydroxide Amines, coco alkylidimete D-Glucopyranose, oligon	1310-58-3 61788-90-7 85515-73-1	Assessed to be Multi-constituent Assessed to be Multi-constituent	No No	
45				Alkohol, C9-11, ethoxylate	68439-46-3	UVCB	Mix number	
46				Above CAS number is the below components accor			na	
47				Decan-1-ol, ethoxylated	26183-52-8		Yes	
48				Undecan-1-ol, ethoxylate	34398-01-1		Yes	
49				Nonan-1-ol	143-08-8		Yes	
50				Decan-1-ol	112-30-1		Yes	
51				Undecan-1-ol	112-42-5		Yes	
52								
53								
54	4	Brake cleaner	Aerosol spray	Hydrocarbons, C6-C7, na	No CAS number provided	Assessed to be Multi-constituent	na	
55				Butan	106-97-8		Yes	
56				Acetone*	67-64-1		Yes	
57				Isopropylalkohol*	67-63-0		Yes	
58				Carbon dioxide	124-38-9		No	
59	5	Lubricant	Aerosol spray	Hydrocarbons, C7, n-alka	64742-49-0	UVCB	Mix number	
60				Propan	74-98-6		Yes	
61				Butan	106-97-8		Yes	
62				Isopropylalkohol*	67-63-0		Yes	
63	6	Lubricant	Aerosol spray	Hydrocarbons, C7, n-alka	64742-49-0	UVCB	Mix number	
64				Propan	74-98-6		Yes	
65				Butan	106-97-8		Yes	
66	7	Carburator cleaner	Aerosol spray	No SDS available on the	na		na	
67	8	Lubricant	Aerosol spray	Propan-2-ol	67-63-0		Yes	

# Trin 1: Database over indholdsstoffer i 82 produkter

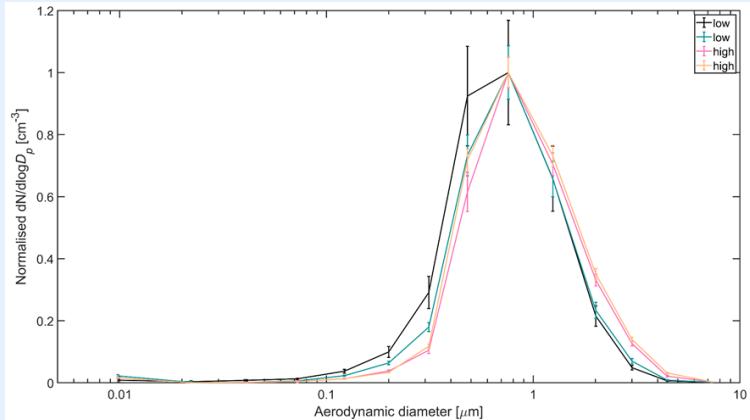
- Ud af 376 indholdsstoffer:
  - 24 potentielt kræftfremkaldende enkeltstoffer
  - 28 potentielt kræftfremkaldende olieblandinger i produkterne
- Potentielt kræftfremkaldende stoffer og olieblandinger i 39 af de 82 produkter
- Kan bruges regulatorisk til at få et overblik over området, samt i *safe-by-design* til at udvikle og vælge produkter uden eller med et lavere kræftpotentiale



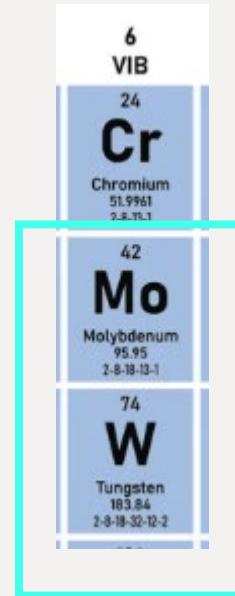
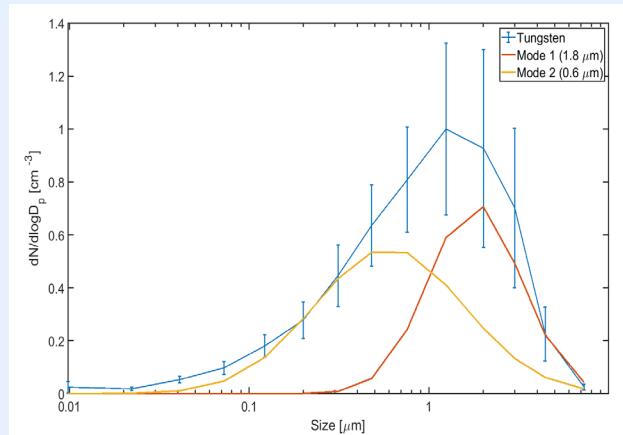
## Trin 2: Subakutte indåndingsforsøg i mus

- Molybdæn disulfid og wolfram kan smøre
- De er ingredienser i mange smøremidler på sprayform

Molybdæn disulfid  $< 2\mu\text{m}$



Wolfram  $< 1 \mu\text{m}$



# Subakutte forsøg molybdæn disulfid

## Metode



Kontrol

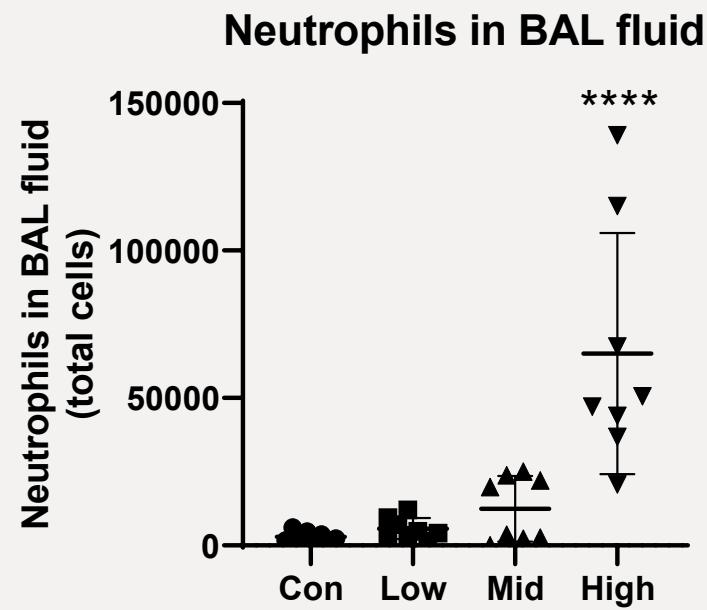
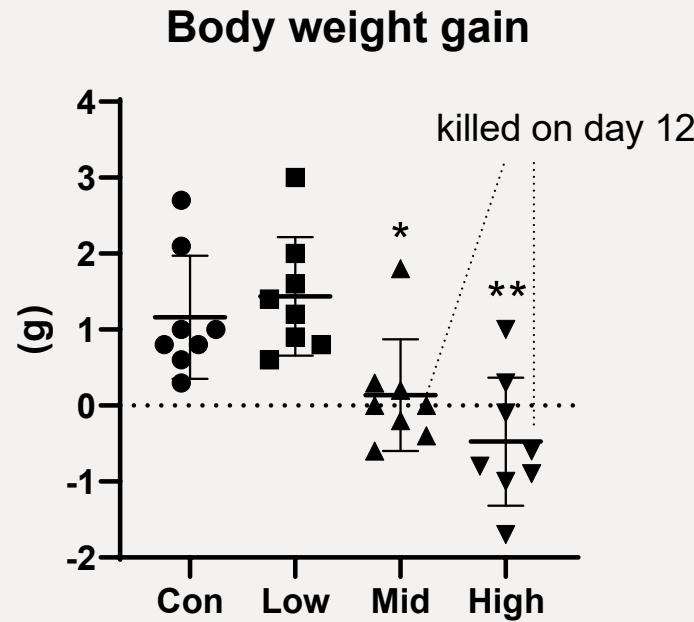
Lav dose: Molybdæn disulfid 13 mg/m<sup>3</sup> (30 minutter/dag)

Mellem: Molybdæn disulfid 50 mg/m<sup>3</sup>

Høj: Molybdæn disulfid 150 mg/m<sup>3</sup>

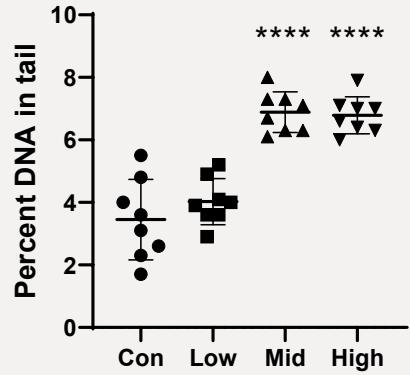
- Legemsvægt
- Bronkoalveolære væske (BAL) cellularitet (inflammation)
- Genotoxicitet ved kometassay in BAL væske celler, lever og lunge
- Patologi, BAL væske LDH/proteiner
- Respiratorisk funktion
- Spermproduktion (kun for wolfram)

# Molybdæn disulfid: Vægt og inflammation

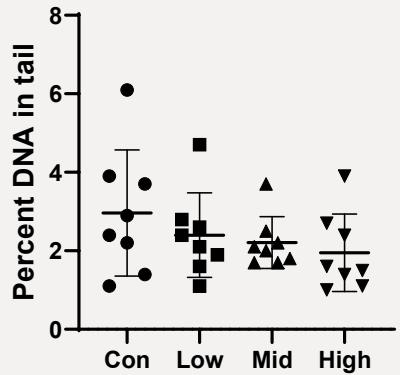


# Molybdæn disulfid: Genotoksicitet

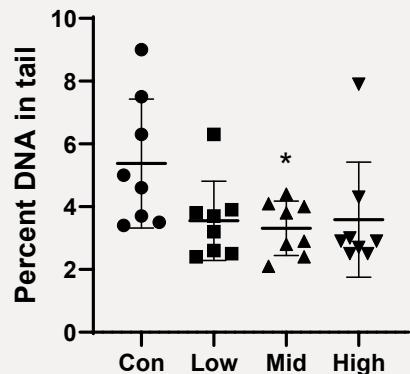
DNA damage in BAL fluid cells



DNA damage in lung



DNA damage in liver



# Subakutte forsøg

- **Molybdæn disulfid**

Effekter på vægt og genotoksicitet: 13 mg MoS<sub>2</sub>/m<sup>3</sup>

- svarende til 0,8 mg/m<sup>3</sup> for en 8-timers arbejdsgang

kunne sættes til *No Observed Adverse Effect Concentration* (NOAEC)

Environmental Toxicology and Pharmacology 98 (2023) 104074

Contents lists available at ScienceDirect

Environmental Toxicology and Pharmacology

journal homepage: [www.elsevier.com/locate/etap](http://www.elsevier.com/locate/etap)





Genotoxicity in the absence of inflammation after tungsten inhalation in mice

Jorid B. Sørli <sup>a,\*</sup>, Alexander C.Ø. Jensen <sup>a</sup>, Alicia Mortensen <sup>a</sup>, Józef Szarek <sup>b</sup>, Eleni Chatzigiannelli <sup>a</sup>, Claudia A.T. Gutierrez <sup>a,c</sup>, Nicklas R. Jacobsen <sup>a</sup>, Sarah S. Poulsen <sup>a</sup>, Iosif Hafez <sup>d</sup>, Charis Loizides <sup>d</sup>, George Biskos <sup>d,e</sup>, Karin S. Hougaard <sup>a,f</sup>, Ulla Vogel <sup>a,g</sup>, Niels Hadrup <sup>a,h,\*\*</sup>

<sup>a</sup> National Research Centre for the Working Environment (NFA), 105 Lerse Parkallé, Copenhagen Ø, Denmark  
<sup>b</sup> Department of Pathophysiology, Forensic Veterinary Medicine and Administration, University of Warmia and Mazury in Olsztyn, Olsztyn, Oczapowskiego 13, 10-719 Olsztyn, Poland  
<sup>c</sup> Department of Public Health, University of Copenhagen, Copenhagen, Denmark  
<sup>d</sup> Climate and Atmosphere Research Centre, The Cyprus Institute, 20 Konstantinou Kavafi Street, 2121, Aglantzia Nicosia, Cyprus  
<sup>e</sup> Faculty of Civil Engineering and Geosciences, Delft University of Technology, Gebouw 23 Stevinweg 1, 2628 CN Delft, the Netherlands  
<sup>f</sup> Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, 1353 Copenhagen K, Denmark  
<sup>g</sup> DTU Food, Technical University of Denmark, Kemitorvet Bygning 202, 2800 Kongens Lyngby, Denmark  
<sup>h</sup> Research group for Risk-benefit, National Food Institute, Technical University of Denmark, Kemitorvet Bygning 202, 2800 Kongens Lyngby, Denmark

- **Wolfram**

Baseret på genotoksicitet kunne en *Lowest Observed Adverse Effect Concentration* (LOAEC) sættes til 9 mg/m<sup>3</sup>

Toxicology 485 (2023) 153428

Contents lists available at ScienceDirect

Toxicology

journal homepage: [www.elsevier.com/locate/toxicol](http://www.elsevier.com/locate/toxicol)





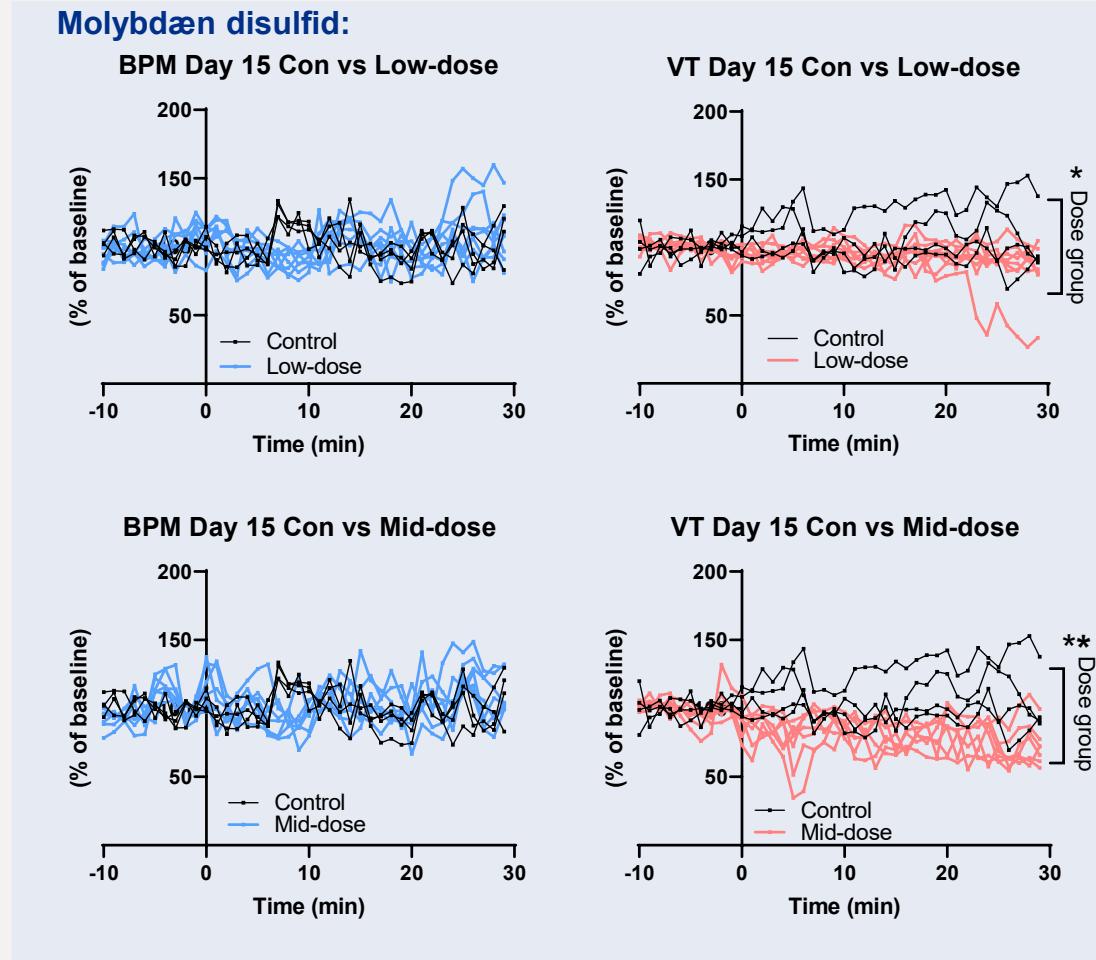
Pulmonary toxicity of molybdenum disulphide after inhalation in mice

Jorid B. Sørli <sup>a,\*</sup>, Alexander C.Ø. Jensen <sup>a</sup>, Alicia Mortensen <sup>a</sup>, Józef Szarek <sup>b</sup>, Claudia A.T. Gutierrez <sup>a,c</sup>, Lucas Givelet <sup>d</sup>, Katrin Loeschner <sup>d</sup>, Charis Loizides <sup>e</sup>, Iosif Hafez <sup>e</sup>, George Biskos <sup>e,f</sup>, Ulla Vogel <sup>a,g</sup>, Niels Hadrup <sup>a,h,\*</sup>

<sup>a</sup> National Research Centre for the Working Environment (NFA), 105 Lerse Parkallé, Copenhagen Ø, Denmark  
<sup>b</sup> Department of Pathophysiology, Forensic Veterinary Medicine and Administration, University of Warmia and Mazury in Olsztyn, Olsztyn, Oczapowskiego 13, 10-719 Olsztyn, Poland  
<sup>c</sup> Department of Public Health, University of Copenhagen, Copenhagen, Denmark  
<sup>d</sup> Research Group for Analytical Food Chemistry, National Food Institute, Technical University of Denmark, DK-2800 Kgs. Lyngby, Denmark  
<sup>e</sup> Climate and Atmosphere Research Centre, The Cyprus Institute, Nicosia 2121, Cyprus  
<sup>f</sup> Faculty of Civil Engineering and Geosciences, Delft University of Technology, 2628 CN Delft, the Netherlands  
<sup>g</sup> DTU Food, Technical University of Denmark, Kgs. Lyngby, Denmark  
<sup>h</sup> Research group for Risk-Benefit, National Food Institute, Technical University of Denmark, Denmark

# Akutte indåndingsforsøg i mus

- 4 enkeltstoffer og 8 formulerede produkter testet i mus
- Et af enkelt stofferne og to af produkterne hæmmede ikke lungesurfaktant-funktionen selv ved den højeste testede koncentration



# Lungesurfaktometer

- Udvalgte stoffer blev testet i lungesurfaktometer



- *Resultaterne er stadigt under evaluering*

# Vi publicerede reviewartikler på den opbyggede viden om bor, molybdæn, wolfram og lithium

Regulatory Toxicology and Pharmacology 121 (2021) 104873

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: [www.elsevier.com/locate/yrtpb](http://www.elsevier.com/locate/yrtpb)

---

Comprehensive Review

Toxicity of boric acid, borax and other boron containing compounds: A review

Niels Hadrup <sup>a,\*</sup>, Marie Frederiksen <sup>a</sup>, Anoop K. Sharma <sup>b,\*\*</sup>

<sup>a</sup> National Research Centre for the Working Environment, Copenhagen, DK, 2100, Denmark

<sup>b</sup> Division for Risk Assessment and Nutrition, Group for Chemical Risk Assessment and GMO, National Food Institute, Technical University of Denmark, Denmark



Toxicology 467 (2022) 153098

Contents lists available at ScienceDirect

Toxicology

journal homepage: [www.elsevier.com/locate/toxicol](http://www.elsevier.com/locate/toxicol)

---

Review

Pulmonary toxicity, genotoxicity, and carcinogenicity evaluation of molybdenum, lithium, and tungsten: A review

Niels Hadrup <sup>a,\*</sup>, Jorid B. Sørli <sup>a</sup>, Anoop K. Sharma <sup>b</sup>

<sup>a</sup> National Research Centre for the Working Environment, Lerø Parkallé 105, DK-2100 Copenhagen, Denmark

<sup>b</sup> Division for Risk Assessment and Nutrition, Group for Chemical Risk Assessment and GMO, National Food Institute, Technical University of Denmark, Kemitorvet, 201, 031, 2800 Kgs. Lyngby, Denmark



# Ekstra mulighed: Risikovurdering af asthma-risiko ved brug af sprays til klargøring af bilkabiner

- *Kasper Mikkelsen DTU-studerende:*
- 1) Database over indholdsstoffer, 2) Eksponeringsmodel, 3) Risikovurdering
- [graf vist til konferencen slettet fra denne udgave Resultat: kun 2 ud af 72 produkter havde en risk ratio der var større end 1]

# Formidling

- Peer-reviewede accepterede videnskabelige artikler
  - 6. Sørli, J.B., Jensen, A.C.Ø., Mortensen, A., Szarek, J., Chatzgianelli, E., Gutierrez, C.A.T., Jacobsen, N.R., Poulsen, S.S., Hafez, I., Loizides, C., Biskos, G., Hougaard, K.S., Vogel, U., Hadrup, N., 2023a. Genotoxicity in the absence of inflammation after tungsten inhalation in mice. *Environ. Toxicol. Pharmacol.* 104074. <https://doi.org/10.1016/j.etap.2023.104074>
  - 5. Sørli, J.B., Jensen, A.C.Ø., Mortensen, A., Szarek, J., Gutierrez, C.A.T., Givelet, L., Loeschner, K., Loizides, C., Hafez, I., Biskos, G., Vogel, U., Hadrup, N., 2023b. Pulmonary toxicity of molybdenum disulphide after inhalation in mice. *Toxicology* 485, 153428. <https://doi.org/10.1016/j.tox.2023.153428>
  - 4. Sørli, Jorid B, Frederiksen, M., Nikolov, N.G., Wedebye, E.B., Hadrup, N., 2022. Identification of substances with a carcinogenic potential in spray-formulated engine/brake cleaners and lubricating products, available in the European Union (EU) - based on IARC and EU-harmonised classifications and QSAR predictions. *Toxicology* 477, 153261. <https://doi.org/10.1016/j.tox.2022.153261>
  - 3. Hadrup, N, Sørli, J.B., Sharma, A.K., 2022b. Response to commentary on "Pulmonary toxicity, genotoxicity, and carcinogenicity evaluation of molybdenum, lithium, and tungsten: A review". *Toxicology* 480, 153323. <https://doi.org/10.1016/j.tox.2022.153323>
  - 2. Hadrup, N, Sørli, J.B., Sharma, A.K., 2022. Pulmonary toxicity, genotoxicity, and carcinogenicity evaluation of molybdenum, lithium, and tungsten: A review. *Toxicology* 467, 153098. <https://doi.org/10.1016/j.tox.2022.153098>
  - 1. Hadrup, N., Frederiksen, M., Sharma, A.K., 2021. Toxicity of boric acid, borax and other boron containing compounds: A review. *Regul. Toxicol. Pharmacol.* 121, 104873. <https://doi.org/10.1016/j.yrtph.2021.104873>
- Videnskabelige artikler indsendt/under udarbejdelse
  - 3. Refinement of the training procedure of mice in holders to minimise stress during the procedure. Jorid B. Sørli, Karin Sørig Hougaard, Niels Hadrup. Indsendt til *Animal Models and Experimental Medicine*
  - 2. Acute toxicity and in vitro lung surfactometer measurements of substances in spray-formulated brake and engine cleaners and lubricants. Jorid B. Sørli et al. tænkes indsendt til: *Inhalation Toxicology*
  - 1. Asthma-inducing potential of substances in spray cleaning products mentioned in the safety data sheet intended for use inside car cabins. Kasper Mikkelsen, Jorid Sørli, Marie Frederiksen and Niels Hadrup. Tænkes indsendt til: *Journal of Applied Toxicology*
- Populærvidenskabelige artikler
  - 2. Accepteret til Miljø og Sundhed i april 2023. Resultater fra AMFF projektet Sikker-Motor: Niels Hadrup, Marie Frederiksen og Jorid B. Sørli.
  - 1. Hadrup, N, Frederiksen, M., Sharma, A.K., 2022. Toksicitet af borsyre, boraks og andre stoffer, der indeholder bor - en oversigt. *Miljø og Sundhed*. 28, 3–14.

# Formidling

- Konferencebidrag

- 4. Abstract indsendt til The 20th International Workshop on (Q)SAR in Environmental and Health Sciences, København, 5–9 juni, 2023: The use of QSAR in occupational toxicology. Jorid B. Sørli og Niels Hadrup.
- 3. Poster-præsentation: ICT/Eurotox konferencen i Maastricht 18-21 september 2022: Identification of substances with a carcinogenic potential in spray-formulated engine/brake cleaners, and lubricating products, available in the European Union – based on IARC, CLP, and QSAR classifications and predictions. Jorid B Sørli, Marie Frederiksen, Nikolai G. Nikolov, Eva B. Wedebye, Niels Hadrup.
- 2. Foredrag: ICT/Eurotox konferencen i Maastricht 18-21 september 2022: Pulmonary toxicity and genotoxicity of molybdenum disulfide and tungsten after inhalation in mice. Jorid B. Sørli, Alexander C.Ø. Jensen, Alicja Mortensen, Jozef Szarek, Ulla Vogel, Marie Frederiksen, and Niels Hadrup.
- 1. Der blev indsendt abstract til Eurotox konferencen som i september skulle afholdes i København i 2021 (aflyst p.g.a Covid-19-epidemien): Chemicals in degreasing agents - QSAR based prioritisation for selecting candidates for further toxicity testing. Niels Hadrup, Marie Frederiksen og Jorid B Sørli.

- Andre formidlingsaktiviteter

- Projektet (Sikker Motor) er blevet formidlet i forbindelse med undervisning på Københavns Universitet (Folkesundhedsvidenskab, marts 2020 til 2023).
- Ved undervisning på kursus i Miljøkemi ved Københavns Universitet (september 2020 til 2023).
- Samt ved foredrag ved gymnasium TEC Ballerup som opstart på elevernes arbejdsmiljøuge i Uge 6 i hvert af årene 2020 til 2023.
- Projektet er blevet præsenteret for ansatte ved Arbejdstilsynet ved Centerfora møde i Kolding 30. marts 2022.
- Er formidlet ved Arbejdsmiljøforskningsfondens Årskonference 2023
- Herudover er publikationerne blevet formidlet på det sociale medie LinkedIn i opslag på de publicerede artikler i årene 2021 til 2023 (6 opslag). Profil tilhørende Niels Hadrup.

# Konklusioner

- Database over indholdsstoffer i sprayprodukter til vedligeholdelse af maskiner
- Afdækket
  - Genotokiske og karcinogene potentielle
  - Subakutte lungetoksicitet af molybdæn (disulfid), wolfram (bor og lithium)
  - Akutte lungetoksicitet i mus og effekt på lungesurfaktant funktion af 12 og 20 stoffer/produkter.
- Database og risikovurdering af stoffer til indvendig bilpleje
- Resultaterne bidrager signifikant til farvurdering i området og til forbedring af arbejdsmiljøet i branchen
  - Producenter kan udfase uønskede stoffer i en safe-by-design proces
  - Brugere/konsulenter kan vælge produkter der indeholder færrest potentiel sundhedsskadelige stoffer
  - Regulatorisk overblik over området

# Perspektiver

## ***Vi har lært meget som vi kommer til at bruge i et nuværende EU projekt:***

Indoor air quality in the context of health and safety of airline passengers and crew members



© Sven Schuchardt

The quality of the air that passengers and aircrews are exposed to on board commercial transport aircraft has been at the core of a continuing debate for the past 60 years, both from the health and the safety points of view. This debate about cabin or cockpit air quality (CAQ) addresses most specifically single cabin/cockpit air contamination (CAC) events – e.g. due to potential oil leaks – and the intrinsic quality of the cockpit/cabin air in normal operating conditions.

A number of investigations and research projects have been conducted by various scientific teams, involving in-flight measurements, but so far has not allowed a complete characterization of the chemical compounds involved in CAC events, determination of sources and exposure levels to contamination, nor performance of comprehensive toxicological risk assessment for such events.

EASA, supported by the European Commission, has launched the new research project "Cabin air quality assessment of long-term effects of contaminants" aimed at collecting additional scientific evidence concerning CAC events to root more extensive assessment of health risks and to support the evolution of aviation standards in this subject area.



**EASA**  
European Union Aviation Safety Agency

**EASA – the European Union Aviation Safety Agency**

EASA is an agency of the European Union which has been given specific regulatory and executive tasks in the field of aviation safety. The Agency constitutes a key part of the European Union's strategy to establish and maintain a high uniform standard of safety and environmental protection in civil aviation at the European level.

**Forhåbentligt fortsættelse med: *Sikkert på arbejde med køle og smøreolier indsendt til AMFF 2023***

# Tak for i dag

Tak til Arbejdsmiljøforskningsfonden  
(Projektnr./sagsnr.: 29-2019-09 / 20195100792).

Tak til projektdeltagere: Jorid B. Sørli og Marie Frederiksen (NFA)

Tak til DTU studerende: Kasper Mikkelsen

Tak til NFA's teknikere

Tak til medforfattere og interessentgruppe

Niels Hadrup  
Seniorforsker  
[nih@nfa.dk](mailto:nih@nfa.dk)  
3. Maj 2023

