EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B - Director

Brussels, 14 March 2016
B4/CRP/cvi/D(2003) 341126

Subject: Endocrine Disrupters –
Stakeholder consultation meeting, 15-16 October 2003, Brussels

Dear Dr [redacted]

In the context of the Community Strategy for Endocrine Disrupters (COM(1999)706 and COM(2001)262), the Commission is in the process of implementing a priority list of substances for further evaluation of their role in endocrine disruption.

An informal consultation meeting with stakeholders will take place **on 15-16 October 2003, starting at 10.00**. The main objectives of the meeting are to consult stakeholders on two studies recently launched by the Commission on candidate endocrine disrupting substances, and to update stakeholders on recent Commission R&D activities and policy discussions relevant to endocrine disrupters (A draft agenda is attached). I would anticipate that agenda item 2 is likely to constitute the majority of the discussion on 15 October.

I would like to invite you, or one of your staff, to participate in this meeting in order to present the results of the study "Endocrine Disrupters: gathering on information on 435 substances with insufficient data" (which BKH was contracted to perform) and to provide technical support during the discussions. The meeting will take place at the following venue:

Avenue de Beaulieu 5, B-1160 Auderghem (Ground floor, Salle C)

Travel expenses, in accordance with normal Commission rules (ie. economy fare + a daily allowance of 150 EURO/per day) will be reimbursed for one person.

For further information you may contact the desk officer responsible for endocrine disrupters, Ms [redacted], tel +32.2.2[redacted], fax: +32.2.299.43.62, e-mail: [redacted]@cec.eu.int.

Yours sincerely,

[signed]
[redacted]

Encls. Draft Agenda

[redacted]
2628 XG Delft
Postbus 5094 - 2600 GB Delft

EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B - Director

Brussels, 01 October 2003
B4/CRP/cvi/D(2003) 341170

NOTE FOR THE ATTENTION OF **MR [redacted], DG ENTR/E.3**
MR [redacted], DG SANCO/B.3
MR [redacted], DG SANCO/C.7
MR. [redacted], DG SANCO/E.1
MR [redacted], DG RTD/E.2
MR [redacted], DG RTD/I.3
MR. [redacted], DG JRC.A.1
MR [redacted], JRC.I
MR [redacted], DG JRC.I.2
MR [redacted], DG JRC.I.3
MR. [redacted], DG JRC.I.5
MR. [redacted], EXECUTIVE DIRECTOR-EFSA.

Subject: **Endocrine Disrupters –**
Stakeholder consultation meeting, 15-16 October 2003, Brussels

In the context of the Community Strategy for endocrine disrupters (COM(1999)706 and COM(2001)262), an informal consultation meeting with stakeholders will take place on 15-16 October 2003, Brussels, starting at 10.00. The meeting will take place in BU5, 0/C.

A draft agenda is attached.

You may wish to send a representative to this meeting, in which case I would request that you inform the meeting secretary, Ms [redacted], tel +32-2-296.[redacted], fax +32-2-299.43.62, e-mail [redacted]@cec.eu.int by **6th October 2003**.

Yours sincerely,

[signed]
[redacted]

Encl. Draft Agenda

Cc: [redacted], Directors DG ENV, HoU B.1, C.3, C.4, B4, [redacted], C. [redacted], [redacted] (DG ENV); [redacted] (DG ENTR), [redacted] DG SANCO), [redacted] (DG RTD); [redacted] (JRC); [redacted] (EFSA) [redacted], Cabinet Wallström

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.
Office: BU-5 2/117. Telephone: direct line (32-2) 2990409. Fax: (32-2) 2966233.

EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B - Director

Brussels,
B4/CRP/cvi/D(2003) 341120

NOTE FOR THE ATTENTION OF MS. [redacted] – HEAD OF UNIT C.3
MR [redacted] - – HEAD OF UNIT B.1
MR [redacted] – HEAD OF UNIT C.4

Subject : "Endocrine Disrupter Strategy" – Policy discussions relevant to EDs.

In the context of the Community Strategy for endocrine disrupters (COM(1999)706 and COM(2001)262), an informal consultation meeting with stakeholders will take place on 15-16 October 2003 in Brussels.

The main objectives of the meeting are to consult stakeholders on technical studies recently launched by the Commission on candidate endocrine disrupting substances, and to update stakeholders on recent Commission R&D activities and policy discussions relevant to endocrine disrupters (A draft agenda is attached.).

The topics identified includes:

-- Overall chemicals policy
-- Water Framework Directive
-- Thematic Strategy on Pesticides and Directive 91/414/EEC and
-- the study on endocrine disrupting chemicals in Drinking Water

I would like to invite you to nominate a delegate from your Unit in order to give a short-oral presentation (20-25 minutes) regarding each of the topics. For further information, you may contact the desk officer responsible for endocrine disrupters, Ms [redacted], tel +32-2-299 [redacted].

Thanks in advance for your collaboration,

Yours sincerely,

[redacted]

cc.: [redacted]

EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B - Director

Brussels, 14 March 2016
B4/CRP/cvi/D(2003) 341130

Subject: Endocrine Disrupters –
Stakeholder consultation meeting, 15-16 October 2003, Brussels

Dear Dr [redacted],

In the context of the Community Strategy for Endocrine Disrupters (COM(1999)706 and COM(2001)262), the Commission is in the process of implementing a priority list of substances for further evaluation of their role in endocrine disruption.

An informal consultation meeting with stakeholders will take place **on 15-16 October 2003, starting at 10.00**. The main objectives of the meeting are to consult stakeholders on two studies recently launched by the Commission on candidate endocrine disrupting substances, and to update stakeholders on recent Commission R&D activities and policy discussions relevant to endocrine disrupters (A draft agenda is attached). I would anticipate that agenda item 2 is likely to constitute the majority of the discussion on 15 October.

I would like to invite you, or one of your staff, to participate in this meeting in order to present the results of the study "Scientific evaluation of 12 substances in the context of the endocrine disrupters priority list of actions" (which WRc-NSF was contracted to perform) and to provide technical support during the discussions. The meeting will take place at the following venue:

Avenue de Beaulieu 5, B-1160 Auderghem (Ground floor, Salle C)

Travel expenses, in accordance with normal Commission rules (ie. economy fare + a daily allowance of 150 EURO/per day) will be reimbursed for one person.

For further information you may contact the desk officer responsible for endocrine disrupters, Ms [redacted], tel +32.2.299.[redacted], fax: +32.2.299.43.62, e-mail: [redacted]@cec.eu.int.

Yours sincerely,

[signed]
[redacted]

Encls. Draft Agenda

[redacted]
WRc-NSF, Henley Road, Medmenham, Marlow,
Buckinghamshire, SL7 2HD

EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B - Director

Brussels, 14 March 2016
B4/CRP/cvi/D(2003) 341128

TO REPRESENTATIVES OF INDUSTRY, NGOS AND OTHERS

Subject: Endocrine Disrupters –
Stakeholder consultation meeting, 15-16 October 2003, Brussels

In the context of the Community Strategy for Endocrine Disrupters (COM(1999)706 and COM(2001)262), I would like to invite you to an informal consultation meeting with stakeholders on **15-16 October 2003**, starting at **10.00.** The meeting will take place at the following venue:

5 Avenue de Beaulieu, B-1160 Auderghem (Ground floor, Room C)

A draft agenda is attached. The main objectives of the meeting are to consult stakeholders on two studies recently launched by the Commission on candidate endocrine disrupting substances, and to update stakeholders on recent Commission R&D activities and policy discussions relevant to endocrine disrupters.

No interpretation will be provided at this meeting. Travel expenses will not be reimbursed.

I would appreciate if you could confirm your participation to Ms [redacted], tel +32-2-296 [redacted], fax +32-2-299.43.62, e-mail [redacted]t@cec.eu.int by **1st October 2003**. For further information, you may contact the desk officer responsible for endocrine disrupters, Ms [redacted], tel +32-2-299 [redacted].

Yours sincerely,

[signed]
[redacted]

Encls. Annex 1 : Draft Agenda
Annex 2 : Invitation list – Member States
Annex 3 : Invitation list – Industry, NGOs and Others

ENDOCRINE DISRUPTERS

Stakeholder Consultation Meeting

Wednesday, 15 October 2003, 10.00–17.00
Thursday, 16 October 2003, 10.00-17.00

5 Avenue de Beaulieu, B-1160 Auderghem (Ground floor, Salle C)

DRAFT AGENDA

1. Welcome

2. Technical Studies funded by the Commission under the action "Establishment of a priority list of substances for further evaluation of their role in endocrine disruption"

   -- Study concerning in-depth evaluation of 12 candidate ED substances – Presentation and discussion

   -- Study concerning 435 candidate ED substances – Presentation and discussion

3. Other technical Studies funded by the Commission

   -- Study concerning "Information Exchange and International Co-ordination on Endocrine Disrupters" Presentation and discussion

   -- Other relevant studies – status update. Website / Drinking water

4. R&D on EDs under 5th Community R&D Programme – status update

5. Community policy discussions relevant to EDs

   -- Overall chemicals policy
   -- Water Framework Directive
   -- Thematic Strategy on Pesticides and Directive 91/414/EEC
   -- General Product Safety

6. OECD Testing Strategy

7. Endocrine Disrupters under the new Environment and Health Strategy.

8. Different approaches on EDs.

- Industry's view
- MS proposal

9. Special issues under the ED problem
   Mixtures
   Low dose and lower doses
   LPV

10. Tour de table

11. Any other business

12. Conclusions

ANNEX 3

INVITATION LIST - INDUSTRY, NGOS AND OTHERS
Informal Stakeholder Meeting on Endocrine Disrupters (15-16 October 2003)

Type of Organisation	*Name*	*Address*	*Tel - Fax - e-mail*
EEA/EFTA	[redacted]	Universität Zürich Institut für Pharmakologie Winterthurerstrasse 190 CH-8057 Zürich	T=+41.1.635.[redacted] F=+41.1.635.57.08 E=[redacted]@pharma.unizh.ch
EEA/EFTA	[redacted]	State Pollution Control Authority P.O. Box 8100 Dep Strønsveien 96 N-0032 Oslo 0663 Oslo	T=+47.22.573.[redacted] F=+47.22.676.706 E=[redacted]@sft.telemax.no
EEA/EFTA	[redacted]	State Pollution Control Authority P.O. Box 8100 Dep Strønsveien 96 N-0032 Oslo 0663 Oslo	T=47.2.257.[redacted] F=47.2.267.6706
EEA/EFTA	[redacted]	EFTA Secretariat Rue de Trèves 74 1040 Bruxelles	T=+32.2.289.1[redacted] F= E=[redacted]@secrbru.efta.be
IND	[redacted]	CONCAWE - The Oil Companies European Organisation for Environment, Health and Safety Bld du Souverain 165 B-1160 Bruxelles	T=+32.2.220.[redacted] F=+32.2.219.46.46 E[redacted]@CONCAWE.be
IND	[redacted]	UROMETAUX Avenue de Broqueville 12 B-1150 Bruxelles	T= +32.2.775.[redacted] F= +32.2.779.05.23 E=[redacted]@eurometaux.be
IND	[redacted]	EUROMETAUX Avenue de Broqueville 12 B-1150 Bruxelles	T=+32.2.775.[redacted] F=+32.2.779.05.23 E=[redacted]@eurometaux.be
IND	[redacted]	Bayer AG Leverkusen	T=+49.214.30-[redacted]

Type of Organisation	*Name*	*Address*	*Tel - Fax - e-mail*
		Corporate Center Governmental & Product Affairs (BGA-GPA) D-51368 Leverkusen	F=+49.214.30-52762 E=[redacted]@bayer-ag.de
IND	[redacted]	CEFIC Av. E. Van Nieuwenhuyse 4 bte 1 B-1160 Bruxelles	T=+32.2.676.7[redacted] F=+32.2.676.73.47 E=[redacted]@cefic.be
IND	[redacted]	A.I.S.E. Square Marie Louise 49 B-1000 Bruxelles	T= + 44 1784 474[redacted] F= + 44 778710555711 E=[redacted]@pg.com
IND	[redacted]	ECPA Av. E. Van Nieuwenhuyse 4 1160 Brussels	T= + 32 (0)2 663 [redacted] F= + 32 (0)2 663 1560 E=[redacted]@ecpa.be
IND	[redacted]	Dow Europe SA	T= + 41 17282[redacted] F= + 41 17282965 E=[redacted]@dow.com
NGO	[redacted]	Toxics Science and Policy Advisor WWF-UK 17 The Avenues UK-Norwich NR2 3PH England	T=+44.1603.507[redacted] F= +44.1603.507.363 [redacted]@aol.com
NGO	[redacted]	Director of Toxics Programme WWF-UK Panda House Weyside Park Catteshall Lane Godalming Surrey GU7 1XR England	T= +44-1483-412-[redacted] F= +44 -1483-426-409 E=[redacted]@wwf.org.uk

Type of Organisation	*Name*	*Address*	*Tel - Fax - e-mail*
NGO	[redacted]	C/o E.E.B. Technical University of Denmark Building 424 DK-2800 LYNGBY	T=+45-45.25.[redacted] F=+45-45.93.26.93 E=[redacted]@ipt.dtu.dk
NGO	[redacted]	European Environmetal Bureau -EEB Av. du Feuillage 42 1180 Brussels	T=+32.(0)2.375.5[redacted] F=+ E=[redacted]@skynet.be
NGO	[redacted]	C/o E.E.B 81 B av. Jan Stolbaerts 1030 Bruxelles	T=+322.242.[redacted] E : [redacted]@skynet.be
NGO	[redacted]	Friends of the Earth 26-28 Underwood Street UK-London N1-7JQ	T=+44.171.5661.[redacted] F=+44.171.4900.881 E=[redacted]@foe.co.uk
NGO	[redacted]	European Crop Care Association –ECCA- Secretary-General Poenaardlaan 7 B-3090 OVERIJSE, Belgium	T= +32-02-687 [redacted] F= +32-02-687 98 67 E=[redacted]@skynet.be
OTHERS	[redacted]	BEUC, Bureau Européen des Unions de Consommateurs Av. E. Van Nieuwenhuyse 4 bte 1 B-1160 Bruxelles	T=+32.2.743.[redacted] F=+32.2.735.74.55 E=[redacted]@beuc.org
OTHERS	[redacted]	T.U.T.B (Trade Union Technical Bureau) Bld. Du Roi Albert II, 5/5 B-1210 Bruxelles	T=+32.2.224.[redacted] F=+32.2.224.05.61 E=[redacted]@etuc.org
OTHERS	[redacted]	EMCEF	T= +32.(0)2.626.2[redacted] F= +32 (0)2 646 06 85 E=[redacted]@emcef.org

Type of Organisation	*Name*	*Address*	*Tel - Fax - e-mail*
OTHERS	[redacted]	OECD Environment, Health and Safety Division 2, rue André-Pascal 75775 Paris Cédex 16	T= +33.1 45 24 [redacted] F= E=[redacted]@oecd.org
OTHERS	[redacted]	Environment, Health and Safety Division Environment Directorate OECD 2, rue André-Pascal 75775 Paris Cedex 16, France	Tel. +33-(0)1-45 24 [redacted] Fax. +33-(0)1-45 24 16 75 [redacted]@oecd.org
EEA	[redacted]	Emerging Issues and Scientific Liaison, European Environment Agency, Kongs Nytorv, 6, DK-1050, Kobenhavn K Denmark	T= + 45 333 [redacted] F= + 45 333 671 28 E= [redacted]@eea.eu.int
OTHERS	[redacted]	WHO-IPCS 20 avenue Appia CH-1211 Geneva 27	T=+41.22.791.3[redacted] F==41.22.791.4848 E=[redacted]@who.int

ANNEX 2

INVITATION LIST - MEMBER STATES
Stakeholder Meeting on Endocrine Disrupters (15-16 October 2003)

Country	*Name*	*Address*	*Tel - Fax - e-mail*
Austria	[redacted]	Federal Ministry for Agriculture, Forestry, Environment & Water Management Dep. V/2 (Chemicals Policy) Stubenbaslei 5 A-1010 Vienna	T=+43.1.51 522 [redacted] F= +43 1 51 E= [redacted]@bmlfuw.gv.at
Austria	[redacted]	Umweltmanagement, Verkehr & Lärm Spittelauer Lände 5 1090 Wien	T= 01/31304-[redacted] F= 01/31304-5400 E= [redacted]@ubavie.gv.at
Belgium	[redacted]	Ministère des Affaires Sociales, de la Santé Publique et de l'Environnement Cité administrative de l'Etat, Quartier Vésale local V 23 04 Boulevard Pacheco, 19 BT 5 B-1010 Bruxelles	T=+32.2.210.4[redacted] F=+32.2.210.47.04 E=[redacted]@health.fgov.be
Denmark	[redacted]	Danish Environmental Protection Agency Biocides & Chemicals Assessment Division Strandgade 29, DK-1401 Copenhagen Denmark	T=+45 32 66 [redacted] F=+45 32 66 03 69 E= [redacted]@mst.dk
Denmark	[redacted]	Danish Environmental Protection Agency Biocides & Chemicals Assessment Division Strandgade 29, DK-1401 Copenhagen Denmark	T=+45 32 66 [redacted] F=+45 32 66 03 69 E= [redacted]@mst.dk
Finland	[redacted]	National Product Control Agency for Welfare and	T=+

Country	*Name*	*Address*	*Tel - Fax - e-mail*
		Health,Finland Pl 210, 00531 Helsinki	F=+358.9.3967.2[redacted] E=[redacted]@sttv.fi
Finland	[redacted]	Finnish Environment Institute P.O. Box 140 Fin-00251 Helsinki	T=+358.9.403.00.[redacted] F=+358.9.403.00.591 E=[redacted]@ymparisto.fi
France	[redacted]	Ministère de l'Ecologie et du Développement Durable Direction de la Prévention des Pollutions et des Risques Sous-Direction des Produits et des Déchets Bureau des Substances et Préparations Chimiques 20, Avenue de Ségur – 75302 PARIS 07 SP	T=+33.1.42.19.[redacted] F=+33.1.42.19.14.68 E=[redacted]@environnement.gouv.fr
Germany	[redacted]	Umweltbundesamt, IV2 Pf 33 00 22 14191 Berlin	T=+49.30-8903-[redacted] F= +49(30)8903 3350 E=[redacted]@uba.de
Germany	[redacted]	Federal Institute for Health and Protection of Consumers and Veterinary Medicine FG 825 Thielallee 88-92 D 14195 Berlin	T=+49.(0) 188 84 12 [redacted] F=+49.(0) 188 84 12 30 03. E=[redacted]@bfr.bund.de
Greece	[redacted]	National and Capodistrian -University of Athens Mediacal School Micras Asias 75 11527 Athens Greece	T=+30.107.462.[redacted] F=+30.106.840.488 E=[redacted]@ath.forthnet.gr
Ireland	[redacted]	Environmental Protection Agency Richview Clonskeagh Dublin 14	T=+01 268 [redacted] F=+01 268 01 99 E=[redacted]@epa.ie

Country	*Name*	*Address*	*Tel - Fax - e-mail*
Ireland	[redacted]	Pesticide Control Service Dept. of Agriculture, Food & Rural Development Abbotstown Laboratory Complex Castleknock Dublin, 15 Ireland	T=+353.1.607.[redacted] F=+353.1.820.4260 E=[redacted]@agriculture.gov.ie
Ireland	[redacted]	Hazardous Substances Assessment Unit, Health and Safety Authority 10 Hogan Place Dublin 2 Ireland	T= + 353 1 614 [redacted] F= + 353 1 614 7017 [redacted]@hsa.ie
Italy	[redacted]	Laboratorio Tossicologia Comparata Istituto superiore di sanita Viale Regina Elena 299 00161 Rome	T=+39.06.499.02.[redacted] F=+39.06.493.87.139 E=[redacted]@iss.it
Italy	[redacted]	Laboratory of Applied Toxicology Istituto superiore di sanita Viale Regina Elena 299 00161 Rome	T= F= E=[redacted]@iss.it
Luxembourg	[redacted]	Ministère de l'Environnement Montée de la Pétrusse, 18 L-2918 Luxembourg	T=+352.478.[redacted] F=+352.400.410 E=[redacted]@mev.etat.lu
Netherlands	[redacted]	Ministry of Health Welfare and Sport Department for Nutrition and Health Protection Product Safety and Injury Prevention Division P.O. Box 20350 2500 EJ Den Haag The Netherlands	T=+31.703.40.[redacted] F=+31.703.40.55.54 E=[redacted]@minvws.nl
Netherlands	[redacted]	Ministry of Transport, Public Works and Water Management Institute of Inland Water Management and Waste	T=+31.320.298.[redacted] F=+31.320.298.373 E=[redacted]@riza.rws.minvenw.nl

Country	*Name*	*Address*	*Tel - Fax - e-mail*
		Water Treatment P.O. Box 17 8200 AA Leystad The Netherlands	
Portugal	[redacted]	Ministério do Ambiente Dir. Geral do Ambiente Rua da Murgueira-Zambujal Apartado 7585 P-2720 Amadora	T=+351.1.472.8[redacted] F=+351.1.471.90.74 E=[redacted]@dga.min-amb.pt
Portugal	[redacted]	Direccão-Geral do Ambiente - DG da Saúde Alameda D. Alfonso Henriques 45 P-1000 Lisboa	T=+351.1.472.[redacted] F=+351.1.843.06.55
Spain	[redacted]	Departamento de Radiología y Medicina Física Facultad de Medicina Universidad de Granada Avda. de Madrid s/n 18071-GRANADA	T=+34.958.24.[redacted] F=+34.958.24.28.65 E=[redacted]@ugr.es
Spain	[redacted]	Subdirección General de Sanidad Ambiental y Salud Laboral Dirección General de Salud Pública y Consumo Ministerio de Sanidad y de Consumo C/Paseo del Prado 18-20 E-28071 Madrid	T=+34.91.596.2[redacted] F=+34.91.360.13.41 E=[redacted]@msc.es
Spain	[redacted]	Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (on behalf of Spanish Ministry for Environment) Ctra. La Coruña, km 7.5 28040 Madrid	T=+34-91-347.[redacted] F=+34-91-357.22.93 E=[redacted]@inia.es
Sweden	[redacted]	National Chemicals Inspectorate, KEMI Risk Assessment	T=+468.78.31.[redacted] F=+468.73.57.698

Country	*Name*	*Address*	*Tel - Fax - e-mail*
		P.O. Box 1384 S-171 27 Solna Sweden	E=[redacted]@kemi.se
United Kingdom	[redacted]	DEFRA 3/E4 Ashdown House, 123 Victoria Street SW1E 6DE London UK	T=+44 T=+44 E=[redacted]@defra.gsi.gov.uk
United Kingdom	[redacted]	DEFRA Chemicals & GM Policy Division	T=+44. (0)20 7944 5[redacted] F=+44. (0)20 7944 5229 [redacted]@defra.gsi.gov.uk

EUROPEAN COMMISSION
DIRECTORATE-GENERAL
ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B4 - Health & Urban
Head of Unit

Brussels, 07 November 2003
B4/CRP/cvi/D(2003) 341208

NOTE FOR THE ATTENTION OF MEETING PARTICIPANTS

Subject: Endocrine disrupters –
Informal Stakeholder Consultation Meeting on Endocrine Disrupters, 15-16 October 2003 - Draft Meeting Report

Please find attached the draft report of the above-mentioned meeting which took place in Brussels on 15-16 October, 2003.

If you have comments on this draft report, please send them to ***Ms*** [redacted] (fax +32-2-299[redacted], e-mail: [redacted]@cec.eu.int), by **28 November, 2003,** following which the report will be finalised.

[signed]
[redacted]

Cc: [redacted]

Encl. Draft Meeting Report, 15-16 October, 2003.
For information: Progress update of the Resorcinol Task Force.

U:\7. COMREL\7.5 CITIZENS\ADO\Replies 2016\838\Documents\COVER NOTE - DRAFT MEETING REPORT_341238_4 Dec 2003.doc

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.
Office: BU-9 4/17. Telephone: direct line (32-2) 2990409. Fax: (32-2) 2994362.

INFORMAL STAKEHOLDER CONSULTATION MEETING ON ENDOCRINE DISRUPTERS (ED)

15-16 October, 2003. Brussels

DRAFT MEETING REPORT

1. INTRODUCTION

The chair of the meeting, Ms. [redacted] (DG Environment), gave a brief welcome and introduction. She explained that the main objectives of the meeting were to consult stakeholders on two studies recently launched by the Commission on candidate endocrine disrupting substances, and to update stakeholders on recent Commission R&D activities, policy discussions and activities of other organisations relevant to endocrine disrupters. The agenda (Annex 1) was approved. A list of participants is attached in Annex 2.

2. TECHNICAL STUDIES FUNDED BY THE COMMISSION UNDER THE ACTION "ESTABLISHMENT OF A PRIORITY LIST OF SUBSTANCES FOR FURTHER EVALUATION OF THEIR ROLE IN ENDOCRINE DISRUPTION".

The chair of the meeting briefly introduced the general framework of the two studies as it has been stated in the Commission document COM(2001)262 on the implementation of the Community Strategy for Endocrine Disrupters.

2.1. Study concerning in-depth evaluation of 12 candidate ED substances

Presentation

Dr. [redacted], WRc-NSF Ltd, (UK) presented the approach adopted for reviewing the 12 substances (9 industrial chemicals + 3 natural/synthetic hormones). The key elements of the framework were presented, which includes: i) the assessment of relevance of test methods and endpoints, ii) study validity and significance and iii) evaluation of effects in target groups. A review of the conclusions obtained by the weight of evidence approach and the uncertainties of 2,2 Bis(4-(2,3-Epoxypropoxy)phenyl)propane -BADGE-, Resorcinol and ethyniloestradiol were shown as an example of the framework.

The consultant indicated that the approach adopted on this study makes part of an integrated procedure which goes all the way from the identification of candidate substances to policy discussions and which needs to identify and focus on substances of concern.

It was pointed out that there are areas of uncertainty, which requires further activity to enhance the evaluation of the extent of endocrine disrupting effects of substances of concern and the risks that they present to humans and/or wildlife, including:

- The development of validated methods which provide robust information on endocrine disrupting effects in particular target groups, specifically invertebrates where there is a lack of knowledge on the endocrinology of many taxonomic groups.

- The conduct and interpretation of mammalian and non-mammalian tests in relation to potential low-dose effects.

- Collation (and if required generation) of information on the normal background variability in reproduction and developmental responses of mammalian and wildlife species.

- Assessment of the risks presented by the potential endocrine disrupting effects of synthetic substances in relation to background exposure to natural compounds (for example vertebrate steroids and phyto-oestrogens)

- Consideration of the effects of mixtures since target groups of humans and/or wildlife may be exposed to combinations of both natural and/or synthetic substances with varying degrees of endocrine disrupting potency.

Discussion

IT considered that the approach taken is good and stated that this type of studies includes an important amount of work. IT raised some questions regarding Resorcinol and its potential testing in amphibians, and whether it will be possible to observe an effect depending on the different degree of purity of the components used. Dr. [redacted] commented that consideration is being given to the need and availability of a suitable test for assessing potential thyroid effects in the amphibians group. In addition, it is expected that due to the potential effects of resorcinol it will be more relevant to focus on invertebrates. Regarding the second question, Dr. [redacted] said that different responses to resorcinol, have been observed in mammals (e.g. rats are more susceptible) but the relevance of these results for humans are not known.

Dr. [redacted] emphasized that the available data for resorcinol is old and Ms. [redacted] invited CALEB to briefly report on the developments of the "Resorcinol Task Force".

CALEB informed that the objective of the "Resorcinol task force" is to fill data gaps. One study in Daphnia magna has been finalised in August and the final report will be available next month. Preliminary results shown that there are no effects on the adrenals glands and/or at the thyroid level, at concentrations 10 times higher than those found normally in the drinking water. The second study is a multigeneration mammalian reproduction study, which involves exposure through drinking water and it is expected to be concluded in 2004, the final report will be available at the end of 2004 / early 2005. Regarding the potential testing in amphibians, the question will be analyzed by the Task Force

GR required clarification on the existence of information regarding neurodevelopmental disorders, due to the potential effect of resorcinol on the thyroid in the foetus development. CALEB informed that on the tests performed, non adverse effects have been observed on the behavioural tests conducted.

WWF-UK questioned i) if the degradation patterns of BADGE and the leaching of this product from pipes have been studied, ii) if there is a potential exposure when this product is used in coatings in cans and iii) if it has been studied the potential thyroid effects.

Dr. [redacted] stated that the chemical hydrolysis of BADGE produces bis-diol of BADGE (bisphenol A bis(2,3-dihydroxypropyl ether) and it has been observed that the body systems do not transform BADGE to Bisphenol A. In cans there is a potential threat, however if the production process is correct, no increase in the exposure will be expected. Regarding the thyroid effects this information will be checked by Dr. [redacted] (Annex 4).

EEB asked whether to focus on "workers and consumers" if it is known that the most affected group is children. Dr [redacted] clarified that children were included under "consumers".

2.2. Study on gathering information on 435 substances with insufficient data

Presentation

Dr. [redacted] RPS Group (NL) presented the final results of the study. The main objective is to define a methodology by which to investigate 435 candidate substances identified in the BKH 2000 report with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption. The work undertaken includes 4 tasks:

Task 1. Review work done, in the context of the Community Strategy for Endocrine Disrupters, leading to the identification of the 435 candidate substances.

Task 2. Define a methodology by which to investigate the 435 candidate substances identified in the BKH 2000 Report with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption

Task 3. Further selection, inventory and evaluation of the group of 435 chemicals, in accordance with the methodology.

Task 4. Define an iterative mechanism by which new substances may be included or existing substances removed from the candidate list of substances as new evidence comes to light.

Discussion

Ms [redacted] emphasized that difference should be made between categorisation, which is the objective of this study and prioritisation which includes the assessment of actions

to be undertaken in the future, i.e: testing, research, weight of evidence approach and input into policy discussions.

D considers that a big step forward has been made in this area during the last years and if we compared the actual situation with the initial one, a considerable amount of information has been collected. WWF expressed that this approach -with the new refined methodology-, is a good "starting point". However inclusion of new studies/information in the process is required to improve it (also to include data from studies conducted in USA and Japan). EEB supports the views of WWF and considers that the Commission should act in a more pro-active way.

For the inclusion of chemicals in the list, BAYER said that information to support this request, must be included.

D requested clarification concerning classification of chemicals, inclusion criteria, and the reasons not to include all the Nonylphenol compounds in category 1. Dr. [redacted] informed that Nonylphenol is included in category 1 (BKH 2000) and other nonylphenol related compounds which are, for example not HPV, are classified in other categories. I expressed concern regarding the necessity to take into account by-products and the way to deal with them, since sometimes they might be more dangerous than the original product. Dr. [redacted] said that there is room in research for studying by-products, but at this stage we have just given priority to the original product.

EEB said that this study referred to groups of substances i.e. if one substance in a group is related to potential endocrine disrupter effects, the rest of the group might also be considered a risk, and they question if the Commission will take this approach further. Ms [redacted] emphasized that the objective of grouping is to make priorities for further activities and that the consequences of grouping have to be consider and discussed in the Commission.

BAYER considers that an intermediate step is required before deciding on exposure concerns, in order not to overload the system. Being aware that this situation could exist and to avoid overloading and increase efficiency the evaluation of the legal status of the substance is done in a further step, after the evaluation of exposure concern.

FR expressed concerns regarding the exclusion of chemicals from the list. Ms [redacted] said that at this stage we are not excluding substances from the list and the aim is to make priorities for future activities/actions.

BAYER pointed out that it is also important to include natural/synthetic hormones and phytoestrogens, which can also pose a risk.

Regarding the slides, D and WWF disagree with the figure presented, which compares the "Potency of category 1 substances in relation to the effect observed for 17-B-estradiol". They consider that this type of comparison is misleading and incorrect.

BAYER proposed the use of "Expected high exposure" instead of "Expected high exposure concern".

As a general recommendation it was proposed to identify from the working list the substances which are used and in production and those which are not, which could be done as an additional step by the Commission.

2.3. Study concerning "Information Exchange and International Co-ordination on Endocrine Disrupters". Presentation and discussion – MRC-IEH (UK)

Presentation

Dr. [redacted], MRC-IEH (UK) presented the final results of the study. The main objectives are i) to assess international progress in endocrine disrupter research, in the development and implementation of testing programmes and in policy actions, ii) to compare and contrast the situation in the EU, USA and Japan, iii) to analyse the extent of cooperation and coordination of research and testing between the EU, USA and Japan; and iv) to make recommendations on ways to improve coordination and the sharing of workloads (worldwide and within the EU). In order to ensure the currency of information gathered, these activities were undertaken within a short-time scale.

Discussion

Ms. [redacted] said that with a view of transparency the final reports are going to be included in the website. Different participants (EEB, I, GR) pointed out the importance to disseminate information/knowledge using the adequate language especially for the non-technical public and to inform the readers on the general context of the studies.

2.4. Other relevant studies – status update. Endocrine Disrupters Website / Drinking water Study.

Ms. [redacted] said that the Commission plays an active role in collecting, exchanging, assessing and providing information, as well as in monitoring ongoing activities concerning the ED issue. Early this year a website has been created in order to provide information on EDs. It includes background info as well as the EU Strategy on EDs. This website has been designed to be easily accessible to different target groups (general public to specialized one). In the future it will be implemented to include some other different activities on EDs. The internet address is: http://europa.eu.int/comm/environment/endocrine/.

Mr. [redacted], DG Environment, presented the main results of the study on endocrine disrupters in Drinking water. This study had been requested by the Council in the context of Directive 98/83/EC. The aim of the study is to provide information on the exposure to endocrine disrupters through water intended for human consumption. It has been found that raw water frequently contains potential ED, but the water treatments should be very effective at removing them. Regarding the concentrations of EDC measured in drinking water, they were generally at or below the level of quantification, but the study was limited in geographical scope and additional data from other MS are required. It has also

been identified that the contribution of EDCs in drinking water to total exposure is of minor importance.

Some of the gaps identified, includes:

- Current database is to small, more substances, more sources and more countries are required

- Further analysis and research is needed

- Approval process needed for use of materials in waterworks and water pipes.

The results of the study are going to be submit to consultation with all the relevant stakeholders, during the "Seminar on Drinking Water", which will take place in Brussels, on 27-28 October, 2003. (Website of the Seminar: http://europa.eu.int/comm/environment/endocrine/)

D considered that the conclusions are too drastic and before being able to get a final conclusion, more research/data is necessary. S asked about the possibility of identifying preventive measures to keep EDCs out of drinking water entirely and Mr. [redacted] said that this is a separate issue which requires further discussion.

2.5. Community policy discussions relevant to EDs

- **Proposed EC Chemicals Regulation – REACH-**

Ms. [redacted], DG Environment, presented a summary on the latest developments towards a new EU chemicals policy. An internet consultation process was held, from 15 May, 2003 to 10 July 2003 and more than 6.400 responses were received. She said that the adoption is expected on 29th October, 2003 and then the proposal is expected to be presented to the Council and the European Parliament later this year.

REACH can be considered as a single, coherent system for new/existing chemicals, which includes new elements, for example: i) Duty of Care, ii) Registration of substances above 1 tonne, iii) Authorisation for substances of very high concern iv) Agency to manage the system.

As it has been stated in the White Paper, the system includes Registration (>1 tonne), Evaluation (>100 tonnes + priorities) and Authorisation of CMR (carcinogenic, mutagenic or toxic to reproduction) Category 1 and 2, PBTs, vPvB and other substances with similar level of concern.

Discussion

EEA questioned on the contents of the Environmental Impact Assessment and Ms. [redacted] commented that it contains an evaluation of cost-benefits; including, estimations

of direct costs for testing and registration, indirect costs, macroeconomic effect and evaluation of cost-savings.

EEB requires clarification about the inclusion of EDs in REACH, Ms [redacted] replied that even if ED is a complicated area, by the nature of their effects most of the Endocrine disruptors would normally qualify as CMR (carcinogenic, mutagenic or toxic to reproduction). Such chemicals (category 1 and 2) are envisaged in line with the proposal in the White Paper to undergo authorisation under the REACH system. Furthermore, adverse effects on the endocrine system of wildlife species have been causally linked to certain persistent, bioaccumulative and toxic (know as PBTs) substances, which are going to be subject to authorisation, as well as vPvBs and other substances with similar level of concern.

Ms. [redacted] pointed out that ED should go under authorisation, but it is important that this decision relies on solid scientific information and evaluation.

Several participants (D, A, BAYER, WWF) raised different questions about REACH, including: the reduction of use of animal testing, the shift in the burden of proof (from MS to Industry), the duty of care, the advantages/potential problems of the implementation of the new system.

Thematic Strategy on Pesticides and Directive 91/414/EEC.

Mr. [redacted], DG Environment gave a presentation on the Thematic Strategy on Sustainable use of Pesticides. The main objectives of the strategy are to minimise hazards and risks to health and environment, to improve controls on use and distribution, to encourage low-input or pesticide free farming, to promote the substitution of most harmful active substances and to establish a transparent system for reporting and monitoring progress (indicators). A first indication of the measures under discussion was also presented. It has been also pointed out that this Thematic strategy is nor specifically targeting ED, it is aimed at generally reducing risk resulting from use op pesticides (including ED aspects).

Mr. [redacted], DG Health and Consumer Protection gave a presentation on the Directive 91/414/EEC and the implications for evaluation of EDs. Under the current provisions of the directive, (annexes II & III) it is foreseen that new data can be requested if there are suspicion of adverse effects. Actually, an amendment proposal is under preparation, which is expected to be adopted by the Commission in 2004.

Questions were raised by the participants regarding the revision of the Directive and the involvement of different stakeholders, the consideration of additive effects, food and feed and monitoring of effects.

Water Framework Directive -WFD-

Ms. [redacted], DG Environment gave a presentation on the Water Framework Directive (Directive 2000/60/EC). The purpose is to establish a framework for protection

of surface and ground waters, which among other things prevents further deterioration and protect and enhance the status of the aquatic ecosystems.

The Directive stipulates that the Commission shall produce proposals for emission controls and quality standards. The Directive identifies priority substances (toxicity criteria take into account human health as most sensitive endpoint), priority hazardous substances (toxicity criteria) and other main pollutants (substances with steroidogenic, thyroid, reproduction and/or other related endocrine functions). It should be noted that, of the 33 priority substances proposed in the field of water policy, 11 are candidate ED substances for which evidence of ED or potential ED was found in the BKH report. It is foreseen that the list of "priority hazardous substances" will be reviewed in December, 2004.

Discussion

GR pointed out that certain countries like Greece or Italy, faced a specific problem regarding radioactive compounds and questioned about their status under this Directive. Ms. [redacted] said that they are not excluded from the scope of the Directive, however at this stage they are not specified.

GR also asked about the status of legislation for "recycled water" and medicinal compounds. Ms. [redacted] replied that there is a specific legislation on waste water ("recycled water") and medicinal compounds can be included in the WFD.

Several participants (CEFIC, EEB) raised questions about the way that this Directive is going to deal with the different water bodies (specifically coastal waters), inclusion of natural hormones, coordination with the activities in OSPAR and the effect of contaminated soils into water quality.

Ms. [redacted] commented that in a first step different types of water bodies/areas will be identified for specific actions, coastal waters are included in the WFD. The WFD will set overall quality standards and identify NOECs for pollutants and natural hormones are not excluded, in addition the need for monitoring programmes for this type of compounds has been highlighted. The issue of the leaching of chemicals into water from waste (contaminated soils, sites, sediments, etc) is currently being addressed to determine the best policies and approach.

D commented about the importance of peak concentrations as well as annual averages, and the fact that for certain substances short-term measurements will be appropriate. In addition point sources as well as diffuse sources will have to be taken into account.

- **General Product Safety**

Mr. [redacted], DG Health and Consumer Protection gave a presentation on the Directive 2001/95/EC on General Product Safety, which has been revised in 2001 and it will become applicable as from 15 January 2004. The revision includes a clarification and enlargement of the scope of the Directive, a stronger role for European standards, additional obligations for producers and distributors, a ban on export of products prohibited on Community level, reinforcement of the obligations and powers of the Member States for market surveillance, collaboration between Member States and the

Commission, improvement of the RAPEX system, a simplification of conditions and procedures for urgent measures at Community level and last but not least an improvement in transparency to the general public.

WWF raised a question regarding information flow and the fact that if there is a product concern how can consumers access this information and Mr. [redacted] said that there is no current provision for this, because there are formal steps that need to be followed to elaborate/verify the information, but this is an important question that needs to be addressed. Some examples of the application of RAPEX were requested by WWF, the most known is phtalates, other includes, the banned of azo-dyes in consumer products, yo-yo balls and lead in candle wicks.

EEB asked if it has been considered to establish a link with REACH to register articles, products and materials, without request for confidentiality. It is a complicated issue, which requires more reflection in the future and in general it will depend on the type of product, because some of them are extremely "complex" like a car or a computer. REACH covers chemicals in products with the intention or likelihood of release.

2.6. Endocrine Disrupters under the new Environment and Health Strategy.

Ms. [redacted] gave an overview of the recent adopted "European Environment and Health Strategy" COM(2003)338. This strategy presents a "**vision**" on how to address environment and health topics.

Due to the broad scope and the complexity of the Environment and Health issue, the strategy, is going to be implemented in cycles with a full involvement of stakeholders (representatives from international organisations, industry, civil society and academia) at the different phases.

The strategy takes a long-term view where the ultimate objectives are:

- To reduce the disease burden caused by environmental factors in the EU
- To identify and to prevent new health threats caused by environmental factors
- To strengthen EU capacity for policy making in this area.

In order to achieve those objectives and due to the broad nature of the problem, we will need to identify and focus on some of the key environmental factors in the EU and their potential /associated effects. In the first cycle we are going to focus on the following priority diseases or conditions:

- Childhood respiratory diseases, asthma, allergies
- Neurodevelopment disorders
- Childhood cancer
- Endocrine disrupting effects

and their related environmental factors including: indoor & outdoor air, dioxins, heavy metals, endocrine disrupters, electromagnetic fields and the urban environment.

Three Technical Working Groups –TWGs- have been created in order to provide a picture of the actual situation for all the items of the first cycle, establishing the state of

knowledge in its specific area, detecting data gaps/needs, identifying measures to improve public health or to enable decision making that can be taken based on current knowledge and identifying also new elements for the next cycle. In addition, a set of actions or recommendations are going to be proposed.

- Indicators and Priority diseases, including: indicators, childhood cancer, neurodevelopmental and respiratory diseases.
- Integrated monitoring, including biomonitoring of children and pilot projects on dioxins, heavy metals and endocrine disrupters
- Research needs.

The kick-off meeting of the ED-TWG were held in Poland, on 6-7 October and Dr. [redacted] the chair of the group informed on the main conclusions from the meeting:

- Monitoring for every candidate chemical is not feasible - additional criteria is needed *e.g.* production volume, toxicological information in order to make a better informed choice.
- A new monitoring system is not proposed. An interface between many relevant databases and datasources should be developed in order to exploit the interaction among them.
- This integrated system must provide the tools for (a) making a realistic exposure assessment, in order to assess the role of man-made chemicals with ED activity on the burden of disease, and (b) driving risk management to reduce this burden.
- To have an efficient monitoring system, a tiered approach should be developed to monitoring - look for "signals" (*e.g.* exposure hotspots), from which several directions can be taken.
- Therefore, there is a strong need to integrate early warning biomarkers and biosensors in a monitoring system.
- Emphasis therefore must be placed on development, validation and widespread availability of tests.
- There is a very important need for generating reference values in order to interpret data.
- Need to address issues of data quality and comparability between databases/sources.

To facilitate the collation of large amounts of information a baseline report structure had been developed during the meeting and Ms. [redacted] invite the participants to give inputs into this process filling with information on Monitoring Activities on their respective countries. It was agreed that the deadline for inputs will be 25th October.

Discussion

Participants (D, CEFIC) pointed out the necessity to develop new monitoring programmes or to improve the existing ones, even if those are not specifically designed and labelled as monitoring programmes for EDs. Dr. [redacted] pointed out that after analysing the actual situation (which is the aim of the Baseline Report) those are the type of recommendations that will beidentified and proposed in the Action Plan.

In the future development of monitoring programmes, RHODIA expressed that it is important to consider different ways of exposure (not only by ingestion of food), other compounds not only chemicals (CEFIC) and uncertainties and other confounding factors.

GR expressed that prospective studies could be used as well as information from BIOBANKS (Breast milk and cord blood), for example the specimen bank in Germany and the BIOBANK in Sweden.

One of the key points is to establish and coordinate different ongoing exercises and information.

2.7. R&D on EDs under 6th Community R&D Programme – status update: - CREDO Cluster and The problem of "mixtures".

Mr. [redacted], DG Research presented the status of the Research projects on ED in the EU, under the 4th and 5th Framework Programmes –FP-. He commented on the clustering strategy for projects/fields/programmes in the FP5 and detailed on the main clusters, e.g. Pharma, CREDO and SedNet. Under the FP5 a new call for proposals will be published on November, 10, 2003 on the website: http://www.cordis.lu/food/. Mr. [redacted] invite the participants to give inputs on specific research needs identified.

Mr. [redacted], London School of Pharmacy presented the activities under the CREDO Cluster. The aims of CREDO are to produce scientific data to support the Community Strategy on Endocrine Disrupters, to establish a focus for ED research in the EU and exchange scientific know-how and data. Mr. [redacted] commented in general, on the developments of the four issues under study, including: exposure assessment, novel endpoint and biomarkers, human studies and low-dose, mixture and regulatory issues. More information is available at the website: http://credocluster.info.

Ms. [redacted], London School of Pharmacy presented in detail the activities regarding low dose and mixtures, undertaken in EDEN, one of the participants of the CREDO Cluster. More information is available at the website: http://edenresearch.info.

General agreement has been expressed on the fact that the Commission is making a lot of efforts for increasing research activities in the EU, however inputs are needed on development of tests and testing strategy.

2.8. OECD Testing Strategy

Ms. [redacted], OECD presented the developments on the OECD initiatives in the framework of the Endocrine Disrupters Testing and Assessment Task Force –EDTA-. The main objective of the Task Force is to develop an internationally harmonised testing strategy and to co-ordinate and oversee the work of different sub-groups charged to develop new test guidelines or revise existing ones to assess the potential of endocrine disrupting chemicals.

The work on the EDTA has been organised on different Validation Management Group on screening and testing established for:

- Mammalian effects (VMG-Mam): Feb 1999.
- Ecotoxicity tests /VMG-Eco): March 2001
- In vitro/non-animal tests (VMG-in vitro): Nov. 2002

Ms. [redacted] presented in detail the main developments on each one of the tests.

CEFIC express their willingness to collaborate, on specific needs identified, closely with the testing and assessment process at OECD. Ms [redacted] said that one limiting factor is the financial one.

EEB request clarification about the grouping of chemicals. Ms [redacted] replied that it is not done by OECD, but the Japanese approach associate substances by chemical structure.

Different participants expressed the need for a better EU coordination (e.g. test for REACH) as well as with OECD.

2.9. Different approaches on EDs.

Mr. [redacted], BAYER, presented the industry's point of view for the regulation of endocrine disrupting substances.

Ms. [redacted], Danish EPA, presented proposal for a dynamic process, for the priority list/candidate list of substances for further evaluation in ED. Ms [redacted] commented that the proposal reflects both the conclusions regarding from the Environment Council (2000) and the critical issues that have been raised based on the experience gained from the prioritisation exercise until now. The overall purpose for preparing this proposal has been to ensure a dynamic process and to make a simple, transparent and flexible concept with a high workability in relation to existing and future EU legislation, and to develop a tool which easily "plays" together with other international activities on EDS. The key point of the proposal is to "convert" the existing priority list/candidate list (the BKH work) to – a dynamic working-list database - containing information about substances with potential endocrine disrupting properties that are systematically organised, as a basis for the dynamic process.

Different views have been expressed on the two approaches. D said that it is important for the validity of all the process to have a dynamic procedure. The outcome of the final list should help to give advice for other directives/services in the Commission- (EEB). Attention should be paid to LPV substances as well as those in Category 2 (around 200).

2.10. Special issues under the ED problem: Low dose and LPVs.

This point will be discussed in a further meeting.

2.11. Any other business

- A Workshop on Low Dose Effects on Endocrine Active Compounds, will take place in Berlin, in Nov 20 -22, 2002. More information available in the website: http://low-dose.de/

- A Workshop on the Gonadal Histopathology of Small Laboratory Fish, has been postponed and now will take place on 25-26 February, 2004. CEFIC will send to the participants additional information.

2.12. Conclusions

Ms [redacted] concluded the meeting by thanking participants for their time and contributions and summarised the various action items arising from the meeting and the future Commission activities regarding ED, especially those related with the follow-up of the BKH and WRc-NSF studies.

In a first phase, the analysis of the legal status of Category 1 and 2 substances, from the BKH studies will be done, in order to identify substances which require a "weight of evidence" evaluation and to update information of substances from BKH 2000 study in the light of new results of the risk assessments conducted under different Directives, e.g. Directive 91/414/EEC and Directive 793/93/EEC.

In a second phase and according to the results of the "weight of evidence approach" of the 12 substances, input into policy discussions will be done on a case by case basis.

In this priority-setting exercise, both studies have been submitted to consultation to the Scientific Committee of Toxicity, Ecotoxicity and Environment (SCTEE), Stakeholders and other existing expert groups and it is expected that the SCTEE adopt and publish its opinion in November.

Finally, Ms. [redacted] commented that the Commission is preparing an implementation report to the Council and to the Parliament on EDs, next year and would carefully consider the many aspects referred to by stakeholders during this meeting as well as other comments from the consultation process.

RESORCINOL TASK FORCE

Progress Update – October 2003

The WRc Report, recently distributed by the European Commission, elaborates in some detail the current state of knowledge on the toxicology of resorcinol and specifically its impact as a thyroid peroxidase inhibitor. As is consistent with many industrial chemicals, WRc reached the conclusion that several key data-gaps remain, particularly in the area of reproductive toxicity. The Resorcinol Task Force[1] (formed in 1998) had already identified the need to fill these data gaps and was able to liaise with WRc throughout the preparation of their Report about its intentions in this respect. This Progress Update provides a brief overview of the work that has been conducted since November 2002 (the point at which the WRc Report was finalised), its significance to the assessment of the risks posed by resorcinol and the direction of planned future work.

Reproductive Toxicity Testing

The Resorcinol Task Force (RTF) reached a decision in early 2002 to progress with a full two-generation reproductive toxicity study. Drinking water was the chosen delivery mechanism (see Appendix 1 for rationale) and the Sprague Dawley rat was selected as the animal of test. The study was envisaged in three phases:

- A 14-day Palatability Study to confirm acceptability of resorcinol to the rats at planned doses
- A comprehensive dose range finding (DRF) study with targeted thyroid end-points and with developmental neuro toxicity screening inbuilt[2]
- A guideline compliant two-generation study with full thyroid histopathology

The Contract Laboratory selected for the study was WIL Research in Ashland, Ohio. The work commenced in August 2002 with confirmation from the 14-day Palatability Study that concentrations up to 360 mg/l were fully acceptable to the rats in question. The DRF Study design was then finalised (see Appendix 2) and commenced in October 2002. The study completed its in-life study phase in early March 2003 and the preliminary results were reviewed. The following points of significance emerged:

- Animals were treated with 0, 10, 40, 120, and 360 mg/l resorcinol in drinking water based on the literature evidence available on adverse thyroid effects (e.g. Cooksey & Seffner).
- Even at the highest drinking water concentration, no effects on the thyroids were observed in either the F0 or the F1 generations that might be categorized as adverse in spite of previously reported results by Cooksey & Seffner at levels as low as 40mg/l. This assessment included all parameters evaluated during gestation as well as those related to reproductive function.
- At the highest concentration level some colloidal changes in the thyroid were observed in the F0 generation. However, there was no change in hormonal levels leading to any functional effect in either F0 or F1 generations.
- There was no indication of any significant changes in neural function in the F1 generation that could be attributed to hormonal disturbance in the F0 generation.
- No effect on the adrenals was found.

These results were somewhat unexpected and led to considerable discussion amongst the Resorcinol Task Force in the period to May 2003 when the decision was made to conduct a further 14-day Palatability Study to confirm that the guideline compliant two-generation study could proceed at levels significantly in excess of 360mg/l. In carrying out this work, levels of 360, 540, 720 and 1080 mg/l were initially chosen. However, after seven days, it emerged that there were no palatability problems at the selected levels and this led to a decision to increase the lower dosages (360, 540 mg/l) to 3000mg/l and 10,000mg/l respectively in order to explore the upper boundaries of taste aversion. The study was also

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[1] Members include the three key producers (2 Japanese + 1 USA) with liaison to key user groups

[2] This was proposed by the Study Laboratory as a means of assessing DNT aspects at an early stage to ensure that the guideline compliant two generation study design could take into account any findings

extended for a third week in order to achieve 14-days exposure. It was also agreed to introduce a review of thyroid weight changes and histology at these higher doses to achieve an early indication of likely effect in the guideline compliant two-generation study. The subsequent examination revealed that thyroid histology was affected in the females at levels of 720, 1080, 3000 and 10000 mg/l, while male histology was only affected at the highest dose of 10000 mg/l.

The Resorcinol Task Force reviewed the significance of these results at its September meeting in Düsseldorf and has since decided to conduct a four concentration guideline compliant two-generation study using concentrations of 120, 360, 1080 and 3000 mg/l (10,000 mg/l was felt to elicit too many general toxicity characteristics that would mask the importance reproductive effects). This four concentration study (with its inherent additional cost) will commence in December 2003 and its in-life phase will run for 45 weeks. The report of the work will follow in Q1 2005.

In the meantime, the report of the DRF study will be publicly available in November 2003 and the Resorcinol Task Force is open to suggestion about possibly means of dissemination.

Risk Assessment

In January 2002, Germany made a submission to the International Programme on Chemical Safety (IPCS) for the inclusion of resorcinol in the Concise International Chemical Assessment Document (CICAD) programme. This provides the opportunity for toxicological data-set of resorcinol to be reviewed in the context of its applications. The degree to which a CICAD can be seen as a genuine risk assessment depends on the access to reliable exposure data which, in itself, requires industry co-operation. The Resorcinol Task Force has been in dialogue with IPCS since the latter part of 2002 and has clearly indicated its willingness to co-operate fully in the process. It is likely that the CICAD will focus on specific risk scenarios in a variety of end-use applications. These will probably include uses in the tyre industry, the wood adhesives industry, the hair dyes sector and the pharmaceutical sector (topical ointments). Fraunhofer will be lead researchers on the CICAD in view of their previous involvement in the preparation of BUA Report No. 99 (1993) on resorcinol. IPCS has indicated that it will want to wait until the output of the guideline compliant two-generation study before finalising the CICAD draft. This means that publication of the CICAD is likely to take place in 2006, because of the annualised cycle of review and approval.

With respect to existing HPV Challenge and ICCA programmes, the Resorcinol Task Force will make its submissions in accordance with programme schedules. Robust Summaries are already in preparation to this end. Resorcinol has been selected as a pilot chemical for joint consideration within IPCS and ICCA processes. As such, the precise nature of the ICCA submission through Japan is still unclear. The timing of the CICAD process may have some impact on this.

Meanwhile, the Resorcinol Task Force continues to work actively with end-users to gain further insight into environmental emissions. Since resorcinol is readily biodegradable, the tracking of emissions is not always easy. Indeed, resorcinol's history as a chemical of low regulatory concern means that there is little institutionalised monitoring. Active consideration is being given to a dedicated monitoring study, but there is a need to identify appropriate protocols at both site level and at regional treatment plants.

Aquatic Toxicity

In accordance with the WRc observations, the Resorcinol Task Force has recently completed a two-generation Daphnia Magna Study. This is currently in the process of being written-up and should be available shortly. In summary, no effects were observed at concentrations below those previously anticipated to generate acute effects. However, the ready bio-degradability of resorcinol at low concentrations made the experimental design quite challenging.

The Resorcinol Task Force has noted comments made at the recent ED Stakeholders' Meeting in Brussels and will be considering the rationale for an amphibian study once the OECD test method has been further developed.

APPENDIX 1 – Rationale behind the selection of drinking water as a dose vehicle

The summary of the Mackay Level 1 Fugacity model presented by WRc in their recent report indicated that over 99% of free resorcinol is likely to find its way into the aquatic compartment. Although the chemical's ready biodegradability is likely to prevent significant human exposure from this source, many researchers (e.g. Gaitan) have spent time evaluating the impact of thyroid active chemicals in surface water and drinking water. Since these can often be available from shale deposits and other natural sources, there can be (and often is) a confused picture concerning cause and effect. Nonetheless, societal epidemiologists are interested in factors influencing the prevalence of goiters in the population since the background level is typically of the order of 5%. In reality, it is found that financial income is a more important factor than any other, since diet has a significant effect on thyroid issues. Despite this, the Resorcinol Task Force has been of the view that a better understanding of the potential role of resorcinol in drinking water would be valuable.

The interest of the Resorcinol Task Force in the drinking water vehicle was also stimulated by two studies conducted independently by Cooksey and Seffner[3] that indicated observable thyroid impacts at relatively low levels (40 mg/l; ~5mg/kg body weight). Both of these studies have been evaluated in detail by independent sources since they were conducted, even to the point of dialogue with the researchers. However, it has emerged that key parameters within the studies were poorly documented and that other procedural inconsistencies make reliance on these studies equivocal[4]. Nonetheless, the Resorcinol Task Force was aware that no other relevant (GLP) drinking water study was available to offer a better context for considering risks based on drinking water intake. The other possible oral exposure route, oral bolus (gavage) had been previously rejected, partly because such a method is unrepresentative of normal human exposure patterns but, more significantly, because a two year NTP study up to 450 mg/kg body weight did not report any effects on the thyroids of rats and mice.

An alternative argument, as advanced at the recent ED Stakeholders Meeting, has been that the medical case study history has been from dermal treatment (i.e. topical ointments). This would support the conduct of a dermal study rather than a drinking water study. Indeed, there is no question that the use of topical ointments with high free resorcinol contents[5] on broken and ulcerated skin can create a reversible thyroid reaction. However, the self-policing mechanisms of the pharmaceutical sector, the introduction of basic toxicological legislation on other dermal end-uses and good handling practices during manufacture have meant that there have been virtually no medical case studies since the 1950s.

Bearing in mind that dermal uses of resorcinol represent less than 1% of total resorcinol consumption, it was felt that undue focus on the dermal route would be inappropriate. There were additional aspects of practicality. These were as follows:

(1) It is well documented in rats that resorcinol is a skin irritant. Therefore dermal application in a guideline compliant two-generation reproductive toxicity study must be anticipated to cause serious skin irritation problems that could jeopardise an entire study soon after initiation[6].

(2) Furthermore, when a dermal irritant chemical is being evaluated, the test animals need to be restrained (e.g. by neck collar) to prevent them from licking the site of application which would otherwise lead to a mixed dermal and oral exposure that could not be quantified. Such restraint also causes stress – a factor that could be a serious confounder in the interpretation of the study outcome.

(3) That long-term dermal studies are rare and are not viewed by many as appropriate in terms of animal welfare

These arguments were well supported by information from the hair dye industry which provided extensive information (made available to WRc) on the exposure levels likely via intact skin from hair dye use. The Resorcinol Task Force therefore concluded that the drinking water approach was the most beneficial and informative under the circumstances.

Resorcinol Task Force October 2003

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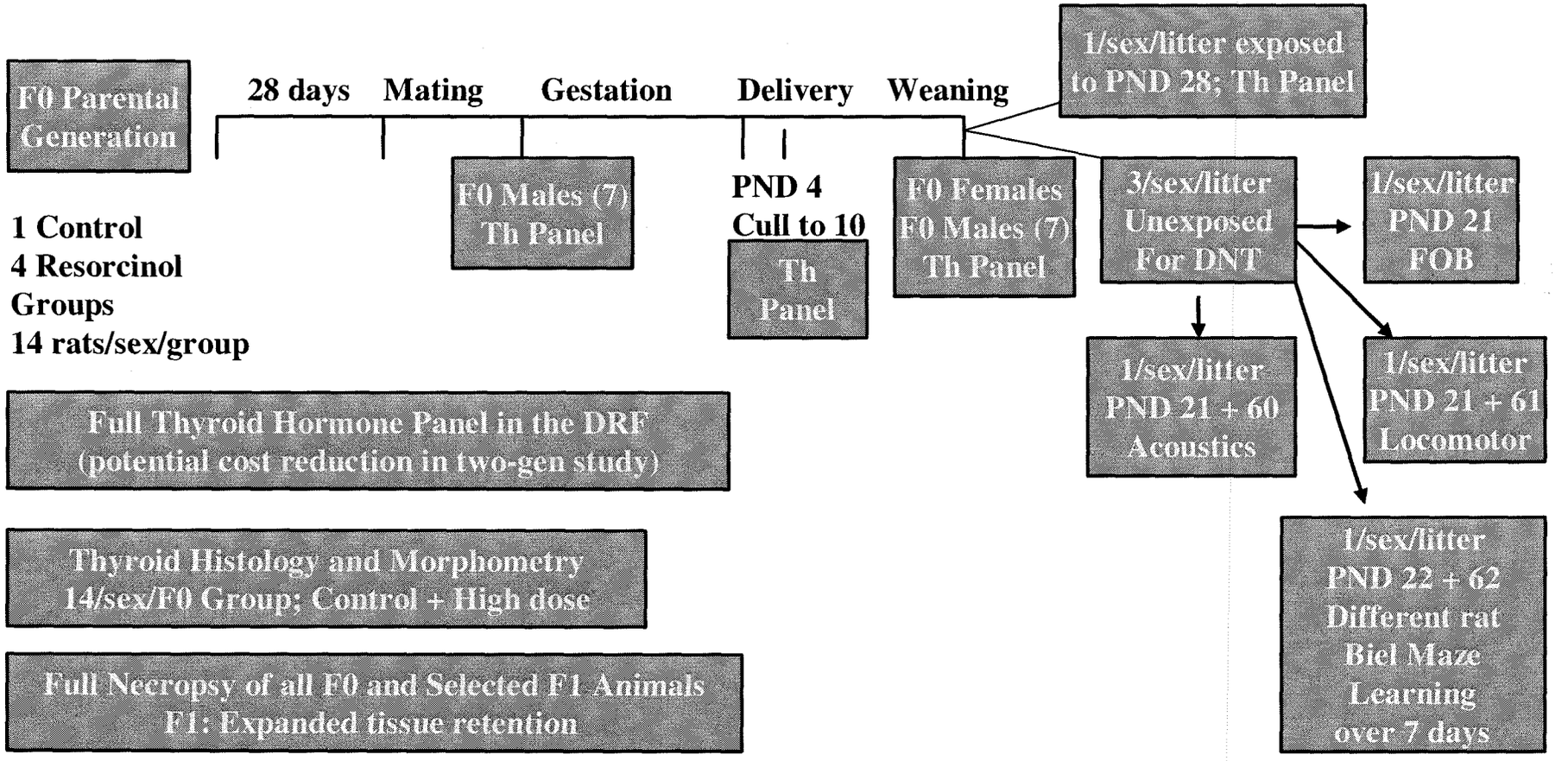
[3] Variation of thyroid fresh weights with Cooksey et al and altered thyroid histology with Seffner et al

[4] There is some concern that concentrations may have been mis-reported

[5] Up to 50% free resorcinol in some formulations used in the early 1900s

APPENDIX 2 – DRF Study Design



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ENVIRONMENT
Directorate B - Quality of Life, Health, Nature & Biodiversity
ENV.B4 - Health & Urban

ANNEX 1

AGENDA

INFORMAL STAKEHOLDER CONSULTATION MEETING ON ENDOCRINE DISRUPTERS

5 Avenue de Beaulieu, B-1160 Auderghem (Ground floor, Salle C)
Wednesday, 15 October 2003, 10.00–17.00
Thursday, 16 October 2003, 10.00-17.00

Wednesday, 15 October 2003, 10.00–17.00

1. Welcome

2. Approval of the Draft Agenda

3. Technical Studies funded by the Commission under the action "Establishment of a priority list of substances for further evaluation of their role in endocrine disruption" – Introduction by the Commission–

   --- Study concerning in-depth evaluation of 12 candidate ED substance. Presentation and discussion. –WRc-NSF Consultants (UK)

   --- Study concerning 435 candidate ED substances. Presentation and discussion – RPS Group (NL)

4. Other technical Studies funded by the Commission.

   --- Study concerning "Information Exchange and International Co-ordination on Endocrine Disrupters". Presentation and discussion – IEH (UK)

   - Other relevant studies – status update. Website / Drinking water.

5. Community policy discussions relevant to EDs

   - Overall chemicals policy

   - Thematic Strategy on Pesticides and Directive 91/414/EEC

6. Endocrine Disrupters under the new Environment and Health Strategy.

7. "Tour de table" regarding the different activities on Endocrine Disruption in the different MS and other organisations.

Thursday, 16 October, 2003 10.00–17.00

1. Community policy discussions relevant to EDs

   - Water Framework Directive

   General Product Safety

2. OECD Testing Strategy

3. R&D on EDs under 6th Community R&D Programme – status update

   --- CREDO Cluster.

   --- The problem of "mixtures".

4. Different approaches on EDs.

   --- Industry's view –
   --- MS. Working list on Endocrine Disrupters.

5. Special issues under the ED problem

   --- Low dose and LPVs

6. Any other business

   --- Workshop on Low Dose Effects on Endocrine Active Compounds – Nov 20 - 22, 2003 Berlin, Germany.

7. Conclusions

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ANNEX 2

ENDOCRINE DISRUPTERS: STAKEHOLDER CONSULTATION MEETING

15 & 16 October 2003, Brussels.

List of Participants

Member States

Ms. [redacted]	Austria
Ms. [redacted]	Belgium
Ms. [redacted]	Denmark
Ms. [redacted]	Denmark
Ms. [redacted]	Finland
Mr. [redacted]	France
Mr. [redacted]	Germany
Mr. [redacted]	Germany
Ms. [redacted]	Germany
Ms. [redacted]	Greece
Ms. [redacted]	Ireland
Mr. [redacted]	Italy
Mr. [redacted]	Spain
Ms. [redacted]	Sweden
Mr. [redacted]	UK

Industry

Mr. [redacted]	BSEF
Mr. [redacted]	BAYER AG
Mr. [redacted]	CEFIC
Mr. [redacted]	CALEB Group
Mr. [redacted]	CONCAWE
Mr. [redacted]	ECCA
Ms. [redacted]	ECPA
Mr. [redacted]	Hill & Knowlton
Mr. [redacted]	Rhodia

NGOs

Mr. [redacted]	EEB
Mr. [redacted]	EEB
Ms. [redacted]	EEB
Mr. [redacted]	Green Facts Foundation
Mr. [redacted]	ISDE
Ms. [redacted]	WWF-UK

Others

Mr. [redacted]	EEA
Mr. [redacted]	MRC-IEH (UK)
Ms. [redacted]	OECD
Mr. [redacted]	RPS Group
Ms. [redacted]	University of London
Mr. [redacted]	University of London
Mr. [redacted]	WRc-NSF (UK)

Commission Staff

Ms. [redacted]	DG ENV
Ms. [redacted]	DG ENV
Mr. [redacted]	DG ENV
Mr. [redacted]	DG ENV
Mr. [redacted]	DG ENV
Ms. [redacted]	DG ENV
Ms. [redacted]	DG ENV (*Chair*)
Mr. [redacted]	DG RTD
Mr. [redacted]	DG SANCO
Mr. [redacted]	DG SANCO
Ms. [redacted]	DG SANCO
Ms. [redacted]	DG SANCO
Ms [redacted]	DG SANCO
Ms. [redacted]	JRC
Mr. [redacted]	JRC

ANNEX 3

TOUR DE TABLE ON ED ACTIVITIES.

Austria
Different monitoring programmes are under development in the framework of the ARCEM project. Substances included are Nonylphenol, Octylphenol and natural/synthetic hormones.

Belgium
In the region of Flanders monitoring programs in surface and ground waters, are been carried out.

Denmark
ED has been a hot issue in Denmark and it has been included in the priority working agenda. The 66 substances identified in the BKH study 2000, in Category 1 have been included on the Danish List of Undesirable Substances. Research on QSAR modelling and on the use of OECD conceptual framework for regulatory purposes are being developed. There is also an ongoing study on monitoring of estrogenic substances on surface water.

EEA
EEA is carrying out monitoring studies on EDs in water, air and soil.

Germany
A survey programme on Children has been established by the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety and the Federal Ministry of Education and Research. In addition an Environmental Specimen Bank has been created, in the context of environmental monitoring.

Greece
There is a network of universities, food industry and research centres, dealing with EDs which conduct a project on fertility and factors that affect them. At the University of Athens a working group on communication of ED issues is actually in place.

France
No national actions specifically for EDs are established. Risk Assessments of New and Existing Chemicals are being carried out.

Italy
No regulatory actions have been taken specifically for EDs at national level. Current activities include a monitoring programme on hormones in meat and a national project funded by the Health Ministry, mainly targeting ED and food safety. No national environmental monitoring programmes exist, only some regional ones. Activities on information to the public and health professionals at national level via the website of the Italian National Health Institute and workshops are being developed.

Spain
Mainly research programmes on the effects of ED on invertebrates and some monitoring programmes. Each year a meeting on EDs take place, but there is not a real network

Sweden
Monitoring programmes in surface water.

UK
DEFRA developed an ED database, known as REDIPED, a website and a newsletter which summarizes the activities on EDs. In addition, different research activities have been conducted.

WWF
WWF UK has established working groups on E&H and on OECD guidelines and testing procedures. Emphasis has been done on information to the public and dissemination through a website.

CALEB
Responsible of the Resorcinol Task Force.

CEFIC – BAYER
The Long Research Initiatives –LRI- program conduct research on development and validation of methods, including for example: Enhancement of OECD 407, Hershberger and Uterotrophic assays and fish screen.

Information on specific activities can be found in the final report of the Study on "Information Exchange and Internationl Co-ordination on Endocrine Disrupters", varied out by MRC-IEH.

ANNEX 4

Notes on issues from the WRc-NSF study raised at the Stakeholder Consultation Meeting on Endocrine Disrupters.
Prepared by: Dr. [redacted].

There is no indication that potential effects on thyroid were evident in a 90 day subchronic oral toxicity study (Stebbins and Dryzga, 2001) investigating the effects of BADGE (Bisphenol A Di Glycidyl Ether) on laboratory mammals.

A one generation reproduction study in rats in which animals were exposed by oral gavage (Smith *et al* 1989) did not show any histological changes in the reproductive tracts in either sex of the F0 generation. It is not clear whether this includes subtle effects such as ano-genital distance. However, it needs to be recognised that the OECD procedure as defined at the time of testing was not specifically designed to assess potential endocrine disrupting effects. In the ECETOC Monograph on Guidance on Evaluation of Reproductive Toxicity Data (ECETOC 2002) the issue of endocrine disruption was considered as an emerging issue. It was stated that

"Endocrine disruption can be detected in a number of suitably adapted 'routine' reproductive toxicity assays. This is achieved by the incorporation of endpoints that are under hormonal control, and thus sensitive to disturbance by endocrine disrupters, and some amendments to the overall protocol where appropriate. Such endpoints include the age of sexual maturation of offspring (for example preputial separation in males and vaginal opening in females), disturbance of sexual differentiation (for example anogenital distance), sperm parameters (for example number, morphology, motility), circulating hormone levels and regularity and duration of the oestrous cyclicity, as well as more conventional endpoints such as histopathology and weights of organs of the reproductive tract. However, it must be borne in mind that many of these endpoints are not specifically indicative of an endocrine mediated mechanism of toxicity per se, but may also be influenced by overall growth and health status of the animal, or by toxicants that influence homeostasis through other mechanisms. For example, the oestrous cycle is perturbed in cases of bodyweight reduction, and reduced sperm counts may be indicative of a male germ cell cytotoxicant. Consequently, these endpoints must be interpreted with reference to other endocrine-sensitive endpoints and to additional observations on growth and histopathology. They are most useful as a measure of effect rather than a mechanism of toxicity".

In a teratogenic evaluation of BADGE in rabbits following dermal exposure (Breslin *et al* 1988) no evaluation of subtle effects, such as changes in ano-genital distance in fetuses, were measured. The developmental test provides information on the potential hazard to the unborn that may arise from exposure of the mother during pregnancy. However, the ability to detect effects on sexual differentiation is rather limited unless really profound endocrine disruption has occurred. There is only a gross external and internal morphological examination of the offspring that cannot detect subtleties in their intra-uterine development that is sensitive to an altered hormonal environment.

Information in the public domain on the potential release of BADGE from epoxy resins used to line water mains pipes is limited because the results of tests on pipes or other related products prior to use is generally confidential to the relevant regulator

(in the United Kingdom the Drinking Water Inspectorate). Available information in the public domain indicates that after lining 100m sections of water mains with epoxy resins and flushing with 10000 l of mains water only trace levels (around the Limit of Detection) of BADGE were found. This substance was not detectable 6 months after return to public use.