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Extensive Training Course on the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) to be Implemented in Uruguay

Final Report

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unitar United Nations Institute for Training and Research

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ORANGE HOUSE PARTNERSHIP vzw

Report prepared by:

Herman B.W.M.Koëter, MSc, DTox, ERT
Managing Director
Orange House Partnership$_{vzw}$

Brussels, 21 June 2010

"Even if you're on the right track, you'll get run over if you just sit there"

(Will Rogers)

Funded by:
- Orange House Partnership$_{vzw}$, Brussels, Belgium
- Asociación Química y Farmacia, Montevideo, Uruguay
- Faculty of Chemistry, University of the Republic of Uruguay, Montevideo, Uruguay
- UNITAR, Geneva, Switzerland

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CONTENTS

ACKNOWLEDGEMENTS

All experts involved in this project (Iona Pratt, Helmut Fleig, Steve Vaughan and Klaus Wettig) are acknowledged for their high quality lectures, outstanding performance during the training course and for donating their technical contributions, time and efforts to Orange House Partnership voluntarily without any financial compensation. Their generosity allows Orange House Partnership to provide to developing countries and countries with emerging economies training, assistance and support with the development of sustainable human and environmental food and chemical safety.

A special thanks is in order for Paula Viapiana who took the initiative to organise this training and contacted Orange House Partnership (OHP) in September 2009 with the request to develop a broad GHS training course. She has been closely involved in all stages of the project, provided assistance whenever needed and anticipated and dealt with potential issues before they would become a problem.

The support of the Toxicology and Environmental Hygiene Department of the Faculty of Chemistry of the University of the Republic of Uruguay is greatly appreciated. OHP is thankful to Professor Nelly Mañay for allowing her team to assist with the organisation, logistics and administrative issues which has been essential for the smooth operation of the project.

The Asociación Química y Farmacia of Uruguay is acknowledged for its financial support of the project and for hosting the meeting. OHP is particularly grateful to Silvia Etcheverry for the effectuation of this support.

OHP is grateful to Mr Jonathan Krueger of UNITAR for sharing the pilot version of the Basic GHS Course and other training material which were indispensable for the success of the project.

PROJECT REPORT SUMMARY

Project nr:	RT(2009)04
Subject:	In-depth Training Course on the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) to be implemented in Uruguay.
Sponsored by:	The GHS training in Montevideo, Uruguay was supported by the Ministry of Labour and Social Security, the Ministry of Health and the Ministry of Environment. The Asociación Química y Farmacia (AQF) in Uruguay (non-profit national society of chemistry and pharmacology) and the Faculty of Chemistry of the University of the Republic also contributed financially and in kind, respectively. Furthermore, a modest admission fee was charged to participants from the private sector. OHP covered the expenses of the 5 expert volunteers who gave the training.
Start and end-dates:	Monday 31 May – 3 June 2010.
Experts involved:	OHP Experts: • Dr Helmut Fleig, independent consultant, BASF retiree, and OHP, Germany • Dr Herman Koëter, OHP, Belgium; • Dr Iona Pratt, Food Safety Authority of Ireland and OHP, Ireland; • Dr Steve Vaughan, InsideOutWorks, independent consultant, formerly of the Ministry for the Environment New Zealand, and OHP, New Zealand; • Dr Klaus Wettig, BfR retiree and OHP, Germany. UNITAR: • Mr Jonathan Krueger, UNITAR; Uruguay Officials: • Dr Carmen Ciganda, Ministry of Health, Uruguay; • Dr Silvia Etcheverry, AQF, Uruguay; • Dr Nelly Mañay, University of the Republic, Uruguay; • Dr Maria Narducci, Ministry of Labour, Uruguay; • Dr Judith Torres, Ministry of Environment, Uruguay; • Dr Paula Viapiana, University of the Republic, Uruguay. •
Background and Objectives:	First contacts were made in September 2009 in South Africa where Herman Koëter gave a presentation on OHP at a conference on chemical and food risk assessment for developing countries. At that conference OHP was approached by Ms Viapiana with the request for training on classification and labelling as described in the newly established GHS. Next, OHP approached UNITAR (UN Institute for Training and Research) being the secretariat of the Programme Advisory Group (PAG) of the UN.ECOSOC Sub Committee of Experts on the GHS (SCEGHS). The PAG is in charge of technical updating and extension of the GHS and is responsible for GHS training. UNITAR was very pleased with the OHP initiative to give training in Uruguay without charging fees and provided its recently developed draft training manual and slides. Unfortunately UNITAR did not have funds to support

	the training course or to participate in the training. To streamline possible future cooperation, including document exchanges, a Memorandum of Understanding (MOU) was developed between UNITAR and OHP which came into effect on 1 May 2010. The objective of the project was to assist the Uruguayan authorities (MoL, MoH, MoE) with the formal implementation of the GHS in Uruguay. To that end a technical training course was developed by OHP experts covering all aspects of the GHS, including its history of development. Extensive use was made of the UNITAR training manual and other materials. The target audience of this training course included technical experts responsible for classification and labelling, occupational health officers and officials responsible for hazard communication. The training course was intended for both the public and private sector. Unfortunately, the budget did not allow simultaneous interpretation and all lectures were given in the English language.
Meetings:	• Orientation meeting with UNITAR staff on 15 February 2010 at the UNITAR offices in Geneva, Switzerland; • In-depth Training Course on the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), from 31 May-3 June 2010 in Montevideo, Uruguay.
Main Topics and observations:	There were 27 registered participants and national speakers from the public (13) and the private (14) sector. The latter group included 5 experts from state-owned dairy products and oil/alcohol businesses. The training course comprised both plenary lectures (16) and practical training sessions of break-out groups (4). Main areas covered were: health hazards, environmental hazards, physical/chemical hazards, and hazard communication. The participants were very interested, pro-active and eager to learn. Break-out sessions were generally more appreciated than plenary lectures but the limited time available did not allow to further extend these sessions. At the end of the training, participants were requested to complete an evaluation questionnaire. The overall impression score was 4.3 on a scale from 1 (poor) to 5 (excellent). Negative comments were mostly on the language problem during the work on example case studies. Introspective informal evaluation of the training by the trainers revealed that in future training courses more time should be invested in developing case examples as a learning tool including both simple examples to illustrate material and more complex 'real world' cases. It was also concluded that all lectures and example cases should be in the language of the country concerned or, alternatively, there should be simultaneous interpretation. The first of these aspects will result in substantial additional costs which were not available for the current training in Uruguay. The atmosphere was excellent throughout the training course.

TRAINING COURSE FACULTY

The Training Course faculty comprised the following experts (in alphabetical order):

- Dr. Helmut Fleig, Germany, email: helmutfleig@t-online.de
  Completed his studies of Natural Sciences at the University of Heidelberg (Germany). From 1970 he worked in BASF in the areas of toxicology/product safety and was mainly engaged in classification & labeling and risk assessment. After his retirement in 2005 Dr Fleig became independent consultant (Helmut Fleig Consultant/HFC). Dr Fleig's professional memberships and extra-curricular activities include: the German Chemical Industry Association, German Advisory Board; German EU delegation for C&L from 1980-2002 and international bodies such as CEFIC and BIAC. He participated in the GHS development process in OECD/UN since 1994 and in EU-ECHA guidance development for C&L. He is also expert member of the UN-GHS SCE (nominated by UNITAR and UNIDO). Dr Fleig has given numerous presentations and trainings in chemicals management (C&L, risk assessment, risk management, chemicals regulations) in Europe (for the chemical and other industries and for EU Twinning projects in Asia, Australia, South America and North Africa.

- Dr. Herman B.W.M.Koëter, Belgium, email: herman.koeter@orangeOhouse.eu
  Herman Koëter is the founder and Managing Director of the Brussels based Orange House Partnership, which is a non-profit partnership organization providing scientific expertise, assistance, advice, training and interim management in the areas of food and chemical safety to the public and private sector primarily in developing countries and emerging economies. Before establishing Orange House Partnership, from 2003 through 2008 Herman Koëter held several positions at the European Food Safety Authority (EFSA) in Parma, Italy, including Scientific Director, Deputy Executive Director and Acting Executive Director. Dr Koëter started his professional career in 1967 at the TNO Toxicology and Nutrition Institute, Zeist, the Netherlands where he held several positions before he was appointed in 1986 as Associate Head of the Department of Biological Toxicology. From 1991-2003 Herman Koëter was Principal Administrator at the Paris based OECD Environment, Health and Safety Division. There he was responsible for the Programme on Harmonization of Classification and Labelling of Chemical Substances. He was also responsible for the OECD Test Guidelines Programme, the OECD Special Activity on Endocrine Disrupters and OECD's Special Activity on Animal Welfare Policies. Dr Koëter was also senior adviser for OECD on human health hazard and risk assessment policies.

- Dr. Iona Pratt, Ireland, email: ipratt@fsai.ie
  Dr Iona Pratt is a consultant toxicologist and risk assessor, who has worked for many years in the area of assessment of hazardous chemicals under the EC legislation on classification, labelling and packaging, risk assessment and notification of new substances. She is based in Dublin, Ireland, and is self-employed, having retired from senior positions with the National Authority for Occupational Safety and Health of Ireland and the Food Safety Authority of Ireland. She has extensive experience of the Globally Harmonised System for Classification and Labelling and was chair of the ILO Working Group on Hazard Communication, responsible for developing proposals for the Hazard Communication parts of the GHS.

- Dr. Steve Vaughan, New Zealand, email: srv@insideoutworks.co.nz
  Dr Vaughan is a director of a consultancy which specialises in risk management – including managing hazardous substances risk. He originally trained as a chemical engineer and worked part of his career in process research and development in the agricultural and biofuels areas before moving to central government where he managed the reform of the law, regulation, and administrative systems for the control of hazardous substances and new organisms (including genetically modified organisms) in New Zealand. The hazardous substance component of these systems was designed to implement the GHS and includes the lifecycle management of chemical risks. He

represented New Zealand on a number of the committees responsible for the development of the classification scheme component of the GHS and later on other UN and World Bank bodies responsible for aspects of sustainable development. He is currently also part time Executive Director for the New Zealand Society for Risk Management and as such maintains a working interest in the international standardisation of risk management methods.

- Pharm. Chem. Paula Viapiana, Uruguay, email: paulavia@yahoo.com
  Paula Viapiana is lecturer at the Toxicology and Environmental Hygiene Department of the Faculty of Chemistry at the University of the Republic, Montevideo, Uruguay. Her current area of research is environmental and occupational toxicology. She is also Chief Environmental Health and Safety at Adium Pharma, a pharmaceutical industry. Prior to her current positions she was Quality Inspector at the Ministry of Health and Private Consultant on good manufacture practices (GMP). She has extensive experience in Environmental issues, Quality Assurance and Occupational Health and Safety.

- Prof. Dr. Klaus Wettig, Germany, email: ke.wettig@t-online.de
  Klaus Wettig performed his studies of chemistry and toxicology in East-Germany (Humboldt-University, Berlin). His later study objects were carcinogenic substances in the environment (PAH and nitrosamines) and the endogenous synthesis of nitrates in humans. After 1990 he worked as department leader (toxicokinetics and biochemistry) in the division of evaluation of chemicals at the Federal Institute of Health. He represented Germany in different groups of international organizations (UN, WHO, OECD, EU) and helped to establish GHS. After 2004 he worked over 3 years as Resident Twinning Advisor in Romania and Poland (both as head of about 40 European experts), UN lecturer on REACH and GHS in Albania, chief-advisor of the Russian caprolactam industry and advisor of Waste Disposal Regeneration Projects in East Germany.

INTRODUCTION

The Globally Harmonised System of Classification and Labelling of Chemicals and Chemical Mixtures (GHS) was approved by the UN Committee of Experts on Transport of Dangerous Goods and the GHS (UNCETDG/GHS) in 2003. The GHS is maintained by the Committee's Sub-Committee of Experts on the GHS (UNSCEGHS). The two main tasks of the Sub-Committee are to promote the implementation of the GHS at a global level and maintain and update the system taking into account areas not yet adequately covered and available new science and technology. With respect to its global implementation, under the auspices of the Inter-Organisation Programme for the Sound Management of Chemicals (IOMC), UNITAR and ILO have taken the lead in a training and capacity building programme to familiarise countries with the GHS and facilitate its implementation. Meanwhile, the Programme Advisory Group (PAG) for this activity has initiated awareness raising and comprehensibility testing in several parts of the world, including South America. Uruguay has the lead role in the Mercosur (Latin American Common Market) implementation of the GHS and, in anticipation, in April 2009 UNITAR arranged for a national GHS workshop in Montevideo, Uruguay, organised by the Laboratorio Tecnológico del Uruguay (LATU). This was followed up In March 2010 by a private initiative of the international consultancy firm: ChemADVISOR which organised a half day introduction to the GHS for the chemical industry association of Uruguay (ASIQUR).

In September 2009 Orange House Partnership (OHP) was approached by a representative of the Toxicology and Environmental Hygiene Department of the Chemistry Faculty of the University of the Republic of Uruguay with the request to develop a broad and extensive GHS training course for representatives of the public and private sector. This initiative was supported by the Ministry of Health, the Ministry of Labour, the Environmental Authority (DINAMA) and the Chemistry and Pharmacology Association (non-profit organisation). As this

request was fully in line with its mission and objectives, OHP responded positively and informed UNITAR of its intention to assist Uruguay by developing the requested training. The dates of the training course were provisionally set for May 2010. Although UNITAR was not in the position to co-organise and co-fund the project, it provided to OHP the pilot version of the newly developed 'UNITAR Basic GHS Course' and the accompanying PowerPoint presentation. It was agreed that OHP would use this training material in developing the training programme for Uruguay and would report its experience at a next meeting of the PAG following the training. In order to facilitate possible future cooperation between UNITAR and OHP, an MOU was agreed which came into force on the 1st May 2010 (see Annex1).

OBJECTIVE

The objective of the project was to familiarise Uruguayan authorities and technical representatives with all aspects of the GHS and to train professionals from both the public and private sector in applying the GHS for the classification and labelling of substances and mixtures. To that end, a four-days technical training course was developed by OHP experts covering the fundamental concepts of hazard and risk assessment and all aspects of the GHS, including its history of development. The target audience of this training course included technical experts responsible for classification and labelling, occupational health officers and officials responsible for hazard communication.

In addition, the training course would provide ample opportunity to use the May 2009 pilot version of the UNITAR Basic GHS Course and share this experience with the PAG at its next meeting following the Uruguay experience.

OBSERVATIONS

The Training Course was held from the 31st of May through the 3rd of June 2010 at the meeting facilities of the Asociación Química y Farmacia (AQF) in Montevideo, Uruguay. The details of the programme are provided in Annex 2. There were 27 registered participants and national speakers from the public sector (13) and the private sector (14). The private sector attendants were largely from the state-owned dairy, petrochemical and the pharmaceutical industry. A list of all registered participants is provided in Annex 3.

The Training Course comprised an opening session and 7 plenary sessions. In addition there were 4 break-out working sessions dedicated to the 4 main aspects of the GHS (health hazards, environmental hazards, physical hazards and hazard communication). The various plenary sessions included a total of 16 lectures covering:

- Principles of hazard and risk assessment and the scientific basis of the GHS;
- History, background, scope and application of the GHS, including principles, practical aspects, oversight and updating;
- Health hazards, including: acute-, skin- and eye toxicity hazards, sensitisation hazards, aspiration hazards, CMR hazards (carcinogenicity, mutagenicity, reproductive toxicity) and other specific target organ toxicity hazards;
- Environmental hazards including: acute- and chronic aquatic toxicity hazards, chemical fate in the environment and hazards to the ozone layer;
- Physical hazards including: classification of explosive, flammable, pyrophoric and self-heating substances, self-reactive substances, organic peroxides, oxidising and corrosive substances and substances which emit flammable gases in contact with water;
- Hazard communication, including hazard- and precautionary statements, other label elements and the preparation of safety data sheets;
- Openness and transparency in hazard classification.

PDF copies of all presentations are provided in Annex 7. During the four break-out working sessions the participants were subdivided in three subgroups of 7-9 participants each. All subgroups were given the same assignments and following each exercise results of the subgroups were compared and differences discussed. During the respective break-out sessions the participants were given the following assignments the details of which are provided in Annex 8:

- Practising health hazard classification (1): the example of classification as provided in Annex 8 of The GHS 3rd edition (the Purple Boo) but without the proposed classification; participants were requested to classify for as many health hazards as possible;
- Practising health hazard classification (2): the part of the public version of the Draft Assessment Report of Flonicamid with all developmental and reproductive toxicity studies; participants were requested to find NOAELs and classify for possible reproductive toxicity hazards;
- Practising environmental hazard classification (1): participants were requested to classify a series of 10 substances with full or partly information on fish, Daphnia, algae, biodegradation/accumulation to be classified;
- Practising environmental hazard classification (2): participants were requested to classify an imaginary mixture of 5 components. Emphasis was on chronic toxicity hazards in the absence of bioaccumulation data;
- Practising environmental hazard classification (3): participants were requested to classify a complex paint mixture of 6 components with no data on the mixture as a whole and no data for a similar mixture (bridging principles cannot be applied) by using the summation method;
- Practising physical hazard classification (1): classify a set of 5 examples for 5 different physical hazard endpoints, respectively (pyrophoric, oxidising, water-reactive, corrosive and self-heating hazards);
- Practising physical hazard classification (2): four cases, case 1: participants were requested to classify a mixture of 5 components with a paste-like consistency (which did not meet the GHS definition of a liquid) and an article; they were requested to classify the mixture again after being modified (hazards considered: explosivity, flammability, oxidising properties); case 2: participants were requested to classify an explosive article with limited information provided, case 3: participants were requested to classify two jet fuels based on flash point and boiling point; case 4: consider classification of a substance as organic peroxide;
- Practising hazard communication: a completed SDS for ethanol was provided in Spanish as an example of a simple SDS. Participants were requested to prepare an SDS for a methylated spirits, a mixture of 4 components based on the physical hazard data and substantial health hazard data provided.

Participation during the 4-days training was very active. The relatively small size of the group made it easy to interact with individual participants and questions and comments were invited during presentations, rather than at the end of each presentation only. Although the plenary introductory lectures were essential as preparation for the break-out sessions, it appeared that most participants had difficulty absorbing all the information from each, rather densely packed, lecture. The participants also had a problem with the many acronyms used and a provisional list of acronyms was distributed. This list, extended with additional, useful acronyms is attached as Annex 4. This apparent overload of information appeared to be the case in particular on day 1 when there were no break-out sessions. By the end of the first day participants seemed to be somewhat saturated with information and several showed signs of considerable fatigue.

The break-out sessions were very successful in that all participated very actively in all 4 sessions. Time was the limiting factor and none of the break-out subgroups managed to finish all assignments. However, after the introduction of each case generally there was no substantial need for further assistance and all subgroups worked quite independently,

although some initial prompting towards the right direction was found to be useful – largely in the interests of keeping to available time.

Other observations include:

- copies of the respective case studies were not for all cases available to each participant.
- Of the rather voluminous reference documents, only 4 copies were available for all participants together. Such reference documents included: the Purple Book on GHS, the Orange Book on Model Regulations, the UN Manual of Tests and Criteria, and the Draft Assessment Report on Flonicamid. A list of references to these documents and other useful documents or websites is provided in Annex 5.
- The budget did not allow for simultaneous interpretation English/Spanish, hence the language of the training course was English. However, although all participants understood English, for many it was hard to understand fine details and to participate in discussions.
- Paper copies of most plenary presentations (those received in advance of the meeting) were made available to all participants and these were useful for those whose English was not perfect.
- The atmosphere during the full training can be characterised as relaxed, open and very friendly.

At the end of the training course participants were requested to complete the OHP Standard Training Evaluation Questionnaire anonymously. Nineteen completed questionnaires were received and a summary of the evaluation is provided in Annex 6. From this summary it appears that the general appreciation of the participants was rather high (4.33 on a scale from 1-5). Comments made by individuals are very much in line with the general observations made by the OHP experts.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

The training project was developed with a view to cover all aspects of the GHS and provide a considerable level of detail in each area of the system. That this could be achieved is thanks to the contributions of 4 highly experienced international experts in the field. It is acknowledged that the areas covered by the GHS are diverse (health hazard, environmental hazards, physical hazards) and that rather different expertises and backgrounds are needed to comprehend the detail of many of the hazard endpoints. In addition, the experience of this programme suggests that a 4-days training course is barely adequate to cover all aspects of the GHS at a detailed level. On the other hand, courses which are longer than 3 or 4 days are generally not preferred by participants as being away from one's workplace/office for a full week or more is considered a luxury hardly anybody with management responsibilities can afford these days.

The communication part of the training course was too short (three-quarter of a day) to be able to cover hazard and precautionary statements, in particular if one wishes to provide the background and relevance of the various statements. It already needs basically a full day to adequately practise the completion of one or two SDS's (with different elements of relevance) even when the necessary information is provided in an orderly manner and at the appropriate level of detail.

The pilot version of the UNITAR Basic GHS Course provided a wealth of information and background, both in the various chapters and the accompanying PowerPoint slide presentation. The course content was extensively used by all OHP experts and is best visible in the PowerPoint presentations of the trainers. Also the questions provided in the course were very useful: they were interspersed with the other questions trainers posed to the audience.

However, the UNITAR course as it is today seems most appropriate as a reference and guidance document for trainers to prepare (more detailed) course material. It would certainly be very useful if the course would be extended with a series of examples and practical exercise cases.

A lesson learned was that all participants should be provided with their own copy of any case assignment and that working sessions are best held in the mother language of the participants. However, this may in some cases substantially increase the costs of the training which in turn would work against the objective of disseminating knowledge of the GHS widely.

Finally, without exception, the expert trainers all had extensive expertise in hazard assessment and the GHS and delivered first class training. The participants were generally very pro-active, highly intelligent and eager to learn. The atmosphere was very positive which made it pleasant for the trainers to work with the audience. Although both the breadth and the amount of information exchanged was somewhat overwhelming, participants greatly appreciated the training and indicated they would appreciate a follow-up training, probably focussed on one or a few aspects of the GHS instead of the whole system.

Recommendations

The following recommendations can be made:

- To meet the objectives of the GHS, training courses for individuals responsible for classification and labelling do need to cover the full range of hazards within the system – and to cover mixtures. This does require time, depending on the starting expertise of the participants. If time constraints are an issue then consideration should be given to separating the classification and hazard communication aspects into separate and possibly sequential courses.
- Considering the diversity of the areas covered by the GHS and the frequently applied 'weight of evidence' approach, additional and separate training of specialists in each of the areas (physical hazards, health hazards and environmental hazards) is recommended. Both substances and mixtures should be part of such training.
- Training courses should dedicate a substantial part of the training (at least 50%) to practical work: case studies work best when the assignment is put on paper, together with the information needed or with the key to find such information. All participants should be provided with their personal copy of the work assignment, even when done as a group exercise.
- Adequate time should be invested in developing case examples as a learning tool including both simple examples to illustrate material and more complex 'real world' cases.
- To this end, it is essential that courses are developed so they can be tailored to the needs, backgrounds and skill level of each audience and that this information is available to the organisers of the training and to the trainers and used to tailor courses appropriately.
- Participants should be provided after the training course with the answers, responses and/or solutions to the case studies assigned to them for later use as reference or reminder.
- Providing participants with PDF copies of slide presentations at the start of the training or, preferably, immediately after the presentation is useful as a reference document; however, providing such presentations well before the meeting, while useful to help with any language issues, may lower the attention span during the presentation.
- Training courses are most efficient when given in the mother language of the participants or, alternatively, with simultaneous interpretation; however, the costs involved may make this difficult to achieve in all cases.
- The UNITAR Basic GHS Course and accompanying PowerPoint presentation is an excellent introduction to the GHS and reference tool for trainers but, as such, functions

more as a guidance document than a true training course. Therefore, it is recommended to (i) expand the course with a number of examples and work assignments, (ii) expand the course with more details of the essential elements and (iii) rework the course into an e-learning course in 2 levels: an introduction to the GHS and an advanced user training course. This last step needs to bear in mind that e-learning programmes necessarily lose some of the value from tailoring to specific audiences – in practice both e-learning and tailored face-to-face learning will be needed to promulgate the GHS fully.

- When trainers are well-prepared, well-experienced and show involvement with the subject they will find an enthusiastic audience, willing to start early in the morning and stay late in the day and even willing to absorb an overload of information, as experienced in Uruguay!

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ANNEX 1

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unitar United Nations Institute for Training and Research

MEMORANDUM OF UNDERSTANDING

1. The non-profit expert organization **Orange House Partnership** (OHP), located in Beersel (Dworp), Belgium, and the **United Nations Institute for Training and Research** (UNITAR), headquartered in Geneva, Switzerland; agree to strengthen collaboration as set forth in this Memorandum of Understanding (MOU).

2. In order to contribute to globally sustainable human and environmental safety by providing expertise, training, assistance, advice, and management in the areas of chemical classification and hazard communication and risk assessment and risk management, to governmental authorities and the public and private sectors, in particular in developing countries and emerging economies , OHP and UNITAR agree to enhance their cooperation based on the following considerations:

   - The importance of developing national or regional systems in developing countries and emerging economies to ensure that chemicals are properly classified and labelled and that safety data sheets are made available for the use of stakeholders to help trigger protective behavior using as a basis the UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS);
   - The urgent need for developing countries and emerging economies to adopt the GHS as soon as possible since it is a practical and coherent global standard for chemical hazard communication in the workplace, for those involved in work-related activities, for the transport and health sectors, and for consumers;
   - The role of the two organizations (OHP and UNITAR), along with the International Labour Organization (ILO), in chemicals management which could create significant opportunities to assist developing countries and emerging economies to achieve sound chemicals management-related goals, including those related to the Strategic Approach to International Chemicals Management (SAICM) and the Millennium Development Goals (MDGs).

3. The objectives of the partnership and enhanced cooperation between OHP and UNITAR are as follows:

   - Assist developing countries and emerging economies with the introduction of compliance monitoring systems for chemicals and strengthening of existing programmes for the harmonization of national regulations on chemical safety based on the GHS;
   - Involve governmental agencies, NGOs, academia and the private sector for the development and implementation of National GHS Implementation Strategies (NIS) in developing countries and emerging economies;
   - Raise awareness of the relevant sectors about the GHS and its benefits for sustainable development.

4. The modalities of collaboration between OHP and UNITAR may include the following:

   - To share expertise and experiences about national implementation of the GHS, as well as respective networks of experts involved in the chemicals and risk management areas, through national and regional workshops;
   - To seek sustainable financial resource mobilization to offer to developing countries and emerging economies the required expertise and training for chemical management, GHS implementation, and risk assessment;
   - To include OHP in the UNITAR/ILO GHS Programme Advisory Group (PAG) with an invitation to attend the biennial meetings;
   - To provide GHS training materials and relevant documents to national GHS implementation workshops and training sessions that may be jointly organized by OHP and UNITAR, as well as resource persons(s) (subject to available resources);
   - To share annual work plans and coordinate activities relevant to this MOU in order to avoid duplication of work and use resources in the most efficient manner .

5. The implementation of activities envisaged in the present MOU shall depend on the availability of the necessary financial resources and shall be made in accordance with the regulations and procedures in force in OHP and UNITAR.

6. OHP and UNITAR will also cooperate in other mutually agreed upon areas whenever such opportunities arise. Agreements and project documents will be developed on a case-by-case basis. Staff will be requested to facilitate such cooperation in as expedited a manner as possible, to the full satisfaction of both organizations.

7. The focal point of OHP for implementing this MOU will be the Managing Director of the OHP. The focal point for UNITAR for implementing this MOU will be the Manager, Chemicals and Waste Management Programme. OHP and UNITAR will inform each other as soon as possible of changes in their respective focal points.

8. This MOU is signed for an initial period of two (2) years and may be renewed by mutual agreement of the Parties.

9. This MOU may be changed or amended by written agreement between the Parties.

10. Either Party shall have the right to terminate this MOU by giving one month's advance notice in writing to the other Party. If this MOU is terminated by either Party, steps shall be taken to ensure that the termination does not affect any prior obligation, project or activity already in progress.

11. Nothing in or relating to this MOU shall be deemed a waiver of any of the privileges and immunities of OHP and UNITAR.

12. In the event of a dispute, controversy or claim arising out of or relating to this MOU, or the breach, termination or invalidity thereof (a "dispute"), the Parties shall use their best efforts to settle promptly such dispute through direct negotiation. Any

dispute that is not settled within fourteen (14) days from the date either Party has notified the other Party of the nature of the dispute and of the measures that should be taken to rectify it shall be resolved through consultation between the Managing Director of OHP and the Executive Director of UNITAR.

13. This Memorandum of Understanding shall enter into force upon signature.

The present Memorandum of Understanding is signed in two authentic copies in English on 1 May 2010 in Geneva, Switzerland and in Beersel, Belgium.

For UNITAR		For Orange House Partnership npo
[signed] Charlotte Diez Special Assistant to the Executive Director On behalf of Carlos Lopes, Executive Director Cleared by: C. Boljkovac, Manager, CWM		*[signed]* Herman B.W.M Koëter Managing Director

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ANNEX 2

IN-DEPTH TRAINING COURSE ON THE GLOBALLY HARMONISED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS) TO BE IMPLEMENTED IN URUGUAY

WITH ASSISTANCE AND SUPPORT OF THE UN INSTITUTE FOR TRAINING AND RESEARCH (UNITAR)

31 May-3 June 2010, Montevideo, Uruguay

Final Training Programme

Chair: Herman Koëter, Orange House Partnership (OHP), Belgium
Co-Chair: Paula Viapiana, Facultad de Química, Montevideo

Day 1: Monday 31 May

09:00-10:45 Opening of the Training Course:

- **Official opening address**
  - Silvia Etcheverry (Asociación Química y Farmacia, Uruguay)
  - Paula Viapiana (Toxicology and Environmental Hygiene Department, Faculty of Chemistry);
- **Objectives and approach of the training** (Herman Koëter, OHP);
- **Introduction of the trainers and participants** (Herman Koëter, OHP);
- **Brief introduction of the Toxicology and Environmental Hygiene Department , Faculty of Chemistry, University of the Republic, Uruguay** (Nelly Mañay, Faculty of Chemistry);
- **Brief introduction of the Ministry of Labour and Social Security, Uruguay** (Maria Narducci, Ministry of Labour and Social Security);
- **Brief introduction of the DINAMA (MVOTMA, Environmental Authority), Uruguay** (Judith Torres, DINAMA);
- **Brief introduction of the Ministry of Health, Uruguay** (Carmen Ciganda, Ministry of Health)
- **Brief introduction of the role of UNITAR** (Herman Koëter, OHP, representing Jonathan Krueger of UNITAR);
- **Brief introduction to Orange House Partnership** (Herman Koëter, OHP).

10:45-11:00 *Coffee/tea break*

Session 1 (Plenary): History and background of the GHS, principles of hazard and risk assessment

11:00-11:30 **History, background and context of the GHS; parties involved in its development and adoption; GHS oversight and updating** (Iona Pratt, Ireland).

11:30-12:00 **General introduction to chemical hazard and risk assessment approaches and procedures being the scientific basis of the GHS** (Herman Koëter, OHP).

12:00-12:45 **Scope and application of the GHS: principles, practical aspects, implementation and responsibilities** (Helmut Fleig, Germany).

12:45-14:00 *Lunch break*

14:00-14:30 **Status of preparation for GHS implementation in Uruguay and work done to date** (Paula Viapiana, Uruguay).

Session 2 (Plenary): Health Hazards: the GHS explained

14:30-15:45 **Health hazards, Part 1: Classification based on acute toxicity, aspiration, skin and eye toxicity, and sensitisation hazards**. (Klaus Wettig, Germany)

15:45-16:15 *Coffee/tea break*

16:15-17:30 **Health hazards, Part 2: Classification based on mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity hazards.** (Iona Pratt, Ireland)

17:30-18:00 **General discussion, questions and answers.**

18:00 *Training course adjourns for the day*.

Day 2: Tuesday 1 June

Session 3 (Breakout Groups): Practicing health hazards classification (Iona Pratt and Klaus Wettig)

09:00-09:05 **Introduction to the Breakout Groups session and assignments**.
09:05-10:30 **All breakout groups will be requested to classify selected chemicals for a variety of health hazards into the respective classes as defined in the GHS**.

10:30-11:00 *Coffee/tea break*

Session 4 (Plenary): Reports from the Breakout Groups on health hazards classification (rapporteurs of each break-out group)

11:00-12:00 **Reports from the Breakout Groups: discussion, mistakes made, lessons learned**.

12:00-13:30 *Lunch break*

Session 5 (Plenary): Environmental Hazards: the GHS explained

13:30-14:15 **Environmental Hazards, Part 1a: Acute and chronic (long-term) aquatic environment hazards for substances**. (Helmut Fleig, Germany)

14:15- 15:00 **Environmental Hazards, Part 1b: Acute and chronic (long-term) aquatic environment hazards for mixtures.** (Steve Vaughan, New Zealand)

15:00-15:15 **Environmental Hazards, Part 2: Hazards to the ozone layer**. (Helmut Fleig, Germany)

15:15-15:45 *Coffee/tea break*

Session 6 (Breakout Groups): Practicing environmental hazards classification (Steve Vaughan and Helmut Fleig)

15:45-15:50 **Introduction to the Breakout Groups session and assignments.**
15:50-17:00 **All breakout groups will be requested to classify selected chemicals for a variety of environmental hazards into the respective classes as defined in the GHS.**

Session 7 (Plenary): Reports from the Breakout Groups on environmental hazards classification (rapporteurs of each break-out group)

17:00-17:30 **Plenary reports from the Breakout Groups: discussion, mistakes made, lessons learned.**

17:30 *Training course adjourns for the day*

Day 3: Wednesday 2 June

Session 8 (Plenary): Physical Hazards: the GHS explained

09:00-10:00 **Physical Hazards, Part 1: Classification of explosives, flammables (gases, aerosols, liquids and solids), self-reactive substances and organic peroxides.** (Steve Vaughan, New Zealand)

10:00-10:30 *Coffee/tea break*

10:30-11:30 **Physical Hazards, Part 2: Classification of pyrophorics (solids and liquids) , self-heating and oxidising substances and mixtures, substances and mixtures which are corrosive to metals, and substances and mixtures which emit flammable gases on contact with water.** (Helmut Fleig, Germany)

Session 9 (Breakout Groups): Practicing physical hazards classification (Helmut Fleig and Steve Vaughan)

11:30-11:35 **Introduction to the Breakout Groups session and assignments.**
11:35-12:30 **All breakout groups will be requested to classify selected chemicals for a variety of physical hazards into the respective hazard classes as defined in the GHS.**

12:30-14:00 *Lunch break*

14:00-14:30 **All breakout groups continue classify selected chemicals for a variety of physical hazards into the respective hazard classes as defined in the GHS.**

Session 10 (Plenary): Reports from the Breakout Groups on physical hazards classification (rapporteurs of each break-out group)

14:30-15:00 **Plenary reports from the Breakout Groups: discussion, mistakes made, lessons learned.**

Session 11 (Plenary): Transport of Dangerous Goods and the GHS

15:30-16:30 **History and working practices and the process of harmonisation of the UN-CETDG with the GHS** (Iona Pratt, Ireland)
16:30-17:15 **Overview of UN Recommendations on the Transport of Dangerous Goods and comparative analysis of the GHS and RTDG** (Helmut Fleig, Germany)
17:15-17:30 **General discussion; questions and answers**

17:30 *Training course adjourns for the day*

Day 4: Thursday 3 June

Session 12 (Plenary): Hazard Communication: the GHS explained

09:00-09:30 **Introduction to hazard communication** (Klaus Wettig):

09:30-10:30 **Hazard communication, Part 1: Hazard statements, label elements, codification of statements, precautionary statements**. (Iona Pratt, Ireland)

10:30-11:00 **Hazard communication, Part 2: Preparation of Safety Data Sheets (SDS).** (Klaus Wettig, Germany)

11:00-11:30 *Coffee/tea break*

Session 13 (Breakout Groups): Practicing hazard communication: preparing an SDS (Iona Pratt and Klaus Wettig)

11:30-11:40 **Introduction to the Breakout Groups session and assignments**.
11:40-12:45 **All breakout groups will be requested to prepare parts of an SDS for a given chemical or mixture.**

12:45-13:45 *Lunch break*

13:45-14:30 **Each Breakout Group will continue with the SDS and review and correct, as appropriate, the SDS's prepared by the other break-out groups.**

Session 14 (plenary): Reports from the Breakout Groups on completed SDS's (Rapporteurs of the break-out groups)

14:30-15:00 **Plenary discussion of all SDS's prepared and commented on by all break-out groups; agreement on the SDS's and discussion of other hazard communication aspects**.

15:00-15:15 *Coffee/tea break*

Session 15 (plenary): Plenary discussion and Training Course summary (Chair & Co-Chair)

15:15-15:30 **Openness and transparency in hazard assessment, labelling and communication** (Herman Koëter, OHP).

15:30- 16:00 **Loop holes and pitfalls, achieving truly global harmonisation, responsibilities with respect to the implementation of the GHS, etc.**

16:00-16:15 **Training Course summary, recommendations, take-home messages and possible follow-up** (Herman Koëter, OHP)**.**

16:15 *Training Course adjourns*

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ANNEX 3

LIST OF REGISTERED PARTICIPANTS AND INVITED NATIONAL SPEAKERS

Name, first name	Affiliation	Contact
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ANNEX 4

LIST OF FREQUENTLY USED ACRONYMS

The list below should not be considered as complete: acronyms are invented almost daily and the ones listed are derived from a personal list of one of the OHP trainers with a few additions made by others.

AF	Assessment factor
CA	Competent Authority
CBI:	Confidential Business Information
CG/HCCS:	Coordinating Group for the Harmonization of Chemical Classification Systems
C&L	Classification and Labelling
CMR	Carcinogenic, mutagenic, toxic to reproduction
CSR	Chemical Safety Report
CWM	Chemicals and Waste Management Programme
DNA	Designated National Authority
DNEL	Derived No-Effect Level
DU	Downstream Users
EASE	Estimation and Assessment of Substance Exposure
EC_{50}:	Median Effect Concentration
ECB	European Chemicals Bureau
ECHA	European Chemicals Agency
ECOSOC	Economic and Social Council
EDEXIM	European database export import of dangerous chemicals
EU:	European Union
GHS:	Globally Harmonized System of Classification and Labelling of Chemicals
ILO:	International Labor Organization
IOMC:	Inter-organization Program on the Sound Management of Chemicals
IPCS	International Programme on Chemical Safety
ISO:	International Standards Organization
JRC	Joint Research Center
LC_{50} :	Median lethal concentration
LD_{50} :	Median or 50% lethal dose
MCA	Multi-Criteria Analysis
mg/kg:	Milligrams per kilogram
MS	Member State(s)
NEC:	No-Effect concentration
NOAEC:	No-Observed Adverse Effect Concentration
NOAEL:	No-Observed Adverse Effect Level
OD	Oily dispersion
OECD:	Organization for Economic Cooperation and Development
OHP:	Orange House Partnership
OSHA	Occupational Safety and Health Agency
OSOR	Open source Observatory & Repository
PAG	Programme Advisory Group
PBT	Persistent, Bioaccumulative, Toxic
PEC	Predicted Environmental Concentration
PIC	Prior Informed Consent
PNEC	Predicted No-effect Concentration
POP	Persistent Organic Pollutant
PPE	Personal Protection Equipment
PPORD	Product and process orientated research and development
PPP	Plant Protection Products
QSPTF	Quick Start Program Trust Fund

SAICM:	Strategic Approach to International Chemicals Management
SDS:	Safety Data Sheet
SIEF	Substance Information Exchange Forum
SME:	Small and medium sized enterprises
STOT	Specific Target Organ Toxicity
SVHC	Substance of very high concern
UN:	United Nations
UNCED:	UN Conference on Environment and Development
UNCETDG:	UN Committee of Experts on the Transport of Dangerous Goods
UNCETDG/GHS:	UN Committee of Experts on Transport of Dangerous Goods and on the GHS
UNDP	United Nations Development Programme
UNECE:	UN Economic Commission for Europe
UNEP	UN Environment Programme
UNITAR:	United Nations Institute for Training and Research
UNSCEGHS	United Nations Sub-Committee of Experts on GHS
vPvB	very persistent, very bioaccumulative
WSSD:	World Summit on Sustainable Development

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ANNEX 5

LIST OF USEFUL WEBSITES

- The IOMC general guidance page which provides a number of links to documents for GHS implementation – including usefully for the Uruguay programme participants the versions in all UN languages including Spanish:
  http://www.who.int/iomc/publications/publications/en/index.html

- The GHS 3rd edition itself can be obtained here in each of the UN official languages:
  http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

- The latest UN recommendations for the Transport of dangerous goods can be obtained here – again in each of the UN official languages:
  http://www.unece.org/trans/danger/publi/unrec/rev16/16files_e.html

- The UNECE dangerous good page which provides (in the sidebar) access to documents such as the ADR (this same sidebar also provides an access point to the UNRTDG, GHS etc):
  http://www.unece.org/trans/danger/danger.htm

- In terms of acronyms the ECHA glossary page is a useful resource:
  in English: http://guidance.echa.europa.eu/public-2/glossary.htm?lang=en
  in Spanish: http://guidance.echa.europa.eu/public-2/glossary.htm?lang=es

- The OECD test guidelines page provides access to many of the tests referenced in the tox and ecotox sections of the GHS. It can be found in English here...
  http://www.oecd.org/document/23/0,2340,en_2649_34379_1948503_1_1_1_1,00.html

- The OECD GLP guidances and requirements can be found here:
  http://www.oecd.org/document/63/0,3343,en_2649_34381_2346175_1_1_1_1,00.html

- The Websites of countries in our part of the world which have implemented the GHS are ERMA New Zealand (Hazardous Substances) . in English only:
  http://www.ermanz.govt.nz/hs/index.html

- An outline of Japan's activities and policies in relation to implementing the GHS is given (in English) on the following page. See the links across the top of the page for more detail on specific elements:
  http://www.meti.go.jp/policy/chemical_management/english/index.html

- UNITAR Chemicals and Waste Management Programme:
  http://www.unitar.org/cwm/

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ANNEX 6

Standard training evaluation questionnaire

In-Depth Training Course on the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) to be Implemented in Uruguay
31 May-3 June 2010, Montevideo, Uruguay

Summary of scores given by participants

Question number	Question	Score on a scale from 1-5 (mark one)					
		1	2	3	4	5	Mean
	Number of registered attendants: 27 **Number of responses received: 19**	**Total score**					
1	Overall training structure (lectures, break-out sessions, breaks, etc.):	0	0	2	9	8	4.3
2	Quality of the training content, appropriate level of detail, coverage of subjects:	0	1	1	8	9	4.3
3	Clarity and quality of the presentations (didactical aspects, clearness, responsiveness to feedback from participants:	0	0	7	3	9	4.1
4	Opportunities for audience participation:	0	0	1	4	14	4.7
5	Quality of responses to specific audience's questions:	0	0	1	12	6	4.3
6	Quality of interpretation/translations	Not relevant: no interpretation					
7	Other aspects (summary of comments made; number of commentors in brackets): *Language is an issue (4); preferably the training material should be available prior to the start of the training (1); not all training material was available for all (we had to share),the training is not sufficiently in-depth, and one trainer was not as good as the others (1); trainers are very kind, good communication (2), very intense course(1).*						
8	Overall impression (time invested/benefits)	0	1	2	6	10	4.3
	Mean score:	0					**4.33**

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ANNEX 7

PLENARY POWERPOINT PRESENTATIONS:

(See at the end of the report)

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ANNEX 8

WORKING ASSIGNMENTS FOR THE RESPECTIVE BREAK-OUT SESSIONS

SESSION 3 & 4:

CASE 1: AN EXAMPLE OF CLASSIFICATION IN THE GLOBALLY HARMONIZED SYSTEM

QUESTION: Classify this substance for as many hazards as available time allows.

The following classification proposal draws on the GHS criteria. The document includes both brief statements about the proposal for each health hazard class and details of all the available scientific evidence.

Proposed classification	

Identification of the substance

1.1 EINECS Name **If not in EINECS IUPAC Name**	2-Hazanol
	CAS No. 999-99-9 EINECS No. 222-222-2
1.2 Synonyms (state ISO name if available)	Globalene Hazexyl Systemol Globalethylene
1.3 Molecular formula	$C_xH_yO_z$
1.4 Structural formula	
1.5 Purity (w/w)	
1.6 Significant impurities or additives	
1.7 Known uses	*Industrial:* Solvent for surface coatings and cleaning solutions. Chemical intermediate for Globalexyl UNoxy ILOate. *General public:* Toilet cleaner

Physico-chemical characteristics

2.1 Physical form	Liquid
2.2 Molecular weight	146.2
2.3 Melting point/range (°C)	-45
2.4 Initial Boiling point/ boiling range (°C)	208.3
2.5 Decomposition temperature	
2.6 Vapour pressure (Pa(°C))	7
2.7 Relative density (g/cm3)	0.887 - 0.890
2.8 Vapour density (air = 1)	5.04

2.9	**Fat solubility (mg/kg, °C)**	
2.10	**Water solubility (mg/kg, °C)**	Slightly soluble (0.99% w/w)
2.11	**Partition coefficient (log Pow)**	
2.12	**Flammability** **flash point (°C)** **explosivity limits (%,v/v)** **auto-flammability temp. (°C)**	**closed cup:** 81.7 **open cup:** 90.6 **lower limit:** 1.2 **upper limit:** 8.4
2.13	**Explosivity**	No data available
2.14	**Oxidising properties**	
2.15	**Other physico-chemical properties**	

Health

Acute toxicity, *Oral*

Species	LD_{50} (mg/kg)	Observations and remarks	Ref.
Rat	1480	No further details were available.	2
Rat	1500 (males) 740 (females)	The LD_{50} values in mg/kg were calculated from ml/kg using the known density for EGHE of 0.89 g/cm^3.	8

Acute toxicity, *Inhalation*
There were no deaths or signs of overt toxicity in animals exposed to the saturated vapour concentration of approximately 0.5 mg/L

Species	LC_{50} (mg/l)	Exposure time (h)	Observations and remarks	Ref.
Rat	> 83 ppm. (approx equal to 0.5 mg/l).	4	No deaths, clinical signs or gross lesions occurred at 83 ppm (85 ppm is stated to be the saturated vapour concentration at room temperature).	3
Rat	Not stated	6	The animals were exposed to the saturated vapour concentration at room temperature (assumed to be 85 ppm). No deaths occurred and no signs of gross pathology were observed.	8
Rat	Not stated	8	No deaths occurred with exposure to the "saturated vapour concentration" at room temperature (assumed to be 85 ppm).	2

Acute toxicity *Skin*

Species	LD_{50} (mg/kg)	Observations and remarks	Ref.
Rat	790	No further details were available.	2
Rabbit (5/sex/ group)	720 (males) 830 (females)	Animals were exposed to up to 3560 mg/kg for 24 hours. All but 2 of the animals that died did so during the application period. Following the exposure period, local toxicity (erythema, oedema, necrosis and ecchymoses) was reported in an unstated number of animals, and persisted throughout the 14 day post-application observation period. Ulceration was also noted in an unstated number of animals at the end of the observation period.	8

Skin irritation/corrosion

There are conflicting reports concerning the irritant nature of this substance. In a dedicated skin irritation study reported in the same paper as the acute dermal study, the author states that "necrosis" was observed in 3 of 6 treated rabbits which was still present on the last day of observation (day 7), along with mild to moderate erythema. Mild to marked oedema was also observed during the course of the study but had resolved within the 7-day observation period. Given that one animal showed no evidence of any skin response in this study and that only slight to moderate skin irritation was observed in the other animals the observation of "necrosis" in three of the animals is somewhat surprising. An acute dermal (skin) toxicity study in rabbits also reported signs of skin irritation including the description "necrosis" and ulceration but did not quantify the number of animals affected. In contrast to these findings, an old and briefly reported study indicated that there was little or no indication of skin irritation in rabbits.

Similarly mixed skin irritation findings have been observed with a closely related substance, for which both necrosis and no skin irritation has been reported. In addition a secondary source indicates that some other similar substances cause "moderate" skin irritation, and that prolonged exposure to these group of substances may cause burns. However, much shorter chain similar substances are not considered to be skin irritants.

Species	No. of animals	Exposuretime (h)	Conc. (w/w)	Dressing: (32cclusive, semi-occlusive, open)	Observations and remarks (specify degree and nature of irritation and reversibility)	Ref.
Rabbit	6	4	0.5 ml of 100%	Occlusive	No signs of irritation were observed in one animal, and only slight erythema (grade 1) in another on day 1, which had resolved by day 7. Four animals showed a mild to moderate erythema (grade 1-2) and a mild to marked oedema (grade 1-3) after removal of the dressing. The oedema had resolved by day 7 post-exposure. "Necrosis" at the application site was reported in 3/6 rabbits from day 1 until the end of the observation period on day 7. Desquamation was observed in 4/6 rabbits on day 7.	8
Rabbit (albino)	5	24	100% (volume not stated)	Not stated	Little or no signs of skin irritation were found in this poorly reported study.	2

Serious damage to eyes/eye irritation

The only available study involved exposure of rabbits to considerably lower amounts of the test substance than the standard protocols for this endpoint recommend. Relatively severe (eg. Conjunctival redness grade 3) but reversible effects were seen. It is predictable that under standard test conditions, the effects on the eye would be very severe.

Species	No. of animals	Conc. (w/w)	Observations and remarks (specify degree and nature if irritation, any serious lesions, reversibility)	Ref.
Rabbit	6	0.005 ml of 100%	One hour post-instillation conjunctival redness (grade 3) and discharge (grade 2.8) observed. The mean scores for the 24, 48 and 72 hour readings for corneal opacity, iris, conjunctival redness, chemosis and discharge were all approx 0.5. All lesions had resolved by day 7.	8
Rabbit	60	1 and 5%	A report in the secondary literature of severe eye injury observed in rabbits associated with instillation of an unstated amount of 5%, could not be substantiated as the information was not found in the reference stated.	1

Skin and respiratory sensitization

No data are available. There are no additional grounds for concern (eg. Structure activity relationships).

Specific target organ/systemic toxicity following single or repeated exposure

Toxicity following single exposure

There is no reliable information available about the potential of this substance to produce specific, non-lethal specific target organ/systemic toxicity arising from a single exposure.

Toxicity following repeated exposure: Oral
No oral repeat dose studies or human evidence are available.

Toxicity following repeated exposure: Inhalation
There was no evidence of adverse toxicity in a 13-week rat inhalation study at 0.43 mg/l (approx. 72 ppm), an exposure level close to the saturated vapour concentration.

Species	conc. mg/l	Exposure time (h)	Duration of treatment	Observations and remarks (specify group size, NOEL, effects of major toxicological significance)	Ref.
Rat (F344) 20/sex / group (plus 10/ sex/group - 4 week recovery groups)	0.12, 0.24 and 0.425	6	5 d/wk for 13 weeks	No deaths occurred. Decreased weight gain was observed in high dose animals of both sexes and medium dose females. There were no toxicologically significant changes in haematological or urinalysis parameters. High dose females showed an increase in alkaline phosphatase. High and medium dose males showed a statistically significant increase in absolute and relative kidney weight. A small increase in absolute liver weight (12%) was observed in high dose females. However, there were no gross or histopathological changes in any organs examined.	3

Toxicity following repeated exposure: Dermal
Unquantified haematological changes were reported in rabbits exposed to 444 mg/kg dermally for 11 days. However, due to the limited information provided, no conclusions can be drawn from this study.

Species	Dose mg/kg	Exposuretime (h)	Duration of treatment	Observations and remarks (specify group size, NOEL, effects of major toxicological significance)	Ref.
Rabbit	0, 44, 222 and 444	6	9 doses applied over 11 days	This is an unpublished study reported in the secondary literature. Unquantified decreases in haematological parameters were noted in top dose animals. No description of local effects was provided.	1

Carcinogenicity (including chronic toxicity studies)

No data available.

Germ cell mutagenicity
Negative results have been reported *in vitro* from Ames, cytogenetics, and gene mutation tests reported in the secondary literature. There are no *in vivo* data available. .

***In vitro* studies**

Test	Cell type	Conc. range	Observations and remarks	Ref.

Ames	Salmonella (strains unstated)	0.3-15 mg/plate	**Negative**, in the presence and absence of metabolic activation. This is an unpublished study described in a secondary source and no further information is available.	5
IVC	CHO	0.1-0.8 mg/ml (-S9), 0.08-0.4 mg/ml (+S9)	**Negative**, in the presence and absence of metabolic activation. This is an unpublished study described in a secondary source and no further information is available.	6
Gene mutation	CHO	Not stated	**Negative**. This is an unpublished study described in a secondary source and no further information is available.	7
SCE	CHO	Not stated	**Negative**. This is an unpublished study described in a secondary source and no further information is available.	7

Reproductive toxicity-Fertility

No data available

Reproductive toxicity

There was no evidence of reproductive toxicity in rats or rabbits following inhalation exposure to levels inducing slight maternal toxicity. It is noted that although shorter chain related substances are classified for reproductive toxicity, this toxicity decreases with increasing chain length such that there is no evidence of this hazard.

Species	Route	Dose	Exposure	Observations and remarks	Ref.
Rat	Inhalation	21, 41 and 80 ppm (0.12, 0.24 and 0.48 mg/L)	days 6-15 of gestation	The substance was tested up to approximately the saturated vapour concentration. Decreases in dam body weight gain, associated with decreases in food consumption, were observed in the medium and high dose groups during the exposure period. There was no evidence of reproductive toxicity.	4
Rabbit	Inhalation	21, 41 and 80 ppm (0.12, 0.24 and 0.48 mg/L)	days 6-18 of gestation	The substance was tested up to approximately the saturated vapour concentration. Decrease in absolute body weight during the exposure period was observed in the high dose animals. There was no evidence of reproductive toxicity.	4

ANSWERS:

Flammable liquid: Category 4
Acute oral toxicity: Category 4
Acute dermal toxicity: Category 3
Skin irritation/corrosion: Category 1C
Eye irritation/serious eye damage: Category 1
No other hazards are classified

SESSION 3 & 4:

CASE 2: AN EXAMPLE OF CLASSIFICATION FOR REPRODUCTIVE TOXICITY

Draft Assessment Report of FLONICAMID:
Initial risk assessment provided by the rapporteur Member State France for the new active pesticide ingredient Flonicamid, July 2005

Part B.6.6. Reproductive and developmental Toxicity: Page 242- 263 which can be found at the following links:

- Flonicamid_DAR_04_Vol 3_B6_part1_public.pdf (for pages 242-251)
- Flonicamid_DAR_05_Vol 3_B6_part2_public.pdf (for pages 252-263)

QUESTION:
Participants are requested to find the NOAELs for all available studies related to reproduction and fertility hazards and to suggest whether Flonicamid should be classified for reproductive toxicity hazards (Chapter 3.7 in the Purple Book) and if so how it should be classified.

ANSWER:
Based on study B.6.6.2.4: Reproductive toxicity study in rabbits and the effects seen in foetuses this should be classified as Category 2:

SESSION 6 & 7

CASE 1: PRACTICING ENVIRONMENTAL HAZARD CLASSIFICATION: A SERIES OF 10 SUBSTANCES

QUESTION: Classify each substance for environmental toxicity hazards

Example 1
Data:
- Fish LC_{50} 0.002mg/l
- Daphnia EC_{50} 4.6mg/l
- Algae E_rC_{50} 88mg/l

Example 2
Data:
- Fish LC_{50} no data
- Daphnia EC_{50} 5.6mg/l
- Algae E_rC_{50} 88mg/l

Example 3
Data:
- Fish LC_{50} 0. 8 mg/l (study with flaws)
- Daphnia EC_{50} 5.6mg/l
- Algae E_rC_{50} *88mg/l*

Example 4
Data:
- Fish Early life stage: NOEC 0.75 mg/l
- Daphnia Reproduction: NOEC 1.6 mg/l

- Rapid degradation

Example 5
Data:
- Fish Early life stage: NOEC 0.045 mg/l
- No data on degradation

Example 6
Data:
- Fish LC50 8.2 mg/l
- Daphnia EC50 56 mg/l
- Algae ErC50 122 mg/l
- Biodegradability <5%
- log Kow 2.1

Example 7 (Variation)

Data:
- Fish LC50 8.2 mg/l
- Daphnia EC50 56 mg/l
- Algae ErC50 122 mg/l
- Daphnia reproduction NOEC > 1mg/l
- Biodegradability <5%
- log Kow 2.1

Example 8 (Variation)
Data:
- Fish LC50 8.2 mg/l
- Daphnia EC50 56 mg/l
- Algae ErC50 122 mg/l
- Fish Early Life Stage NOEC > 1mg/l
- Biodegradability <5%
- log Kow 2.1

Example 9
Data:
- Fish LC50, Daphnia EC50, Algae ErC50 all > water solubility
- Water solubility 35 mg/l
- Biodegradability <5%
- log Kow 2.1

Example 10
Data:
- Fish LC50, Daphnia EC50, Algae ErC50 all > water solubility
- Water solubility < 1mg/lmg/l
- Biodegradability <5%
- log Kow 6

ANSWERS

ANSWER Example 1:
Classification: *Acute aquatic toxicity Cat 1 (see Table 4.1.1)*
M-factor: *100 (s. Table 4.1.5)*
Hazard statements: *H400=Very toxic to aquatic life*
Rationale for classification:

The LC50 in a valid study is below the cut-off level of <= 1 mg/l, and thus the criteria are clearly fulfilled.
Remark: Classification with respect to chronic toxicity generally will be performed if respective appropriate chronic data are available. Using a conservative approach Cat 4 could be assigned if there is some grounds for concern in absence of data (see decision logic 4.1.5.2.1)

ANSWER Example 2:
Classification: *Acute Cat 2*
Rationale: (s. Table 4.1.1 a) and refer Example 1

ANSWER Example 3:
Classification: Acute Cat 2 NB: Application of a very conservative approach would lead to Cat 1
Rationale: Based on the lowest valid value of 5.6 mg/l the criteria for Cat 2 are fulfilled
Proposals for proceeding:
- Evaluate the the Fish study in order to decide if it is really in total invalid and not usable even in part
- Perform a new fish study in order to clarify the toxicity in this species (Not required by GHS)

ANSWER Example 4:
Classification: *Chronic Cat 3.*
Rationale: s. Table s. 4.1.1 b. ii. For Acute toxicity no data available, thus classification not possible

ANSWER Example 5:
Classification: *Cat 1*
Rationale: Assumption not readily biodegradable. Therefore Table 4.1.1(b) ii has to be applied.

ANSWER Example 6:
Classification: *Acute and chronic aquatic toxicity Cat 2*
Rationale:
Acute toxicity >1 and <=10 mg/l (Table 4.1.1 a)
Not readily biodegradable, therefore Table 4.1.1b (iii) to be used
Log Kow not taken into account

ANSWER Example 7:
Classification: *Acute and chronic Cat 2*
Rationale:
Acute Cat 2 from Fish data and table 4.1.1a
Not readily biodegradable so this combined with acute data for fish gives chronic 2
log Kow not taken into account, No BCF
Chronic data NOEC > 1mg/l (daphnia) cannot be used since not from species for which acute classification is based on (fish)

ANSWER Example 8:
Classification: *Acute Cat 2, but no classification for chronic*
Rationale:
- Acute fish data gives Cat 2
- Not readily biodegradable
- log Kow not taken into account, No BCF
-Chronic data NOEC > 1mg/l (fish) are used for declassification since from same species for which acute classification is based on (fish). (see Table 4.1.2and Decision logic 4.1.5.2.3). Otherwise chronic classification would have been requested due to no ready biodegradability

ANSWER Example 9:
Classification: *Acute and chronic no classification*
Rationale:
- Acute toxicity values > water solubility
- Not readily degradable, but log Kow< 4 nor a BCF
- No chronic data
(see Table 4.1.1 (c)

ANSWER Example 10:
Classification: *Chronic Cat 4*
Rationale:
- Acute toxicity values > water solubility
- Not readily biodegradable and log Kow > 4; no BCF data
- No chronic data
See Table 4.1.1 (c) and Decision logic 4.1.5.2.3

CASE 2: MIXTURE TO BE CLASSIFIED FOR ENVIRONMENTAL TOXICITY

A mixture is made up of the following components

Name	%	Acute LC_{50} (mg/l)	Rapidly degradable?	Bioaccumulation?
Component A	80	None	No	No
Component B	10.5	2	Yes	No data
Component C	3.4	8	No	No
Component D	1	None	Yes	No
Component E	5.1	50	Yes	No

QUESTION:
Classify the mixture using the summation method and comment on the limitations of the classification you derive.

ANSWER:
1. No class 1 components so classification as class 1 not possible
2. Class 2: sum of the % of components in class 2: 10.5% +3.4% = 13.9% not class 2
3. Class 1,2, 3:
   (M X class 1 X 100) + Class 2 X 10 + Class 3
   (10 X 13.9) + 5.1 = 144.1 so class C
4. Matters to consider : chronic eco-toxicity, absence of bioaccumulation data for one component

SESSION 6 & 7

CASE 3: PRACTICING ENVIRONMENTAL HAZARD CLASSIFICATION: A COMPLEX PAINT MIXTURE

QUESTION: Classify the following paint mixture

Ingredient	%	GHS-Classification of ingredients	Relevant ingredient	M-Factor (M) <1 on basis of available data
Pigmentgreen XYZ	0,2	Aqu.chron. Cat 3; H 412	No; < 1%	NA*
Cyclohexane	0,15	Aqu. akut Cat 1; H 400 Aqu. chron. Cat 1; H 410	Yes; > 0,1 % Yes; < 0,1 %	None based on data None based on data
Propargylalkohol	0,4	Aqu. chron. Cat 2; H 411	No; < 1%	NA*
Tetrahydrthiophene	5,5	Aqu. chron. Cat 3; H 412	Yes; > 1%	NA*
2-Naphthol	24,9	Aqu. acute Cat 1; H 400	Yes; > 0,1 %	None based on data
4-(4-Tolyloxy)biphenyl	21	Aqu. chron. Cat 4; H 413	Yes; > 1%	NA*

***NA= Not applicable since not classified in Cat 1**

Procedure:
- No test data for the mixture as a whole so cannot classify directly
- No test data for similar mixtures, there for Bridging principles not applicable
- No complete data sets for the ingredients

ANSWER:

Summation method (§ 4.1.3.5.5) on basis of classified ingredients

1.Acute aquatic toxicity (Table 4.1.1):

Cat 1: Sum relevant Cat 1- ingredients x M) >= 25%

0,15%x1 + 24,9%x1 = 25,05% → **Cat 1**

2.Chronic aquatic toxicity (Table 4.1.2):

Cat 1: Sum (relevant chronic Cat 1- ingredients x M)>= 25%

0,15x1 < 25% →**No Classification (NC)**

Cat 2: Sum (M x 10x rel. chron. Cat 1-ingredients) + rel. chron. Cat2-ingredients >= 25%

1x10x0,15 + 0= 1.5 < 25% → **NC**

Cat 3: Sum (Mx100xrel. Chron. Kat 1-ingredients)+ (10x rel. chron. Cat2-ingredients) + rel. chron. Cat 3-ingredients)

1x100x0,15 +0+5.5 = 20,5 < 25% (Remark: The Cat 2-ingredient is no relevant ingredient according to EU-GHS; see above) → **NC**

Cat 4: Rel. chron. Cat 1-ingredients+ rel. chron. Cat 2-ingrdients + rel. chron. Cat 3-ingredients rel. chron. Cat 4-ingredients

0,15 +0 + 5,5 + 21 = 26,65 >25% → **Cat 4**

SESSION 9 & 10

CASE 1: PRACTICING PHYSICAL HAZARDS CLASSIFICATION: A SET OF 5 EXAMPLES

QUESTION: Classify the following substances for the hazard mentioned

Example 1 : Pyrophoric Liquids
Data:
- Suspected to be pyrophoric
- Test 1: Addition to diatomaceous earth in an open porcelain cup does not cause ignition within 5 min
- Test 2: Addition of 0.5 ml to a filter paper : charring started after 5 min and 20 sec
- Test 3: Addition of 0.5 ml to a filter paper: ignition at 4 min ant 50 sec

Example 2: Oxidising Gases
Data:
Composition: 5 % O2 + 70% N2 + 0.5% O3

Example 3: Water reactive Substances & Mixtures
Data:
Maximum rate 11 l/kg substance of a flammable gas per hour at ambient temperature. No spontaneous ignition

Example 4: Corrosive to Metals
Data:
Mass loss after 10 days 21%

Example 5: Self-heating
Data:
Tests with packages of 400 litres:
1. A positive result using a 100 mm sample cube at 140 °C.
2. A negative result using a 100 mm sample cube at 100 °C.
3. A negative result using a 25 mm sample cube at 140 °C.

ANSWER Example 1:
Classification: *Cat 1*
Rationale: In one valid test (No 3) the criteria for classification are met; see Table 2.9.1; Decision logic 2.9

ANSWER Example 2:
Classification: *Cat 1*
Rationale: Use guidance in § 2.4.4.2; Decision logic 2.4:
5%x1 + 0 0.5%x40=25 > 21

ANSWER Example 3:
Classification: *Cat 3*
Rationale: The criteria for Cat 3 (>= 1l/kg/h) are fulfilled , but not the criteria for Cat 2 (>020l/kg/h)

ANSWER Example 4:
Classification: *Cat 1*

ANSWER: Example 5:

Classification: *None*
Rationale:
- Cat 1: Exclusion since package volume <450 l
- Cat 2a: Exclusion since test 3=negative and volume <3 m3
- Cat 2b: Exclusion since volume < 450 l
*- Cat 2c: Exclusion since test 2 negative; thus condition " …**and** a positive results is obtained in a test using a 100 mm sample at 100 °C " is not fulfilled*
Rationale: Use f the Table with Mass loss (see Presentation) and interpolation allows the conclusion that after 14 days the mass loss would be > 26.5%

SESSION 9 & 10

CASE 2: PRACTICING PHYSICAL HAZARDS CLASSIFICATION: 3 LINKED EXAMPLES OF SUBSTANCES AND MIXTURES

Case example 1a – physical hazards

1. A mixture made up of the following components
   Ammonium Nitrate 71%
   Water 16%
   Diesel fuel 8%
   An emulsifier composed of
   Oleic Acid 3%
   Sodium Hydroxide (50% aq. soln.) 2%

The mixture has a paste like consistency which does not meet the GHS definition of a liquid.

QUESTION:
Considering the components, identify the possible physical hazard classifications for this mixture, providing reasons for your choice.

Case example 1b - physical hazards

1. The ammonium nitrate based substance referred to in case example 1 is subjected to the following tests from the UN Manual of Tests and Criteria with the results shown.
   a. The substance as described is intended to provide one component of a substance which forms part of an explosive chain, but is itself not manufactured to produce an explosive or pyrotechnic effect
   b. The following results are obtained when the substance is subject to UN test series 8 (see figure 10.4 UNRTDG Manual of Tests and Criteria 4th Edn or Figure 2.1.4 GHS 3rd Edn)
   c. Test 8(a) – substance is reported as thermally stable
   d. Test 8(b) (large scale gap test) – substance is reported as not too sensitive to shock to be accepted as an oxidising liquid or oxidising solid
   e. Test 8(c) (Konen test) – substance is reported as not too sensitive to heat under confinement
   f. When tested using the UN standard test methods for oxidising solids the following results were obtained

   The mean burn time of the substance when mixed with cellulose and ignited as prescribed in UN Test Series O.1 is as follows
      i. Greater than the mean burn time of a 3:2 mixture of potassium bromate and cellulose
      ii. Less than the mean burn time of 2:3 mixture of potassium bromate and cellulose

QUESTION:
Determine the physical hazard classification for the substance, explaining how you obtained the classification.

2: The manufacturer of the ammonium nitrate based substance previously described changes to emulsifier to a proprietary form. This emulsifier now makes up less than 2% of the total mixture but the ratio of other ingredients to each other remains unaltered. As the regulator you insist that the substance is re-tested by the same certified laboratory that previously tested this substance. The laboratory reports the following results:

When the substance is subject to UN test series 8 (see figure 10.4 UNRTDG Manual of Tests and Criteria 4th Edn or Figure 2.1.4 GHS 3rd Edn)

a. Test 8(a) – substance is reported as thermally stable
b. Test 8(b) (large scale gap test) – substance is reported as not too sensitive to shock to be accepted as an oxidising liquid or oxidising solid
c. Test 8(c) (Konen test) – substance is reported as too sensitive to heat under confinement

The laboratory then subjects the modified substance to UN test series 5 (for explosive hazard). The substance 'fails' the shock test and thermal test (i.e. is insufficiently sensitive to mechanical shock and does not show any tendency to transition from deflagration to detonation). However the substance does detonate when subject to test 5(c) (package exposed to intense fire over an extended period)

QUESTION:
Classify the modified substance, explaining your reasoning.

Case example 2:
You are presented with a number of small round disks about 30mm in diameter apparently made of a soft metal of some sort. The disks are marked "railway fog signal."

QUESTION:
Classify these articles, explaining how you derived the classification.

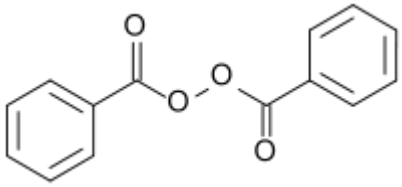
Case example 3: Physical hazards
Jet A and Jet A-1 fuel are the commonest forms of jet aircraft fuel in general use. This fuel is described in the open literature as having the following Flash point and boiling point range:
Flash point 38^{0}C – 66^{0}C; Boiling point 160^{0}C - 300^{0}C

In certain parts of the world Jet B fuel is used in aircraft operations. Jet B fuel has the following flash point and boiling point ranges:
Flash point < -31^{0}C; Boiling point 50^{0}C - 270^{0}C

QUESTION:
Classify Jet B fuel and comment on the consequences of the classification in comparison with Jet A fuel.

Case example 4 : physical hazards
Benzoyl peroxide (IUPAC name dibenzoyl peroxide) is used widely in various formulations to

- Initiate polymerisation reactions
- Treat certain skin conditions
- As a bleach



QUESTION:
Given the molecular structure of dibenzoyl peroxide (as shown)

1. Calculate the lowest concentration of this substance in an inert diluent which would be classified as an organic peroxide

2. Benzoyl peroxide is to be shipped as a 38% dispersion in water for use as a polymeriser in the fibre reinforced composite boat building industry. Determine its physical hazard classification.

ANSWER Example 1a:
Possible classifications

- Explosive – question is this substance intended as an explosive?
- Oxidising substance - ammonium nitrate component
- Flammable – discuss whether or not the emulsified diesel fuel would ignite]

Not intended as explosive so not classified as explosive and in any case test series 8 results show no explosive effect as defined.
Substance is not a liquid so consider test for oxidising solid chapter 2.14 GHS
Substance is class 2 oxidising solid]

ANSWER Example 1b:
The substance Ammonium nitrate emulsion (ANE) is an explosive precursor and a very common way of making explosives which can be easily handled/transported to the detonation site. Test series 8 is designed specifically to test for explosive effect in this mixture. Following through this test series shows that the modified substance should be considered for classification as an explosive. Test series 5 then indicated that the substance should be classified class 1.5 – an explosive.

ANSWER Example 2:
These are articles so only possible classification is as an explosive.

- Check to see if the listed articles in the orange book list something like this. Look first in the alphabetical index in volume 1 UNRTDG.
  Ans. yes there are entries for "signals railway track explosive" with transport classifications and UN numbers
- Use UN number(s) 0192, 0492, 0193, 0493 with different classes. Look up these number is in the dangerous goods list (part 3 volume 1) for further information
- Possible classifications are class 1.1 class 1.3, class1.4
- Consider intended use – fog signals are intended to be placed on a railway line to be run over by a train and produce a noise to warn of fog on the line ahead. – minor blast or projection hazard so class 1.3

Discussion points

- Classification for explosives requires information about the intended (designed) use
- Articles with similar descriptions require more information for effective classification.]

ANSWER Example 3:
Jet fuel B is Flammable liquid class 2. (Jet fuel A is class 3) As the flashpoint is at a very low temperature, jet fuel B would be easily ignited in use and so require more precautions. So why use Jet fuel B? Ans. for this very reason – Jet engines can be started at very cold temperatures with Jet fuel B. Commonly used in Canada – especially in the winter.

ANSWER Example 4:
Solve formula in section 2.15.2 GHS for concentration of benzoyl peroxide – no hydrogen peroxide present.

1 = 16 X C / (MW benzoyl peroxide) [242]
Lowest concentration = 15.13%

Look up benzoyl peroxide in table of section 2.5.3.2.4 UNRTDG. 38% benzoyl peroxide is < 42% as stable dispersion in water so UN number is 3109. Look up this UN number in the table in part 3 dangerous goods list classification is organic peroxide type F]

SESSION 13 & 14

CASE 1: PRACTICING HAZARD COMMUNICATION AND SDS PREPARATION

[Data abstracted with permission from the ERMA New Zealand application for reassessment under the NZ Hazardous Substances and New Organisms (HSNO) Act for methylated spirits.]

Table: Chemical and Physical Properties of a methylated spirits mixture

Chemical Name	**Methylated spirit**	**Components**			
		Ethanol 96%	**Methanol 2.0%**	**Denatonium benzoate 10 ppm**	**Methyl violet 1.5%**
Appearance (colour, odour, physical state or form)	Purple-coloured liquid when dyed, colourless without dye; alcoholic odour.	Colourless liquid. Pleasant alcoholic odour detectable between 49 and 716 ppm in air	Colourless liquid with a characteristic pungent odour detectable between 4 and 6000 ppm in air	White crystals, odourless, bitter taste.	Blue/green crystals.
pH	Not applicable	NA	NA	NA	NA
Density	0.812	0.789	0.791	No data located	No data located
Vapour pressure A3	5.86 kPa @ 25 °C	7.87 kPa @ 25 °C	16.8 kPa @ 25 °C	NA	NA
Melting / Boiling point	77°C (b.p.)	78.3°C (b.p.)	64.7°C (b.p.)	168°C (m.p.)	137°C (m.p.)
Solubility in water	miscible	miscible ≥10 g/100 mL at 23 °C	miscible	soluble	soluble
Flash point	13°C	13°C	12°C	NA	NA

Chemical Name	Methylated spirit	Components			
		Ethanol 96%	**Methanol 2.0%**	**Denatonium benzoate 10 ppm**	**Methyl violet 1.5%**
Octanol/Water partition log Kow	NA	-0.32	-0.77	1.78	0.43

Additional Information:
Denatonium benzoate and methyl violet, when present, are below the relevant classification thresholds of the GHS as no evidence could be located of adverse effects from these components below the classification thresholds.

Denatonium benzoate and methyl violet are both present at relatively low levels. Although for certain hazards either or both may be below the cut-off value for being considered a "relevant ingredient" for other they may not. Solely for practical reasons and for making this exercise not overly complicated they do not need to be considered further in the hazard classification of this exercise.

QUESTION:
Classify this mixture for all possible hazards listed below. Where information is available on the substance, this is used for classification. When information on the substance is not available, classification of the hazardous properties is based on the major components, ethanol and methanol.
Prepare an SDS for this mixture

Possible hazards:

Physical Hazards:
- Explosiveness
- Flammability
- Flammable Gases and Aerosols
- Flammable Liquid
- Liquid Desensitised Explosives, Flammable Solids, Oxidisers; Metallic Corrosives

Biological Hazards
- Human toxicity (acute and chronic)
- Environmental toxicity(acute and chronic)

Physical hazards

See data in table above for information for classification

Biological hazards

Human toxicity

Metabolism and kinetics

- Ethanol is metabolised by the enzyme alcohol dehydrogenase (ADH) to acetaldehyde, and then by the enzyme acetaldehyde dehydrogenase to acetate which becomes incorporated into normal cellular metabolic cycles.

- A key study in relation to toxicity of methanol is the report by an NTP-CERHR Expert Panel on the reproductive and development toxicity of methanol, published in April 2002. This report also includes evaluation of data in relation to other aspects of methanol metabolism and toxicity.
- Methanol is metabolised by a three-step process, initially being converted by ADH in the liver to formaldehyde and then to formic acid (formate) by another enzyme formaldehyde dehydrogenase. The formate is then converted to carbon dioxide and water, a process that requires the presence of folic acid (folate). Alcohol dehydrogenase has an approximately nine-fold greater affinity for ethanol than for methanol. This means that when both ethanol and methanol are present in the body at the same time the ethanol is metabolised by ADH at approximately nine times the rate that methanol is metabolised, which will tend to reduce the toxic effect of formaldehyde generated from methanol.
- Some people may eliminate a proportion of the methanol through a catalase system without the production of formate. This system of elimination in the lungs and kidneys may be more developed in some patients who chronically abuse methanol.

Acute Oral Toxicity

Ethanol
Many studies have been conducted on the acute oral toxicity of ethanol. A wide range of values are reported for the rat (in the range of LD_{50} ~ 6300-12,000 mg/kg bw).
An LD_{50} (mouse) of 9488 mg/kg bw is adopted as representative of reported oral toxicity values for ethanol.

Methanol
There are numerous studies on the toxicity of methanol, but data that can be directly attributable to its toxicity to humans is limited. Humans and non-human primates are uniquely sensitive to its toxic effects. Overall methanol has a low acute toxicity to non-primate animals. The LD_{50} values and minimal lethal doses after oral exposure range from 7000 to 13,000 mg/kg bw in the rat, mouse, rabbit and dog and from 2000 to 7000 mg /kg bw for the monkey.

The normal blood concentration of methanol from endogenous sources is less than 0.5 mg/L (0.02 mmol/L), but dietary sources may increase the levels. Generally, central nervous system (CNS) effects appear at blood methanol levels > 200 mg/L (6 mM); ocular symptoms appear above 500 mg/L (16 mM), and fatalities have been reported in untreated patients with initial methanol levels in the range 1500-2000 mg/L (47-62 mM).

For the purpose of this classification, another value was found of LD_{50} (mouse) of 870 mg /kg bw for methanol. This value was used to provide an estimate of the maximum acute oral toxicity of methylated spirits.

The minimum lethal dose of methanol for humans in the absence of medical treatment is between 300 and 1000 mg /kg bw.

Acute Dermal Toxicity
No data is available for the dermal toxicity of methylated spirits. No data is available for the dermal toxicity of ethanol. The dermal LD_{50} for methanol (rabbits) of 20,000 mg/kg bw exceeds the classification threshold of 5000 mg /kg bw.

Acute Inhalation Toxicity

Ethanol LC_{50} (mouse):	39 mg/L (4 hours)
Methanol LC_{50} (mouse):	64,000 ppm (4 hours) ≡ 83.4 mg/L

Skin Irritation/Skin corrosion

These two subclasses are mutually-exclusive and are addressed together, i.e. if a substance is classified as a skin irritant (reversible adverse effects) it cannot also be classified as a skin corrosive (irreversible adverse effects), and vice versa.

No test data is available for methylated spirits.

Test data referred to in relation to skin irritancy indicates that ethanol and methanol are not corrosive to skin. Methylated spirits is thus not classified as corrosive to skin.

Test data for ethanol (rabbit) obtained following the OECD test guideline 404 "Acute Dermal Irritation/Corrosion", gave a mean Draize score for erythema of 1.0 after 1 and 24 hours. Scores for erythema were 0 at all other times. This is below the threshold for classification under subclass 6.3.

Where no testing on the substance as a mixture has occurred, consideration should be given to whether any of the components may enhance skin irritation or have an additive effect on a component with low skin irritation. For example, a component that degreases the skin will enhance the action of a skin irritant.

Eye Irritation/Serious eye damage

These two subclasses are mutually-exclusive and are addressed together, i.e. if a substance is classified as an eye irritant (reversible adverse effects) it cannot also be classified as an eye corrosive (irreversible adverse effects), and vice versa.

Test data referred to in relation to eye irritancy indicate that ethanol and methanol are not corrosive to ocular tissue.

Ethanol is described as moderately irritating based on average scores for redness of the conjunctivae of 2.5 (at 24 hours) and 2.61 (48 hours), with significant ocular lesion persisting for at least 24 hours. Methanol is described as a moderate irritant to the eyes as solution or vapour. A broad range of ocular effects have been associated with longer-term exposure to lower levels of methanol.

Sensitisation

Respiratory Sensitisation
No evidence could be located for respiratory sensitisation in humans for either methanol or ethanol.

Skin Sensitisation
Tests with ethanol (95%) and methanol indicate that neither is sensitising to the skin.
In a modified Magnusson-Kligman maximization test with 10 female guinea-pigs no sensitization was found after intracutaneous or percutaneous induction and challenge with 50% methanol solution in distilled water or with Freund's adjuvant. No skin irritation effects were observed.

Mutagenicity

Ethanol
There are some studies that suggest ethanol causes DNA damage, but at excessive doses. The UK Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM) in 1995 concluded that "the consumption of alcoholic beverages does not provide any significant concern with respect to their mutagenic potential." The COM concluded that there was no evidence to suggest that ethanol had mutagenic potential. With regard to the metabolite acetaldehyde the COM concluded there was evidence that acetaldehyde had "…a direct acting mutagenic potential *in vitro* but would only be

expected to have the potential of *in vivo* activity at sites where it is not rapidly metabolised to acetic acid."

In May 2000, the COM reaffirmed its opinion with respect to ethanol and acetaldehyde reached in 1995, agreeing that that conclusion with regard to acetaldehyde should take into consideration the rapid metabolism of acetaldehyde to acetic acid.

Methanol
The most recent study, and the one considered key for this classification is the NTP-CERHR Expert Panel Report. This is an extensive review of the information available on the reproductive and developmental toxicity of methanol.

In relation to genetic toxicity, the report states that the "results of *in vivo* genetic toxicity assays in mice have been mixed, with both negative and positive results in micronuclei formation and chromosomal aberration assays and negative results in SCE (sister chromatid exchange) and murine mutagenicity assays. Negative results were obtained in the majority of in vitro assays that examined mutations in bacteria and yeast, DNA repair in bacteria, and SCE and cell transformation in mammalian cells; positive results were obtained in a chromosomal mal-segregation assay in yeast only in the absence of metabolic activation and in a mutation assay in mammalian cells only with metabolic activation. IPCS (the International Programme on Chemical Safety) concluded that "The structure of methanol (by analogy with ethanol) does not suggest that it would be genotoxic".

Carcinogenicity

There is no entry specifically for ethanol or methanol in IARC, the California EPA or the National Toxicology Program 10th Report on Carcinogens (U.S. Department of Health and Human Services Public Health Service).

The International Agency for Research on Cancer (IARC) has determined that there is sufficient evidence for the carcinogenicity of alcoholic beverages in humans (thus classified as IARC Group 1) but it is not known what role if any ethanol plays in this. The causative agent could be ethyl carbamate or some other product of fermentation. However, ethanol is metabolised to acetaldehyde and this is a suspected human carcinogen.
The NTP-CERHR report on methanol concludes that there are no reliable data for evaluating its carcinogenicity.

Reproductive or Developmental toxicity

Ethanol
Doses used in animal studies are above the normal thresholds for classification, and human developmental effects are difficult to evaluate from animal models.

There is a large body of data on foetal alcohol syndrome arising from consumption of alcoholic beverages, but these effects may be secondary to maternal toxicity; some of the effects may be attributable to ethanol or to other congeners in the beverages.

Methanol
The Expert Panel, in its report on the reproductive and developmental toxicity of methanol, recognised the need to consider species differences in methanol metabolism and toxicity in its evaluation of the risk to reproduction posed by human exposure to methanol. Some observations suggest there may be overlap between exposures resulting in clinical signs of acute toxicity and those that might result in developmental toxicity in humans.

Toxicity data in monkeys provides suggestive but insufficient evidence that adverse developmental effects may occur in primates exposed by inhalation to methanol at maternally non-toxic doses.

The Expert Panel concluded that there is insufficient evidence to determine if the human foetus is more or less sensitive than the most sensitive rodent species (i.e. mouse) to methanol teratogenesis.

The blood methanol levels associated with reproductive toxicity in rodents are 700 mg/L and greater. Levels of this magnitude in humans would be associated with methanol (formate) toxicity.

The Expert Panel did note that other factors (e.g. maternal folate status) may predispose humans to developmental toxicity at lower blood methanol concentrations (<100 mg/L).

The Expert Panel concluded that developmental toxicity was the most sensitive endpoint of concern with respect to evaluating the risk to reproduction posed by methanol exposure in humans.

Other conclusions of relevance from the report are:

- The Expert Panel has minimal concern that methanol exposures resulting in low (<10 mg/L) blood methanol concentrations may result in developmental toxicity in humans. These methanol concentrations have been associated with consumption of a common American diet and with work exposures that are below U.S. occupational exposure limits.
- The Expert Panel has concern that methanol may be a developmental toxicant in pregnant women following exposure to high levels of methanol.
- The Expert Panel has negligible concern that methanol may be a male reproductive toxicant in humans under dietary conditions or occupational exposure that result in blood methanol concentrations <10 mg/L. However, there were not sufficient data to rule out the possibility that high, acutely toxic, doses of methanol might affect male reproduction.
- The Panel determined that the data are insufficient to assess whether or not methanol is a reproductive hazard in females.

The panel identified critical data needs to provide information that could substantially improve an assessment of human reproductive risks. This included studies on exposure from all sources, translation of studies from Japanese studies and reanalysis of some statistical data. Data from concurrent exposures to methanol and ethanol were also considered to be helpful.

An earlier report on methanol toxicity records reproductive and developmental effects arising from inhalation exposure of pregnant rodents for 7 hours per day to methanol vapour. These occurred at doses of 6.5 mg/L and up to 26 mg/L. Some maternal toxicity occurred at the highest level, and at 9.8 mg/L there was increased embryo/foetal death. [The HSNO upper threshold for classification in this subclass is 20 mg/L in a 6 hour/day exposure]. This report also referred to increased incidences of exencephaly and cleft palate in mice exposed to methanol vapour concentrations below the level at which maternal toxicity was observed.

As the Expert Panel notes, more work is required to resolve some aspects of reproductive or developmental toxicity. In endeavouring to determine the classification of methanol, these points are considered to be key:

- the high methanol levels at which adverse effects were observed in test species (rodents);
- the possibility of overlap between exposures resulting in clinical signs of acute toxicity and those that might result in developmental toxicity in humans; and

- the possibility that maternal folate status may predispose humans to developmental toxicity at lower blood methanol concentrations (<100 mg/L).

Specific Target Organ Toxicity

Ethanol
Ethanol is a central nervous system (CNS) depressant, and there is well-established evidence of the effects of alcohol consumption commonly described as intoxication. Chronic consumption of large amounts of ethanol over an extended period may lead to hepatic cirrhosis. Foetal Alcohol Syndrome (FAS) was named originally to describe the presumed cause of a range of anomalies found in children of severely and chronically alcoholic women. The full pattern of FAS usually occurs in children of chronic alcohol abusers, most often in women who drink four to five drinks or more daily, but it has occurred in women who drink less. The description Foetal Alcohol Effects (FAE) is sometimes used to describe less extensive dysmorphology suggested to be associated with lower levels of ethanol drinking. Less is known about the long-term outlook for children with FAE than about those with FAS. It is said that it can occur in babies of women who drink moderately or lightly during pregnancy.

The effects cannot be totally separated from maternal toxicity, but the doses required for CNS and hepatic effects are above the repeat dose cut-off level for classification (100 mg /kg bw). There is no data available for target organ-related effects through dermal, inhalation or other routes.

Methanol
Nearly all of the available information on methanol toxicity in humans relates to the consequences of acute rather than chronic exposures. The vast majority of poisonings appear to have occurred from drinking adulterated beverages and from methanol-containing products (such as methylated spirits).

Humans (and non-human primates) are uniquely sensitive to methanol poisoning. The toxic effects are characterised by formic acidaemia, metabolic acidosis, ocular toxicity (including temporary or permanent blindness), nervous system depression, coma and death. Ocular toxicity is linked to the increase in blood formate concentrations; the minimum dose causing permanent visual defects is unknown.

The adverse effects of methanol intake may be increased in persons who are folate-deficient as the subsequent metabolism of formate to carbon dioxide is through the folate-dependent pathway. Folate deficiency may arise in a number of circumstances, including amongst those who have a history of chronic alcohol abuse.

In situations where ethanol and methanol are consumed together (or where dosage with ethanol is used as the treatment for methanol poisoning), eventually the ethanol will be completely metabolised, thus allowing ADH metabolism of methanol to formaldehyde and ultimately formic acid. There is a clear inference that it is the total dose of methanol that is the critical factor, rather than the concentration of methanol in the product consumed (such as methylated spirits).

The evidence for a causal relationship between exposure of humans to methylated spirits and the development of target organ/systemic toxicity, particularly ocular toxicity is thus well-established.

Environmental toxicity

Aquatic Effects
Test data is not available for aquatic toxicity of methylated spirs, so the major components are considered separately.

Ethanol
Studies indicate that the aquatic acute ecotoxicity to fish exceeds the thresholds for classification.

Data is varied for crustaceans, with some toxicity values falling within the 1-10 mg/L range. The acute ecotoxicity for Daphnia magna is 9.3 mg/L (48 hr LC_{50}), and the chronic ecotoxicity 9.6 mg/L (NOEC).

No data is available for algae or other species.

Ethanol is readily biodegradable. Its low octanol/water partition coefficient indicates that it will not bioaccumulate.

Photolysis experiments indicated a half-life in water of 0.27 days.

There is no data indicating design or use of ethanol as a biocide, and ethanol is not on the EU biocide list.

Methanol
Ecotoxicity values for methanol, where available, exceed the upper threshold for classification. It is not persistent and does not bioaccumulate.

Methanol is included in the EC biocide list for the following product types: human hygiene, biocidal products; private area and public health area disinfectants; food and feed area disinfectants; fibre, leather, rubber and polymerised materials preservatives; slimicides (i.e. algicidal); embalming and taxidermist fluids.

ANSWERS

Classification:

Flammable liquid class 2

Acute toxic class 5

Eye irritant class 2A

Human reproductive toxicant
Category 2

Specific target organ toxicity
Category 2

Ecotoxic class 4