APPENDIX E

PROVISIONAL C4SLs FOR BENZO(A)PYRENE AS A SURROGATE MARKER FOR PAHS

CONTENTS

APPENDICES

FIGURES

TABLES

1. INTRODUCTION

This appendix presents provisional Category 4 Screening Levels (pC4SLs) for benzo(a)pyrene (BaP) based on the methodology described in Section 5 of the main report. Section 1.1 provides brief background information on BaP, while Section 2 summarises the toxicological review from which Low Levels of Toxicological Concern (LLTCs) are identified (Steps 1 and 2 of the methodology). Section 3 presents the exposure modelling aspects for the generic land-uses under consideration (Step 3), while Section 4 presents the remaining steps of the methodology (Steps 4 to 7). The pC4SLs presented herein can be used for the setting of final C4SLs by relevant authorities (e.g., Defra).

1.1 BACKGROUND INFORMATION ON PAHS

Polycyclic aromatic hydrocarbons (PAHs) are a large group of hydrocarbons containing two or more benzene rings fused to each other or to other hydrocarbon rings. They are formed mainly as a result of pyrolytic processes, especially the incomplete combustion of organic materials. Man-made sources include motor vehicle engines, coal and wood fires, refuse incineration and cigarette smoke; PAHs are also present in many foodstuffs. Natural sources include volcanoes and forest fires. Crude oil, shale oil and coal tar contain small amounts of PAHs (Defra and the EA, 2002).

PAHs are prevalent in most urban soils in the UK, largely as a result of the historic burning of coal at both a domestic and industrial scale, and through the processing and use of petroleum hydrocarbons (SoBRA, 2011). Sources of PAHs in UK soil include:

- atmospheric deposition of combustion particles;
- ash fill and clinker from industrial processing;
- coal tar from gasworks;
- fuel oil (diesel, heating oil, lube oil);
- asphalt; and
- industrial processing of oil and coal tar derivatives.

Further background information on PAHs relevant to land contamination risk assessment can be found in the above-referenced documents, as well as the relevant Health Protection Agency (HPA) profile (HPA, 2008).

It should be noted that the approach adopted herein has been to derive C4SLs for BaP as a surrogate marker for genotoxic PAHs, in line with the relevant HPA Contaminated Land Information Sheet (HPA 2010). This approach enables land contamination risk assessors to consider the combined carcinogenic risk associated with all genotoxic PAHs that might be present at a site, despite the absence of toxicological information for many of them, on an individual basis. Further information on the surrogate marker approach, including how and when it should be used, is provided below.

2. LOW LEVEL OF TOXICOLOGICAL CONCERN FOR BENZO(A)PYRENE

2.1 FRAMEWORK FOR DEFINING A LOW LEVEL OF TOXICOLOGICAL CONCERN (LLTC)

A framework for evaluating chemical-specific toxicology data for the purposes of LLTC derivation is presented in the form of a flowchart in Figure 2.2 of the main report. The remainder of this section demonstrates the application of this framework to BaP.

As indicated in Figure 2.2 in the main report, the first task of the toxicological framework is to perform a review of existing health based guidance value (HBGV) evaluations for all routes of exposure. A checklist of information from authoritative bodies has been collated, as per the process in SR2, although pertinent primary literature in peer reviewed journals has also been searched and included, if relevant (although it should be noted that, as described in the main report, reviews by authoritative international and national bodies are preferred to the open scientific literature, for the purpose of LLTC derivation). A "Human Toxicological Data Sheet (HTDS)" for BaP has also been completed, as shown in Appendix E1.

2.2 ORAL ROUTE

2.2.1 FLOWCHART ELEMENT 1: COLLATE THE EVALUATIONS FOR THE CONTAMINANT AS PER SR2: IDENTIFY ALL KNOWN TOXICOLOGICAL HAZARDS; COLLATE HBGVS FROM RELEVANT AUTHORITATIVE BODIES AND SPECIFY THE CONDITIONS OF MINIMAL RISK

All oral HBGVs from authoritative bodies, together with a brief description of how they were derived, are given in descending order in Section II of the HTDS (see Appendix E1).

In 2002, the Environment Agency (EA) published the TOX2 report for BaP (Defra & EA 2002). This has been used as the starting point of the data search, with more recent information being considered, as appropriate.

In 2013, the key data packages for BaP toxicology evaluation comes from two sources; European Food Safety Authority (EFSA 2008) and the Joint Food & Agriculture Organisation and World Health Organisation (FAO/WHO) Expert Committee on Food Additives (JECFA) (WHO 2006 a & b).

Both expert bodies carried out benchmark dose (BMD) modelling of BaP and PAH mixtures, using data from two pivotal studies, namely a rat study by Kroese (2001) and a mouse study by Culp *et al.* (1998).

2.2.2 FLOWCHART ELEMENT 2: REVIEW THE SCIENTIFIC BASIS OF EACH HBGV. CHOOSE THE PIVOTAL STUDY

Flowchart element 2 requires a suitably qualified individual who sufficiently understands the nature of toxicological data to review the scientific basis of all existing HBGVs and choose the pivotal toxicology study for the LLTC calculation for the oral route. Three possible options are provided for the type of pivotal study that could be chosen at this point, i.e. in the form of: 1) animal toxicology data; 2) human toxicology/epidemiology data; and 3) anevidence informed policy choice (i.e. based on an existing guideline from another regime, with or without a toxicological rationale).

2a) Animal Toxicology Data

For BaP, the critical toxic endpoint selected in all toxicity studies is carcinogenicity, including tumours of the liver, forestomach, lung, gastrointestinal tract, oesophagus, larynx or tongue.

Evaluations by Environment Agency (2002), RIVM (2001), WHO drinking water standard (1993), USEPA (1994) and CCME (2008) were based on an old mouse study by Neal and Rigdon (1967) using BaP alone, whereas later assessments by JECFA (WHO 2006a&b) were based on a rat study by Kroese (2001) and a mouse study by Culp *et al*.

(1998) which were based on PAH mixtures containing BaP. Similarly, EFSA (2008) used the Culp *et al*. (1998) study as a basis of their evaluation.

Overall the HBGVs proposed by all authoritative bodies (Appendix E1), indicating minimal risk, ranged from 0.004 to 0.05 μg kg^{-1} bw day^{-1} for BaP alone and not in the context of BaP as a component of a PAH mixture. Various points of departure (POD) have been selected by different authoritative bodies from the different studies. Both JECFA and EFSA calculated the 95^{th} percentile of the benchmark dose (BMD), relating to a 10% tumour incidence rate ($BMDL_{10}$) in the Culp *et al*. (1998) study. Environment Agency (2002), RIVM (2001) and USEPA (1994) used the dose (from animal data) that is related to a excess lifetime cancer risk (ELCR) of 1 in 100,000.

The recent evaluations carried out by EFSA and JECFA, used the 2 year mouse carcinogenicity study on coal tar mixtures carried out by Culp *et al*., (1998). Both Committees derived a $BMDL_{10}$ based on the dose response of total tumours in tumour-bearing mice, expressed in terms of BaP as a surrogate marker (SM) for the carcinogenic potential of the PAH mixture. Due to the choice of mathematical model used to derive the $BMDL_{10}$, data are slightly different (EFSA. 0.07 to 0.20 mg kg^{-1} bw day^{-1}; JECFA. 0.1 to 0.23 mg kg^{-1} bw day^{-1}).

EFSA and JECFA have not derived a HBGV from their evaluations, favouring instead the use of a margin of exposure approach to risk assessment. This involves comparing the exposure to PAHs in food to the POD ($BMDL_{10}$), case by case assessing the margin of exposure, and deciding whether it is adequate.

In the UK, the current oral HCV published in 2002 was based on the WHO guideline for drinking water. WHO based their derivation on mouse forestomach cancer data by Neal and Rigdon (1967). Using default physiological assumptions, the oral HCV (index dose) was 20 ng kg^{-1} bw day^{-1} for BaP alone (EA 2002). This value is the current minimal risk value available at present for UK contaminated land risk assessment. It is based on an ELCR derived from an animal study that the UK COC does not now endorse. This view from COC means that two evaluations should be the focus, going forward, for LLTC derivation, namely those by EFSA and JECFA, where a POD in the form of a BMD/BMDL has been derived from a study (Culp *et al.,* 1998) on a mixture of PAHs including BaP. The Health Protection Agency (HPA) recently published a Contaminated Land Information Sheet (CLIS) (2010), on the approaches by EFSA and JECFA, and considers the benchmark dose modelling approach appropriate to use.

Based on the data available, the 2 year mouse carcinogenicity study on coal tar mixtures carried out by Culp *et al*., (1998) has been selected as the pivotal study to form the basis of the LLTC as it measures the carcinogenic potential of a mixture of PAHs in coal tar, hence is scientifically appropriate for the risk assessment of PAHs in soil rather than using a study on BaP alone. Moreover, this study was also considered to be the most appropriate study by EFSA (2008) and JECFA (WHO 2006 a & b).

GO TO FLOWCHART ELEMENT 3.

2b) Human Toxicology/Epidemiology Data

Not applicable as no human epidemiology data were used in the evaluation of the oral toxicity of BaP.

2c) Policy choice, with or without a toxicological rationale

Not applicable.

2.2.3 FLOWCHART ELEMENT 3: ARE THERE ADEQUATE DOSE-EFFECTS DATA FOR THE CHOSEN PIVOTAL STUDY – ANIMAL DATA?

Yes	No	Not applicable
X		

In the Culp *et al*., (1998) study there are sufficient dose-effects data to carry out dose-response modelling. Modelling was based on the total number of tumour bearing animals

exposed to soil mixture 1 used in the original study (as reported by Schneider *et al.,* (2002) and used by EFSA (2008).

GO TO FLOWCHART ELEMENT 3b

2.2.4 FLOWCHART ELEMENT 3b: PERFORM BMD MODELLING

The most recent version of the USEPA BMD software (BMDS) version 2.3.1 (USEPA 2012) was used to re-evaluate the dose-response modelling of total tumours in tumour bearing mice. Several dose-response models were used to fit the data, including:

- Gamma multihit model
- Logistic model
- LogLogistic model
- LogProbit model
- Multistage model
- Multistage-Cancer model
- Probit model
- Weibull model
- Quantal-Linear model

To assess the acceptability of the different models, various criteria were evaluated. For nested models, a likelihood ratio test to evaluate goodness of fit was used. For comparing the fit of non-nested models, the Akaike information criteria (AIC) was appropriate. Smaller AIC values indicate a better fit of data. In addition, the BMDS software provides statistics on the suitability of the fit of the model, by providing chi square and p-values. The lower the chi-square value the better the fit and the p-value should be significantly larger than 0.05, which EFSA selected as the rejection level (Falk Filipsson *et al.*, 2003; EFSA 2008, COC 2007).

A BMR of 10% incidence above the control is typically selected for minimal risk derivations, based on the limit of sensitivity of cancer bioassays (Benford *et al.*, 2010) and a 95th lower confidence limit is used to take into account the inherent uncertainty in the pivotal toxicity study and to ensure (with 95% confidence) that the selected BMR is not exceeded.

Data on the BMD modelling is presented in Table IV of appendix E1 and in Table 2.1 below.

Table 2.1: Dose response modelling of the Culp data.

Range	**BMR_{10}**
BMD (mg kg^{-1} bw day^{-1})	0.13-0.33
BMDL (mg kg^{-1} bw day^{-1})	0.08-0.2
Best fit	**BMR_{10}**
BMD (mg kg^{-1} bw day^{-1})	0.21
BMDL (mg kg^{-1} bw day^{-1})	0.1*
Model selected	Multistage cancer model

*$BMDL_{10}$ value similar to that derived by JECFA

The BMD and $BMDL_{10}$ representing a 10% risk of tumours above background in the experimental species was estimated by performing 250 iterations. All models were assessed using the criteria described above and the most appropriate model, namely the multistage cancer model, was selected, as shown in Table 2.1.

The BMD lower limit (BMDL) corresponding to the lower limits of a one-sided 95% confidence interval on the BMD is commonly used as the POD. However, the BMD may also be selected for the derivation of the LLTC.

2.2.5 FLOWCHART ELEMENT 4: DOES THE CRITICAL ENDPOINT EXHIBIT A THRESHOLD?

Yes	No	Not applicable
	X	

IARC concluded that there is sufficient evidence in experimental animals for the carcinogenicity of BaP and classified it as group 1 – carcinogenic to humans (IARC 2010). BaP is a known genotoxic carcinogen (EA 2002) hence, in the absence of data to the contrary, it is assumed not to exhibit a threshold for toxicity. Therefore a CSM may be derived.

GO TO FLOWCHART ELEMENT 4a

2.2.6 FLOWCHART ELEMENT 4a: DEFINE A SUITABLE CHEMICAL-SPECIFIC MARGIN

The default margin for establishing a "minimal risk" level for non-thresholded carcinogens from animal data using a $BMDL_{10}$ is 10,000. For the derivation of a LLTC for genotoxic carcinogens, three alternative methods could be considered for deriving a CSM or generic margin:

a) Using scientific evidence on the specific uncertainties relating to the data from the pivotal study, a CSM may be derived by adjusting factors relating to :

- Intraspecies variability: Due to the lack of human data available regarding the carcinogenicity of BaP following oral exposure, the default value of 10 is proposed to account for intraspecies variability.
- Interspecies variability: BaP is lipophilic and is metabolized by many tissues to form mutagenic metabolites. There is little evidence to suggest that humans are 10 times more sensitive to BaP than mice (species used in the pivotal study) as the default factor implies, suggesting that the humans and mice exhibit a similar sensitivity to the carcinogenic effects of BaP (Fitzgerald *et al*., 2004). However, not all genotoxic PAHs are considered to have the same mechanism of action, and the sensitivity of humans to other PAHs indeed may notbe similar to that of the test species. Therefore, for interspecies variability, the default factor of 10 is proposed.
- Additional uncertainties: A default factor of 100 is commonly used for genotoxic carcinogens to account for additional uncertainties such as quality of the data, severity of endpoint. As the mouse 2 year carcinogenicity study carried out by Culp *et al*., (1998) was a well carried out study, with the appropriate number of animals per dose group and adequate dose levels, a factor of 50 is proposed. .

Therefore a CSM of 5000 is proposed supported by the above scientific rationale.

b) Previously, a $BMDL_{10}$ divided by a default uncertainty factor of 10,000 has been equated to a risk level of 1 in 100,000 for genotoxic carcinogens (EA 2009), which has been defined as a minimal level of risk (Defra 2008). Therefore, a low level of risk could be defined as a notional cancer risk level of 1 in 50,000 (using $BMDL_{10}$ and a generic margin of 5000). It should be noted that this risk estimate is an approximation as it is derived in the context of animal data and not human data.

c) The choice of generic margin used to derive the LLTC could be communicated on a purely risk management basis. A margin of 5000-fold less than the POD could be considered as an acceptable margin. The ideal situation is when the scientific information corroborates that this is a pragmatic margin, as is the case here. In the context of setting the LLTC we would propose using a margin of 5000 that can be justified using both a) and b) rationales above.

2.2.7 FLOWCHART ELEMENT 5a: CALCULATE THE LLTC FOR NON-THRESHOLDED CHEMICALS

For non-thresholded chemicals, the LLTC is calculated by dividing the POD by the CSM (or default margin)

POD/margin = LLTC (units as per POD)

In Table 2.2 the choices of POD are presented, along with the choices of margins and the resultant LLTCs.

Table 2.2: Proposed choices of oral LLTC values using different PODs and/or CSMs

	POD	Value (mg kg^{-1} bw day^{-1})	Margin /CSM	HCV/LLTC (μg kg^{-1} bw day^{-1})
Alternative	$BMDL_{10}$	0.1	10000*	0.01
Current HCV for BaP alone (EA 2002)	-	-	-	0.020
Alternative	$BMDL_{10}$	0.1	5000	0.020
Alternative	BMD_{10}	0.21	10000*	0.021
Proposed LLTC	**BMD_{10}**	**0.21**	**5000**	**0.042**

*Default margin

GO TO FLOWCHART ELEMENT 7

2.2.8 FLOWCHART ELEMENT 7: ASSESS LLTC for BENZO(A)PYRENE

Based upon a scientific evaluation (BMD modelling) of carcinogenic effects in mice (Culp *et al.* 1998), an oral LLTC of **0.042 μg kg^{-1} bw day^{-1}** is proposed, based on a BMD_{10} as the POD and a CSM of 5000. This value:

a) is 2-fold higher than the current EA minimal risk value of 0.02 μg kg^{-1} bw day^{-1} (EA 2002)

b) is based on a dose that corresponds to a 10% increased incidence of a tumorigenic response (above the control) in the test species and an uncertainty factor of 5,000

c) is higher than the mean dietary intakes in adults and children from food and water (0.0016 and 0.0043 μg kg^{-1} bw day^{-1}, respectively; Annex 1)

Therefore this LLTC is considered to be a pragmatic level for setting a C4SL, and is suitably protective of all health effects from genotoxic PAHs in the general population.

2.3 INHALATION ROUTE

2.3.1 FLOWCHART ELEMENT 1: COLLATE THE EVALUATIONS FOR THE CONTAMINANT AS PER SR2: IDENTIFY ALL KNOWN TOXICOLOGICAL HAZARDS; COLLATE HBGVS FROM RELEVANT AUTHORITATIVE BODIES AND SPECIFY THE CONDITIONS OF MINIMAL RISK

As with the oral route, the original 2002 TOX2 report for BaP has been used as the start of the data search, with more recent information being included, as appropriate. In 2013, the main data comes from WHO (WHO 2000 and 2010) and Expert Panel on Air Quality Standards (EPAQS) (DETR, 1999). These expert groups use occupational epidemiology data from two main occupational studies, namely by Redmond (1976) and Armstrong (1994), respectively.

2.3.2 FLOWCHART ELEMENT 2: REVIEW THE SCIENTIFIC BASIS OF EACH HBGV. CHOOSE THE PIVOTAL STUDY

As above. flowchart element 2 requires a suitably qualified individual who sufficiently understands the nature of toxicological data to identify the scientific basis of all existing HCVs for the inhalation route. Again, three possible options are provided for the type of pivotal study that could be chosen at this point, i.e. in the form of: 1) animal toxicology data; 2) human toxicology/epidemiology data; and 3) an evidence informed policy choice (i.e. based on an existing guideline from another regime, with or without a toxicological rationale).

2a) Animal Toxicology Data

No animal data were used as the pivotal data in the evaluation of the inhalation toxicity of BaP. However, animal data were used to support the WHO epidemiology evaluation as lung tumour rates in a rat inhalation study of coal tar/pitch aerosols were the same order

of magnitude (cancer risk of 2 in 100,000 per ng m^{-3} BaP) as that seen in the epidemiology study (WHO 2000).

2b) Human Toxicology/Epidemiology Data

For BaP, the critical toxic endpoint in all inhalation studies is lung carcinogenicity. Evaluations have predominantly been based on human epidemiology data following occupational exposure to PAH mixtures. Early evaluations by RIVM were based on epidemiological studies of workers in UK gas works (Doll *et al*., 1965, 1972), in Chinese women exposed during cooking (Mumford *et al*., 1987) and in workers in the coal ovens of US steel works (Redmond 1976) (RIVM 1989).

Latterly, a surrogate marker (SM) approach was used by EPAQS and WHO to assess the carcinogenic risk following inhalation exposure to PAH mixtures, although different pivotal occupational studies were used by both groups.

WHO based their evaluation on occupational data from coke-oven workers (Redmond 1976). Using BaP as a SM, the corresponding BaP doses producing a ELCR of 1 in 10,000, 100,000 and 1,000,000 were calculated to be 1.2, 0.12 and 0.012 ng m^{-3}, respectively (WHO 2000, 2010). They concluded this was the same order of magnitude as the cancer risk observed in rat studies mentioned above. Moreover, based on the WHO derivation, an EC Working Group proposed 'possible limit values' of 1, 0.1 and 0.01 ng m^{-3} of BaP as a surrogate marker based on an ELCR of 1 in 10,000, 100,000 and 1,000,000, respectively (EC 2001).

Conversely, EPAQS used cancer mortality data in workers at a Canadian aluminium smelter (Armstrong *et al*., 1994). A lowest observed adverse effect level (LOAEL) was selected as the POD and an UF of 1000 applied, resulting in a standard of 0.25 ng m^{-3} as a SM for inhalation exposure to a total mixture of PAHs in the atmosphere. A later meta-analysis of human epidemiology studies of lung cancer in different occupational settings, also carried out by Armstrong (2004), and included here for completeness (though has not been reviewed by an authoritative body to date for HBGV setting) supports 0.25 ng m^{-3} as a minimal risk value.

This value of 0.25 ng m^{-3} was recommended by EPAQS to be incorporated into the UKs Air Quality Strategy (Defra 2007) as the target Air Quality Objective.

In the UK, the inhalation HCV published in 2002 was also based on 0.25 ng m^{-3}. Using default assumptions that a 70 kg adult inhales 20 m^{-3} of air per day, the inhalation HCV (index dose) was 0.07 ng kg^{-1} bw day^{-1} (EA 2002).

GO TO FLOWCHART ELEMENT 6

2c) Policy choice, with or without a toxicological rationale

Due to technical achievability an annual ambient air concentration of 1 ng m^{-3} has been set as an EU target. This higher value was adopted in the UK Air Quality Standards Regulation (2010), to be achieved in England by 2012.

This target value of 1 ng m^{-3} has been selected as the basis of the inhalation LLTC, to avoid disproportionately targeting exposures from soil. Based on data from WHO, it corresponds to an ELCR of approximately 1 in 10,000. Using default assumptions that a 70 kg adult inhales 20 m^{-3} of air per day, this results in an inhalation LLTC of 0.3 ng kg^{-1} bw day^{-1} of BaP.

2.3.3 FLOWCHART ELEMENT 6c: ARE THERE ADEQUATE DOSE-EFFECTS DATA FOR THE CHOSEN PIVOTAL STUDY – HUMAN DATA?

Yes	No	Not applicable
		X

As described above, various expert bodies have presented data outlining carcinogenic risk of BaP via inhalation.

GO TO FLOWCHART ELEMENT 6c

2.3.4 FLOWCHART ELEMENT 6c. SPECIFY AN ELCR ABOVE 1 IN 10^5

EPAQS derived a value of 0.25 ng m^{-3} as the minimal risk value, equating to 0.07 ng kg^{-1} bw day^{-1}, which was supported by a meta-analysis from Armstrong (2004).

WHO presented BaP concentrations of 1.2, 0.12 and 0.012 ng m^{-3} that correspond to an ELCRs of 1 in 10,000, 100,000 and 1,000,000, respectively. Therefore, the target concentration of 1 ng m^{-3} adopted in the UK Air Quality Standards Regulation (2010) would approximately correlate to a cancer risk of 1 in 10,000. Table 2.3 presents the resultant LLTCs based on different air concentrations and consequently varying levels of cancer risk.

Table 2.3: Proposed choices of inhalation LLTC values using different PODs and/or CSMs

	ELCR	Air concentration (ng m^{-3})	HCV/LLTC (ng kg^{-1} bw day^{-1})
Alternative	1 in 1,000,000	0.01	0.003
Alternative	1 in 100,000	0.1	0.03
Current HCV for BaP	1 in 40,000	0.25	0.07
Proposed LLTC*	**1 in 10,000**	**1**	**0.3**

*based on UK AQS

GO TO FLOWCHART ELEMENT 7

2.3.5 FLOWCHART ELEMENT 7: ASSESS LLTC for BENZO(A)PYRENE

Based upon a scientific evaluation of carcinogenic data in humans, an inhalation LLTC of **0.3 ng kg^{-1} bw day^{-1}** is proposed, based on an ELCR of 1 in 10,000 derived from the UK Air Quality Regulations of 1 ng m^{-3}. This value:

a) is 4-fold higher than the EA minimal risk value (EA 2002);

b) describes a 1 in 10,000 lifetime cancer risk;

c) is higher than the adult mean intake from ambient air in indoor environments (0.05 ng kg^{-1} bw day^{-1}); and

d) gives the same intake level to adult intakes of BaP from ambient air (if BaP concentrations in air are equal to the UK Air Quality Standards Regulations 2010).

Therefore this LLTC is considered to be a pragmatic level for setting a C4SL, and is suitably protective of all health effects in the general population.

2.3.6 CALCULATION OF A CHILD-SPECIFIC LLTC for BENZO(A)PYRENE

The above LLTC, which is based on the Air Quality Standard of 1 ng m^{-3}, equates to 0.3 ng kg^{-1} bw day^{-1} based on default physiological parameter values for an adult receptor that would only be considered in the commercial land use scenario. Inhalation LLTCs for other land use scenarios are derived based on receptor-specific physiological parameter values (i.e. for bodyweight and inhalation rate) and are detailed in Table 2.4.

Table 2.4: Proposed inhalation LLTCs for C4SL land use scenarios

Land use	Critical receptor	Receptor age classes	Average bodyweight (kg)	Inhalation rate (m^3 day^{-1})	HCV/LLTC (ng kg^{-1} bw day^{-1})
Residential	Female child	1-6	13.3	8.8	0.66
Allotments	Female child	1-6	13.3	8.8	0.66
Commercial	Female worker	17	70[1]	20[2]	0.30
POS-residential	Female child	4-9	21	11	0.52
POS-park	Female child	1-6	13.3	8.8	0.66

2.4 DERMAL ROUTE

In 2010 USEPA carried out a comprehensive scientific review of toxicity data of PAHs, during which dermal toxicity of PAHs was evaluated. Also ATSDR (2012) covered a review of dermal studies. They have reported BaP being a multi-species skin carcinogen, acting through both genotoxic and non-genotoxic mechanisms. However, to date no authoritative body has published a quantitative evaluation of potential carcinogenic risk following dermal exposure to PAHs. The nature of the data in the USEPA (2010) report indicates that skin carcinogenicity is a potential hazard. However, the data in relatively old reports and in the authoritative evaluations do not allow for a route specific quantitative dose-response evaluation for local toxicity for a HBGV to be derived.

Therefore, as there are no new data for this route, it would seem pragmatic to carry out the assessment of systemic cancer risk following dermal exposure by using the oral HBGV, as has been the case previously in EA (2002).

2.5 BENZO(A)PYRENE AS A REPRESENTATIVE FOR PAHS

BaP exists in the environment as part of a mixture of PAH. In order to evaluate the carcinogenic potential of the PAH mixture, two toxicological methods have been used by authoritative bodies, namely using a Toxic Equivalency Factor (TEF) approach and a surrogate marker (SM) approach. A third approach would be to carry out a toxicity study using the exact mixture to which humans are exposed, but this is rarely carried out and none of the expert groups have proposed this methodology.

Toxic equivalency factor approach

In the TEF approach, each PAH is assigned a TEF value that is an estimate of its carcinogenic potency relative to the reference compound, which is assigned a TEF of 1. BaP is often used as the reference compound due to the vast amount of toxicity data available and its carcinogenic potency, as it has been proposed to significantly contribute to the carcinogenicity of a PAH mixture (USEPA 2010).

Exposure to the PAH mixture is expressed in terms of reference-compound equivalents, by multiplying the concentration of each PAH by its TEF value to produce a series of toxic equivalences (TEQ). These are summed together to arrive at a total TEQ of the mixture (USEPA 2010).

The TEF approach relies on a number of assumptions (HPA 2010; USEPA 2010).

- All PAHs congeners must act through the same molecular mechanism of action.
- The potency-correct doses of each compound in the mixture should be additive and synergistic or antagonistic interactions should not occur at low levels of exposure encountered in the environment.

[1] Default adult physiological parameter values for conversion of media concentrations to intake values detailed in EA, 2009a. Values for other receptors are the average bodyweight and inhalation rate for the age class range taken from EA, 2009b.

- Robust data showing the toxicological endpoint by a relevant route of exposure must be available to use as a basis for the derivation of the TEF values.

There are several problems in using the TEF approach for PAHs. Firstly, whilst a number of PAHs act through binding to the Ah-receptor, DNA binding and induction of mutations also contribute to the PAH's carcinogenic potential. Hence there is evidence that PAHs do not have the same mechanism of action (EFSA 2008). In contrast USEPA assumed a similar toxicological action for PAHs, although stated that the carcinogenic process for individual PAHs is related to a unique combination of molecular events. They also assumed a common mutagenic mode of action based on available information for BaP (USEPA 2010).

Secondly, the EU Scientific Committee on Food (SCF) concluded that mixtures of individual PAHs have shown the potential for synergistic and/or antagonistic interactions (EC 2002). Lastly, as there are little oral toxicity data on individual PAHs on which to base TEF values, many of the TEF schemes are based on various study types and model systems such as in vitro and in vivo assays, using routes of exposures that may not be directly applicable i.e. dermal route of exposure.

As with the SM approach, high potency PAHs cannot be assessed using the TEF approach as there are no toxicity data on which to derive a TEF value. Overall, it was suggested that TEFs based on BaP as the reference compound do not adequately describe the potency of PAHs and may lead to the underestimation of the carcinogenic potencies (EFSA 2008).

Overall, the recent report by USEPA stated that the 'database for PAHs still does not meet the criteria for the derivation of TEFs' and therefore considered the more generalized relative potency factor (RPF) approach would be more appropriate (USEPA 2010)[2].

Based on all these uncertainties, the TEF approach is considered unsuitable for the risk assessment of PAH mixtures in soil. However, it is still worthy to note that several organisations have endorsed this approach as the best method available to assess mixtures of PAH in soil. This is, in part, due to uncertainties surrounding the SM approach (HPA 2010).

Surrogate marker approach

The SM approach estimates the toxicity of a mixture of PAHs in an environmental matrix by using toxicity data for a PAH mixture for which the composition is known. Exposure to the SM is assumed to represent exposure to all PAHs in that matrix therefore the toxicity of the SM represents the toxicity of the mixture. In most cases, BaP is chosen as the SM due to its ubiquitous nature and the vast amount of data available and has been used by various authoritative bodies to assess the carcinogenic risk of PAHs in food (EFSA 2008). However, RIVM considered that 'it would not be suitable to use BaP as a SM for carcinogenic risk assessment of PAH mixtures in soil due to the wide variety in composition of PAH mixtures in Dutch land contamination sites', although little data was provided in the report to support this statement (RIVM 2001). Similarly, the Canadian Council of Ministers of the Environment (CCME) also stated that contaminated soil is likely to contain a diverse range of carcinogenic and non-carcinogenic PAH of varying potency (CCME, 2008).

The SM approach relies on a number of assumptions (HPA 2010).

- The SM (BaP) must be present in all soil samples.
- The profile of the different PAH relative to BaP should be similar in all samples.
- The PAH profile in the soil samples should be similar to that used in the pivotal toxicity study on which HBGV was based i.e. the Culp study.

[2] The difference between TEF and RPF approach is that TEFs are applied to all health endpoints, routes or durations whereas RPFs and limited to specific endpoints, routes of durations. RPFs are derived when the mode of action is less certain of is known only for some health endpoints.

In order to aid making a robust decision regarding the most appropriate risk assessment methodology to use for PAH mixtures, a recent study was carried out in the UK to address some of these assumptions (HPA 2010; Bull *et al*., 2013). Data showed that BaP was present in all soil samples tested. Although the absolute concentrations of PAHs varied between sites, the levels of PAH relative to BaP showed little variability. Moreover, the relative profile in soil samples was also similar to the coal tar mix used in the Culp study (HPA, 2010; Bull *et al.*, 2013). The authors concluded that BaP is a suitable SM to represent mixtures of PAH in soil.

As with the TEF approach, there is some uncertainty surrounding high potency PAH using the SM approach. Dibenzo[a,l]pyrene (DBaIP) is a very potent genotoxic carcinogen with a cancer potency like to be 10 to 100 times that of BaP (COC 2003). However, it is rarely measured in routine sampling hence it is unknown whether the SM is representative of DBaIP in soil samples.

Based on the recent study carried out in the UK mentioned above as well as opinions of various expert bodies, it is proposed that the SM approach should be used to carry out the risk assessment of PAH mixtures in soil.

In order to risk assess the PAH mixture using a HBGV, the assumptions described above must be verified. To assess the PAH profile in the test soil sample, the ratio of the seven genotoxic PAHs (benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[g,h,i]perylene, chrysene, dibenz[a,h]anthracene and indeno[1,2,3-c,d]pyrene), relative to BaP, should be calculated to ensure it is similar to the test material used in the Culp study (HPA 2010). To be considered sufficiently similar, the ratio relative to BaP should fit within the upper and lower limits (representing an order of magnitude above and below the mean ratio to BaP of test material used in the Culp study) as shown in Table 2.5 and Figure 2.1. In such cases BaP is considered an adequate SM and the LLTC for BaP may be used in the risk assessment.

If the site falls outside the order of magnitude limits, it may be appropriate to considering a LLTC for groups of surrogate markers, such as groups of 2, 4 or 8 PAHs, as used by EFSA for the evaluation of PAHs in food (EFSA 2008). Expert judgement should be sought in such situations where there is uncertainty as to whether BaP is sufficiently representative (HPA 2010).

Table 2.5: Profile of the genotoxic PAHs relative to BaP in the Culp study with order of magnitude upper and lower limits.

PAH	Mean ratio to BaP	Lower limit	Upper limit
Benz[a]anthracene	1.24	0.12	12.43
Chrysene	1.16	0.12	11.61
Benzo[b]fluoranthene	1.08	0.11	10.85
Benzo[k]fluoranthene	0.37	0.04	3.72
Dibenz[ah]anthracene	0.14	0.01	1.38
Indeno[123-cd]pyrene	0.73	0.07	7.27
Benzo[ghi]perylene	0.82	0.08	8.22

Systemic exposure from oral, inhalation and dermal routes should be considered as additive as PAHs are multi-site systemic carcinogens. Therefore, oral, inhalation and dermal exposures should be combined and compared against the oral LLTC to assess the systemic cancer risk following exposure. In contrast, the inhalation LLTC is based on carcinogenicity attributed solely to local pulmonary effects and therefore inhalation exposure alone should be compared against the inhalation LLTC to assess the localised cancer risk following inhalation exposure.

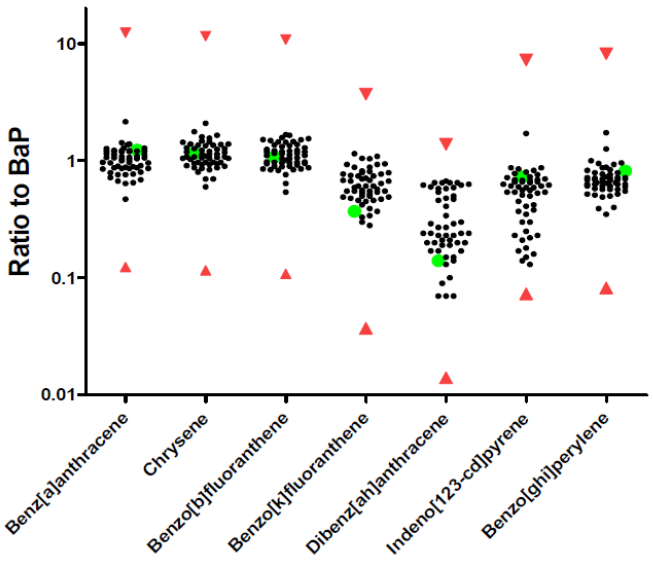

Figure 2.1: Ratio of genotoxic PAHs relative to Bap in soil from potentially contaminated sites (HPA, 2010).

The ratio of the mean concentrations of the 7 genotoxic PAH relative to BaP in individual sites are shown, with the upper and lower limits (arrows), which represent an order of magnitude above and below the test material (circles) used in the Culp study.

3. EXPOSURE MODELLING FOR BENZO(A)PYRENE

As described in step 4 of the framework (see Section 5.1 of the main report), the CLEA model has been used deterministically with the LLTCs to derive provisional C4SLs (pC4SL) for the following six land-uses:

- Residential with consumption of homegrown produce;
- Residential without consumption of homegrown produce;
- Allotments;
- Commercial;
- Public open space (POS):
    - The scenario of green space close to housing that includes tracking back of soil (POS_{resi}); and
    - A park-type scenario where the park is considered to be at a sufficient distance that there is negligible tracking back of soil (POS_{park}).

The CLEA model has then been used probabilistically to determine the probability that exposure of a random individual within the critical receptor group would exceed the LLTC values for a range of different soil concentrations (step 5). This probabilistic step helps to illustrate the level of precaution provided by each pC4SL and, if necessary, can be used to guide any modifications judged necessary. The approach and key assumptions for both types of exposure modelling are discussed in the following sections. The results of the modelling are presented in Section 4.

Although the previous section adopts a "surrogate marker" approach to the toxicological assessment of BaP in soil and utilises this in the derivation of a LLTC, the focus of this section is on the modelling of potential exposure to BaP alone. The consequences of this approach, in terms of any additional uncertainty it may introduce, are identified, as appropriate.

3.1 DETERMINISTIC MODELLING

Deterministic modelling uses a single value for each parameter input and derives one estimate of ADE for each exposure pathway. ADEs are then summed for some or all exposure pathways for comparison with the LLTC. The pathways considered in the summation are dependent on the critical toxicological effects that the LLTC is based on. In the case of BaP, the $LLTC_{inhal}$ is based on carcinogenicity attributed solely to local pulmonary effects and therefore the ADE for inhalation routes of exposure are compared with the $LLTC_{inhal}$. As discussed in Section 2 the $LLTC_{oral}$ is based on systemic effects and therefore the ADE for all routes of exposure (oral, dermal and inhalation) are compared with the $LLTC_{oral}$.

CLEA uses iteration to find the soil concentrations at which the summed ADEs equal the respective LLTC values and these are termed 'assessment criteria' (AC). As described in the CLEA SR2 and SR3 documents (EA, 2009 a & b), the AC are integrated by CLEA to determine an overall AC where the critical toxicological effects via both routes of exposure are systemic. Where the critical toxicological effect is localised for either the oral or inhalation routes of exposure, the assessment criteria are not integrated and the lowest of the two criteria is chosen as the overall assessment criteria. Given that the $LLTC_{inhal}$ is based on localised effects the latter approach has been taken to determine the pC4SL.

The assumptions and non-contaminant specific parameter values used for the derivation of the C4SLs are presented in Section 3 of the main report. For residential, allotments and commercial land-uses the assumptions and parameter values are as those described in the SR3 report (EA, 2009d) with the exception of those summarised in Section 3.5.7 of the main report. Note that for consumption of homegrown produce CLEA predicts the greatest exposure to BaP from root vegetables and tuber vegetables for both the residential and allotments scenarios. Therefore, in accordance with the "top two"

approach (see Section 3.5.5.3 of the main text for further details), 90th percentile consumption rates have been used for these two produce types and mean consumption rates have been used for the remaining produce types. For the POS land-uses the assumptions and parameter values are described in Section 3.6 of the main report.

Note that the C4SLs have been derived assuming a sandy loam soil type (i.e. as used for deriving SGVs). Given that BaP is non volatile and that empirical soil to plant concentration factors have been used, soil organic matter content has a negligible influence on the C4SLs for this chemical. However, to retain consistency with the approach used for the derivation of C4SLs for benzene, a soil organic matter (SOM) content of 6% has been chosen.

CLEA requires a number of contaminant specific parameter values for modelling exposure. Contaminant specific parameter values used for BaP are shown in Table 3.1. Note that the physico-chemical properties of BaP are considered sufficiently similar to the other genotoxic PAHs to assume that the prediction of exposure to BaP will be a good surrogate for prediction of exposure to the other genotoxic PAHs.

Table 3.1: Contaminant specific parameter values used for derivation of pC4SLs for BaP

Parameter	Units	Value	Source/Justification
Air-water partition coefficient	$cm^3\ cm^{-3}$	1.76E-06	CLEA SR7, EA 2008
Diffusion coefficient in air	$m^2\ s^{-1}$	4.38E-06	CLEA SR7, EA 2008
Diffusion coefficient in water	$m^2\ s^{-1}$	3.67E-10	CLEA SR7, EA 2008
Relative molecular mass	$g\ mol^{-1}$	252.31	CLEA SR7, EA 2008
Vapour pressure	Pa	2E-08	CLEA SR7, EA 2008
Water solubility	$mg\ L^{-1}$	0.0038	CLEA SR7, EA 2008
Log Koc	Log $cm^3\ g^{-1}$	5.11	CLEA SR7, EA 2008
Log Kow	-	6.18	CLEA SR7, EA 2008
Dermal absorption fraction	-	0.13	CLEA SR3, EA 2009b
Soil-to-plant concentration factor (green vegetables)	mg g^{-1} FW plant over mg g^{-1} DW soil	0.000412	Geomeans of empirical soil to plant concentration factors derived from from literature sources (Environment Agency, unpublished data)
Soil-to-plant concentration factor (root vegetables)		0.00178	
Soil-to-plant concentration factor (tuber vegetables)		0.000889	
Soil-to-plant concentration factor (herbaceous fruit)		0.000508	
Soil-to-plant concentration factor (shrub fruit)		5.63E-06	
Soil-to-plant concentration factor (tree fruit)		4.69E-05	
Soil-to-dust transport factor (g g-1 DW)	-	0.5	Default value from CLEA SR3, EA 2009b
Sub-surface soil to indoor air correction factor	-	1	Default value from CLEA SR3, EA 2009b
Relative bioavailability soil	-	1	Conservative assumption made that bioavailability of BaP in soil and dust is the same as bioavailability of BaP in critical toxicological studies used to derive the LLTC
Relative bioavailability dust	-	1	

The key contaminant specific parameter values used for the derivation of pC4SLs for BaP as a surrogate marker for genotoxic PAHs are discussed below. Given that BaP is not volatile and empirical factors have been used for the soil to plant concentration factors, and as demonstrated by the sensitivity analysis summarised in the main body of the report, the remaining parameters have negligible influence on the C4SLs derived.

Dermal absorption factor

The dermal absorption factor is the proportion of contaminant mass in the adhered soil that enters the blood stream. It is a contaminant specific property and is an important parameter for contaminants where dermal contact is a key pathway. The Environment Agency SR3 guidance (EA, 2009b) provides recommended dermal absorption factors for some contaminants/groups of contaminants including BaP and other PAHs, which are based on USEPA recommended values.

The recommended dermal absorption for BaP is 0.13. This means that in each exposure event 13% of the mass of BaP in soil adhered to skin is assumed to diffuse through the skin surface and into the bloodstream. This dermal absorption factor is based on a study by Wester *et al*.,(1990) who applied soil mixed with C14 labelled BaP to skin on female rhesus monkeys for a 24 hour period. The average absorption of BaP from soil from the in vivo study was 13.2%. There is an increasing body of evidence that dermal absorption from aged BaP soil contamination may be significantly lower (e.g. Stroo *et al.*, 2005 , Moody *et al*., 2007 , Turkall *et al*., 2009 and Abdel-Rahman *et al.*, 2002).

Soil to plant concentration factors

The Environment Agency recently undertook a review of the scientific literature on the plant uptake of BaP and naphthalene by fruit and vegetables based on findings from literature searches conducted during November 2008 and October 2009 (Environment Agency, unpublished data). As part of this review they collated soil to plant concentration factors from available studies. These were calculated from the ratio of concentration of the contaminant in the plant (mg^{-1} kg^{-1} fresh weight [FW]) to the concentration of the contaminant in soil (mg^{-1} kg^{-1} fresh weight [DW]). The summary statistics for the collated concentration factors are shown in Table 3.2. Note that soil organic matter was generally not reported from the studies.

Table 3.2: Summary statistics for soil to plant concentration factors for BaP.

Produce Category	Soil-to-plant concentration factors (mg kg^{-1} FW per mg kg^{-1} DW)				
	GM [1]	Minimum	Maximum	SD [2]	N [3]
Green vegetables	4.12E-04	5.24E-05	3.90E-03	1.81E-03	4
Root vegetables	1.78E-03	2.73E-05	1.39E-02	4.30E-03	10
Tuber vegetables	8.89E-04	7.33E-06	4.57E-02	1.57E-02	8
Herbaceous fruit	5.08E-04	3.33E-06	2.07E-01	8.40E-02	6
Shrub fruit	NA	5.63E-06	5.63E-06	NA	1
Tree fruit	4.69E-05	5.21E-06	4.22E-04	2.95E-04	2

1. Geometric mean (GM) of data is reported as it is a more suitable representation of experimental ratios
2. Standard deviation (SD)
3. Number of studies (N)

NA: Not applicable because only one value is available

In line with the approach used for the existing SGVs, the geomean of the concentration factors for each produce type have been used for the derivation of pC4SLs for BaP as a surrogate marker for genotoxic PAHs. The collated concentration factors and geomean values are illustrated graphically in Figure 3.1.

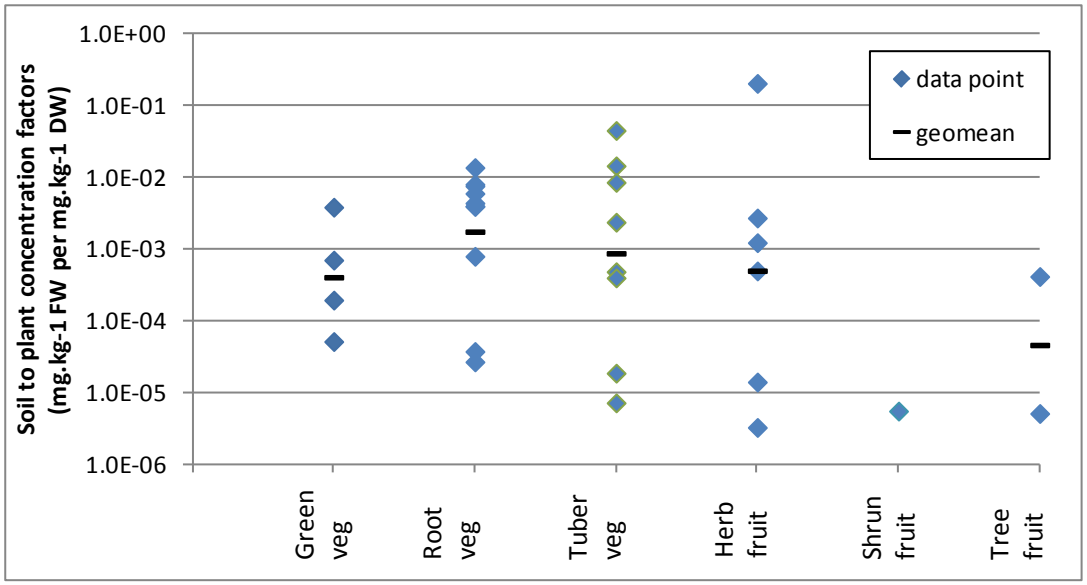

Figure 3.1: Summary of soil to plant concentration factors for BaP.

Relative bioavailability

The relative bioavailability (RBA) is the ratio of the bioavailability of the contaminant in soil to the bioavailability of the contaminant in the critical study used to derive the health criteria (i.e. the LLTCs in this context). For the derivation of the pC4SLs for BaP, this is conservatively assumed to be 100% for both the oral and inhalation routes of exposure.

The proposed values for the $LLTC_{oral}$ are based on the study by Culp *et al.,* (1998) where mice were fed on a diet of NIH-31 meal mixed with coal tar or BaP in acetone. The bioavailability of the BaP in coal tar or acetone was not reported but is likely to be significantly higher than typical PAH contamination of soils (e.g. that associated with ash and clinker).

In-vitro bioaccessibility testing can be used to give an indication of the oral bioavailability of PAHs in soil. Cave *et al.,* (2010) used the FOREhST and SHIME techniques to derive estimates of the oral bioaccessible fraction of PAHs in soils from UK gasworks. The reported oral bioaccessible fraction for BaP ranged from 17 to 50%.

3.2 PROBABILISTIC MODELLING

The sensitivity analysis described in Section 3.4 of the main report helped to identify the key uncertain parameters contributing to the greatest uncertainty in the model results. The CLEA model has been used probabilistically, substituting the single deterministic values for these parameters with a probability density function and using Monte Carlo analysis to derive a distribution of possible ADE results for a given soil concentration. All other parameters in CLEA remain unchanged as deterministic single values. Although there is uncertainty in the remaining parameters, the sensitivity analysis demonstrated that this does not give rise to significant uncertainty in the CLEA model outputs and these remaining parameters have not therefore been modelled probabilistically. Key parameters modelled probabilistically together with an indication of where and how they are correlated are shown for the residential and allotments land-uses in Table 3.3.

Table 3.3: Parameters modelled probabilistically for BaP

Parameter	Generic Land-use				Correlation
	Residential		Allot-ments	Comm-ercial	
	With home grown prod.	Without home grown prod.			
Body weight	✓	✓	✓	✓	Correlated between age classes, i.e. a heavy one year old is assumed to become a heavy six year old. Body weight is also correlated with inhalation rate, i.e. a child in the upper percentile body weight will also have an upper percentile inhalation rate
Soil ingestion rate	✓	✓	✓	✓	Correlated between age classes
Exposure frequency outdoors	✓	✓	✓		Correlated between age classes
Soil to skin adherence factor outdoors	✓	✓	✓		Correlated between age classes
Maximum exposed skin fraction outdoors	✓	✓	✓		Correlated between age classes
Inhalation rate	✓	✓		✓	Correlated between age classes and with body weight
Dust loading factor	✓	✓		✓	Not correlated with other parameters
Soil to dust transport factor	✓	✓		✓	Not correlated with other parameters
Produce consumption rate	✓		✓		Correlated between age classes. Also, consumers of homegrown produce assumed to be within the upper quartile of consumers of fruit and vegetables
Homegrown fraction	✓		✓		Correlated between produce types, i.e. an individual who consumes potatoes, most of which are homegrown will also consume mostly homegrown root and green vegetables and fruit
Dermal absorption fraction	✓	✓	✓		Not correlated with other parameters
Soil to plant concentration factors	✓		✓		Correlated between produce type, i.e. if a soil allows high plant uptake for potatoes, it will also allow high plant uptake for the remaining produce types

A probability density function (PDF) has been derived for each of these parameters. The type of distribution (e.g. normal, log normal, beta etc.) and associated attributes (e.g. mean, standard deviation or 95th percentile) selected for each parameter have been chosen to best represent the range of distribution families considered. The PDF type and associated attributes for contaminant specific parameters are summarised in Table 3.4 below for contaminant specific parameters. The PDF types and attributes for the remaining parameters modelled probabilistically are summarised in Appendix B of the main report.

Table 3.4: PDF attributes for contaminant specific parameters for Monte Carlo analysis for BaP.

Parameter	Units	Basis of PDF	PDF attributes
Soil-to-plant concentration factor (green vegetables)	mg g^{-1} FW plant over mg g^{-1} DW soil	Log normal distribution assumed based on geomean and SD from Environment Agency, unpublished data. Values truncated at 2.5 and 97.5 %iles.	Log normal (gm 4.12e-4, SD [ln CFs] 1.56)
Soil-to-plant concentration factor (root vegetables)			Log normal (gm 1.78e-3, SD [ln CFs] 1.23)
Soil-to-plant concentration factor (tuber vegetables)			Log normal (gm 8.89e-4, SD [ln CFs] 2.3)
Soil-to-plant concentration factor (herbaceous fruit)			Log normal (gm 5.08e-4, SD [ln CFs] 3.48)
Soil-to-plant concentration factor (shrub fruit)			Log normal (gm 4.69e-5, SD [ln CFs] 1.75)
Soil-to-plant concentration factor (tree fruit)			Log normal (gm 4.69e-5, SD [ln CFs] 1.75)
Soil to dust transport factor	g g^{-1} DW	Triangular distribution with min and max based on reported range in literature values from Oomen & Lijzen (2004). Most likely value = mid range of these values.	Triangular (min 0.08, mode 0.5, median 0.47, max 0.8)
Dermal absorption fraction	-	Normal PDF assumed based on Wester *et al*. 1990 (in vivo rhesus monkey, mean = 13.2%, SD = 3.3), but divided by factor of 2 which is considered a reasonably conservative estimate for aged BaP contamination in soil. Evidence: (1) Turkall *et al*., 2009 - in vitro pig skin DAF reduced 1.9 to 2.3 times for 3 month aged soil, mean = 1.8 / 3.7 (2 soils), SD = 0.5/0.2 (2) Moody *et al*.,2007 - in vitro human skin - mean = 14.8%, SD = 6.17, (3) Stroo *et al*. 2005 - Soils contaminated with lampblack - 0.14 to 1.05%	Normal (m 0.065, sd 0.017)

4. PROVISIONAL C4SLs FOR BENZO(A)PYRENE AS A SURROGATE MARKER FOR GENOTOXIC PAHS

As described in the framework (see Section 5.1 of the main report), the setting of C4SLs involves an initial deterministic stage, whereby modified CLEA exposure modelling is combined with LLTCs to produce provisional C4SLs (pC4SLs) (Step 4), followed by quantitative (Step 5) and qualitative evaluations of uncertainty (Steps 6a and 6b), using probabilistic modelling and other methods, to examine their likely levels of precaution. Other considerations are also brought to bear (Steps 6c and 6d), such that any final C4SLs (Step 7) can most closely match Defra's defined policy objectives.

4.1 PROVISIONAL C4SLs

The pC4SLs for BaP (used as a surrogate marker for genotoxic PAHs), derived from the deterministic CLEA modelling using the proposed LLTC values, are presented in Table 4.1 below, along with BaP's existing generic assessment criteria (GACs).

Table 4.1: Provisional C4SLs and GACs

Exposure parameters	HCV or LLTC µg kg^{-1}(bw) day^{-1}		pC4SL (mg.kg^{-1})					
			Residential					
	Oral	Inhal	With home grown prod.	Without home grown prod.	Allot-ments	Commer cial	POS_{resi}	POS_{park}
Current GAC [1]	0.02	7E-5	1.0	-	2.1	14	-	-
pC4SL with exposure changes only [2]	0.02	7E-5	2.4	2.5	2.7	36	4.9	10
pC4SL with LLTC but exposure parameters as SR3 [2,3]	0.042	3.0e-4 - 6.6e-4 [4]	3.2	3.4	5.1	77	-	-
pC4SL with changes in exposure and LLTC	0.042	3.0e-4 - 6.6e-4 [4]	5.0	5.3	5.7	77	10	21

1. GAC assuming 6% SOM from Nathanail *et al*., 2009
2. Parameters as described in Section 3 and include non integration of assessment criteria
3. Chemical specific parameters as Section 3.1. Non contaminant specific parameters as SR3.
4. Note age specific adjustments used for residential and POS land-uses as shown in Table 2.5

The relative contribution of each exposure pathway to total ADE is shown for each land-use in Table 4.2.

Table 4.2: Relative contributions of exposure pathways to overall exposure

Exposure pathway	Relative contribution to total exposure (%)					
	Residential		Allot-ments	Comm-ercial	POS_{resi}	POS_{park}
	With home grown prod.	Without home grown prod.				
direct soil & dust ingestion	88	94	27	81	92	88
sum of consumption of homegrown produce and attached soil	7	0	55	0	0	0
dermal contact (indoor)	2	2	0	7	4	0
dermal contact (outdoor)	3	3	18	10	4	11
inhalation of dust (indoor)	0.2	0.2	0	0.6	0.3	0
inhalation of dust (outdoor)	2E-04	2E-04	0.01	4E-3	1E-03	0.05
inhalation of vapour (indoor)	4E-03	4E-3	0	5E-4	0	0
inhalation of vapour (outdoor)	1E-03	1E-3	0.04	0.01	4E-03	0.2
oral background	0	0	0	0	0	0
inhalation background	0	0	0	0	0	0

Note: Exposure contributions based on changes to exposure parameters described in Section 3 of the main report

4.2 PROBABILITY OF EXCEEDING THE LLTCS

Monte Carlo probabilistic modelling has been conducted for the residential, allotments and commercial land-uses to estimate the possible distribution in ADE exposures for the critical receptor for a given soil concentration. This has been repeated for various soil concentrations to cover the range of pC4SLs presented in Table 4.1.

The results of this modelling are discussed in the following sections. The results are presented graphically as:

- Reverse cumulative frequency (RCFs), i.e. graphs of the reverse cumulative frequency versus ADE for alternative pC4SLs. The alternative pC4SLs have been derived using the deterministic CLEA model but making different choices for the exposure parameter values. These RCF graphs provide an indication of the probability of the ADE to a random individual within the critical receptor group exceeding the LLTC from a given soil concentration. As explained in Section 5.1 of the main report, this probability is one of the considerations that is relevant to deciding whether a pC4SL is appropriate. These graphs also show the potential magnitude of exposures above the LLTC, which is also a relevant consideration when setting the C4SL; and
- Probability of exceedence versus soil concentration graphs. These show how the probability of the ADE exceeding the LLTC varies with soil concentration.

It should be noted that the accuracy of these graphs is dependent on the accuracy of the underlying PDFs used to conduct the probabilistic modelling. Residual uncertainty in the underlying PDFs and remaining parameters modelled as set deterministic values (such as RBA) are discussed in Section 4.3.

4.2.1 RESIDENTIAL (WITH CONSUMPTION OF HOMEGROWN PRODUCE) LAND-USE

Figure 4.1 shows the RCFs of total exposure for three alternative values of pC4SLs using alternative sets of exposure parameters. These are:

1. pC4SL = 3.2 mg kg^{-1}. This is the pC4SL derived using an $LLTC_{oral}$ of 0.042 μg kg^{-1} bw day^{-1} and an $LLTC_{inhal}$ of 3 x 10^{-4} μg kg^{-1} bw day^{-1} but making no changes to the exposure parameters from the CLEA SR3 report;
2. pC4SL = 5.0 mg kg^{-1}. This is the pC4SL derived using LLTCs as above but with the proposed modifications to exposure modelling parameters described in Section 3.5.7 of the main report; and
3. pC4SL = 6.4 mg kg^{-1}. This is the pC4SL derived as above, but with additional modifications to exposure modelling parameters that had been proposed in the draft interim methodology document produced in advance of the first Stakeholder Workshop. These additional modifications are soil ingestion rate reduced to 80 mg d^{-1}, homegrown fraction halved for all produce types and dust loading factor reduced to 25 μg $.m^{-3}$.

The coloured curves on Figure 4.1 show the RCFs for the alternative pC4SLs. These curves show that there is a high probability of exposure exceeding a low ADE value but a low probability of exposure exceeding a high value. Figure 4.1 also shows the $LLTC_{oral}$ (as a dashed line) along with estimates of average background exposure from non soil sources for comparison with the RCFs of average daily exposure. As discussed below, the probability of inhalation exposure exceeding the $LLTC_{inhal}$ is negligible and so RCFs are not presented for inhalation exposure in Figure 4.1.

Note that the probabilistic modelling for residential (with consumption of home-grown produce land-use) is based on the assumption that the property has a garden and the critical receptor consumes produce grown in that garden (albeit to varying degrees).

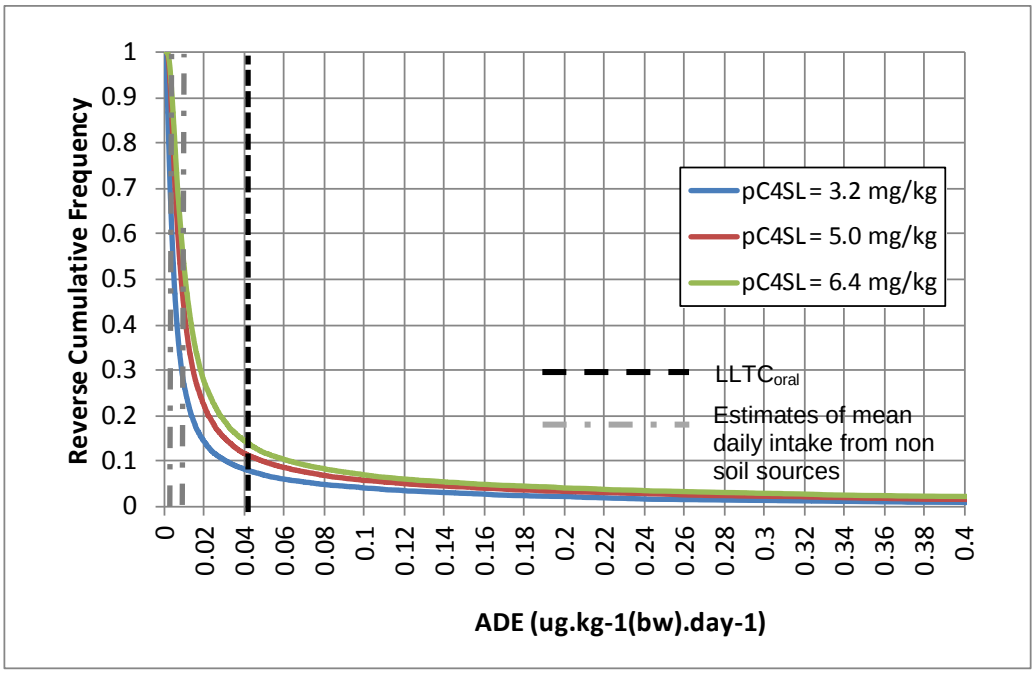

Figure 4.1: Reverse cumulative frequency graph of ADE for alternative values of pC4SL for BaP for residential (with consumption of homegrown produce) land-use

Figure 4.1 can be used to estimate the probability that exposure to a random individual within the critical receptor group would exceed the $LLTC_{oral}$ by reading off the probability from the y axis where the RCF curve intersects the LLTC vertical dashed line. Thus, the probability that exposure would exceed the LLTC is 8% for a soil concentration of 3.2 mg kg^{-1}, increasing to 11% and 13% for soil concentrations of 5 and 6.4 mg kg^{-1}, respectively. For comparison purposes, the probabilities of exposure exceeding a value of ten times the LLTC (0.42 μg kg^{-1} bw day^{-1}) are significantly lower, ranging from 1 to 2%

for the alternative pC4SL. As discussed in Section 4.3, a generally conservative approach has been adopted for the probabilistic modelling and it is possible that the true probabilities of exceedence are significantly lower.

Figure 4.1 can also be used to assess the relative importance of background exposure to exposure from soils. In this figure (and Figure 4.4 below) two estimates of average background exposure for a child are given. These are based on estimates of average dietary intakes given by FSA (2002) and EFSA (2008) (see Appendix E1). In the case of BaP for residential (with consumption of homegrown produce) land-use, exposures from the three alternative pC4SLs are generally expected to exceed background exposure, i.e. exposure from soils is likely to be the main contributor of exposure to PAHs for the range of alternative pC4SLs presented.

Figure 4.2 presents the probability of exceedence graphs for residential (with consumption of homegrown produce) land-use. This graph shows two curves: the probability that the total exposure from soil (i.e. from oral, dermal and inhalation routes) exceeds the $LLTC_{oral}$ and the probability that exposure from soil via the inhalation route alone exceeds the $LLTC_{inhal}$. Like Figure 4.1, this graph can also be used to estimate the probability that exposure to a random individual in the critical receptor group exceeds the LLTCs for alternative pC4SLs, but has the added advantage that the relationship between probability of exceedence and soil concentration can be seen more easily.

Figure 4.2 shows that the probability of total exposure exceeding the $LLTC_{oral}$ is far greater than the probability of inhalation exposure exceeding the $LLTC_{inhal}$. This is because inhalation is a relatively unimportant exposure pathway for BaP (see Table 4.2). For the three alternative pC4SLs of 3.2, 5.0 and 6.4 $mg.kg^{-1}$, the probability of inhalation exposure exceeding the $LLTC_{inhal}$ is negligible.

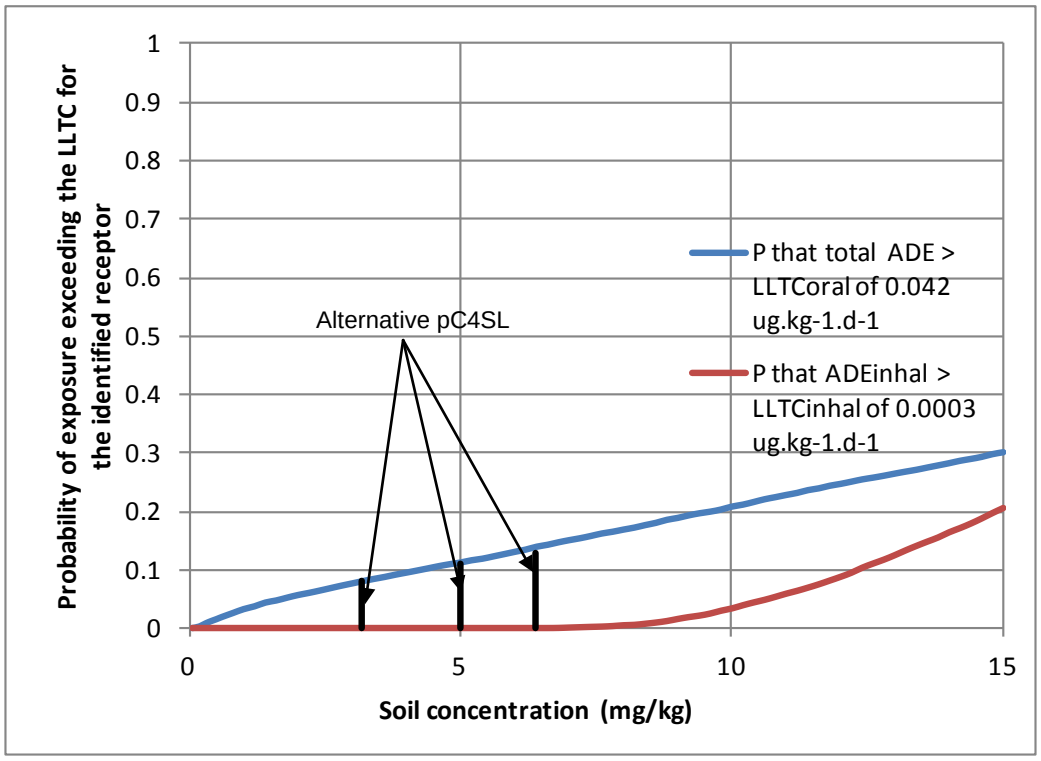

Figure 4.2: Probability of exposure exceeding the LLTC with alternative values of pC4SL for BaP for residential (with consumption of homegrown produce) land-use

4.2.2 RESIDENTIAL (WITHOUT CONSUMPTION OF HOMEGROWN PRODUCE) LAND-USE

Figure 4.3 shows the probability of exceedence graph for the residential (without consumption of homegrown produce) land-use for three alternative values of pC4SL using alternative sets of exposure parameters. These are:

1. pC4SL = 3.4 mg kg^{-1}. This is the pC4SL derived using an $LLTC_{oral}$ of 0.042 μg kg^{-1} bw day^{-1} and an $LLTC_{inhal}$ of 3 x 10^{-4} μg kg^{-1} bw day^{-1} but making no changes to the exposure parameters from the CLEA SR3 report;
2. pC4SL = 5.3 mg kg^{-1}. This is the pC4SL derived using LLTCs as above but with the proposed modifications to exposure modelling parameters described in Section 3.5.7 of the main report; and
3. pC4SL = 6.6 mg kg^{-1}. This is the pC4SL derived as above, but with additional modifications to exposure modelling parameters that had been proposed in the draft interim methodology document produced in advance of the first Stakeholder Workshop. These additional modifications are soil ingestion rate reduced to 80 mg d^{-1} and dust loading factor reduced to 50 μg $.m^{-3}$.

The predicted probabilities of exceedences of the LLTCs are significantly lower than those for the residential (with consumption of homegrown produce) land-use. The predicted probabilities of exceedence are 0.4%, 2% and 3.5% for the pC4SLs of 3.4, 5.3 and 6.6 $mg.kg^{-1}$, respectively.

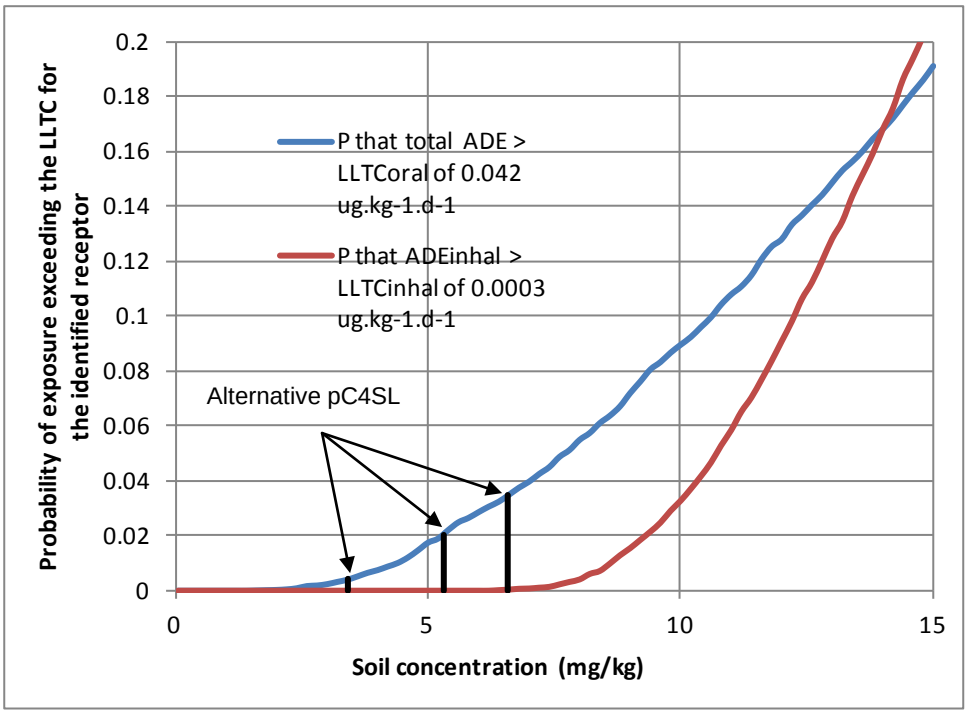

Figure 4.3: Probability of exposure exceeding the LLTC with alternative values of pC4SL for BaP for residential (without consumption of homegrown produce) land-use

4.2.3 ALLOTMENTS LAND-USE

Figure 4.4 shows the RCFs of total exposure for three alternative values of pC4SL using alternative sets of exposure parameters. These are:

1. pC4SL = 5.2 mg kg^{-1}. This is the pC4SL derived using an $LLTC_{oral}$ of 0.042 $ug.kg^{-1}(bw)day^{-1}$ and an $LLTC_{inhal}$ of 3 x 10^{-4} $ug.kg^{-1}(bw)day^{-1}$ but making no changes to the exposure parameters from the CLEA SR3 report;
2. pC4SL = 5.7 mg kg^{-1}. This is the pC4SL derived using the LLTCs as above with proposed modifications to exposure modelling parameters described in Section 3.5.7 of the main report; and
3. pC4SL = 10.4 mg kg^{-1}. This is the pC4SL derived as above, but with additional modifications to exposure modelling parameters that had been proposed in the draft interim methodology document produced in advance of the first Stakeholder Workshop. These additional modifications are soil ingestion rate reduced to 80 $mg.d^{-1}$ and exposure frequency outdoors for children halved.

Figure 4.4 also shows the $LLTC_{oral}$ and estimates of average background exposure from non soil sources for comparison with the RCFs of average daily exposure. Figure 4.5 shows the relationship between the probability of exceedence of the LLTCs and soil concentration. As for residential land-use, the probability of inhalation exposure exceeding the $LLTC_{inhal}$ for the range of alternative pC4SLs is negligible and so RCFs are not presented for inhalation exposure in Figure 4.4.

Figures 4.4 and 4.5 show that the probability that exposure to a random individual from the critical receptor group would exceed the LLTC is 35% for a soil concentration of 5.2 mg kg^{-1}, increasing to 37% and 53% for soil concentrations of 5.7 and 10.4 mg kg^{-1}, respectively. The probabilities of exposure exceeding a value of ten times the LLTC (0.42 μg kg^{-1} bw day^{-1}) are significantly lower, ranging from 10 to 15% for the alternative pC4SLs. As discussed in Section 4.3, a generally conservative approach has been adopted for the probabilistic modelling and it is possible that the true probabilities of exceedence are significantly lower.

As can be seen from Figure 4.4 exposures from the three alternative pC4SLs are generally expected to exceed background exposure, i.e. exposure from soils is likely to be the main contributor of exposure to PAHs for the range of alternative pC4SLs presented.

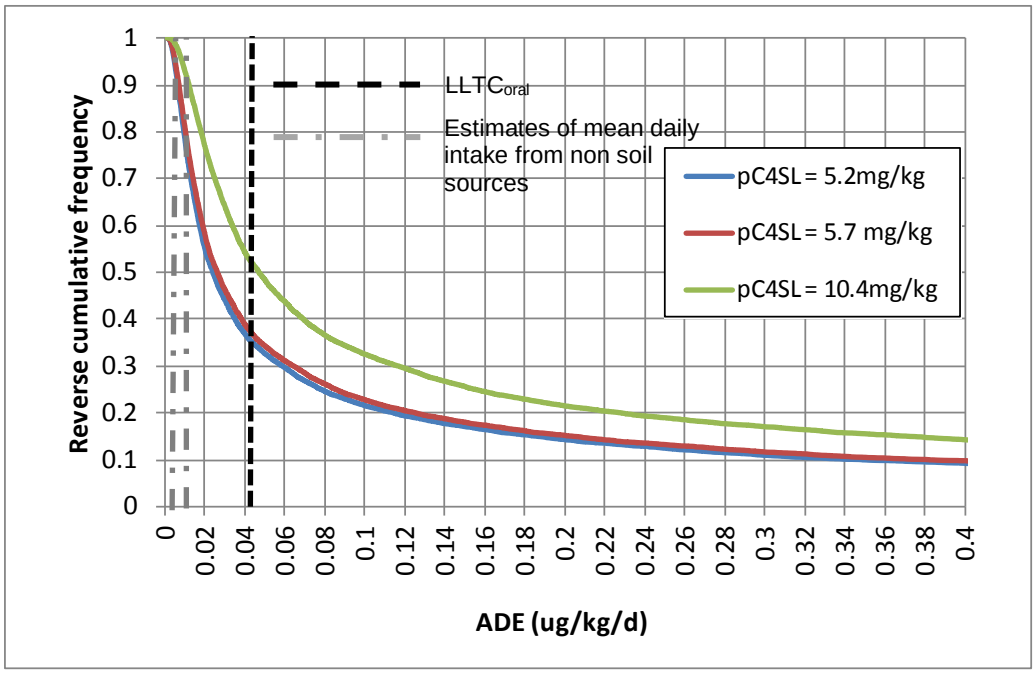

Figure 4.4: Reverse cumulative frequency graph of ADE for alternative values of pC4SLs for BaP for allotments land-use

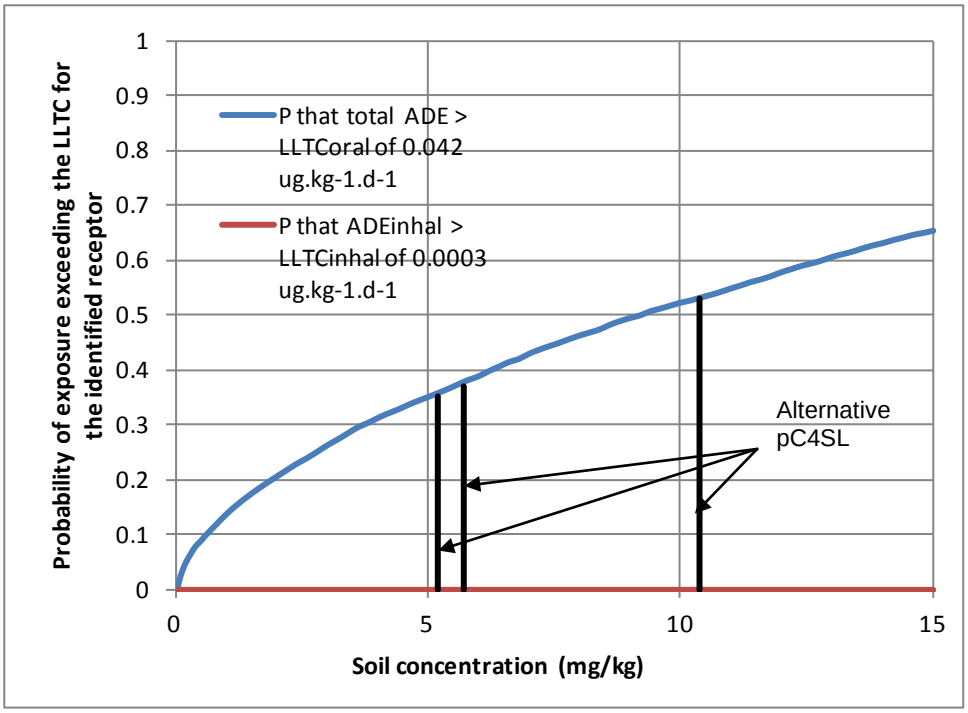

Figure 4.5: Probability of exposure exceeding the LLTC with alternative values of pC4SL for BaP for allotments land-use.

4.2.4 COMMERCIAL LAND-USE

Figures 4.6 and 4.7 show the RCFs of total exposure and inhalation exposure, respectively, for two alternative values of pC4SL using alternative sets of exposure parameters. These are:

1. pC4SL = 77 mg kg^{-1}. This is the pC4SL derived using an $LLTC_{oral}$ of 0.042 $ug.kg^{-1}(bw)day^{-1}$ and an $LLTC_{inhal}$ of 0.0003 μg kg^{-1} bw day^{-1} with the proposed modifications to exposure modelling parameters described in Section 3.5.7 of the main report; and
2. pC4SL = 91 mg kg^{-1}. This is the pC4SL derived as above, but with additional modifications to exposure modelling parameters that had been proposed in the draft interim methodology document produced in advance of the first Stakeholder Workshop. These additional modifications are soil ingestion rate reduced to 40 $mg.d^{-1}$ and dust loading factor reduced to 50 μg $.m^{-3}$.

Unlike the residential and allotments scenarios only two sets of exposure parameters have been tested. This is because there is no difference between the pC4SL with the proposed exposure parameter changes described in Section 3.5.7 of the main report and pC4SL using the SR3 parameters. The only difference in exposure parameters for commercial land-use is a slight reduction in adult inhalation rate and this has no effect on the pC4SL for BaP for this land-use.

Figures 4.6 and 4.7 also show the $LLTC_{oral}$ and estimates of average background exposure from non-soil sources for comparison with the RCFs of average daily exposure. Figure 4.8 shows the relationship between the probability of exceedence of the LLTCs and soil concentration.

Figures 4.6 and 4.8 show that the probability that total exposure to a random individual from the critical receptor group would exceed the $LLTC_{oral}$ is 11% for a soil concentration of 77 mg kg^{-1}, increasing to 16% for a soil concentration of 91 mg kg^{-1}. Figures 4.7 and 4.8 show that the probability that inhalation exposure to a random individual from the critical receptor group would exceed the $LLTC_{inhal}$ is 17% for a soil concentration of 77 mg kg^{-1}, increasing to 35% for a soil concentration of 91 mg kg^{-1}. This indicates that inhalation could be a relatively important exposure pathway for BaP for commercial land-

use, largely as a result of the low inhalation LLTC relative to the oral LLTC. As discussed in Section 4.3, a generally conservative approach has been adopted for the probabilistic modelling and it is possible that the true probabilities of exceedence are significantly lower.

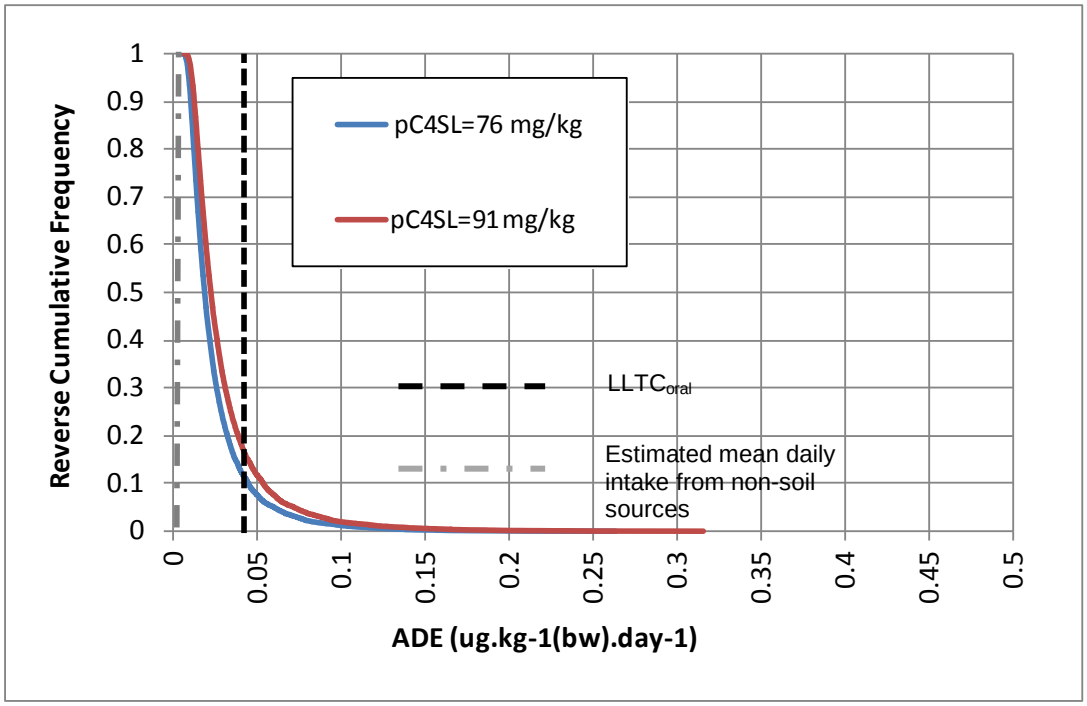

Figure 4.6: Reverse cumulative frequency graph of ADE (all routes) for alternative values of pC4SL for BaP for commercial land-use

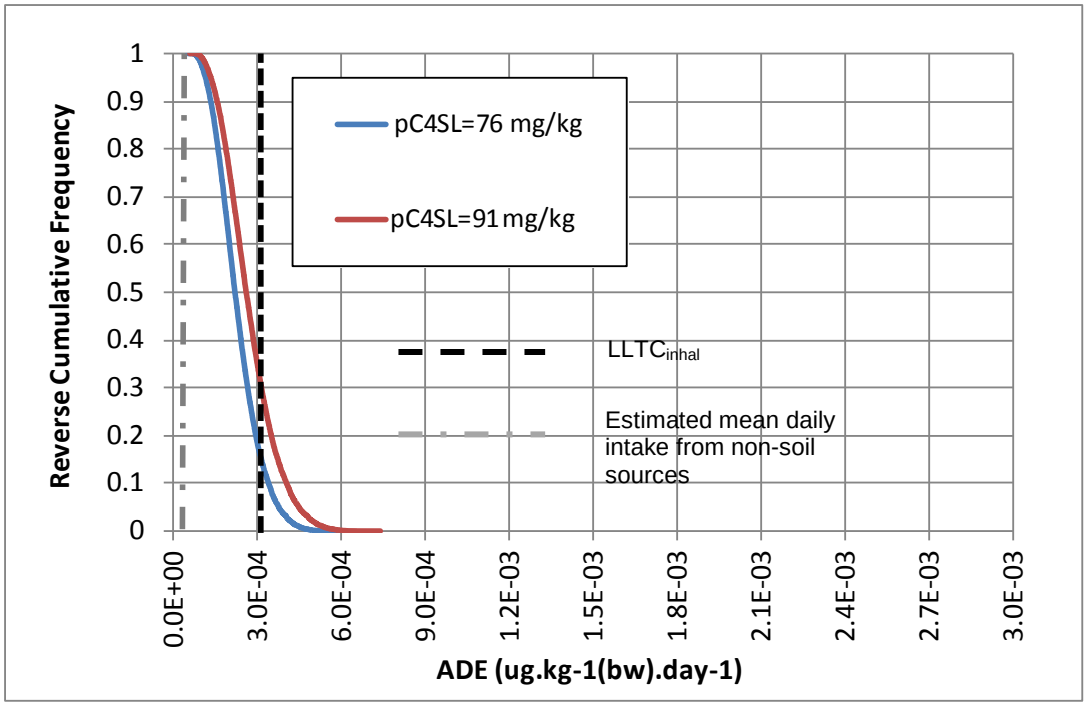

Figure 4.7: Reverse cumulative frequency graph of ADE (inhalation) for alternative values of pC4SL for BaP for commercial land-use

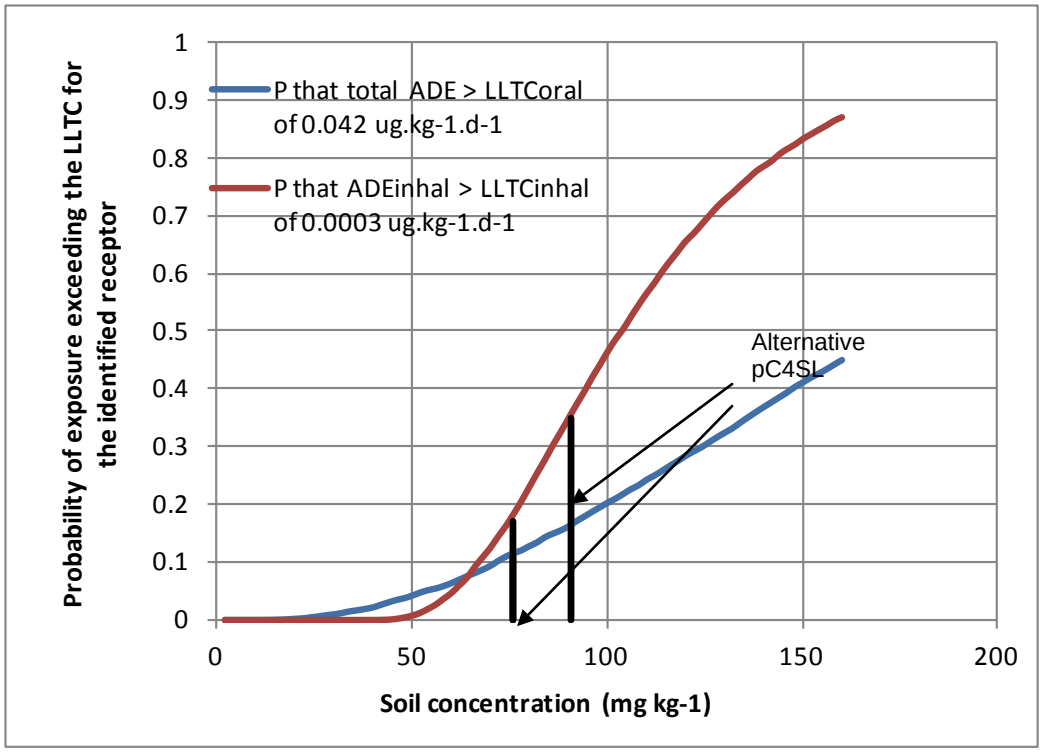

Figure 4.8: Probability of exposure exceeding the LLTC with alternative values of pC4SL for BaP for commercial land-use

As can be seen from Figures 4.6 and 4.7 exposures from the two alternative pC4SLs are generally expected to exceed background exposure, i.e. exposure from soils is likely to be the main contributor of exposure to BaP for the range of alternative pC4SLs presented for the commercial land-use.

4.3 QUALITATIVE APPRAISAL OF UNCERTAINTY

As described previously, there are a number of uncertainties that have not been captured by the probabilistic modelling. These include uncertainty in the LLTCs and uncertainty in the PDF attributes used for the probabilistic modelling.

A qualitative appraisal of these residual uncertainties has therefore been conducted, using a tabular approach adapted from EFSA (2006 as described in Section 5.1.2 of the main report.

Tables 4.3 and 4.4 describe the key residual uncertainties and their impact on toxicity and exposure estimates for the exposure modelling of these pathways, respectively. The residual uncertainties are listed in the left hand column of the table, whilst the right hand column contains a subjective evaluation of the impact of each uncertainty on the estimated LLTC and exposures, using plus (+) and minus (-) symbols.

The number of symbols indicates the approximate magnitude of the over- or under-estimation, based on the scale, shown in Figure 4.9. A dot (●) represents a negligible impact (< ±10 %), while symbols separated by a forward slash represent an uncertain impact (e.g. -/++ indicates between 0.5x underestimate and x5 overestimate). Note that the implications of the symbols differ between toxicity and exposure: a + for exposure implies overestimation of exposure and hence overestimation of risk, while a + for the LLTC implies overestimation of the LLTC which results in underestimation of risk.

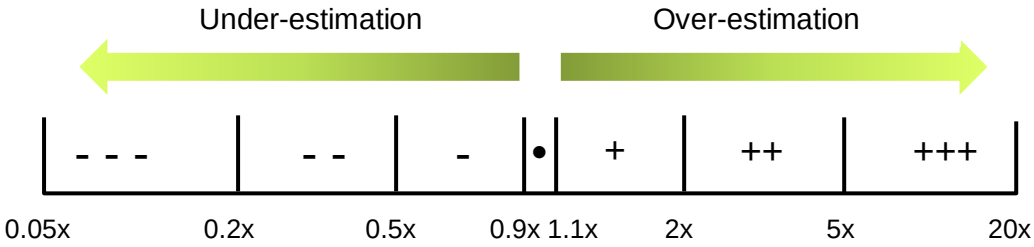

Figure 4.9: Key for symbols used to express judgements about the magnitude of potential over- or under-estimation of the LLTC and exposure in Tables 4.3 and 4.4 respectively.

Finally, at the foot of the table, a subjective evaluation is given of the overall impact of the combined uncertainties, using the same symbols. The assessment of the overall impact is necessarily a subjective judgement, taking into account the evaluation of the individual uncertainties (as shown in the individual rows) and how they might combine (including potential dependencies between them where relevant)., with equal weight being given to over- and under-estimates.

4.3.1 TOXICOLOGICAL ASSESSMENT

Table 4.3 describes the key residual uncertainties and their impact on the toxicology evaluation.

Table 4.3: Qualitative appraisal of key residual uncertainties in the toxicology evaluation (see Figure 4.9 for key to symbols)

Source of Uncertainty	Evaluation of uncertainty
ORAL LLTC	
Choice of pivotal study: the Culp study is considered the most appropriate study by EFSA (2008) and JECFA (WHO 2006 a&b) due to the use of PAH mixtures rather than BaP alone. However, this use of a PAH mixture also presents other uncertainties, as the exact composition of the chemical profile in the coal tar mix is unknown. Although the concentration of 20 PAHs was measured, it is conceivable that other contaminants may be present that may contribute to the toxicity of the mixture, leading to an over estimation of the cancer risk and therefore underestimation of the LLTC.	**-/--**
Choice of data and endpoint from pivotal study: in the critical study coal tar mix 1 or 2, or BaP alone was administered to female mice (Culp *et al.*, 1998). Data showed that for BaP alone, forestomach tumours were the most sensitive endpoint (46 tumour bearing mice/47 total at the top dose used for modelling) whereas for coal tar mix 1 containing a mixture of PAHs, lung tumours were the most sensitive endpoint (25/47). We selected to use data for coal tar mix 1 as it is considered to be the most appropriate to use to risk assess mixtures of PAH in contaminated soil but use the total tumour bearing animals as the endpoint (40/48). Based on the Culp data, WHO (2006b) presented BMDLs for forestomach and lung tumours as well as total tumour bearing mice. Modelling the coal tar mix data the BMDL for forestomach tumours was approximately 1.5x higher than for total tumours. If the BMDL for forestomach tumours was used as the POD a less conservative $LLTC_{oral}$ would be derived. The $LLTC_{oral}$ would also be higher if a BMDL for BaP alone would be used as the POD. Thus the values given for $LLTC_{oral}$ may be underestimates.	**-/●**
Interspecies uncertainties: uncertainties arise during extrapolation between mice (species used in the pivotal toxicology study) and humans. Based on in vitro and in vivo data metabolism and mutagenicity data a factor of 5 was assigned as it was thought that there were little data to suggest that humans are ten times more sensitive to BaP carcinogenicity than mice (as the default value of 10 implies). However, it remains possible that a larger factor is required, between 5 and 10, in which case the $LLTC_{oral}$ of 0.042 μg kg^{-1} bw day^{-1} would be an overestimate.	●/+

Source of Uncertainty	Evaluation of uncertainty
Intraspecies uncertainties: there are little human data on the variability hence a conservative value of 10 was used to represent the variability of the human population. Cytochrome (CYP) P450 enzymes involved in the metabolism of PAH to the toxic metabolite have been shown to be different in different ethnic populations (Polimanti *et al.* 2012), although few studies have quantified such differences. CYP450 enzymes are also polymorphic although the role of such polymorphisms on PAH carcinogenesis is yet unknown. It has been suggested that polymorphisms of some CYP isoforms may not be strongly related to alter risk for cancer in following exposure to PAHs (Ingelman-Sundberg 2004). However, the influence of polymorphisms is likely to be more important at low doses of exposure (EFSA 2008). Other enzymes such as glutathione-S-transferase may also vary in the population, or systems such as DNA repair and may impact the outcome.	**--/++**
Uncertainty surrounding adequacy of database: A conservative factor of 2 was selected to represent the adequacy of the database leading to a higher CSM and a more conservative $LLTC_{oral}$. It is plausible that a factor of 1 could have been selected, in which case the values given for the $LLTC_{oral}$ are underestimates.	**-/●**
Choice of BMD model: the choice of the model used to derive the BMD as the POD has some uncertainty surrounding it. We have selected the model according to its best fit to the data. Alternatively, the average value from all models that adequately fit the data could be used (NHMRC 1999).	**-/+**
Choice of BMD or BMDL: the choice of a BMD or BMDL has an influence on the $LLTC_{oral}$ value. The lower confidence limit tends to be conservative and may lead to over estimation of the actual level of risk (NHMRC 1999). On average the BMDL value is 2 fold lower than the BMD, hence resulting in a more conservative lower $LLTC_{oral}$ than if the BMD is used. Therefore, if the BMDL was considered more appropriate then the $LLTC_{oral}$ of 0.042 $\mu g\ kg^{-1}$ bw day^{-1} is an overestimate.	**●/+**
Choice of BMR: The BMD or BMDL varies according to the incidence of additional risk above the controls in the experimental animals (the BMR). The $LLTC_{oral}$ would be 1.5x higher if a $BMDL_{20}$ is used compared to a $BMDL_{10}$. If that was more appropriate, then the values given for the $LLTC_{oral}$ are underestimates.	**-/●**
Choice of SM approach: the SM approach has some uncertainties surrounding as little is known about high potency PAHs and whether the SM is representative of the levels in either the soil sample or the test mixture in the toxicity study.	**-/+**
Overall evaluation of uncertainty for $LLTC_{oral}$: Although the $LLTC_{oral}$ of 0.042 $\mu g\ kg^{-1}$ bw d^{-1} is less conservative than other values examined (see Table 5.1), it still contains a number of conservative elements (tending to underestimate the LLTC). The largest uncertainty relates to intraspecies variability, for which the factor of 10 is widely accepted in regulatory risk assessment. Overall it is judged that the toxicological assessment is more likely to be conservative (underestimated LLTC, hence overestimating risk) than unconservative for the purposes of setting the LLTC. In essence, the LLTC represents a dose which is 5000 times less than that which was shown to give rise to tumours in 10% of experimental animals.	

INHALATION LLTC	
Basis of LLTC: the $LLTC_{inhal}$ is based on a political decision to avoid disproportionate targeting of exposures from soil, hence an air concentration of 1 ng m^{-3} is used, which was adopted in the UK Air Quality Standards Regulations. If the LLTC was based on an air concentration that would lead to a minimum excess lifetime cancer risk, it would be based on an ambient air concentration of 0.25 ng m^{-3} and would be approximately 4 times lower, which would imply that the $LLTC_{inhal}$ is an overestimate. However, it should be noted that minimal risk is not the policy objective for the C4SLs or LLTCs used to derive them and this should be considered when setting the LLTC	●/++
ELCR modelling: a linearized multistage model was used to estimate the lifetime unit risk associated with exposure to coke-oven emissions in the occupational study. The corresponding concentrations of BaP producing excess lifetime cancer risks were calculated, assuming linearity.	**-/+**

Source of Uncertainty	Evaluation of uncertainty
BaP as a SM: the use of a BaP as a SM assumes that BaP represents the same proportion of carcinogenicity activity in PAH mixtures in air environments as in the occupational setting used as the critical study.	**-/+**
Choice of pivotal study: The PAH mixtures to which workers were exposed in the various occupational studies may also contain other contaminants that may overestimate the toxicity potential of the emissions (and hence underestimate the $LLTC_{inhal}$).	**-/●**
Overall evaluation of uncertainty for $LLTC_{inhal}$: the proposed $LLTC_{inhal}$ is based on the Air Quality Standard of 1 ng m^{-3}, which, based on WHO (2006 a&b), represents approximate ELCR of 1 in 10,000. This is higher than the ELCR that would normally be associated with minimal risk (1 in 100,000) but given that the LLTC represents low risk and is based on an air quality standard it is considered a suitable basis for setting the C4SL.	

Note that the implications of the overall uncertainty for risk can be considered by looking at the RCF graphs in Section 4.2: over- and under-estimation of a LLTC would imply the black dashed lines should be further left or right (respectively).

4.3.2 EXPOSURE MODELLING

As shown by Table 4.2, the principle exposure pathway for BaP for the residential land-use is incidental ingestion of soil and dust. The principle exposure pathways for BaP for the allotments land-use is incidental ingestion of soil and dust, dermal contact outdoors and consumption of homegrown produce. The key uncertainties in estimating exposure for these pathways are described in Table 4.4.

Table 4.4: Qualitative appraisal of key residual uncertainties in exposure modelling not captured by probabilistic modelling (see Figure 4.9 for key to symbols)

Source of Uncertainty	Evaluation of uncertainty
RESIDENTIAL LAND-USE	
Soil and dust ingestion rate. The PDF used is based on the mean and 95th percentile soil ingestion rates estimates by Stanek, et al. (2012) from a meta-analysis of the key soil ingestion studies conducted in the USA. There is uncertainty over how the soil and dust ingestion rates derived from these studies relate to UK receptors and average annual conditions (i.e. winter and summer). It should also be recognised that the estimates for children do not just relate to soil and dust they ingest from their own property, but will also include soil and dust ingested outside the home, in the nursery/school, play park, car etc. There is also some uncertainty in the shape of the PDF, but this uncertainty is unlikely to result in more than a factor of two over or under-estimation in exposure. Overall, it is considered possible that the PDF will over-estimate average annual ingestion of soils from UK residential properties by up to a factor of 2.	**● / +**
Relative bioavailability (RBA). The CLEA modelling (deterministic and probabilistic) is based on the assumption of 100% RBA. As discussed in Section 4.1.2, based on in-vitro bioaccesibility testing on soils, there is some evidence that the oral biovailability of BaP in soils is typically less than 100%. The bioavailability of BaP in the Culp study used as the basis of the LLTC is unknown but given that BaP was administered in acetone or coal tar mixed with food, it is likely to be higher than aged BaP contamination in soils. Thus the assumption of an RBA of 100% may over-estimate oral exposure from ingestion of soils by a factor of 2x or more.	**● / ++**
Surrogate marker approach. The pC4SLs are based on BaP used as a surrogate marker for the risk from the typically analysed genotoxic PAHs. As such the assumption is made that the ratio of soil concentration to exposure from BaP is a reasonable surrogate for this ratio for the other genotoxic PAHs. In essence this implies that the dermal absorption factor and soil to plant concentration factors for BaP are equally applicable to these other PAHs. Like BaP, the other genotoxic PAHs have a relatively high molecular	**- / +**

Source of Uncertainty	Evaluation of uncertainty
weight and consequently have similar physico-chemical properties to BaP. As such, their dermal absorption factors and soil to plant concentration factors are likely to be similar, although it should be recognised that there will be some variability between PAHs. The effect of this variability on overall risk from a PAHs mix is considered small, and unlikely to lead to an over- or under-estimate of overall risk of more than a factor of 2.	
OVERALL EVALUATION OF UNCERTAINTY FOR RESIDENTIAL LAND-USE: Based on the above it is considered that the estimates of total exposure predicted by the probabilistic modelling are likely to be moderately conservative, particularly at specific locations.	
ALLOTMENTS LAND-USE	
Soil and dust ingestion rate. The PDF used for allotments is based on that used for residential. As discussed above there is uncertainty over how the soil and dust ingestion rates derived from the US studies relate to UK receptors and average annual conditions (i.e. winter and summer). There is added uncertainty on how they relate to an allotments scenario. Data from the Netherlands soil ingestion study indicate that children on campgrounds ingest approximately twice as much soil as children in day-care whilst the USEPA (2011) indicate that average daily ingestion of soil outdoors is equivalent to the average daily ingestion of soil indoors. There is also some uncertainty in the shape of the PDF, but this uncertainty is unlikely to result in more than a factor of two over or under-estimation in exposure. Overall, it is considered possible that the PDF over or under-estimates exposure for the allotments scenario by up to a factor of 2.	**- / +**
Relative bioavailability (RBA). As residential	**● / ++**
Surrogate Marker approach. As residential	**- / ++**
Exposure frequency outdoors. The exposure frequencies outdoors are based on children accompanying adults to the allotments for a percentage of time that the adult visits the allotments. The percentages are based on those in the SR3 report and appear to be relatively arbitrary but not unreasonable. The adult exposure frequency is based on a 1993 survey and may be weighted towards retired adults who regularly visit the allotment but rarely bring children. Thus the PDF for exposure frequencies is considered more likely to over- than under-estimate exposure.	**- / ++**
Dermal absorption factor. As discussed in Section 3.1, the dermal absorption fraction (DAF) used for the deterministic modelling has been based on an in-vivo study using soil mixed with BaP in acetone. There is evidence to suggest that dermal absorption from aged soil contamination will be significantly lower. This has been taken account of to a certain extent in the PDF for DAF, but the PDF is still likely to be conservative and likely results in an over-estimation of dermal exposure by a factor of up to 2x.	**+**
Soil adherence factor. PDF is based on data for gardeners and is considered reasonable for allotments land-use.	**●**
Exposed skin fraction. Based on shorts and T-shirt worn when visiting allotment. This assumption is likely to over-estimate exposure by up to 2 x.	**+**
Soil to plant concentration factors. The soil to plant concentration factor (CF) PDFs are based on limited empirical measurements of the concentration of BaP in fruit and vegetables and the soil they have been grown in. The empirical estimates range over several orders of magnitude for each plant type and due to the relatively few data points there is a high degree of uncertainty in the PDFs derived. In addition there is some evidence that CFs for PAHs may decrease with increasing soil concentration (Wild and Jones, 1992; Samsoe-Petersen *et al.*, 2002) and thus the PDFs may under-estimate exposure from consumption of homegrown produce for low soil concentrations and over-estimate exposure for high concentrations. For example, Samsoe-Petersen *et al.*,(2002) found that the CF in potatoes was 3 times less for a soil containing an average of 15 $mg.kg^{-1}$ BaP than a soil with an average of 2 $mg.kg^{-1}$ BaP. It is noted that the majority of CFs obtained from literature sources were for soils with concentrations in the range of 1 to 5 $mg.kg^{-1}$ (i.e. similar to the range of pC4SLs) or less. Thus it is plausible the CFs have been over-estimated in some cases for the purposes	**--/+++**

Source of Uncertainty	Evaluation of uncertainty
of deriving C4SLs. Overall, it is considered that the CF PDFs more likely over-estimate exposure than under-estimate, with the magnitude of under/over estimation ranging from a factor of 0.2x to 20x true values	
Produce consumption rates. PDFs for produce consumption rates are based on NDNS 2008-2011 survey data. It is considered likely that allotment holders and their families tend to be within the upper percentiles of consumers of fruit and vegetables. For the purposes of the probabilistic modelling the assumption was made that consumption rate is within the top quartile. This is likely to be a conservative assumption, as not all individuals who consume homegrown produce will be high level consumers for all produce types. Thus the PDF is considered likely to over- estimate exposure for families who have allotments, possibly by a factor of up to 2x.	● / +
Homegrown fraction. The PDF for fraction of consumed produce grown at the allotment is based on UK Expenditure and Food Survey 2004/5. It was beyond the scope of this project to re-assess the raw data from this survey and so the beta shaped PDF is based on information presented in SR3 and the former CLR10 report (EA, 2002). It is possible that PDF attributes over- or under-estimate exposure by a factor of up to 2.	-/+
OVERALL EVALUATION OF UNCERTAINTY FOR ALLOTMENTS LAND-USE: Based on the above it is considered likely that the estimates of total exposure predicted by the probabilistic modelling likely to be moderately conservative, particularly at specific locations.	
COMMERCIAL LAND-USE	
Soil and dust ingestion rate. The PDF used is based on the mean and 95th percentile soil ingestion rates for children estimated by Stanek, *et al*. (2012) from a meta-analysis of the key soil ingestion studies conducted in the USA. Average soil and dust ingestion by children is expected to be twice that of adults (USEPA, 2011) and therefore the assumed PDF is likely to result in an over-estimation of exposure to adults. Furthermore, the majority of commercial properties have limited exposed soils and this will limit the potential for soil and dust ingestion. For these reasons, the exposure estimates from soil and dust ingestion for the commercial land-use are likely to be over-estimates, possibly by as much as a factor of 10x.	+ / +++
Relative bioavailability (RBA). As residential	● / ++
Dust loading factor. The PDF assumes a triangular distribution with min, max and mode values based on PM10 estimates for commercial properties cited in the literature. There is limited data available on which to base the PDF but the exposure estimates are unlikely to be under- or over-estimates by more than a factor of x0.5 to x2	-/+
Soil-to-dust transport factor. The PDF assumes a triangular distribution with min, max and mode values based on soil to dust estimates for mostly residential properties cited in the literature. The mode is based on the CLEA default of 0.5. This implies that 50% of the dust within the commercial property is derived from outdoor soil at the property. Most commercial properties have little exposed soil outdoors and it is therefore doubtful that outdoor soil contributes significantly to indoor dust in the majority of cases. The PDF is therefore likely to over-estimate inhalation exposure indoors by a factor of x10 or more	+++
OVERALL EVALUATION OF UNCERTAINTY FOR COMMERCIAL LAND-USE: Based on the above it is considered likely that the estimates of total exposure predicted by the probabilistic modelling are likely to be highly conservative, particularly at specific locations.	

Note that the implications of the overall uncertainty for risk can be considered looking at the RCF graphs in Section 4.2: over-and underestimation of the exposure would imply that the RCF should be shifted to the left or right, respectively.

The above qualitative evaluation of uncertainty has indicated that the exposure estimates derived by the probabilistic modelling are likely to be over-estimates.

The overall impact of uncertainty on the estimates of probability of exceedence has been further assessed for the allotments land-use by re-conducting the probabilistic modelling using alternative PDFs for these parameters, as described below:

- Consumption rates. As discussed in Table 4.4 it is possible that the assumption that all consumers of homegrown produce have overall consumption rates within the top quartile for each produce type may be overly conservative. An alternative PDF has been tested based on the assumption that consumers who eat homegrown produce do not eat more produce than consumers who do not eat homegrown produce i.e. there is no correlation between homegrown fraction and consumption rate.
- Homegrown fraction. Modelling the homegrown fraction as 100% in all cases results has been tested to model the allotment holders who are self sufficient.
- Soil to plant concentration factors. As discussed in Table 4.4 there is a large variability in the estimates of soil to plant concentration factors for BaP based on a limited dataset. It is possible that this variability over-estimates the true variability of plant uptake of BaP. The effect of this uncertainty has been assessed by modelling the soil to plant concentration factor for each soil type as a uniform distribution set at the geomean value, i.e. modelling no variability at all.

The results of this sensitivity analysis are presented in Figure 4.10 and show that uncertainty in the PDFs creates considerable uncertainty in the estimates of probability of exceedence. However, in combination with the qualitative assessment of uncertainty presented in Table 4.4, it is considered likely that the probabilities of exceedence shown on the graphs in Section 4.2 are over-estimates.

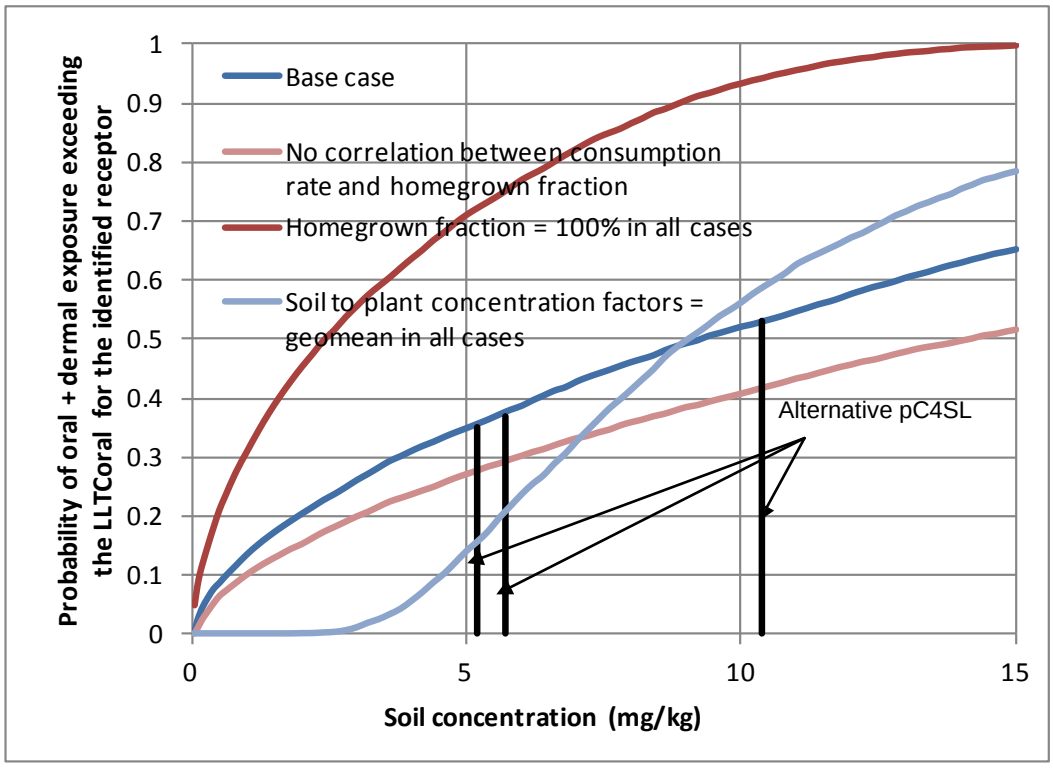

Figure 4.10: Probability of exposure exceeding the LLTC for BaP for allotments land-use with alternative PDFs

4.4 OTHER CONSIDERATIONS

Other considerations that are relevant when setting the C4SLs for BaP include the following:

- The British Geological Survey (BGS) have derived normal background concentrations (NBCs) for BaP (corresponding to the upper confidence limit of the 95th percentile concentrations) for Great Britain. The NBC for BaP for the 'urban' domain is 3.6 mg kg^{-1} (Defra, 2012 and 2013). This is based on only 32 samples and so there is considerable uncertainty in this estimate. Nevertheless, experience from contaminated land investigations of residential properties and allotments in urban areas would suggest that it is not untypical of concentrations of BaP in urban areas. The NBC is within the range of pC4SLs presented for residential and allotments land-uses;
- Modelled exposure from soils with concentrations of BaP at the various pC4SLs are generally in excess of background exposure. By extension, therefore, soil could be a potentially major contributor of BaP exposure on a site-specific basis and its remediation could potentially significantly reduce this.
- With regard to remediation, it should also be noted that, as non-threshold substances, genotoxic PAHs are subject to the "As Low as Reasonably Practicable" (ALARP) principle (see EA, 2009a; 2009b for details). The principle of ALARP automatically applies to the regulation and management of non-threshold chemicals in the UK. It is important to note that ALARP remains the overriding principle even when a margin of exposure or minimal risk level or LLTC suggests there is a minimal/low concern for human health. What is considered practicable is a remediation/risk management decision, and could be lower or higher than the scientific values derived.
- The predicted exposures from the pC4SLs (and thus, by conjecture, from normal background concentrations) when compared to the LLTCs are considered unlikely to result in a measurable increase in cancer within the population.

4.5 SUMMARY AND CONCLUSIONS

Following the methodology described in the main report, deterministic exposure modelling with a modified version of CLEA has been used to estimate the soil concentration that could result in potential exposure to an individual receptor within the critical receptor group for each land-use equating to the LLTCs for BaP, as a surrogate marker for genotoxic PAHs. These soil concentrations are the pC4SLs.

A range of pC4SLs have been derived for BaP, as a surrogate marker for genotoxic PAHs, based on the following options:

Option 1:	Use of minimal risk HCVs with changes to exposure parameters (as summarised in Section 3.5.7 of the main report);
Option 2:	Use of LLTCs with no change to exposure parameters (i.e. as defined in SR3); and
Option 3:	Use of LLTCs with changes to exposure parameters.

These are shown below:

Table 4.5: pC4SLs for BaP as a Surrogate Marker for Genotoxic PAHs (at 6% SOM)

Land-Use	pC4SL (mg/kg)		
	HCVs with suggested changes to exposure parameters	LLTCs with no change to exposure parameters	LLTCs with suggested changes to exposure parameters
Residential (with consumption of homegrown produce)	2.4	3.2	5.0
Residential (without consumption of	2.5	3.4	5.3

Land-Use	pC4SL (mg/kg)		
	HCVs with suggested changes to exposure parameters	LLTCs with no change to exposure parameters	LLTCs with suggested changes to exposure parameters
homegrown produce)			
Allotments	2.7	5.1	5.7
Commercial	36	77	77
POS_{resi}	4.9	NA	10
POS_{park}	10	NA	21

Quantitative probabilistic modelling has been conducted to better understand some of the uncertainty inherent within the exposure modelling aspects of the pC4SLs and the level of protection they may provide. The probabilistic modelling has focused on key exposure pathways and has helped to demonstrate the expected variability in exposures between individuals within the critical receptor group for a given soil concentration (and the probability that exposure to a random individual within the group would exceed the LLTC). Such modelling has not been carried out in relation to toxicological aspects, due to a lack of suitable data and approaches.

The probabilistic modelling has indicated that the greatest uncertainty within the exposure modelling is associated with the consumption of homegrown produce pathway, stemming partly from the large degree of variability in produce consumption rates and the fraction consumed that is homegrown. Furthermore, there is a high degree of uncertainty in the soil to plant concentration factors used for modelling the plant uptake of BaP.

In addition to the probabilistic modelling, a qualitative analysis of uncertainty has been carried out to further elucidate the level of uncertainty within the pC4SLs. This has focused on other aspects of the exposure modelling, as well as the LLTC setting process.

As a final step within the C4SL derivation process, other relevant considerations are identified, which should have a bearing on any final choice of numbers. For BaP, these take the form of recently published background levels in soil, estimates of background human exposure levels and a review of epidemiological evidence of health impacts from BaP in UK soil. As described in the main report, and at the request of the Steering Group, this appendix stops short of providing “final C4SLs” for BaP since: 1) final C4SLs should be set by “relevant authorities” (eg, Defra); 2) the toxicological framework contained herein has recently been submitted for review by the Committee on Toxicity (COT, 2013), with comments pending; and 3) the whole document will also be the subject of peer review.

Since the above pC4SLs have been derived using a modified version of the CLEA model, the Environment Agency’s SR3 document (EA, 2009d) should be referred to for important caveats and supporting information regarding their use. Furthermore, the LLTCs have been derived using similar methods to those outlined in the Environment Agency’s HCV document (EA, 2009c), and the reader is referred to that document for the same reasons.

As described in the main report, the final C4SLs can be used in a similar manner to that described for SGVs in the Environment Agency’s “Using Soil Guideline Values” document (EA, 2009e). Although they are unlikely to represent a “significant possibility of significant harm” (SPOSH), the likelihood of an exceedance of a C4SL being representative of SPOSH may be greater than if the default CLEA settings and toxicological criteria equivalent to minimal risk had been used in their derivation.

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APPENDIX E1

HUMAN TOXICOLOGICAL DATA SHEET FOR BENZO(A)PYRENE

Human Toxicological Data Sheet for C4SL derivation: Reference checklist

Chemical: **Benzo(a)pyrene**

Human Health Hazard Profile - References

Authoratative bodies	Website	Checked (Y/N)	References
EA	http://www.environment-agency.gov.uk/	y	Unpublished data
FSA	http://www.food.gov.uk/	y	PAHs in cereals, ceral products, vegetables, vegetable produts and traditionally smoked foods, 2012
			PAHs in the 2000 total diet study, 2002
COC	http://www.iacoc.org.uk/	Y	COC mixtures
			COC BMDL PAH, 2007
COM	http://www.iacom.org.uk/		
COT	http://cot.food.gov.uk/		
EFSA	http://www.efsa.europa.eu/	y	Polycyclic Aromatic Hydrocarbons in Food, 2008
JECFA	http://www.who.int/foodsafety/chem/jecfa/publications/en/index.html	y	Sixty-fourth meeting, 2005
WHO	http://www.who.int/en/	y	EHC PAHs, 2002
RIVM	http://www.rivm.nl/English	y	Re-evaluation of human-toxicological maximum permissible risk levels, 2001
ATDSR	http://www.atsdr.cdc.gov/		
USEPA	http://www.epa.gov/	y	Development of a relative potency factor approach for polycyclic aromatic hydrocarbon mixtures, 2010
Health Canada	http://www.hc-sc.gc.ca/index-eng.php	Y	No data found
Other references			
IOM		y	Tox review of the risks of exposure to soil containing PAHs, 2009
SCF		y	Opinion of the SCF on the risk to human health of PAHs in food, 2002

Human Toxicological Data Sheet for C4SL derivation: Toxicological Evidence, HBGVs, MDIs and LLTC derivation

Chemical: **Benzo(a)pyrene**

I) Human Health Hazard Profile - Toxicological Evidence

Type of Evidence	POD type	POD value	Units	Species	Study Type	Comments/Study Quality	Reference
1. Toxicokinetics						Oral absorption of BaP is estimated to be 35 - 99% following dietary or gavage exposure. It is distributed to almost all tissues, the highest levels been found in the GI tract and lipid rich tissues. It also crossed the placenta into the foetus. Metabolism of PAHs is required for the toxic, mutagenic and carcinogenic action.	EFSA 2008
Oral							
Inhalation							
Dermal							
2. Acute Toxicity							
Oral	LD50	>1600	mg/kg	Rodents			Defra & EA 2002; EFSA 2008
	NOAEL	3	mg/kg bw/day	Rat	90 day		
Inhalation						No data found	
Dermal						No data found	
3. Irritation and Corrosivity							
Dermal						Adverse skin reactions resulting from respeated dose local application	Defra & EA 2002
Eye						No data found	
4. Sensitisation							
Dermal						Sensitising potential	Defra & EA 2002
Respiratory						No data found	
5. Repeat-dose Toxicity							
Oral	NOEL	3	mg/kg bw/day	Rat		Based on immunosuppressive effects of BaP fed by gavage	EFSA 2008
Inhalation						Few adverse effects following inhalation exposure to BaP alone	IPCS 1998
Dermal						Repeat dermal exposure caused an inflammaotry response in skin.	ATSDR 1995
6. Genetic Toxicology						PAH metabolites form DNA adducts, generallyr regarded as one fo the first steps in carcinogenicity of mutagenic PAHs	EFSA 2008
In vitro							
In vivo							
7. Carcinogenicity						BaP is carcinogenic to humans (group 1)	IARC 2010
Oral				Rat and mouse		BaP alone produces tumours of the tumours of the liver, forestomach, lung, gastrointestinal tract, oesophagus, larynx, tongue and mammary glands - liver and forestomach tumours are the most sensitive; For mixtures of PAHs lung tumorus are the most sensitive endpoint	EFSA 2008; Culp et al 1998
Inhalation						Inhalation causes lung tumours	
Dermal							
8. Reproduction							
Reproductive						No NOAELs derived from thefew available data	EFSA 2008
Developmental							
Teratogenicity							
9. Human epidemiology data							
Oral						Few quantitative data available	EFSA 2008
Inhalation							
Dermal						Mixtures of some PAH may cause skin disorders	ATSDR 1995

Most Sensitive Health Effect: **Carcinogenicity**

II) Health Based Guidance Values (HBGVs) from Authoritative Bodies (in descending order of magnitude)							
A) Oral Route	**HBGVoral**	**Unit**	**UF used**	**PoD**	**Endpoint**	**Pivotal data used & Comments**	**Reference**
RIVM 2001 MRL	0.05	µg kg^{-1} bw day^{-1}			Liver, GI tumours	BaP alone. Based upon a female rat study on BaP by Kroese et al., 2001. Dose related to a lifetime excess cancer risk of 1 in 100,000. TEF approach adopted for other PAHs.	
CLEA 2002	0.02	µg kg^{-1} bw day^{-1}			fore-stomach tumours	BaP alone. 2002 Published Tox2 report. Index dose based on WHO 1993 drinking water guideline value 0.7 µg L-1 for a lifetime cancer risk of 1 in 100 000. (based upon Neal & Rigdon, 1967 study). Approach using quantitiative risk estimate from animal data not endorsed by COC.	
US EPA 1994	0.004	µg kg^{-1} bw day^{-1}			fore-stomach tumours	BaP alone. Neal and Rigdon, 1967. Brune et al., 1981. Rabstein et al., 1973. Combined forestomach tumour data in mice. 1 in 100 000 lifetime cancer risk. Approach using quantitiative risk estimate from animal data not endorsed by COC. **NB. In 2010 USEPA proposed a method for adopting Relative Potency Factors (RPFs) based on dermal study data. Method is under consultation.**	
CCME 2008	0.004	µg kg^{-1} bw day^{-1}		ELCR of 1 in 100,000	fore-stomach tumours	BaP alone. Neal and Rigdon, 1967. Forestomach tumours in mice. 1 in 100,000 lifetime cancer risk. Approach using quantitiative risk estimate from animal data not endorsed by COC.	
JECFA 2006				$BMDL_{10}$; 100 µg kg^{-1} bw day^{-1}	Lung, liver, GI tumours	Based on mouse study by Culp and mouse study by Kroese. MOE calculated to compare against exposure via food.	
EFSA 2008				$BMDL_{10}$; 70 µg kg^{-1} bw day^{-1}	Lung, liver, GI tumours	Based on mouse study by Culp. MOE calculated to compare against exposure via food.	

Comment:

Current UK oral HCV

CLEA 2002	0.02	µg kg^{-1} bw day^{-1}	0	0	fore-stomach tumours	BaP alone. 2002 Published Tox2 report. Index dose based on WHO 1993 drinking water guideline value 0.7 µg L-1 for a lifetime cancer risk of 1 in 100 000. (based upon Neal & Rigdon, 1967 study). Approach using quantitiative risk estimate from animal data not endorsed by COC.

B) Inhalation Route	Converted HBGVinh	ng kg^{-1} bw day^{-1}	HBGVinh	ng m^{-3}	UF used	PoD	Endpoint	Pivotal Study used & Comments	Reference
**US EPA 1989	*5.71*	*ng kg^{-1} bw day^{-1}*	20	ng m^{-3}		ELCR of 1 in 100,000	carcinogenicity	Based on occupational exposure of coke workers. BaP used as surrogate marker. 20 ng m^{-3} related to an ELCR of 1 in 100,000	
**Air Quality Standards Regulation 2010	0.3	*ng kg^{-1} bw day^{-1}*	1	ng m^{-3}			carcinogenicity	Based on the Air Quality Standards Regulation approach that stated that Member States should take necessary measures to ensure that air concentrations of BaP (used as a surrogate marker for carcinogenic risk of all PAHs) do not exceed the target value of 1 ng m^{-3}.	
*CLEA 2002	*0.07*	*ng kg^{-1} bw day^{-1}*	0.25	ng m^{-3}	1000	LOAEL; 0.25 µgm^{-3}	lung tumours	Based on the UK EPAQs, namely the atmospheric concentration of 0.25 ng m-3 which was considered to pose a cancer risk that was so small as to be undetctable.	
**UK AQS, 2007	*0.07*	*ng kg^{-1} bw day^{-1}*	0.25	ng m^{-3}				Based on recommendation of EPAQs of 0.25 ng m^{-3}.	
*EPAQS 1999	*0.07*	*ng kg^{-1} bw day^{-1}*	0.25	ng m^{-3}	1000	LOAEL; 0.25 µgm^{-3}	lung tumours	Based on cancer mortality of workers in an aluminium smelter in Canada (Armstrong 1994). 3 x 10 UF used to account for using a LOAEL, conversion from occupation to continuous exposure, and to account for human variability. 0.25 ng m^{-3} was recommended as AQO but in England, target value of 1 ng m^{-3} is used as the AQ standard. BaP used as a marker for hte total mixture of PAHs.	
** WHO 2000	*0.03*	*ng kg^{-1} bw day^{-1}*	0.12	ng m^{-3}		ELCR of 1 in 100,000	lung tumours	Based on occupational exposure of coke workers (Redmond 1976). BaP is used as surrogate marker for carcinogenic potential of PAHs in a mixture. 1.2, 0.12 and 0.012 ng m^{-3} related to an ELCR of 1 in 10,000, 100,000 and 1,000,000, respectively. Linearised multi-stage model of lung tumour rates in a rat inhalation study giving a cancer risk of 2 in 100,000 per ng m-3 BaP was in the same order of magnitude as that seen in the epidemiology study.	
*WHO AQG 1996	*0.03*	*ng kg^{-1} bw day^{-1}*	0.12	ng m^{-3}		ELCR of 1 in 100,000	carcinogenicity	Based on occupational exposure of coke workers (Redmond 1976). BaP is used as an indicator of total PAH burden. 1.2, 0.12 and 0.012 ng m^{-3} related to an ELCR of 1 in 10,000, 100,000 and 1,000,000, respectively	
**EC working gp 2001 Possible limit values	*0.03*	*ng kg^{-1} bw day^{-1}*	0.1	ng m^{-3}		ELCR of 1 in 100,000	carcinogenicity	Based on the WHO AQG. BaP used as surrogate marker as BaP was likely to make a similar proportional contribution to the total carcinogenicity of mixtures in ambient air as in the occupational setting. Possible limit values of 1, 0.1 and 0.01 ng m^{-3} were proposed, relating to an ELCR of 1 in 1,000,000, 100,000 and 10,000 respectively.	
**RIVM, 1989	*0.003*	*ng kg^{-1} bw day^{-1}*	0.01	ng m^{-3}		ELCR of 1 in 100,000	lung tumours	Based on lung cancer in UK gas works (Doll 1965, 1072), chinese women exposed during cooking (Mumford 1987) and occupational exposure to coal ovens of US steel works (Redmond 1976). ELCR of 1 in 1,000,000 were between 0.002 and 0.02 ng m-3 for BaP as a surrogate marker for PAH. 0.01 ng m^{-3} was deemed probably the most appropriate to use in practice.	

Comment:

* EA 2002 evaluation; ** draft EA 2010 evaluation. Both WHO and UK EPAQs evaluated the risk of lung cancer from occupational exposure to mixtures of inhlaed PAHs, expressed in terms of BaP. The UK EPAQs used data from a Canadian aluminium smelter (Armstrong 1994) whereas WHO favoured occupational data from coke oven workers (Redmond 1976).

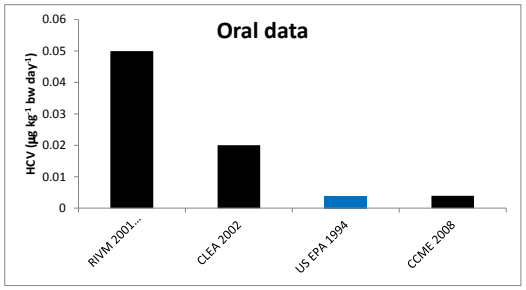
UK inhalation HCV

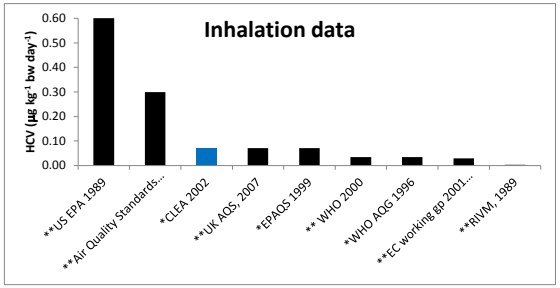
*CLEA 2002	0.07	ng kg-1 bw day-1	0.25	ng m-3	1000	LOAEL; 0.25 mgm-3	lung tumours	Based on the UK EPAQs, namely the atmospheric concentration of 0.25 ng m-3 which was considered to pose a cancer risk that was so small as to be undetctable.

C) Dermal Route	HBGVderm	Units	UF used	POD	Endpoint	Pivotal Study used & Comments	Reference
BAP is a human carcinogen when applied to the skin topically (IPCS 1998). However, no authoritative assessments of dermal skin painting have been performed to yield a quantitative minimum risk estimate for local cancer effects from dermal exposure to PAH mixtures. Topical doses of 100 mg kg-1 bw or 0.001 per cent w/v concentrations have induced tumours in mice. Default: Use Oral HCV and an estimate of skin absorption. Where data allows calculate data driven Dermal HBGV							

COT/COC Opinion: It is inappropriate to use TEFs to assess the oral carcinogenicity of combined exposures to PAHs, most of which have no oral carcinogenicity data. An alternative surrogate marker approach based on the benchmark dose derived the the Culp study

Positioning of UK Minimal Risk HCV vs other HBGV from authoritative bodies





III) Mean Daily Intakes from Other Sources (e.g. Diet)

	Pathways	Units	Adults	Children	Refs
Food (average)	Oral	µg kg^{-1} bw day^{-1}	0.0016		FSA 2002
Food (average)	Oral	µg kg^{-1} bw day^{-1}	0.0043		EFSA 2008
Water	Oral	µg kg^{-1} bw day^{-1}	0.0003	0.05	EA draft 2010
Air	Inhalation	ng kg^{-1} bw day^{-1}	0.05	-	EA draft 2010
Smoking	Inhalation	ng kg^{-1} bw day^{-1}	3	-	EA draft 2010

Comment: Average daily dietary intake is below 'minimum risk' value of 0.01 µg kg^{-1} bw day^{-1}

IV) LLTC derivation

A) ORAL

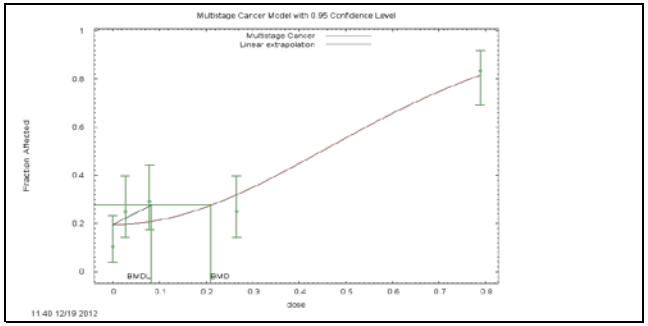
Choice of Pivotal Data	Dosing vehicle	Doses	Units	Species	Study Type	Comments	Reference
Culp et al 1998	Coal tar mix	0, 0.027, 0.079, 0.266 and 0.789	mg kg^{-1} bw day^{-1}	B6C3F1 mouse	2 year carcinogenicity study		Culp et al 1998. A A comparison of the tumors induced by coal tar and benzo[a]pyrene in a two-year bioassay.

BMD Modelling (if relevant)

Software used US EPA BMDS 2.3.1

	BMD1	BMD5	BMD10	BMD15	BMD20
BMD modelling (value) (mg kg^{-1} bw day^{-1})	NA	NA	0.21	0.26	0.31
	BMDL1	BMDL5	BMDL10	BMDL15	BMDL20
BMD modelling (value) (mg kg^{-1} bw day^{-1})	NA	NA	0.08	0.12	0.17

Comments: Modelling carried out for 10, 15 and 20 % tumour incidence. BMDL15 has been selected as the PoD to be sufficiently protective of health but slightly above minimum risk. Alternatively, BMDL20 or BMD10 could be selected.



Point of Departure for ORAL LLTC:	Value	Units
Type of PoD	BMD10	mg kg^{-1} bw day^{-1}
Description of PoD		
Value selected	0.21	mg kg^{-1} bw day^{-1}

Chemical Specific Adjustment Factor to account for uncertainties in the data		
	Range	Selected value
Intraspecies	1 - 10	10
Interspecies	1 - 10	10
Additional uncertainties	1 - 100	50

Thresholded chemical? No

If yes - calculate CSAF
If no - calculate CSM

CSAF = (for thresholded chemical)

CSM = 5000 (for non-thresholded chemical)

ELCR =

Lifetime averaging to be applied in CLEA No

Oral LLTC calculation:

	Units
LLTC (Thresholded chemical)	
LLTC (Non Thresholded chemical)	0.042 µg kg^{-1} bw day^{-1}
LLTC (Human carcinogen)	Classified by IARC as a group 1 human carcinogen

Comments:

B) INHALATION

Choice of Pivotal Data	Dosing vehicle	Doses	Units	Species	Study Type	Comments	Reference
Epidemiology study of cancer mortality of workers in an aluminium smelter in Canada (Armstrong 1994)	NA	NA	NA	Human	Epidemiology study in Aluminium smelter workers	Concentrations of BaP (as a surrogate marker) of 1, 0.1 and 0.01 ng m^{-3} equates to an ELCR of 1 in 10,000, 100,000 and 1,000,000, respectively. 1 ng m^{-3} also is the target value under the Uk Air Quality Standards Regulation (2010).	**UK Air Quality Standards Regulation (2010)**

BMD Modelling (if relevant)

Software used

	BMD1	BMD5	BMD10	BMD15	BMD20
BMD modelling (value)					
	BMDL1	BMDL5	BMDL10	BMDL15	BMDL20
BMD modelling (value)					

Comments:

Paste BMDL graph here

Point of Departure for INHALATION LLTC:	Value	Units
Type of PoD	ELCR = 1 in 10000	ng m^{-3}
Description of PoD		
Value selected	1	ng m^{-3}

Chemical Specific Adjustment Factor to account for uncertainties in the data		
	Range	Selected value
Intraspecies	1 - 10	
Interspecies	1 - 10	
Quality of study	1 - 10	
Severity of Effect	1 - 50	

Thresholded chemical? No
If yes - calculate CSAF
If no - calculate CSM

CSAF = 0 **(for thresholded chemical)**

CSM = 0 **(for non-thresholded chemical)**

ELCR = 10000

Lifetime averaging to be applied in CLEA No

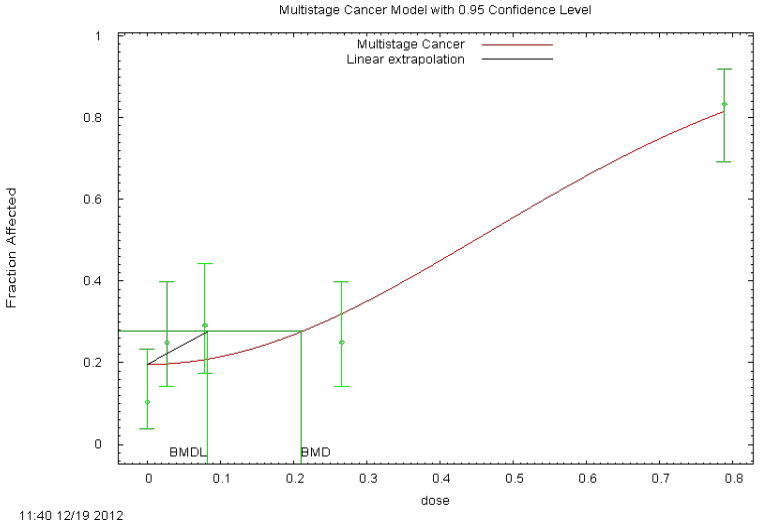
Inhalation LLTC calculation:

	Units
LLTC (Thresholded chemical)	
LLTC (Non Thresholded chemical)	0.3 ng kg^{-1} bw day^{-1}
LLTC (Human carcinogen)	Classified by IARC as a group 1 human carcinogen

Comments:

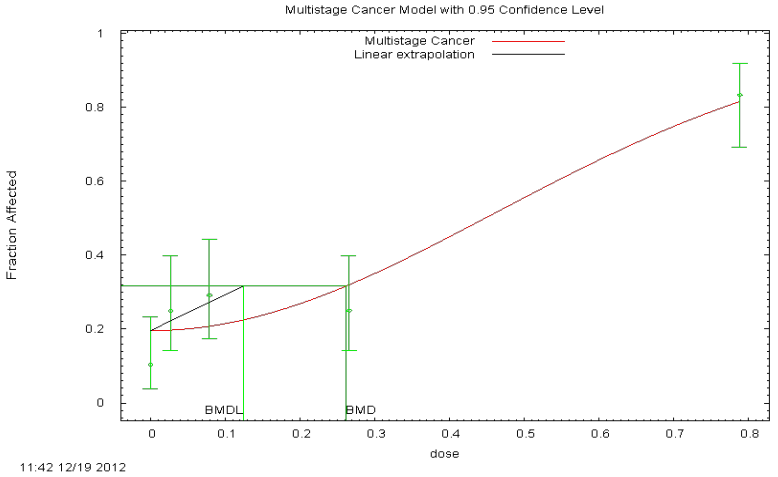
Physiological conversion factors		
	Value	Units
Body weight	70	kg
Inhalation rate	20	m^3

Toxicological data	Culp 1998 (data from Schneider 20			
Endpoint	Total tumours			
Level of modelled response	10%			
Chemical used in study	Coal tar mix II			
Dose (mg/kg bw/day)	**Species**	**Sex**	**n**	**Incidence of**
0	Mouse	f	48	5
0.027	Mouse	f	48	12
0.079	Mouse	f	48	14
0.266	Mouse	f	48	12
0.789	Mouse	f	48	40
1.92	Mouse	f	48	42
3.2	Mouse	f	48	43



Model Name	Maximum number of iterations	AIC	Chi squared value	p value	Specified effect	Accept	BMD	BMDL
Gamma	250	253.244	5.51	0.0637	0.1	yes	0.33	0.16
Logistic	250	252.574	7.24	0.0645	0.1	yes	0.13	0.11
LogLogistic	250	253.235	5.5	0.0638	0.1	yes	0.33	0.18
LogProbit	250	253.247	5.51	0.0637	0.1	yes	0.32	0.20
Multistage	250	254.12	6.6	0.0369	0.1	no	0.22	0.08
Multistage-Cancer	250	252.133	6.63	0.0845	0.1	yes	0.21	0.08
Probit	250	252.639	7.29	0.0632	0.1	yes	0.13	0.11
Weibull	250	253.211	5.5	0.064	0.1	yes	0.33	0.14
Quantal-Linear	250	257.022	11.3	0.0102	0.1	no	0.07	0.05

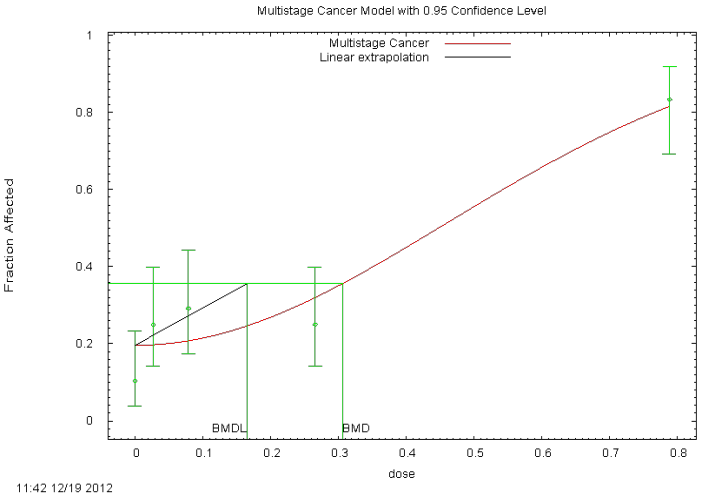
Toxicological data	Culp 1998 (data from Schneider 20			
Endpoint	Total tumours			
Level of modelled response	15%			
Chemical used in study	Coal tar mix II			
Dose (mg/kg bw/day)	**Species**	**Sex**	**n**	**Incidence of**
0	Mouse	f	48	5
0.03	Mouse	f	48	12
0.09	Mouse	f	48	14
0.32	Mouse	f	48	12
0.96	Mouse	f	48	40
1.92	Mouse	f	48	42
3.2	Mouse	f	48	43



Model Name	Maximum number of iterations	AIC	Chi squared value	p value	Specified effect	Accept	BMD	BMDL
Gamma	250	253.244	5.51	0.0637	0.15	yes	0.37	0.21
Logistic	250	252.574	7.24	0.0645	0.15	yes	0.19	0.16
LogLogistic	250	253.235	5.5	0.0638	0.15	yes	0.37	0.22
LogProbit	250	253.247	5.51	0.0637	0.15	yes	0.36	0.23
Multistage	250	254.12	6.6	0.0369	0.15	no	0.27	0.12
Multistage-Cancer	250	252.133	6.63	0.0845	0.15	yes	0.26	0.12
Probit	250	252.639	7.29	0.0632	0.15	yes	0.18	0.15
Weibull	250	253.211	5.5	0.064	0.15	yes	0.38	0.19
Quantal-Linear	250	257.022	11.3	0.0102	0.15	no	0.10	0.08

Toxicological data	Culp 1998 (data from Schneider 20
Endpoint	Total tumours
Level of modelled response	20%
Chemical used in study	Coal tar mix II

Dose (mg/kg bw/day)	Species	Sex	n	Incidence of endpoint
0	Mouse	f	48	5
0.03	Mouse	f	48	12
0.09	Mouse	f	48	14
0.32	Mouse	f	48	12
0.96	Mouse	f	48	40
1.92	Mouse	f	48	42
3.2	Mouse	f	48	43



Model Name	Maximum number of iterations	AIC	Chi squared value	p value	Specified effect	Accept	BMD	BMDL
Gamma	250	253.244	5.51	0.0637	0.2	yes	0.40	0.25
Logistic	250	252.574	7.24	0.0645	0.2	yes	0.24	0.20
LogLogistic	250	253.235	5.5	0.0638	0.2	yes	0.40	0.26
LogProbit	250	253.247	5.51	0.0637	0.2	yes	0.39	0.27
Multistage	250	254.12	6.6	0.0369	0.2	no	0.32	0.17
Multistage-Cancer	250	252.133	6.63	0.0845	0.2	yes	0.31	0.17
Probit	250	252.639	7.29	0.0632	0.2	yes	0.23	0.19
Weibull	250	253.211	5.5	0.064	0.2	yes	0.42	0.23
Quantal-Linear	250	257.022	11.3	0.0102	0.2	no	0.14	0.11

Range (mg/kg bw/day)	BMD1	BMD5	BMD10	BMD15	BMD20
BMD modelling (value)	-	-	0.13 - 0.33	0.1 - 0.38	0.14 - 0.42
	BMDL1	BMDL5	BMDL10	BMDL15	BMDL20
BMD modelling (value)	-	-	0.08 - 0.2	0.08 - 0.23	0.11 - 0.27

Best fit (mg/kg bw/day)	BMD1	BMD5	BMD10	BMD15	BMD20
BMD modelling (value)	-	-	0.21	0.26	0.31
	BMDL1	BMDL5	BMDL10	BMDL15	BMDL20
BMD modelling (value)	-	-	0.08	0.12	0.17