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# Executive summary

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## Scope and procedure

At the request of the Minister of Social Affairs and Employment, the Committee on Occupational Standards (DECOS), a committee of the Health Council of the Netherlands, derives so-called health-based calculated – occupational cancer risk values (HBC-OCRVs) associated with excess mortality levels of 4 per 1,000 and 4 per 100,000 as a result of working life exposure to substances that have been classified by the European Union or the DECOS as genotoxic carcinogen.

In this report the committee derives HBC-OCRVs for benzo[a]pyrene (BaP) and unsubstituted non-heterocyclic polycyclic aromatic hydrocarbons (PAH) from coal-derived sources. PAH (and BaP) are formed by incomplete combustion of these coal-derived sources. Occupational exposure may occur in several industries, such as in: coke ovens and power plants; petroleum refining; aluminium production using Söderberg anodes; manufacture of anodes; and, steel and iron foundries.

Although this report is limited to coal-derived sources, it is not the only source at which PAH may be formed by incomplete combustion; other examples are wood, petroleum, and gas oil. However, a main problem with these sources is that they contain relatively high concentrations of other substances than PAH. Some of these are carcinogenic, just as PAH. Therefore, the committee is not able to combine data from these different sources to estimate reliable cancer risk values for PAH, and thus left these data aside this evaluation.

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HBC-OCRVs associated with the reference cancer risks are derived by using a standard linear non-threshold extrapolation model, unless scientific data indicate otherwise. This model is described in the report 'Calculating cancer risks due to occupational exposure to genotoxic carcinogens' (1995/06 WGD)<sup>50</sup>.

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### **Identity and physical-chemical properties**

Polycyclic aromatic hydrocarbons constitute a large class of organic compounds consisting of at least two fused aromatic rings of carbon and hydrogen atoms. Concerning benzo[a]pyrene, this PAH consists of 5 benzene rings. PAH are not to be confused with polycyclic or polynuclear aromatic compounds (PAC), which contain not only unsubstituted non-heterocyclic PAH, but also substituted and/or heterocyclic PAH-derivates.

Due to differences in number of rings and molecular mass, the physical and chemical properties of a single PAH may differ. However, in general PAH are solids having high melting (~60-450°C) and boiling (~200-600°C) points. In addition, PAH are very little to moderately volatile, in particular the high molecular PAH. This means that PAH can occur in the air as inhalable particles and vapour. Furthermore, PAH are rather inert lipophilic compounds, which easily dissolve in organic solvents.

PAH always occur as complex mixtures, of which the composition may differ by source (*e.g.*, coal-derived *versus* non-coal derived), physical circumstances, and the way these sources are handled in the workplace.

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### **Monitoring**

Airborne benzo[a]pyrene and PAH are collected using pumping systems, filters (for particle-bound PAH) and absorbents (for gaseous PAH). After extraction and purification, BaP and PAH are analysed by chromatographic or spectrophotometric techniques.

Although it is desirable to monitor total PAH or a selection of PAH, considering the vast and consistent amount of data presented for benzo[a]pyrene and the fact that BaP is believed to be one of the more potent PAH carcinogens, the committee prefers the use of BaP as a marker for the overall PAH exposure. Similarly, various other national and international regulatory authorities consider BaP as a suitable marker for PAH exposure in the air.

The recommendation in this report is valid for BaP and PAH derived from coal. Various measurements have pointed out that by current industrial use of coal the variation between BaP and other PAH contributes to a limited degree in

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the whole set of uncertainties. This relationship will be disturbed when, for instance, BaP (but not the other PAH) is filtered out before the PAH mixture is emitted in the air. In those cases, a readjustment of the recommendation is needed.

Internal benzo[a]pyrene and PAH exposure can be assessed using biological monitoring techniques (*e.g.*, 1-hydroxypyrene in urine, and DNA- and protein-adducts in blood and tissues). Biological monitoring is not only useful in protecting worker health and minimising exposure, but also for quantitative occupational cancer risk estimation. However, since biological monitoring represents total body burden, and thus dermal, oral and inhalation exposure cannot be separated, it cannot readily be used for the risk estimation in this document, which is based on inhalation exposure alone.

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## **Kinetics**

PAH are absorbed through the epithelia of the respiratory and gastrointestinal tract. In these epithelia, PAH are metabolised by phase I and II enzymes into various polar and water soluble metabolites. Most of these metabolites are inactive and do not cause harm, but some do and are able to initiate cancer (*e.g.*, diol epoxides and cations). Of all PAH investigated, BaP (five aromatic rings) is considered as one of the more potent carcinogens, whereas PAH with less than five aromatic rings are considered less potent or even non-carcinogenic (*e.g.*, pyrene). After absorption, PAH and its metabolites are distributed via the bloodstream throughout all internal organs, with a preference for organs or tissues that contain high amounts of fat. Finally, they are released from the body in the urine and faeces.

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## **Carcinogenicity**

To cope with the vast amount of data and considering the purpose of this report, the committee extensively evaluated only what it judged to be the most relevant studies, with a main focus on epidemiological studies. Below a summary of the findings is given.

Numerous human and animal studies have been published on the carcinogenic effects of PAH, as a single compound (in animal studies only) or as a mixture, by various routes of exposure. These studies revealed that PAH act mainly as local carcinogens (*e.g.*, lung cancer by inhalation, skin cancer by dermal exposure). Some authors reported also on the risk of systemic cancer, such as bladder cancer in humans after inhalation. However, in none of these studies the presence

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of specific bladder carcinogens could be ruled out (*e.g.*, 2-naphtylamine). Data on cancer at other sites of the body were inconclusive, due to limitations in data presentation and the low number of cases.

Concerning animal studies, in a few carcinogenicity studies lung tumours were reported after chronic feeding of coal tar pitch volatiles. Also other animal data are published on systemic cancer after oral, intraperitoneal and intrarectal administration of single PAH, but the quality of these studies was insufficient to make a final conclusion about systemic carcinogenicity. Overall, no consistent evidence was found that PAH might induce or enhance the development of systemic cancer by inhalation or dermal exposure.

In the literature a vast amount of epidemiological data is presented associating lung cancer with work-related PAH exposure (expressed by job-title or airborne PAH concentrations). However, interpretation and comparison of these data is partly hampered due to: differences in study design (case control *versus* cohort); differences in exposure measurements; not taking into account lifestyle factors; unawareness of co-exposure; and, incomplete data presentation. Nevertheless, despite these confounding factors, the majority of the epidemiological data associated airborne PAH exposures with increased lung cancer risk. In addition, skin cancer has been reported to be positively associated with dermal PAH exposure, but not with inhalation exposure.

Some investigators estimated (excess) lifetime lung cancer risk. For instance, the results of a well-performed meta-analysis have been published recently, which included 39 different cohorts. Exposure in all these cohorts concerned coal-derived PAH sources from various industries (*e.g.*, coke oven, gas works, aluminium production). The unit relative lung cancer risk (URR) at 100  $\mu\text{g}/\text{m}^3$  years BaP was estimated at 1.20 (95% CI, 1.11-1.29,  $p < 0.001$ ; log-linear model). This risk value was not driven by any particular cohort and was not dependent on analysis method.

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### **Evaluation and HBC-OCRVs**

Since lung cancer is strongly associated with airborne BaP and PAH exposure, and a vast amount of data is available on PAH exposure and lung cancer, the excess lifetime cancer risk values are based on lung cancer data.

In selecting the suitable study for estimating HBC-OCRVs, in principle the committee prefers epidemiological studies. According to the committee the meta-analysis constitutes the best starting-point. The committee has thoroughly evaluated this analysis and despite some uncertainties inherent to the design of the single epidemiological studies, none of the 39 cohorts were excluded. The

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authors of this meta-analysis concluded that a log-linear model instead of a linear model best described the relationship between exposure and cancer risk. Therefore, to derive HBC-OCRVs, the committee adopted the log-linear model. The committee likes to add that at the low exposure concentrations, at which cancer risk values are based, the models just differ very little from each other, and the use of the linear model yields comparable outcomes as the log-linear model. Furthermore, lung cancer death values of the general population were adapted to the situation in the Netherlands.

In considering the above, the committee derived HBC-OCRVs corresponding to an excess cancer mortality level of\*

- 4 per 1,000 ( $4 \times 10^{-3}$ ) for 40 years of occupational exposure to benzo[a]pyrene and polycyclic aromatic hydrocarbons from coal-derived sources of 550 ng BaP/m<sup>3</sup>
- 4 per 100,000 ( $4 \times 10^{-5}$ ) for 40 years of occupational exposure to benzo[a]pyrene and polycyclic aromatic hydrocarbons from coal-derived sources of 5,7 ng BaP/m<sup>3</sup>.

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### **Skin notation**

At the request of the Minister of Social Affairs and Employment, the committee judged whether for benzo[a]pyrene and polycyclic aromatic hydrocarbons (PAH) from coal-derived sources a skin notation is needed. Although the committee did not find proof that BaP or other PAH compounds add substantially to systemic non-carcinogenic adverse health effects by dermal exposure, the committee does recommend a skin notation, because direct skin contact may cause skin cancer.

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### **Recommendation of Health-Based Occupational Cancer Risk Values**

The committee derived HBC-OCRVs corresponding to an excess cancer mortality level of

- 4 per 1,000 ( $4 \times 10^{-3}$ ) for 40 years of occupational exposure to benzo[a]pyrene and polycyclic aromatic hydrocarbons from coal-derived sources of 550 ng BaP/m<sup>3</sup>
- per 100,000 ( $4 \times 10^{-5}$ ) for 40 years of occupational exposure to benzo[a]pyrene and polycyclic aromatic hydrocarbons from coal-derived sources of 5,7 ng BaP/m<sup>3</sup>.

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\* Calculation is based on the log-linear model of Armstrong *et al.* (2003).

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