in the urine, but extent of activation was not highly correlated with any single urinary PAH-OH marker.

**Conclusion** Among firefighters, urinary PAH-OH concentrations increase in both entry teams and engineers. The route and extent of dermal and inhalation exposure vary with the specific job task at the fireground. AhR and p53 *in vitro* bioassays demonstrate activation of cancer pathways following occupational exposure in firefighters.

## 53 HUMAN BIO-MONITORING OF EPOXY RESINS AND HARDENERS IN THE PRODUCTION OF ROTOR: BLADES

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**Introduction** In a small company producing rotor blades for aviation from carbon composites, epoxy resins based on Novolac and isophorone diamine as hardener are used. Both compounds can be absorbed via skin contact and were shown to be strong skin sensitizers. As a part of risk assessment, the industrial physician prompted a biological monitoring to determine the internal exposure of the workers.

Methods 6 workers were identified with potential contact to the hardener and resin. We have collected pre- and post-shift urine samples at the beginning and mid of the work week and analysed them for the concentration of isophoronediamine and bisphenol-f-diglycidylethermetabolites as biomarker for the hardener and Novolac via specific mass spectrometric methods.

**Results** We detected isophoronediamine in almost all urine samples with post-shift-values significantly higher than preshift. Median urinary excretion of isophoronediamine over the workweek was 195  $\mu$ g/g crea. (Monday pre-shift), 709  $\mu$ g/g crea. (Monday post-shift), 573  $\mu$ g/g crea. (Wednesday pre-shift) and 1319  $\mu$ g/g crea. (Wednesday post-shift). Results for urinary bisphenol-f-diglycidylether-metabolites were several orders of magnitude lower and near the limit of detection (0.5  $\mu$ g/L).

**Conclusion** We found considerable internal exposures to isophoronediamine in workers producing carbon composite rotor blades. Our results indicate a cumulating internal exposure over the work-week. One of the workers showed clinical symptoms of allergic contact dermatitis in the skin examination. Use of inappropriate gloves was determined to be the cause for these high exposures. Biological monitoring should be part of risk assessment of workers handling epoxy resins.

## 684 EXPOSURE FROM GUN SMOKE ACTIVATES SEVERAL SYSTEMIC INFLAMMATORY PATHWAYS

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Introduction Norwegian Armed Forces reported episodes of acute respiratory symptoms after exposure to fumes from firing small arms weapon HK416 (Heckler and Koch) using unleaded ammunition. These fumes contain a mixture of gases and solid particles, that may be capable of inducing inflammatory immune responses. The aim of the present study was to find out if exposure to fumes from small arms could induce systemic and airway inflammation, and whether there were any differences between the ammunition types (leaded, and two types of unleaded).

Methods Fifty-five healthy men (age 19–62) were recruited and randomised to three groups using HK416 and one of the three types of ammunition. Spirometry and collection of blood and sputum samples were performed 2–4 days before shooting, and 1.5 hour (spirometry), 24 hour (blood and spirometry) and 48 hour (sputum) after shooting under standardised conditions. Exposure was monitored.

**Results** All subjects had a significant increase in median sputum and blood neutrophils (sputum: 46% to 73%, p<0.001; blood:  $2.9 \times 10^6$ /mL to  $7.1 \times 10^6$ /mL, p<0.001). CRP was significantly elevated from 1.3 mg/L to 18.5 mg/L (p<0.001) along with other markers of systemic inflammation (PTX3, YKL-40, SpD, CC16, CXCL16, vWF, MPO, CD25, CD14). CRP and number of neutrophils in blood had a larger increase with unleaded as compared to leaded ammunition. For the whole group, mean FEV<sub>1</sub> and FVC decreased 290 mL (p<0.001) and 130 mL (p<0.001), respectively.

Discussion All subjects displayed elevated airway and in particular systemic inflammation following the use of small arms. The changes in systemic markers were enhanced acute stress response (CRP, PTX3), immune cell upregulation (sCD25, sCD14) and increased vascular inflammation (MPO, vWF, CXL16, YKL40). Increased airway inflammation was present at 48 hour post exposure and was accompanied by reduced spirometry that appeared <1.5 hour and lasted >24 hour after exposure. These results suggest that soldiers may be at increased risk to inflammation-based disorders when repeatedly using small arms.

## 753 COMBINATION OF CELLULAR ASSAYS WITH METABOLOMICS REVEALED MECHANISTIC INSIGHTS ON DOSE-RESPONSE RELATIONSHIP OF 3-NITROBENZANTHRONE IN HUMAN UROTHELIAL CANCER CELLS

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**Introduction** A product of incomplete combustion of diesel fuel, 3-nitrobenzanthrone (3-NBA), has been classified as a cancer-causing substance. It gained attention as a potential urinary bladder carcinogen due to the presence of its metabolite in urine and formation of DNA adducts.

The aim of this study was to characterise the dose-response relationship starting from environmentally relevant to high concentrations by utilising toxicological and metabolomic approaches to determine the toxic potential of 3-NBA in bladder cells.

Method Cells of RT4 cells were exposed against 0.3 nM to 80  $\mu M$  3-NBA for 24 hour. Both activity of enzymes involved in the metabolism of 3-NBA as well as cytotoxicity were