The Interdepartmental Group
on Health Risks from Chemicals

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Final Report for Phase 2 (2003 – 2007) and Forward Plan for Phase 3 (2007 – 2010)

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The Interdepartmental Group on Health Risks from Chemicals aims to stimulate the development of new, improved approaches to the assessment of risks to human health from chemicals.

The Steering Committee of the Interdepartmental Group on Health Risks from Chemicals comprises participants from the Department for Environment, Food and Rural Affairs, the Department of Health, the Department for Business, Enterprise and Regulatory Reform, the Home Office, the Environment Agency, the Health and Safety Executive, the Food Standards Agency, the Medicines and Healthcare Products Regulatory Agency, the Pesticides Safety Directorate, the Veterinary Medicines Directorate, the Biotechnology and Biological Sciences Research Council, the Medical Research Council and the Natural Environment Research Council.

The Secretariat is based at the Institute of Environment and Health, Cranfield University.

The Institute of Environment and Health was established by the Medical Research Council at the University of Leicester in 1993 and moved to Cranfield University in 2005 where it is now part of Cranfield Health.

Published by the Institute of Environment and Health, 2008

ISBN 978-1-899110-42-1

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Foreword

The Interdepartmental Group on Health Risks from Chemicals (IGHRC) comprises representatives from UK government departments, agencies and research councils with an interest in chemical risk assessment. The group was originally established in 1996 as the Risk Assessment and Toxicology Steering Committee, but the name was changed in 1999 to reflect the broader remit of the group.

The overall aim of the IGHRC is to reduce uncertainties and limitations in the conduct of chemical risk assessment. To this end, IGHRC develops and publishes reports and guidance documents aimed at improving chemical risk assessments in the UK, establishes specific-issue working groups to develop and share expertise, and runs training courses in the area of risk assessment. This report explains how the group carried out its work programme during the period October 2003 to September 2007 (Phase 2) and how it intends to carry out its programme of activities during the period October 2007 to September 2010. The report can also be accessed from the IGHRC website[1].

During Phase 2, three documents were prepared: *Guidelines on Route-to-Route Extrapolation of Toxicity Data* (published as Committee Report cr12, 2006), *Chemical Mixtures: a Framework for Assessing Risks and Current Approaches to Exposure Modelling.* The success of the courses run in Phase 1 led to a focus on training provision during Phase 2. A total of seven courses were provided by the IGHRC in Phase 2, with two courses repeated due to good feedback and continuing high levels of interest. The training courses were particularly considered to reflect the aims and objectives of the IGHRC and will be developed further in the future, alongside the production of additional framework and guidance documents.

We hope, in reading this report, you will feel IGHRC continues to make an important contribution to the field of chemical risk assessment.

Dr David Harper
Chairman of the IGHRC
Chief Scientist, Department of Health

[1] http://www.cranfield.ac.uk/health/ighrc

Contents

1. Introduction

The Interdepartmental Group on Health Risks from Chemicals (IGHRC) comprises participants from UK government departments, research councils and agencies, and aims to stimulate the development of new improved approaches to the assessment of risks to human health from chemicals, share experiences to achieve a more consistent and coherent approach on issues related to chemical risk assessment, and increase the clarity and transparency with which risk assessment documents are written. The IGHRC comprises two committees, a Steering Committee and an Executive Committee. Membership of both committees is shown in Annex 1. The Executive Committee (EC) meets every four months and is responsible for the day-to-day operation of the IGHRC, including writing of reports, organising workshops, producing guidance documents, developing training courses and proposing future activities to the Steering Committee. The Steering Committee (SC) meets once or twice yearly to approve and oversee the work of the EC. Both committees are overseen by a chairperson: Dr David Harper for the SC and, for most of the Phase 2 programme, Professor Ian Purchase for the EC. Professor Purchase stepped down from this role towards the end of the programme and has been succeeded by Professor Len Levy, formerly of the IGHRC Secretariat.

The IGHRC Secretariat, which manages the programme of work and activities on behalf of the EC and SC, continues to be provided by the Institute of Environment and Health (IEH). IEH moved from the University of Leicester to Cranfield University in November 2005.

The IGHRC group was originally established in 1996 as the Risk Assessment and Toxicology Steering Committee (RATSC) but changed its name in September 1999 to reflect its broader remit. The aims and objectives of the IGHRC are given in Annex 2. The purpose of this report is to summarise the Phase 2 activities of IGHRC for the period October 2003 to September 2007, and to outline the forward plan and work programme to September 2010 (Phase 3). This report follows on from the First Report (cr7 and cr7A) and the Final Report for Phase 1 (cr 11) (IGHRC, 2000a, 2000b, 2004a).

2. Report of Phase 2 Work Programme (2003-2007)

The *Final Report for Phase 1 and Forward Plan to 2006* (cr11) described four main areas of IGHRC activity: the initiation of research projects, the production of authoritative guidance documents and reports, the formation of specific-issue working groups, and the sharing of experience to initiate change (principally through training courses). The latter three activity areas were continued into Phase 2 and are described in the sub-chapters below. It was determined by the SC that the initiation and support of research projects was now well served by government departments and agencies (solely or in collaboration) who were able to fund specific areas of research of particular concern or interest. Phase 1 of the IGHRC programme had addressed two key areas identified as having minimal research activity across the IGHRC membership (see Section 2.4) and further research was not considered a priority for Phase 2 of the programme. The evaluation of Phase 1 work programme, provided in cr11, further supports the concentration on course/workshop provision and the publication of relevant guidance and framework documents to assist in improving the understanding of chemical risk assessment.

The original 2003-2006 Phase 2 work programme was extended by a further year, financed by an under-spend of funds during Phase 1.

The remainder of this section expands on the work programme outlined in Figure 1 (Schedule of activities, October 2003-September 2007).

Figure 1: Schedule of activities, October 2003-September 2007

ACTIVITY	2003	2004	2005	2006	2007
Guidance documents and reports					
Route-to-route extrapolation					
Chemical mixtures					
Exposure modelling					
Sharing Experience					
Presenting and reporting transparent risk assessment					
Introduction to probabilistic modelling					
Basic aspects of exposure assessment					
Awareness Day					
Epidemiology					
Specific-Issue Working Groups					
RA for skin sensitisers[1]					
Chemical mixtures workshop (leading to guidance)					
Research					
Human chemical exposure model					
Evaluation of IGHRC[2]					
Final Report – Phase 2					

[1] Not progressed further – see Section 2.3

[2] The evaluation of Phase 1 of the IGHRC programme derives from the feedback received from training courses which link to the provision and use of IGHRC-published guidance documents (Annex 3) and a brief independent evaluation (Annex 5).

2.1 'Guidance' documents and reports

The production of guidance documents by the IGHRC is a means of promoting best practice, harmonisation and awareness of different risk assessment approaches between departments and agencies. The IGHRC worked with government agencies and departments, as well as academic experts, to prepare the following guidance documents and reports on various aspects of chemical risk, with the purpose of making risk assessments more coherent and consistent, as described in the Forward Plan to 2006 (IGHRC, 2004; Committee Report cr11).

- Guidelines on route-to-route extrapolation of toxicity data when assessing health risks of chemicals (IGHRC, 2006; Committee Report cr12);
- Chemical mixtures: a framework for assessing risks to human health (in press, Committee Report cr14); and
- Current approaches to exposure modelling in UK government departments and agencies (in final preparation).

These documents have been evaluated or are in the process of assessment by the agencies, departments and expert committees.

2.1.1 Guidelines on route-to-route extrapolation of toxicity data when assessing health risks (cr12)

There is very limited guidance on route-to-route extrapolation available to risk assessors. This document aims to rectify this paucity of information, providing guidance on the extrapolation of toxicity data obtained from one route of exposure (usually oral), to other routes of exposure, specifically dermal or inhalation. Guidance is also given, although more briefly, on extrapolation from inhalation to the oral route. Flow diagrams are included to assist the reader, together with recommendations for default values that can be used in the absence of data. Current use of route-to-route extrapolations of toxicity data by three UK regulatory bodies is included in an Annex. The full document is available through the IGHRC website http://www.cranfield.ac.uk/health/ighrc (IGHRC, 2006).

2.1.2 Chemical mixtures: a framework for assessing risks to human health

This document provides a framework to help risk assessors think about how to address mixture issues. Developed from a workshop that took place in Leicester on 23rd February 2005, the document followed on from other research reports initiated by the COT[2] report *Risk Assessment of Mixtures of Pesticides and Similar Substances* (COT, 2002). It discusses the types of mixtures for which UK government has to conduct risk assessments and the circumstances in which people might be exposed. It considers different regulatory approaches that may be adopted for different types of mixtures and the circumstances in which these approaches could be used. Aimed at both risk assessors and stakeholders, the document draws on the approaches that have been described in publications from other regulatory bodies and presents a flow chart that will help risk assessors to identify key issues that have to be considered depending on the type of mixture that is being assessed and type of data available. The document concludes that risk assessment of chemical mixtures is best dealt with through a series of discrete steps for which clear boundaries can be set.

2.1.3 Current approaches to exposure modelling in UK government departments and agencies

This report summarises current practice in the use of exposure models in risk assessment in a number of UK government departments and agencies, and explores reasons for the similarities and differences in approach. By increasing transparency on why certain models are used, including their default values and underlying assumptions, it is hoped that the document will facilitate harmonisation of exposure modelling approaches both nationally and internationally. As such, it provides guidance to assist those having to undertake or evaluate exposure assessments rather than prescribe the

[2] Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

use of certain models. It is aimed at risk assessors and policy makers within UK government departments and agencies who need to understand the process involved in the undertaking of an exposure assessment. Four exposure models from four government departments and agencies are described in detail.

2.2 Sharing experiences and training

The IGHRC considers that sharing experiences across government agencies and departments on various issues will lead to a more consistent and coherent approach to risk assessment. Such sharing of experience may also initiate changes in procedure, or lead to a better understanding of why different processes occur in different departments. It is a key part of IGHRC activities and follows on from the original training course organised during Phase 1. The Forward Plan to 2006 suggested the running of three courses:

- Presenting and reporting transparent risk assessments;
- Basic aspects of exposure assessment; and,
- A practical introduction to probabilistic modelling of exposures for risk assessment.

Two of the courses, *Presenting and reporting transparent risk assessments* and *Basic aspects of exposure assessment*, were run twice during Phase 2 due to the excellent feedback received and recommendations made by the IGHRC EC. Other courses were also run, as suggested by IGHRC members during the Phase 2 work programme. All course programmes are included in Annex 3.

2.2.1 Presenting and publishing understandable and transparent risk assessments for chemical exposures

This was a modification of the course run by IGHRC at the MRC Institute of Environment and Health (IEH) in Leicester in October 2001. This two-day course aimed to teach individuals how to report and/or evaluate reports of risk assessments in a robust and transparent manner rather than how to conduct chemical risk assessments.

First repeated in March 2004 at MRC IEH in Leicester, there were a total of 23 participants, both scientists and policy makers, from a variety of government departments and agencies and with a variety of risk assessment experience. The EC decided to repeat the course for a third time and it took place in October 2007 as *Developing and explaining chemical risk assessments* with an amended programme to better reflect the framework of a risk assessment and the importance of case studies and practical 'hands-on' sessions. The course was run over two days at IEH, Cranfield University, with 20 participants.

2.2.2 Probabilistic modelling of exposures for risk assessment

A two-day course was conducted at the Health and Safety Laboratory in Buxton during March 2005. An intensive practical course for experienced risk assessors, the course was attended by 19 scientists from across government departments and agencies. The feedback received from the course was excellent and the committee suggested that the course be run again before the end of Phase 2. However, the cost of the course was much higher than for other IGHRC courses, due predominantly to the requirement for IT equipment, and it was not considered cost-effective to run again when there are a number of similar in-house courses offered by member organisations of the IGHRC and other external bodies.

2.2.3 Understanding chemical exposure assessments

Suggested in the Future Plan to 2006 as *Basic aspects of exposure assessment*, this course was first run as a two-day event in May 2005 at MRC IEH in Leicester. It was intended for non-experts required to use or understand chemical exposure assessments and was based upon the IGHRC guidance document *Guidelines for good exposure assessment practice for human health effects of chemicals* (IGHRC 2004; Committee Report cr10). A total of 30 participants attended the course and the feedback was such that the committee suggested that the course be repeated towards the end of the Phase 2 programme. The course, which took place in October 2007 at Cranfield University, was altered to better reflect the structure of the cr10 guidance document and to improve the practical/case study content. While only 12 participants attended this course, the feedback was excellent.

2.2.4 Chemical risk assessments on health effects: current practice within the UK government

An Awareness Day was hosted by the Pesticides Safety Directorate at the University of York in March 2006, which aimed to provide an introduction into the wide range of different regulatory systems that apply to human health risk assessments of chemicals. It was attended by 54 scientists and policy makers with sessions delivered by scientists from a number of government departments and agencies. As a one-off single day course, it attracted a larger than normal number of delegates and was well received.

2.2.5 Understanding epidemiology for chemical risk assessment: an introduction for scientists and policy makers

A two-day course on *Understanding epidemiology for chemical risk assessment* took place at Imperial College London in November 2006. Epidemiology is an important aspect of risk assessment and the IGHRC committee determined that many risk assessors or evaluators of risk assessments are not familiar with epidemiological techniques and applications. The course provided an introduction to epidemiology and how epidemiology informs chemical risk assessment. The course was attended by 32 participants, the vast majority of whom found the course very useful.

2.3 Specific-issue working groups

At the commencement of Phase 1, the IGHRC proposed establishing specific-issue working groups to develop and share expertise on a number of issues. Initially these groups were to be interdepartmental, but the knowledge-base required made it necessary to go further afield for specific expertise. Specific-issue working groups were established to develop and share expertise in physiologically-based pharmacokinetic (PBPK) modelling and probabilistic modelling during Phase 1. The SC agreed that these were valuable and that the groups should continue to form part of the work programme during Phase 2. Two working groups/workshops were proposed for Phase 2:

- Risk assessment for skin sensitisers; and,
- Chemical mixtures.

2.3.1 Skin sensitisers risk assessment

During the development of the Phase 2 work programme, the IGHRC Committees noted that the risk assessment process for skin sensitisers had not been adequately considered and would benefit from the establishment of a specific working group led by the Health & Safety Executive (HSE). However, in the time that elapsed between the development of the Phase 2 work programme and the commencement of the programme, it was felt by the EC that adequate measures had been adopted outside the IGHRC to consider the issue of skin sensitiser risk assessment. As a result, it was agreed that no further action would be necessary and a working group need not be progressed.

2.3.2 Chemical mixtures

An IGHRC working group on chemical mixtures convened at a one-day workshop run by MRC IEH in Leicester on 23rd February 2005. The workshop included presentations from departments and agencies represented on the IGHRC, as well as expert feedback from other meetings/reports regarding chemical mixtures. A total of 13 participants attended the workshop, which resulted in the development of the guidance document described in Section 2.1.2 that is currently being reviewed by UK expert committees.

2.4 The research programme

In Phase 1, five research topics were identified in the document *Priority Research Topics for Improving Chemical Risk Assessments* (IGHRC 2002):

- toxicology and uncertainty factors;
- human variation and susceptibility;
- the role of probabilistic modelling;
- exposure models; and,
- physiologically-based pharmacokinetic (PBPK) models.

Within these five research areas, two were highlighted as having minimal ongoing research: *Human variation in toxicodynamics* and *Evaluation of human exposure models used in UK chemical risk assessments*. Sufficient funding was made

available to enable two pilot research projects to be initiated in these two areas. The first pilot was completed and the Executive Summary published on the IGHRC website within Phase 1 (IGHRC, 2003a). The exposure model study report was received during Phase 1 but has been published during Phase 2 (IGHRC, 2004c).

No further steps were taken with the research programme as it was agreed that sufficient research activities were underway elsewhere.

2.5 Evaluation of the IGHRC initiative during Phase 2 (October 2003 to September 2007)

As part of the remit laid down in the *Annexes to the First Report and Forward Plan to 2002* (IGHRC, 2000b) the SC proposed an independent evaluation of the activities and outputs of the group. Dr Sue Barlow, an independent consultant, was contracted to conduct the evaluation for Phase 1 and her Executive Summary is given in Annex 6 of cr11 (IGHRC, 2004a). The full report is available from the IGHRC Secretariat.

The IGHRC SC decided that a further detailed evaluation of the IGHRC initiative was not necessary owing, in part, to changes made to the work programme resulting from the Phase 1 evaluation. Instead, it was recommended that an evaluation be based upon the feedback received from participants/speakers involved in the courses and workshops, and on the comments received from the external committees reviewing IGHRC documents prior to publication. The SC suggested that an independent evaluator be contracted to carry out a brief audit of Phase 2 activities; Dr Barlow was again approached for this purpose because of her prior experience in this area.

The independent evaluation is provided in Annex 5. Table 5.1 of Annex 5 provides a summary of the feedback forms received from IGHRC course participants and demonstrates the high level of usefulness generally ascribed to all of the courses run. Speakers invited to host the sessions were all recognised experts in their field and this was appreciated by the participants. Speakers achieving the best feedback were included in repeated courses, leading to steady improvements in delegate feedback.

During Phase 2, three documents were developed and two were submitted to external expert bodies for consultation/review. Generally, the comments and feedback received were favourable and constructive, leading to the publication of a useful document contributing to a greater transparency and understanding of chemical risk assessment (Annex 4).

2.6 New issues for consideration

The Phase 1 work programme highlighted genomic and proteomic research and its possible use in risk assessment as a potential area of future interest, proposing the establishment of a 'watching brief'. As the techniques have yet to be applicable to regulatory chemical risk assessment, the 'watching brief' was not progressed over the Phase 2 programme. It is proposed that the 'watching brief' be maintained over the next phase and the formation of a working group be considered to report to the IGHRC EC on any developments in this area. This is expanded further in Section 4.

2.7 Summary of the Phase 2 work programme

The aims and objectives of the IGHRC have been met in a number of ways through the above activities, summarised in Annex 6.

3. Phase 2 Financial Statement (Summary)

A summary of IGHRC income and expenditure for the period October 2003 to September 2007 is summarised in Table 1. This includes the extension of Phase 2 from September 2006 to September 2007 using Phase 1 under-spend.

Table 1: Income and Expenditure Statement for IGHRC: - Phase 2 Actuals - Period: October 2003 to September 2007 Plus Projected Expenditure for Activities in Phase I carried over to Phase II

A) INCOME	Oct'03-Sep'04	Oct'04-Sep'05	Oct'05-Sep'06	Oct'06-Sep'07	**Total Income Oct'03-Sept'07 Actuals £**
Balance b/f from allocated Phase I activities	26,490				**26,490**
Balance b/f from unallocated Phase I activities	44,799				**44,799**
Total balance b/f from IGHRC Phase I	71,289				**71,289**
Actual Claims from Phase 2 contract	90,000	107,249	82,356	N/A	**279,605**
A) TOTAL INCOME	**161,289**	**107,249**	**82,356**	**N/A**	**350,894**
B) EXPENDITURE	Oct'03-Sep'04	Oct'04-Sep'05	Oct'05-Sep'06	Oct'06-Sep'07	**Total Actual Expenditure**
Core staff costs:	38,110	26,142	37,867	37,473	
B) TOTAL EXPENDITURE (CORE ACTIVITIES)	**38,110**	**26,142**	**37,867**	**37,473**	**139,592**
C) SCHEDULED ACTIVITIES (to Sep'07)	Oct'03-Sep'04	Oct'04-Sep'05	Oct'05-Sep'06	Oct'06-Sep'07	**Total Actual Expenditure**
Guidance documents	11,231	9,952	6,771	2,430	30,384
Specific issues - Working Groups:		4,284			4,284
Training Courses x 7 (Oct 2003 – Oct 2007)	6,262	26,951	4,544	17,675	55,432
Final Report (Assume 50 page report-100 copies)				1,100	1,100
C)TOTAL EXPENDITURE (Other scheduled activities)	**17,493**	**41,187**	**11,315**	**21,205**	**91,200**
Summary of Income & Expenditure	Oct'03-Sep'04	Oct'04-Sep'05	Oct'05-Sep'06	Oct'06-Sep'07	**Total Actuals**	***Expenditure carried over to Phase 3 activities***
Summary Total Income to Sep'06	**161,289**	**107,249**	**82,356**	**N/A**	**350,894**	
Total Expenditure to Sep'07 (Core + Scheduled Activities)	**55,603**	**67,329**	**49,182**	**58,678**	**230,792**	**120,102**

Total Income	**£350,894**	
Total Expenditure to date (Phase 2)		£230,792
Unallocated funds carried over to Phase 3		£120,102
Total anticipated expenditure from Phase 2		**£350,894**

The following government departments, agencies and research councils contributed towards the funding of IGHRC Phase 2 activities:

Biotechnology and Biosciences Research Council, Defra, Department of Health, DTI, Environment Agency, Food Standards Agency, Health & Safety Executive, Health Protection Agency, Medical Research Council, Pesticides Safety Directorate.

4. Forward Plan and Work Programme for Phase 3

The forward plan and work programme for the period October 2007 to September 2010 was developed by the EC and agreed at the SC meeting in January 2007, following a 'brainstorming' workshop in June 2006. Further alterations, including the prioritisation of activities, were made at the EC meetings in February and June 2007 and at the SC meeting in November 2007.

4.1 Introduction

The purpose of this section is to outline the proposed strategy and programme of work of the IGHRC for the period October 2007 to September 2010. This period represents the third phase of activities of the IGHRC. The first phase (October 1999 to September 2002) is described in the *Final Report for Phase 1* (cr11) (IGHRC, 2004a) and the second phase is outlined in Sections 2 and 3 of this report. Further details regarding the achievement of IGHRC objectives through Phase 2 and the proposed Phase 3 programme are provided in Annex 6. It should be noted that the future plan describes areas of work considered by the IGHRC committees to warrant greater attention; whilst it is the aim to address as many of these topics, as documents and as courses, as possible, it must be recognised that the programme of work is ambitious and it may not be possible to complete all the activities in the timescale provided for Phase 3.

The work programme has been determined through discussion within both the SC and the EC. Three areas identified for future IGHRC activities are the primary components of risk assessment: hazard characterisation, exposure assessment and risk characterisation. These areas are to be addressed through the provision of training combined with the sharing of experience through workshops and the development of documents (guidance, framework, or mapping) for publication. It was also proposed that several other areas not considered to be high priority, or concerning emerging fields, should be included in a 'watching brief', the findings of which may lead to further workshops and document preparation and publication as appropriate.

4.2 Sharing experience and training

The SC and EC have determined that training for government personnel should remain an essential component of IGHRC activities. The purpose of all the training courses is to maintain a high level of awareness regarding the techniques available to assess the health risks from chemicals and permit the exchange of ideas among government departments and agencies. Five specific training courses were proposed for Phase 3; other courses will be considered when applicable.

4.2.1 Benchmark dose course

It was agreed that a course on the use of the 'benchmark dose' should be included in the IGHRC work programme. FSA opinion on previously organised external courses attended by FSA personnel indicates that such a course would be worthwhile. An IGHRC organised course would be focused to the needs of government departments and agencies and enable discussion of complex issues. It is proposed that steps are taken to arrange the course during mid-2008, having first ascertained levels of interest from IGHRC government departments and agencies.

4.2.2 Descriptive versus quantitative risk assessment of genotoxic carcinogens

It is proposed that a workshop be organised to permit discussion of descriptive versus quantitative risk assessment for genotoxic carcinogens, among IGHRC members and invited experts. A workshop report will form the basis of an IGHRC publication, as described in Section 4.3.6. The workshop may result in a training course for IGHRC government departments and agencies.

4.2.3 Uncertainty in risk assessment

A workshop is proposed to discuss uncertainty in risk assessment and comparisons between quantitative and descriptive types of uncertainty factors applicable to substances with threshold-value effects. The workshop will result in a report that may either be used to update previous IGHRC publications or form a new publication.

4.2.4 Probabilistic approaches to exposure/risk assessment, incorporating sensitivity analysis

A two-day course on the probabilistic modelling of exposures was organised on behalf of the IGHRC by the Secretariat and HSL in 2005, following on from a one-day introductory meeting on the subject in 2002. The feedback from the 2005 course was excellent and there have been repeated calls from the members of the EC for the course to be repeated. However, the cost of the course (in excess of £20,000) was such that it has been recommended that established courses be identified (e.g. Rikilt Institute of Food Safety in the Netherlands) and that the IGHRC alert the government departments and agencies when these become available. Details of such relevent courses will also be sourced by Committee members and supplied to the Secretariat. It is hoped that suitable courses will be identified and steps taken to alert relevant personnel throughout Phase 3. This may be followed by a workshop to discuss approaches applicable to chemical risk assessment and the possibility of developing an IGHRC document for publication.

4.2.5 REACH Awareness Day

A REACH Awareness Day, proposed by the SC, will permit explanation, discussion and sharing of experience between government departments and agencies involved in the REACH regulatory process and with others whose work may be affected by REACH activities. It is proposed that this one-day experience-sharing event be held during the first year of Phase 3 and may result in a short document for circulation to IGHRC member departments and agencies.

4.3 Publications

Seven areas requiring the development of guidance or framework documents were identified. The EC felt, that in terms of priority (importance and timeliness), the documents should be addressed in the order presented below.

4.3.1 Overview document on the use of predictive approaches

The EC and SC have recognised the use and acceptance in certain programmes of predictive approaches, including read-across from toxicity study results in the OECD/ICCA/HPV programme and (Q)SAR by other groups. The REACH regulations provide guidance in this area but there is scope for IGHRC activity to harmonise approaches in government departments and agencies before current methodolgies become too entrenched. Wary of attempting a too broad guidance document, the SC recommended that the approaches used in the OECD HPV chemicals programme should be used as a basis for the document due to its general acceptance, despite it operating as a voluntary scheme. Papers/opinions published by other groups, such as COT, could be used to inform IGHRC decisions regarding the use of predictive approaches. Alternatively, an overview of department/agency activity in the use of predictive approaches would prove to be useful and could be approached through an initial workshop involving all IGHRC members with an interest in this area.

4.3.2 Mapping default values used in exposure assessment

The EC and SC have noted that there is limited exposure assessment capability across the UK, and a mapping document for the default values used in exposure assessments would help increase the transparency of the exposure assessment process. As exposure assessments utilise a variety of very different models, the production of a guidance document to standardise default values would be inappropriate. A review of relevent documentation, such as the CHEMRISK initiative, IPCS's (WHO) default value booklets used by the FSA, and the default values stated by the REACH regulations, would map the various default values or ranges

used in exposure assessment and highlight areas where more information, or more up-to-date information, is required. Documents arising from other initiatives will be identified as a starting point before this activity is progressed further.

4.3.3 Risk assessment for dermal contact (exposure and absorption estimates)

The SC considered that two activities suggested by the EC, namely the production of a guidance document on the use and best practice of *in vitro* data to predict skin adsorption and an exposure assessment document for exposure via the skin, should be combined into one activity. Whilst a document that collates the different approaches used by different departments for exposure assessment was suggested as being more useful than a "how to" guidance document, it has been agreed that there is a need to assess which exposure models are best and indicate their limitations. In particular, a common approach (or approaches) needs to be sought to prevent the use of often contradictory approaches to dermal exposure assessments. Regarding the *in vitro* skin absorption model, the OECD is looking at *in vitro* data for pesticides, biocides and industrial chemicals but work in this area has been slow. An OECD draft report was due in February 2008, and the IGHRC activity will be evaluated in light of the findings reported. The EC has suggested that the VMD, PSD and other interested parties discuss dermal exposure in more detail, perhaps in a formal workshop, and from this the content and format of an appropriate document will be developed.

4.3.4 Guidance on susceptible groups

While there are other relevant ongoing activities within this area, most notably production of the *Children's Environment and Health Action Plan* (HPA, 2007) and the *Variability and Uncertainty in Toxicology* report (COT, 2007), there is much work to be done to determine the acceptable exposures/doses for particular groups in society. Any work towards a guidance document is dependent upon the results of previous studies and reports, and must reflect susceptible groups of interest to the various departments and agencies. The Secretariat will begin by approaching each department and agency for a list of relevant groups, then explore current literature for relevant guidance before addressing the need for further information. A workshop format is suggested to determine which susceptible groups will be addressed and which issues are considered most relevant for further investigation.

4.3.5 Mapping risk management options

While risk management is beyond the remit of the IGHRC, the EC and SC agreed that it would be beneficial to provide a transparent explanation of how government departments/agencies use risk assessments to determine risk management options/criteria. It was agreed that such a document would be of use to the public to explain why certain government departments and agencies select certain risk management options. For example, it may be that some departments and agencies can set limits or ban substances by applying legislation while others may only be able to offer advice.

4.3.6 Descriptive vs. quantitative risk assessment of genotoxic carcinogens

The focus of this document would be an evaluation of the benefits and disadvantages of the application of descriptive and quantitative methodologies to the assessment of risk of genotoxic carcinogens. A workshop, as outlined in Section 4.2.2, would enable views and approaches to be exchanged. Other bodies beyond the IGHRC have established working groups to formulate opinion in this area which the IGHRC should be aware of during preparation of guidance; noting that quantitative risk assessment is often favoured by many international organisations whereas the descriptive approach is predominant in the UK The EC FSA member will inform IGHRC of the findings of one such working group established by the EFSA Scientific Committee.

4.3.7 Uncertainty in risk assessment

Following on from the workshop described in Section 4.2.3 considering uncertainty in risk assessment and comparisons between quantitative and descriptive types of uncertainty factors, further guidance in this area will assist in interpretation and possibly harmonisation of approaches to risk assessment within government departments and

agencies. The IGHRC has already published documents on uncertainty (IGHRC, 2003b; RATSC, 1999f) but more work in this area would provide updates or indicate the need for further document development.

4.3.8 Other topics

Other areas that may benefit from the preparation of guidance documents were also discussed by the EC and SC. However, the work areas were determined to be of lower current priority to the those described above, or are dependent upon the findings or publication of non-IGHRC bodies. For the latter category, a number of the work areas have been included in the 'watching brief' in Section 4.4. The results of work into these areas may require action by the IGHRC - whether as workshop, guidance document or formation of a specific working group.

4.4 Watching brief

A number of other areas of work were discussed by the SC and the EC in developing the future work programme. Most of these other activities were considered to be of lower current priority or under active consideration by other interdepartmental or international groups. Other areas were deemed to have insufficient current information, thus preventing a decision regarding further work/inclusion in the future work programme. Further topic areas including: new techniques ('-omics' and computer modelling) with the potential to reduce animal testing for hazard characterisaton; the use of biomarkers and biomonitoring for exposure assessment; further work on chemical mixtures; and ongoing observation of work in nanotechnology, should be monitored for output and relevance to the remit of the IGHRC. Stem cell research is also an area for horizon scanning, due to evidence that stem cells cultured from individuals may be desensitised to certain chemicals as a result of exposure prior to culture. The IGHRC Secretariat will gather existing guidance documents and project reports for appraisal and will keep the SC and the EC informed of findings. Similarly, EC and SC members will report any observations to their relevant committees as and when appropriate. It is proposed that the 'watching brief' become a feature of the EC agenda and that each of the topics are discussed in sequence (Figure 2), commencing with '-omics'.

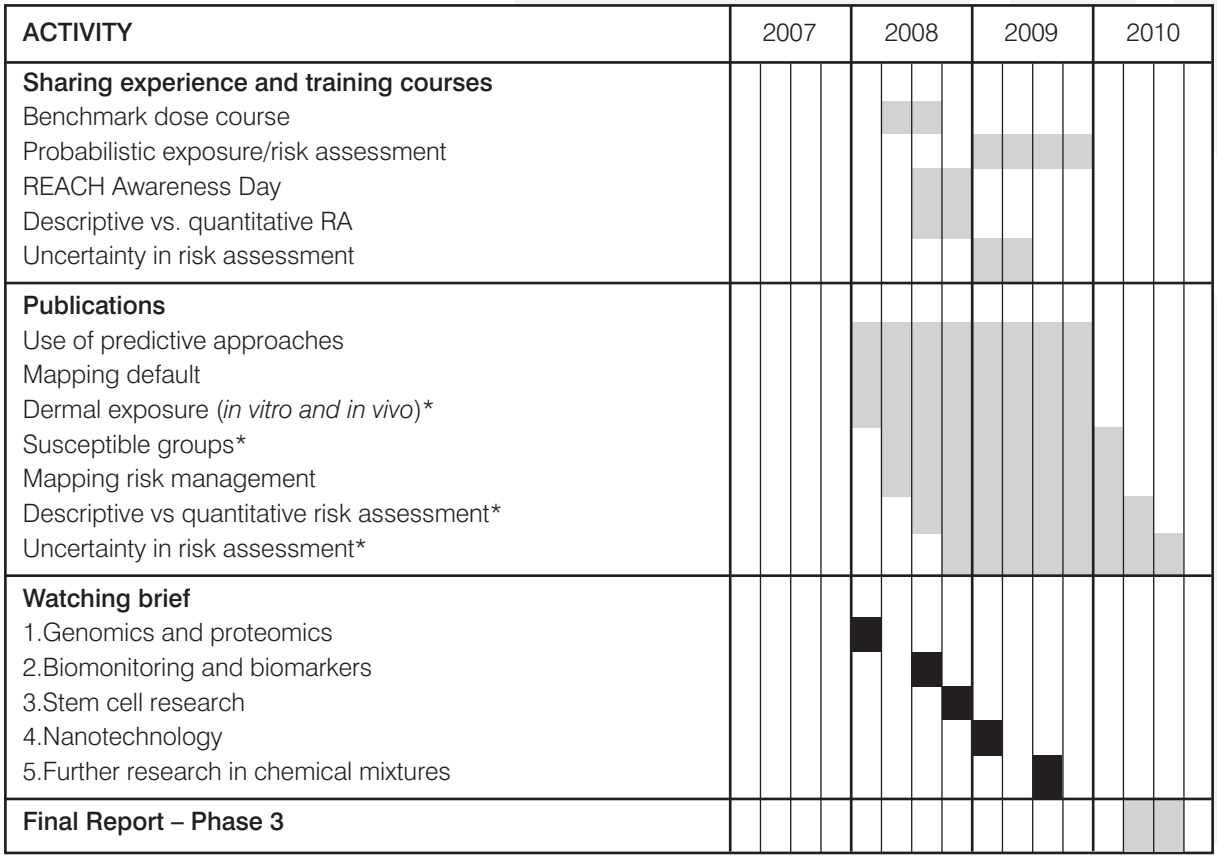
4.5 Contingency

It is possible that items not considered during the development of the Future Plan will gain prominence during Phase 3, necessitating the development of new documentation or the organisation of approproate training courses. As such, a contingency fund has been included in the costings (Annex 7) for this end.

4.6 Outline schedule of activities, October 2007 – September 2010

The proposed IGHRC work programme up to and including September 2010, with outline timings, has been described in Sections 4.2 – 4.4. Figure 2 presents a Gantt summary schedule of the activities. The total cost of the project is forecast in Annex 7.

Figure 2: Schedule of activities, October 2007 – September 2010



*Linked to workshop/training course
Light shading indicates likely period for specific activities e.g. individual training courses and documents
Dark shading for the watching brief indicates likely discussion at EC meetings but all members should be aware of any developments in these areas at any time over Phase 3.

5. Bibliography

Note: All IGHRC publications are available from the website http://www.cranfield.ac.uk/health/ighrc

Committee on Toxicity of Chemical in Food, Consumer Products and the Environment (2002) *Risk Assessment of Mixtures of Pesticides and Similar Substances*. Available [January 2004] on the Food Standards Agency website at http://www.food.gov.uk/science/ouradvisors/toxicity/COTwg/wigramp/

Committee on Toxicity of Chemical in Food, Consumer Products and the Environment (2007) *Variability and Uncertainty in Toxicology of Chemicals in Food, Consumer Products and the Environment* Available [March 2007] on COT website at http://cot.food.gov.uk/pdfs/vutreportmarch2007.pdf

HMSO (1995) *Forward Look of Government-funded Science, Engineering and Technology* (Volume 1), London, UK, HMSO

Health Protection Agency (2007) *Children's Environment and Health Action Plan*, Didcot, UK, HPA.

IGHRC (2000a) *Interdepartmental Group on Health Risks from Chemicals: First Report and Forward Plan to 2002* (cr 7), Leicester, UK, Institute for Environment and Health

IGHRC (2000b) *Interdepartmental Group on Health Risks from Chemicals: Annexes to First Report and Forward Plan to 2002* (cr 7A), Leicester, UK, Institute for Environment and Health

IGHRC (2002) *Interdepartmental Group on Health Risks from Chemicals: Assessment of Chemical Carcinogens: Background to General Principles of a Weight of Evidence Approach* (cr 8), Leicester, UK, Institute for Environment and Health

IGHRC (2003a) *Interdepartmental Group on Health Risks from Chemicals: A Study of Human Variation in Toxicodynamics* (Pump Priming Research Project), Leicester, UK, Institute for Environment and Health

IGHRC (2003b) *Interdepartmental Group on Health Risks from Chemicals: Uncertainty Factors: Their Use in Human Health Risk Assessment by UK Government* (cr 9), Leicester, UK, Institute for Environment and Health

IGHRC (2004a) *Interdepartmental Group on Health Risks from Chemicals: Final Report for Phase I 1999-2003 and Forward Plan to 2006* (cr 11), Leicester, UK, Institute for Environment and Health

IGHRC (2004b) *Interdepartmental Group on Health Risks from Chemicals: Guidelines for Good Exposure Assessment Practice for Human Health Effects of Chemicals* (cr 10), Leicester, UK, Institute for Environment and Health

IGHRC (2004c) *Interdepartmental Group on Health Risks from Chemicals: Evaluation of Currently Used Exposure Models to Define a Human Exposure Model for Use in Chemical Risk Assessment in the UK* (Pump Priming Research Project), Leicester, UK, Institute for Environment and Health

IGHRC (2006) *Interdepartmental Group on Health Risks from Chemicals: Route-to-Route Extrapolation of Toxicity Data when Assessing Health Risks of Chemicals* (cr 12), Silsoe, UK, Institute of Environment and Health, Cranfield University

Risk Assessment and Toxicology Steering Committee (1999a) *Developing New Approaches to Assessing Risk to Human Health from Chemicals* (cr1), Leicester, UK, Institute for Environment and Health

Risk Assessment and Toxicology Steering Committee (1999b) *Risk Assessment Approaches used by UK Government for Evaluating Human Health Effects from Chemicals* (cr2), Leicester, UK, Institute for Environment and Health

Risk Assessment and Toxicology Steering Committee, (1999c) *Risk Assessment Strategies in Relation to Population Subgroups* (cr3) Leicester, UK, Institute for Environment and Health

Risk Assessment and Toxicology Steering Committee (1999d) *Physiologically-Based Pharmacokinetic Modelling: A Potential Tool for Use in Risk Assessment* (cr4) Leicester, UK, Institute for Environment and Health

Risk Assessment and Toxicology Steering Committee (1999e) *Exposure Assessment in the Evaluation of Risk to Human Health* (cr5) Leicester, UK, Institute for Environment and Health

Risk Assessment and Toxicology Steering Committee (1999f) *From Risk Assessment to Risk Management: Dealing with Uncertainty* (cr6) Leicester, UK, Institute for Environment and Health

Annex 1 Membership

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Dr R Slack (from August 2007)

Dr P Harrison (from September 2007)

The MHRA, NERC and VMD do not have representatives on the Executive Committee.

Annex 2 IGHRC aims and objectives

The IGHRC is a committee made up of representatives of all the main government agencies and departments. The main focus of the IGHRC's activities is to seek ways to improve the procedures underpinning chemical risk assessment. In pursuit of this, the specific aims of the IGHRC are to:

- promote the development of methods and techniques that will improve information used in the toxicological risk assessment process;
- promote improved approaches to toxicological risk assessment for use in a regulatory context;
- promote coherence and consistency in the practice of toxicological risk assessment as used within the different risk management and regulatory frameworks used in government; and
- act to disseminate and advance best practice within government.

To address these aims the IGHRC has the following objectives:

Primary Objectives

- to develop and publish for consultation a programme of work aimed at improving the conduct of risk assessments of chemicals in the UK;
- to promote through the identification of research needs the development of innovative methods and improved approaches;
- to provide a forum within government for discussing how greater coherence and consistency of approach can be achieved nationally, and, if feasible, internationally; and
- to identify and disseminate best practice in collaboration with stakeholders and other national and international organisations.

Secondary Objectives

- to report annually to the Interdepartmental Liaison Group on Risk Assessment (ILGRA)[3] and funding bodies; and
- to evaluate the Group's achievements after three years (Phase 2, October 2003 to September 2007).

[3] ILGRA has since been disbanded

Annex 3 Training courses

IGHRC COURSE ON PRESENTING AND PUBLISHING UNDERSTANDABLE AND TRANSPARENT RISK ASSESSMENT FROM CHEMICAL EXPOSURES

PROGRAMME OUTLINE – 4th/5th March 2004

DAY 1

0930 Introduction to the course – Dr Len Levy

0945 Key steps in the risk assessment process – Professor David Coggon

1045 Coffee

1100 Key features of communicating risk assessments – Professor Judith Petts

1230 Lunch

1315 Hazard identification and characterisation – Dr Len Levy

1500 Tea

1515 Exposure characterisation – Dr Martie van Tongeren

1700 Round up of Day One

DAY 2

0900 Introduction to Day Two – Dr Len Levy

0915 Data quality – Dr Sue Barlow

1030 Coffee

1100 Risk assessment from an NGO point of view – Dr David Santillo

1145 Risk Characterisation (Part I) – Dr Steve Fairhurst

1230 Lunch

1300 Risk Characterisation (Part II) – Dr Steve Fairhurst

1415 Course round up, feedback and close – Dr Len Levy

IGHRC-HSL COURSE ON PROBABILISTIC MODELLING OF EXPOSURES FOR RISK ASSESSMENT

PROGRAMME OUTLINE - 16th/17th March 2005

DAY 1

1030 Registration; Tea/Coffee

1100 Introduction and Welcome – Professor Len Levy

1110 Welcome to the Health & Safety Laboratory – Dr Andrew Curran

1120 Essentials of probabilistic modelling – Dr Anna Rowbotham

1200 Good modelling practice – Dr Derek Morgan

1230 Topic 1: Input distributions – Dr Anna Rowbotham

1300 Lunch

1400 Topic 2: Characterising Uncertainty – Dr Nick Warren

1430 Practical Session 1: Matlab Notebook Exercises – HSL Staff

1530 Coffee/tea break

1545 Practical Session 1 (contd)

1615 General Discussion & Round-up of Day 1

1645 Close

DAY 2

0930 Welcome to Day 2 – Dr Anna Rowbotham

0935 Topic 3: Sensitivity Analysis – Dr Martin Spendiff

1015 Probabilistic Exposure Assessment Case Study 1: Crop protection products – Mr Kim Travis

1055 Coffee/Tea Break

1110 Probabilistic Exposure Assessment Case Study 2:

Migration of chemicals from food packaging materials – Dr Mel Holmes

1150 **Interpreting Probabilistic Model Predictions: Implications for Human Health Risk Assessments** – Dr Caroline Harris

1230 Lunch

1330 **Practical Session 2: Hypothetical Case Study Using @Risk Software** – HSL Staff

1500 Tea/coffee break

1515 **Probabilistic Techniques in Complex Exposure Modelling**

- **Bayesian techniques and Markov Chain Monte Carlo** – Dr Nick Warren
- **Probabilistic modelling of systemic exposures** – Dr Anna Rowbotham

1600 **General Discussion, Course Feedback & Close** – Dr Anna Rowbotham & HSL staff

IGHRC COURSE ON UNDERSTANDING CHEMICAL EXPOSURE ASSESSMENT

PROGRAMME OUTLINE - 16th/17th May 2005

DAY 1

1030 Registration; Tea/Coffee

1100 **Introduction and welcome** – Professor Len Levy & Mr Bob Scott

1115 **General principles of exposure assessment** – Dr Sue Barlow

1200 **Exposure sources and pathways** – Dr Kate Vizard

1245 **Discussion**

1300 Lunch

1400 **Gathering exposure data** – Dr Martie van Tongeren

1500 Tea/coffee break

1515 **Exposure modelling** – Dr Martie van Tongeren

1600 **The use of exposure data in risk assessment** – Mr Mark Selby

1700 **General discussion and round-up of Day 1** – Len Levy & Bob Scott

DAY 2

0900 **Welcome to Day 2** – Len Levy & Bob Scott

0905 **Case Study 1: Consumer Exposure (phthalate plasticiser migration)** Mr Ian Axford

0950 **Practical Session 1 – Consumer Exposure** – Ian Axford & Bob Scott

1050 **Feedback and discussion of Practical Session 1** – Ian Axford & Bob Scott

1105 Coffee/Tea Break

1115 **Introduction to Occupational Hygiene Exposure** – Len Levy

1230 Lunch

1330 **Case Study 2: Environmental Exposure (benzene)** – Dr Raquel Duarte-Davidson

1415 **Practical Session 2 – Environmental Exposure** – Dr Raquel Duarte-Davidson

1515 Tea/coffee break

1530 **Feedback and discussion of Practical Session 2** – Dr Raquel Duarte Davidson

1545 **General Discussion & Course Feedback** – Len Levy & Bob Scott

1600 **Close**

IGHRC AWARENESS DAY ON CHEMICAL RISK ASSESSMENT ON HEALTH EFFECTS: CURRENT PRACTICE WITHIN THE UK GOVERNMENT

PROGRAMME OUTLINE - 16th March 2006

0930 *Registration; Tea/Coffee*
1000 **Introduction and welcome**
– Prof Len Levy & Mr Richard Davis
1015 **General principles** - Dr Sue Barlow
1045 **Pesticide risk assessments**
– Dr Ian Dewhurst
1115 *Coffee*
1130 **Food risk assessments**
– Dr Diane Benford
1210 **Human pharmaceutical risk assessments** - Mr Henry Stemplewski
1250 *Lunch*
1330 **Industrial chemicals risk assessments**
– Dr Peter Evans
1410 **Environmental risk assessments**
– Ms Albania Grosso
1450 **Discussion forum**
1510 *Tea/Coffee*
1530 **Case Studies (small group work)**
– introduced by Ian Dewhurst
1610 **Discussion on case studies and feedback on the day**
1630 **Close**

IGHRC COURSE ON UNDERSTANDING EPIDEMIOLOGY FOR CHEMICAL RISK ASSESMENT: AN INTRODUCTION FOR SCIENTISTS AND POLICY MAKERS

PROGRAMME OUTLINE – 13th/14th November 2006

DAY 1
1000 *Registration and coffee*
1030 **Introduction – a brief overview of epidemiological methods and some statistical topics** - Dr Lesley Rushton
1100 **Introduction to critical reviewing – reviewing a single paper**
– Dr Lesley Rushton
1230 *Lunch*
1330 **Introduction to qualitative research methods** – Dr Petra Boynton
1530 *Refreshment break*
1600 **Biomarkers and genetic epidemiology**
– Professor Alan Boobis
1730 *Course Reception*

DAY 2
0900 **Design and analysis of cohort and case-control studies** – Dr Lesley Rushton
1100 *Refreshment break*
1130 **Bias, confounding and chance in epidemiological studies**
– Dr Lesley Rushton
1300 *Lunch*
1400 **Introduction to advanced epidemiological techniques – demystifying statistical modelling** – Dr John Molliter
1530 *Refreshment break*
1600 **Narrative review** – Dr Lesley Rushton

DAY 3
0900 **Ecological epidemiology, including time series, point sources and clustering**
– Professor Paul Elliott
1030 *Refreshment break*
1130 **Systematic review and an introduction to meta-analysis** – Professor David Jones
1300 *Lunch*
1400 **Evaluating all the evidence – the decision-making process: the role of epidemiology in risk assessment**
– Professor David Coggon
1530 *Refreshment break and end of course*

IGHRC COURSE ON UNDERSTANDING CHEMICAL EXPOSURE ASSESSMENT

PROGRAMME OUTLINE – 4th/5th October 2007

DAY 1

1030	*Registration; Coffee/Tea*
1100	**Introduction and Welcome**
1115	**General Principles of Exposure Assessment** – Dr Sue Barlow
1200	**Exposure Assessment Strategy** – Dr Susan Hodgson
1245	**Discussion**
1300	*Lunch*
1345	**Exposure Modelling** – Dr Anna Rowbotham
1430	**Exposure Characterisation** – Dr Martie Van Tongeren
1515	**Discussion**
1530	*Tea/Coffee break*
1545	**Critical Evaluation and Application to Risk Assessment** – Prof Simon Pollard
1630	**CASE STUDY 1 – Consumer Exposure** – Mr Ian Axford
1700	**Practical Session 1 – Consumer Exposure** – Mr Ian Axford
1800	**General Discussion & Round-up of Day 1**

DAY 2

0900	*Welcome to Day 2*
0905	**CASE STUDY 2 – Exposure** – Mr Neil Byron
0950	**Practical Session 2 – Exposure** – Mr Neil Byron
1050	**Feedback and Discussion of Practical Session 2**
1100	*Coffee/Tea*
1115	**CASE STUDY 3 – Environmental Exposure** – Dr Raquel Duarte-Davidson
1200	**Practical Session 3 – Environmental Exposure** – Dr Raquel Duarte-Davidson
1300	*Lunch*
1345	**Feedback and Discussion of Practical Session 3**
1400	**General Discussion and Course Feedback**
1445	**Course close**

IGHRC COURSE ON DEVELOPING AND EXPLAINING CHEMICAL RISK ASSESSMENTS

PROGRAMME OUTLINE – 29th/30th October 2007

DAY 1

1030	*Registration; Coffee/Tea*
1100	**Introduction and Welcome**
1115	**Key Steps in the Risk Assessment Process** – Dr Lesley Rushton
1215	*Lunch*
1300	**Hazard Identification and Characterisation** – Prof Len Levy
1400	**Dose-Response Assessment & Data Quality** – Dr Sue Barlow
1500	**Discussion/Further Remarks**
1515	*Tea/Coffee*
1530	**Exposure Quantification & Characterisation** – Dr Martie Van Tongeren
1645	**Science, Precaution and Risk Assessment** – Prof Andrew Stirling
1745	**General Discussion & Round-up of Day 1**

DAY 2

0930	*Welcome to Day 2*
0935	**Communicating Risk Assessments** – Dr Peter Bennett
1040	*Coffee/Tea (travel arrangements)*
1100	**Risk Characterisation** – Dr Steve Fairhurst
1145	**CASE STUDY 1 – Government** – Dr Steve Fairhurst
1300	*Lunch*
1345	**CASE STUDY 2 – Industry** – Dr Bob Safford
1500	**Feedback and Discussion**
1530	**Course round-up** *with tea/coffee*
1600	**Course close**

Annex 4 Comments on documents

IGHRC GUIDELINES ON ROUTE-TO-ROUTE EXTRAPOLATION OF TOXICITY DATA

Responses to Expert Committees' Comments

Chapter or Section	Committee Comment	IGHRC response
General Comments	The document was clear and pragmatic and dealt with a commonly encountered problem by researchers and regulators for whom it would provide a useful resource. **(ACHS)** General agreement that the document was useful. Members welcomed the document. They noted that there are usually more route-specific data available for pesticides than for most other classes of chemical, so although the report will be a valuable source of guidance, in practice there is less of a problem in this area for pesticides than for many other chemicals. Members noted that this document provides a more detailed consideration of first pass metabolism than might usually be the case for pesticides. **(ACP)** Generally, this is a useful document. The limitations of route to route extrapolation are well explored and a set of rules for performing such extrapolations when necessary, should find wide application. **(EPAQS)**	Noted.
Omissions	The only major concern with this document relates to the treatment of oral to inhalation exposures for relatively non-volatile aerosols. **(EPAQS)** The question of how some of the correction factors used in the document originated was raised and the issue of factors involved with the plutonium work was noted. Is it possible to translate some figures obtained for metals to organic chemicals? **(ACHS)** Changes and additions included the need for information on the use of PBPK modelling, more information on exposure via the lung and through the dermal route and the inclusion of a summary. In addition, it was considered important to note the difficulty of route-to-route extrapolation for sensitisation of the immune system. Oral exposure tends to reduce susceptibility to sensitisation by other routes of exposure. **(COT)** Many dermal studies use application rates well above those likely to occur in real life exposures. The text should include some comment on this aspect and possibly on the issue of presenting doses on a " /cm2 " basis. One specific issue that members discussed was the potential impact on systemic dose of the total surface area of skin over which a given dermal dose of a toxin is applied. PSD is also aware of some data	Query submitted to WATCH for advice. WATCH recommended change to text to emphasise exposures to volatile aerosols. Comment is unclear. Does the committee mean 'defaults'? The over-riding principle of the document is to be precautionary. Figures given are defaults and are therefore not scientifically derived. A sentence on PBPK modelling has now been included in Section 4. An Executive Summary has now been included. Request for more info on lung has been noted. However, it is felt that the level of detail is appropriate for the document as it stands. Info on sensitisation of the immune system has now been included in Section 3.1.

	which show that dermal exposure to more dilute formulations can increase absorption in comparison with more concentrated solutions. Overall it is possible therefore that the guidance document might gloss over some of these complications associated with estimating systemic exposure via the dermal route. However, it is possible that this level of detail is less relevant to risk assessments for other groups of chemicals. **(letter from ACP Chairman)** The document does not note the general observation that dermal penetration, where measured in animals, tend to exceed that observed in man. This means that the oral to dermal extrapolation is likely to be especially precautionary. **(EPAQS)**	Agreed. New text has been included in Section 3.3 to cover this.
Title	It was suggested that more consideration be given to the title, perhaps with an expansion or explanation of the term 'route-to-route' which was felt to be a little vague. Perhaps a sub-title or strap-line would be helpful in bringing this out. **(ACHS)**	Agreed. Title has been lengthened to clarify.
Introduction	Members highlighted the need to expand the introduction to include an outline of when route-to-route extrapolation should be used and its dependence on the level of exposure and an outline of the content of the annexes. **(COT)**	Agreed. New text included at the end of the Introduction.
Section 2, 1st Para	There is some discussion on the kinetics of uptake by instantaneous doses which is not taken up later in the report – perhaps this could be addressed with some examples. **(ACHS)**	Not agreed. This amount of detail is not warranted in the guidance document.
Page 36, chloroalkanes example	Chloroalkanes have been banned in metal working fluids and leather processing, therefore these examples should be removed from text. **(ACHS)**	Checked with HSE and example determined to be useful.
P42 middle of para 4	'The basis for the cut-offs is unknown' should be replaced by 'These cut-off values are in line with current EU guidance'. **(letter from ACP Chairman)**	Agreed.
Section 7.4	In Section 7.4 inhalation to oral extrapolation, it should be noted that all experimental inhalation exposures also include some oral exposure. This may be negligible in the case of gases, but vapours which dissolve in the surface mucus layer and aerosols both liquid and solid will result in significant concomitant oral exposure at any inhalation dose. Thus, extrapolation involves only a change in proportion rather than a complete change of route. This must make the process less prone to error. **(EPAQS)**	This point was recognised by the WATCH Committee and changes were made to the text.
Annex p 43-44	The section on bystander exposure will need some expansion to make clearer that the risk assessment does not assume that the only exposure for a bystander arises from a single pass of a sprayer. This point has been consistently misrepresented in the press. The single pass is used as a 'marker' for a realistic worst case, as this level of exposure is assumed every day throughout the 3 months plus that agricultural spraying is likely to take place. I understand the PSD will provide an updated draft. **(letter from ACP Chairman)**	New text supplied.

CHEMICAL MIXTURES: A FRAMEWORK FOR ASSESSING RISKS TO HUMANS

Responses to Expert Committees' Comments

The Expert Committees (see below), and individuals who responded to the call to review, frequently provided very detailed comments. A complete copy of the comments received, together with the responses prepared by the IGHRC, is available from the IGHRC Secretariat. The key comments are summarised in the table below.

Committee/ Individual*	Comment	IGHRC response
COT	In several places, the document suggests that the assumption of dose additivity is the most precautionary approach, rather than synergy. The target organ of an individual chemical may not be the same when the chemical is in a mixture and this should be made clear in the document. Worked examples would make the process clearer for the reader.	Noted and amendments made to Step 7a of Chapter 6. Interactive behaviour is discussed in Chapter 3. Noted and text strengthened accordingly. It was not the purpose of the document to provide examples but may be considered for a future publication.
ACHS	The document mainly focuses on (eco)toxicity; environmental persistence, exposure and bioaccumulation potentials are currently lacking, making it difficult to assess the overall risks of chemical mixtures. Does the document imply that the framework provided takes precedence over all other existing approaches? What is a "significant" exposure (Step 3 of decision tree)? How is the judgement made on whether the hazard data are sufficient for whole mixture assessment? The guidance does not seem to adequately address the low dose mixture issue. Some key literatures are missing from the references. Transformation products from human metabolism, biotic and abiotic degradations undergo spatial and temporal changes.	The text has been altered to include these terms where previously no explicit mention was made. It should be noted that the document refers to human health risk and not environmental risk. The text has been altered to enforce the message that regulations have priority. A footnote has been added to define usage of "significance". Wary of including environmental risk assessment data, the text has been altered. While Chapter 3 did include a brief mention of this issue, the text has been altered to reinforce the message. While the key references had been cited, more have been added. The text has been altered to include exposures over time and space.
COC	One comment received which, besides minor points for clarification, refers to the document as helpful and clear.	Points have since been clarified.
COM	Non-mutagens may enhance the properties of mutagens (potentiation). There is limited evidence of synergy in mutagen-mutagen interaction.	Whilst already referred to in the text, the message has been reinforced accordingly. Also clarified by the text.
VPC (VMD)	The VPC provided a revised version of Annex E.	Added to document.

WATCH	Risk and hazard are often used interchangeably in the text. The Committee felt that the document had an environmental bias. The text used in Figure 1 should emphasise exposure.	The text has been altered to prevent the interchangeable use of 'risk' and 'hazard'. Efforts have been made to ensure that the environmental perspective is only referred to when necessary. The text in Figure 1 has been changed.
BTS	No comments received.	n/a
COMEAP	No comments received.	n/a
ACP	Potential hazard of low dose disruption of gene expression in the embryo had not been addressed in text. Concentration on mammalian risk and not wider ecotox application. Possible clarification of a paragraph in the Exec Summary. Addition of further references suggested.	Noted. See note for first comment from ACHS. Clarification provided. Kortenkamp et al. reference has been included in response to other comments; other references not considered appropriate to human health aspect of document.
Dr Dennis Paustenbach (Chemrisk, Inc.)	Comments received were largely favourable and requested addition of "contaminant" to the Glossary, citation of historical mixtures work and reference to OSHA list.	The changes and additions have been carried out. A number of refrences have been included to offer an historical perspective.
Document Steering Group representative	A more explicit view would be helpful for genotoxic carcinogens. Various technical suggestions and recommended changes to text.	This area is currently being reviewed by COM; the UK position may therefore change. Changes to text have been carried out.

*COT (Committee on Toxicity); ACHS (Advisory Committee on Hazardous Substances); COC (Committee on Carcinogenicity); COM (Committee on Mutagenicity); VPC (Veterinary Products Committee); WATCH (Working Group on Action to Control Chemicals); COMEAP (Committee on the Medical Effects of Air Pollutants); ACP (Advisory Committee on Pesticides).

Annex 5 Independent evaluation of Phase 2

Report prepared by Dr Sue Barlow (Consultant in Toxicology)

1.1 Introduction

The objectives of this evaluation of Phase 2 of the work of the IGHRC, running from October 2003 to September 2007, are:-

- To assess the quality of the training courses and workshops, based on feedback from participants[4].
- To assess the quality of IGHRC publications, based on the comments received from external committees that reviewed the documents prior to publication.

1.2 Courses and workshops

The content of the 7 courses/workshops are described earlier in this Final Report for Phase 2, in section 2.2 and Annex 3.

1.2.1 Overall course ratings

Course participants were asked to rate the courses overall and the individual sessions and to submit additional written comments via feedback forms provided in the course handout packs. Overall course ratings are shown below (Table 5.1).

The overall ratings show, with the exception of one course, that a large proportion of participants rated the courses very highly as 'Excellent' or 'Very good'. The lower rating for the 2005 *Exposure assessment* course (1) compared to the 2007 course appears to be due to fewer ratings of individual sessions as 'Excellent' in 2005. For the 2007 course, some changes were made in the programme of speakers.

Overall ratings for the *Epidemiology* course were not available as the participants' questionnaire was different and more detailed than those used for other courses. The evaluation form asked (*inter alia*) to what extent the content of the course met expectations and course objectives, helped

Table 5.1: Summary of feedback received from Phase 2 courses.

Course title	*Date*	*Overall course rating (% of respondents)*				
		Excellent	*Very good*	*Good*	*Fair*	*Poor*
Transparent risk assessments (I)	March 2004	25	65	10		
Probabilistic modelling	March 2005	47	33	18		
Exposure assessment (I)	May 2005	17	38	42	4	
Awareness Day	March 2006	15	56	26	3	
Epidemiology *	Nov 2006					
Exposure assessment (II)	Oct 2007	20	60	20		
Transparent risk assessments (II)	Oct 2007	22	56	22		

* Different feedback form used: 81% of participants felt that the course certainly met course objectives, with 16% finding most objectives were met; 3% did not respond.

[4] It should be noted that the author of this evaluation also lectured on some of IGHRC courses.

learning and understanding on how to apply theory to practice, and helped develop critical attitudes and stimulate interest. The extent of meeting these various criteria was rated highly by 62-84% of participants.

1.2.2 Presentation ratings

The majority of course participants rated the individual presentations as 'Excellent' or 'Very good', with the exception of *Understanding chemical exposure assessment (I)*, for which several of the sessions were rated by the majority of participants as 'Good' or 'Fair'. A rating of 'Poor' was only returned by one or two participants for some individual presentations in *Understanding chemical exposure assessment (I)* and *Awareness Day*.

In the two similar courses *Presenting and reporting transparent risk assessment* and *Developing and explaining chemical risk assessment*, case study sessions were included in the latter but not the former course and the case studies were rated as 'Excellent', 'Very good' or 'Good'.

In the course *Introduction to probabilistic modelling*, practical sessions on case studies were also included and the majority of these were rated as 'Very good' or 'Good'. The practical sessions formed an important component of this course and several participants commented that they would have liked simpler examples and more time.

In the two courses on *Understanding chemical exposure assessment*, the case study sessions were rated as 'Excellent', 'Very good' or 'Good' with only a few rating them as 'Fair'.

For the course on *Epidemiology*, the individual presentations were rated for whether they were professionally presented, pitched at the right level, run at the right pace and sufficiently interactive. These criteria were mostly met either 'To a full extent' or 'To a large extent', with the exception that several participants commented that some presentations were pitched too high. The amount of group work in this course was considered by most of the participants to be about right but some would have liked more group work and smaller groups.

1.2.3 Pre-course information and course materials/handouts

Where available, these were all rated as 'Excellent', 'Very good' or 'Good'. Some courses did not have pre-course materials and some participants felt the provision of such materials would have enhanced understanding.

1.2.4 Course booking arrangements

These were all rated as 'Excellent', 'Very good' or 'Good'.

1.2.5 Venue suitability

The ratings ranged from 'Excellent' to 'Fair' and were mostly 'Very good'.

1.2.6 Catering arrangements

The ratings ranged from 'Excellent' to 'Fair' and were mostly 'Very good'.

1.3 IGHRC publications

IGHRC publications comprise reports and guidance documents aimed at improving chemical risk assessments in the UK. They are available at http://www.cranfield.ac.uk/health/ighrc

Three new documents have been developed during Phase 2:-

- Guidelines on Route-to-Route Extrapolation of Toxicity Data when Assessing Health Risks of Chemicals (cr12)
- Chemical Mixtures: A Framework for Assessing Risks to Human Health
- Current Approaches to Exposure Modelling in UK Government Departments and Agencies

1.3.1 Guidelines on Route-to-Route Extrapolation of Toxicity Data when Assessing Health Risks of Chemicals (cr12)

The previous lack of guidance documents and the need for guidance on route-to-route extrapolation is clearly explained in the publication from the perspective of the scarcity of studies using

inhalation and dermal routes of administration compared with the oral route, the need to make best use of existing data for risk assessment in order to avoid unnecessary use of animals, and the fact that several government departments and agencies are already using route-to-route extrapolation in some risk assessments.

The draft document was sent out for comment to appropriate UK expert scientific committees (ACHS, ACP, EPAQS, COT), which provide advice to the main departments/agencies using route-to-route extrapolation, such as DEFRA, EA, HSE and PSD. The comments from these committees are listed in Annex 4 of this document, together with the IGHRC responses to those comments.

The expert committees welcomed the document as a useful resource which should have wide application. Most of the other comments, on issues which needed to be added or expanded in the text or on specific parts of the text that needed to be amended, were addressed by IGHRC following further discussion with departments/agencies or their committees and this can be verified from the text of the final cr12 publication.

The guidance on route-to-route extrapolation was published to schedule in 2006. It has the potential to be influential beyond the UK since it will be cited as useful guidance in documentation to be published soon by the European Commission on REACH (RIP3.2).

1.3.2 Chemical Mixtures: A Framework for Assessing Risks

This document on chemical mixtures was developed, as requested in the forward plan for 2003-2006, following a one-day workshop in 2005, in which departments and agencies presented their work on mixtures and information from other meetings and reports on mixtures was considered. Progress on it has fallen behind the original planned schedule for completion in 2007. However, the draft document has been publicly available since April 2007 on the IEH website.

The document covers a complex topic on which the risk assessment community worldwide is currently still working to develop appropriate and agreed approaches and methodology. Moreover, the underpinning research is still somewhat limited. Thus a document such as this, which is not prescriptive but rather proposes a framework to guide risk assessors through the issues they need to address, is valuable. In addition to theoretical considerations and a discussion of the various approaches that can be taken, it offers risk assessors practical help in the form of a decision tree for the assessment of chemical mixtures and the use of a tiered approach to target further work that may help refine the risk assessment when data are scarce.

The draft document was sent to 8 UK expert committees for comment following its placing on the web in 2007; several committees have responded with detailed comments but some further responses are still awaited. The chapter covering the decision tree and tiered approach has generated the most comment. In an interesting departure that would allow input, not just from risk assessors, but also from a wide range of stakeholders with an interest in chemicals, the draft was also posted on the website of the British Toxicology Society, but no comments were elicited.

The comments received so far have been considered by the IGHRC Secretariat together with the author of the report in November 2007 and plans have been made for amending the draft, gathering the remaining comments from expert committees and finalising the document for publication in April 2008.

1.3.3 Current Approaches to Exposure Modelling in UK Government Departments and Agencies

The draft document on exposure modelling has fallen behind the original planned schedule but is undergoing final changes prior to being sent out for comment. No evaluation is possible here.

1.4 Conclusions and recommendations

The overall aims of IGHRC are to promote coherence and consistency in human health risk assessment, promote the development of toxicological risk assessment methods and

techniques, and disseminate and advance best practice within Government, sharing experience and initiating change (see IGHRC Final Report for Phase I 1999-2003 and Forward Plan 2003-2006 - cr11, 2004). Both the training courses and the guidance documents contribute to achieving these ends.

1.4.1 Courses

In the forward plan (cr11), it was anticipated that three courses would be run between 2004 and 2005 (transparent risk assessments, probabilistic modelling and exposure assessment). IGHRC fully met these goals. In addition, a further 4 courses were organised during the extension period of Phase II to 2007; two topics were repeated due to extra demand, a new course on epidemiology was run, and a well-attended IGHRC awareness day was held. The feedback from participants shows:-

- Most of the lecture sessions were well executed and well received. Practical/case study sessions were particularly appreciated.
- A mix of lectures and case studies/group work may be a more preferred and instructive format than just lectures. This is further underscored by some of the individual participants' comments from several of the courses, in which more interactive sessions, case studies and worked examples within lectures were requested. More time was requested for practical sessions where participants worked alone or in groups.
- Some individual comments appeared to contradict others in terms of the level at which the content of courses was pitched. This is most likely due to the differing backgrounds of participants, some of whom were policy makers while others were scientists. This suggests consideration should be given to whether future courses, or sections of courses, could be more tailored to participants' backgrounds. For example, on the topic of REACH, there could be separate, shorter courses for policy makers. Alternatively, in order to ensure an opportunity for networking is not lost, there could be an introductory day suitable for all, including generalists and policy makers, followed by more intensive day(s) with an emphasis on 'learning by doing' for scientists who are, or are training to be, risk assessment practitioners.
- The numbers attending indicate there is a need for both general and more in-depth courses and the proposals for Phase 3 appear to offer such a mix.

1.4.2 Publications

The first two guidance documents, on route-to-route extrapolation and on chemical mixtures, have been well generally received by expert committees. There is no feedback as yet from risk assessors in departments and agencies on whether they are finding these two documents of value in their day-to-day work. It may be worth considering some follow-up, towards the end of Phase 3, on whether the suggested decision tree and tiered approach for chemical mixtures are helpful and whether the further experience, nationally and internationally, in assessing chemical mixtures would enable more guidance to be developed.

Of the three planned guidance documents, the one on route-to-route extrapolation, was published to schedule. The document on chemical mixtures is well on track for final publication in 2008 and the third one, on exposure modelling, will shortly be sent out for comment. Thus IGHRC should be able to complete all the planned activities for Phase 2, albeit delivering late on two of the publications.

For Phase 3, seven publications are planned to be developed and completed by 2010. Given the experience from Phase 2, this may be an unrealistic timescale.

Annex 6 Aims of work programme

IGHRC Activities 2003-2007 (Phase 2)	Promote the development of chemical risk assessment methods and techniques	Promote coherence and consistency in chemical risk assessment	Disseminate and advance best practice within government, sharing experience and initiating change	Publish for consultation a programme of work for improving chemical risk assessment in the UK
First Report and Forward Plan to 2006 (cr11, IGHRC 2004a)				√
Guidance Document: Route-to-route extrapolation in health risk assessment (cr12, IGHRC 2006)	√	√	√	
Guidance Document: Chemical mixtures (under review)	√	√	√	
Guidance Document: Chemical exposure modelling (in preparation)	√	√	√	
Specific Issue Working Group: Chemical mixtures workshop (Feb 2005)	√	√	√	
Presenting and Publishing Understandable and Transparent Risk Assessments from Chemical Exposures (two-day course, March 2004; October 2007)	√	√	√	
Probabilistic Modelling (two day course, March 2005)	√	√	√	
Understanding Chemical Exposure Assessment (two-day course, May 2005; October 2007)	√	√	√	
Awareness Day (one-day course, March 2006)	√	√	√	
Epidemiology for Chemical Risk Assessment (two-day course, November 2006)	√	√	√	
Evaluation of the IGHRC Phase 2 by course feedback			√	
October 2007 – September 2010 (Phase 3)				
Final Report and Forward Plan to 2010 (this report)				√
Probabilistic exposure assessment (two-day course)	√	√	√	
Descriptive vs. quantitative risk assessment (two-day course)	√	√	√	
Benchmark dose course (two day course)	√	√	√	
Publication: Use of predictive approaches	√	√	√	
Publication: Mapping default	√	√	√	
Publication: Dermal exposure (in vitro and in vivo)	√	√	√	
Publication: Susceptible groups	√	√	√	
Publication: Mapping risk management	√	√	√	
Publication: Descriptive vs quantitative risk assessment	√	√	√	
Watching brief			√	

Annex 7 Phase 3 financial forecast

Costs include Secretariat staff costs (core activities) and scheduled activities as specified in Section 4. Forecast is based on balance sheets for Phase 1 and Phase 2 activities and include publication of reports/documents.

ACTIVITY	£ '000s			
	2007/8	2009	2010	TOTAL EXPENDITURE
Sharing experience and training courses	**25**	**25**		**50**
Benchmark dose course#	20			20
Descriptive vs. quantitative RA		5		5
Uncertainty in RA		5		5
REACH Awareness Day	5			5
Probabilistic exposure/risk assessment#		15		15
Publications	**25**	**35**	**20**	**80**
Use of predictive approaches*	10	5		15
Mapping default	5	5		10
Dermal exposure (*in vitro* and *in vivo*)*		10	5	15
Susceptible groups*	10	5		15
Mapping risk management			10	10
Descriptive vs quantitative risk assessment*		5	5	10
Uncertainty in risk assessment*		5		5
Other Activities	**10**	**10**	**16**	**36**
Watching brief†				
Final Report – Phase 3			6	6
Contingency fund‡	10	10	10	30
Total Scheduled Activities	**60**	**70**	**36**	**166**
Core Activities§	**35**	**40**	**30**	**105**
TOTAL ACTIVITIES	**95**	**110**	**66**	**271**

#Organisational costs expected to be high but may be mitigated through inclusion of charged non-IGHRC participants
*Linked to workshop/training course and hence likely to require greater allocation of funds
†A core activity
‡A fund to permit running of further training courses (epidemiology, introduction to transparent risk assessment, etc.) or assist in preparation of documents not specifically stated in the Future Plan but deemed necessary during the course of Phase 3
§Includes all activities of the Secretariat including the organisation of EC and SC meetings, overseeing document preparation and organisation of training courses through support of EC leads; collating information from the watching brief.

Risk Assessment and Toxicology Steering Committee publications

cr 1 Developing New Approaches to Assessing Risk to Human Health from Chemicals.

cr2 Risk Assessment Approaches used by UK Government for Evaluating Human Health Effects of Chemicals

cr 3 Risk Assessment Strategies in Relation to Population Subgroups

cr 4 Physiologically-Based Pharmacokinetic Modelling: A Potential Tool for Use in Risk Assessment

cr 5 Exposure Assessment in the Evaluation of Risk to Human Health

cr 6 From Risk Assessment to Risk Management: Dealing with Uncertainty

The Interdepartmental Group on Health Risks from Chemicals (IGHRC) publications

cr 7 The Interdepartmental Group on Health Risks from Chemicals: First Report and Forward Plan to 2002

cr 7A The Interdepartmental Group on Health Risks from Chemicals: Annexes to First Report and Forward Plan to 2002

cr 8 Assessment of Chemical Carcinogens: Background to General Principles of a Weight of Evidence Approach

cr 9 Uncertainty Factors: Their Use in Human Health Risk Assessment by UK Government

cr 10 Guidelines for Good Exposure Assessment Practice for Human Health Effects of Chemicals

cr 11 The Interdepartmental Group on Health Risks from Chemicals: Final Report for Phase 1, 1999-2003 and Forward Plan to 2006

cr 12 Guidelines on Route-to-Route Extrapolation of Toxicity Data when Assessing Health Risks of Chemicals

All reports are available from:

Institute of Environment and Health,
Building 63, Cranfield University, Cranfield,
Bedfordshire MK43 0AL

Tel: +44 (0) 1234 758506
Fax: +44 (0) 1234 758517

IGHRC website:
http://www.cranfield.ac.uk/health/ighrc