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Assessing PAHs

Varying toxicological approaches

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Mixture or single compound assessment?

- PAHs are most likely to occur as mixtures; and
- Behaviour of mixtures is different to that of individual components, in ways that cannot be ascertained.

However,

- Availability of toxicological data for mixtures is limited;
- Testing procedures are costly; and
- PAH mixtures from different sources have different compositions.

Individual PAH approach

Advantages

- Each individual PAH compound is assessed, providing ‘controlled’ results.
- Empirical data is compared to HCV directly, and is not affected by variation in the mixture composition.
- Uses a relatively large body of toxicology data for individual PAHs.
- Risk assessment protocols established for evaluating individual compounds.
- It provides an assessment that doesn’t rely on the source of the PAH, which is relevant when many sources are likely (such as for soil).

Individual PAH approach

Disadvantages

• Will use data for a comparatively limited set of PAHs analysed for, compared to the numerous that will be present in the mixture.

• Availability of individual HCVs for PAHs – further toxicity testing required.

•Does not consider the interaction that may occur due to exposure to a mixture.

• May therefore underestimate risk due to all PAH by considering only a few compounds.

Mixture toxicity – SR2

‘*In the absence of direct conclusive data, evaluation of the potential for combination effects of chemicals must in practice rely on assumptions based on knowledge of the modes of toxicity.*’

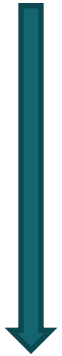
Mixtures are assumed to have a potential for additive effects where the relevant compounds share a **common mode of action**.

‘*Where there is evidence for chemical interaction, this should be taken into account.’*

Mixture toxicity

When undertaking testing, effects from

specific natural /synthetic test material
(in human/experimental animal)



- Different test material
- Possibly different test subject
- Controlled mode of exposure (to enable precise dosing) etc.
- Exclusion of other impurities

‘naturally occurring’, unspecified mixture
(in humans)

Surrogate marker approach

- First adopted in the 1970s
- This approach adopts an indicator compound as a basis for comparison for toxicity of varying mixtures.

Currently for PAHs, we assume that the risk due to **the specified PAH component** of complex mixtures is proportional to that of benzo[a]pyrene in the mixture.

Surrogate marker approach

In practice

E*stimate the carcinogenic risk due to exposure to a PAH mixture, determine what proportion of this is due to B[a]P and use this as a benchmark for other comparisons*.

- PAH profiles within a mixture have been found to be similar.
- Mixtures rich in PAH from similar sources (i.e. for which PAHs are likely to contribute a significant proportion of the risk of the mixture) are very similar in potency.
- Potency can be related to, and therefore expressed ‘per unit amount of benzo [a]pyrene’.

Surrogate marker approach

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Disadvantages

- Uncertainty in choosing benzo[a]pyrene as a surrogate – is there a better/more conservative alternative?
- In research situations, it has been found that it may result in overestimate of the risk of PAH within a mixture.
- Some PAH, such as substituted ones, are not well represented by benzo[a]pyrene and will still need to be considered separately.

Comparative potency approach

First evaluated for PAHs in the early 1980s.

- Estimation of the potency of a PAH containing mixtures, without having to identify or quantify individual compounds.
- It involves extrapolating to the carcinogenic potency of an unknown mixture in humans, based on the potency of the mixture in a bioassay.
- The potency of other mixtures is also used as a means of comparison, in order to provide a constant for extrapolation.

Comparative potency approach

$$\frac{\text{Human risk of carcinogen (mixture)1}}{\text{Bioassay potency of carcinogen (mixture)1}}$$

=

$$\frac{\text{Human risk carcinogen (mixture) 2}}{\text{Bioassay potency carcinogen (mixture)2}}$$

=

k

Comparative potency approach

Examples of source mixtures evaluated include:

- Residue from coke-ovens
- Emissions from coke-ovens
- Roofing tar
- Diesel emissions
- Road tar materials

Comparative potency approach

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- Does not separate the contribution of PAH components from the estimated overall risk.
- Will not provide any means of for assessing speciated components of a mixture.
- Limited availability of data for individual sources of PAH.
- Mixtures from the same source may not actually have similar risks – conditions in which PAHs are produced vary.

Relative potency factor approach

This is commonly referred to as the Toxic Equivalent Factor (TEF) approach, although the values are reported as relative potencies for carcinogenic effect.

• Estimate the potency of the PAH relative to that of benzo *[a]*pyrene, in order to obtain a benzo[a]pyrene equivalent. The levels of these equivalents are then added together.

Relative potency factor approach

In practice, this involves a summation of risks, which can be done either by:

- adding the benzo[a]pyrene equivalents and multiplying by the potency of benzo[a]pyrene; or
- estimating the potency of each PAH in humans (risk for cancer) and then adding the derived potencies.

Relative potency factor approach

Advantages

- Well understood, and widely used methodology for summing risks.
- Scientifically defined ‘TEFs’ for a number of PAHs.
- TEFs available for majority of PAHs within standard analytical suite.

Relative potency factor approach

Limitations in approach

For additivity to apply, all PAHs would need have the same mechanism of action – however, this is not the case.

• Practical studies show that different PAHs result in tumour formation at differing sites.

- Some by a direct genotoxic mechanism.
- For some, the need for metabolic activation to result in genotoxic effects.

•Has been shown that it may under-predict the potency of a mixture.

Relative potency factor approach

Limitations in data

- The data on which TEFs are based relate to exposures that are not typically used in deriving quantitative estimates of risk after oral or inhalation exposure.
- The study populations were relatively small.
- Many of the studies involved only one experimental dose.
- In some cases, dose-response relationships were not reported.
- Study designs varied between PAHs.

Regulatory support – the TEF approach

The approach was made popular by the WHO. The following agencies have adapted or adopted it in some form:

- COT
- EPAQS
- The US EPA (although currently re-evaluating approach)
- The RIVM
- The CCME

Regulatory opinion – the TEF approach

Both SCF and the JECFA concluded that the TEF approach to the assessment of PAHs was not appropriate due to limitations in the available data and because of different modes of action amongst different PAHs.

Regulatory support – surrogate approach

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- Both SCF and the JECFA concluded that benzo[*a*]pyrene could be used as a marker of PAHs in evaluating the risks to human health of PAHs in food.
- The EFSA have also adopted this approach for evaluating PAHs in food.
- It is also supported by the HPA for use in evaluating PAHs in soil.