09.01.2002

EUROPEAN COMMISSION
DIRECTORATE-GENERAL HEALTH AND CONSUMER PROTECTION
Directorate C - Scientific Opinions
Unit C2 - Management of Scientific Committees; scientific co-operation and networks
Scientific Committee on Toxicity, Ecotoxicity and the Environment

Brussels, SANCO.C.2/JCD/jcd.**sanco83**.D(02)CSTEE/00/ .min.09.01.2002

SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)

Minutes of the

29th PLENARY MEETING

9 January 2002
Centre Albert Borschette, rue Froissart 36
B-1040 Brussels

1. Welcoming address, apologies for absence, declarations of interest

Apologies were sent by Prof. S. Kyrtopoulos.

No declarations of interest were made by any committee member. Prof. K. van Leeuwen took this agenda point as an opportunity to confirm his imminent resignation as a committee member given his taking up of his new post in the JRC as Director of the Institute for Health and Consumer Protection, as from 16 January 2002.

2. Adoption of the draft agenda

The draft agenda was adopted.

3. Approval of the draft minutes of the 27th and 28th CSTEE plenary meetings

The draft minutes of the 27th CSTEE plenary meeting were adopted with minor editorial corrections. The adoption of the minutes of the 28th CSTEE plenary meeting was postponed.

4. Health effects of Radio Frequency and Electromagnetic fields – recommendations of the CSTEE for research

The working group chairman informed that he was still in the process of trying to collate contributions from experts. He also informed that he would not be able to attend the next CSTEE plenary. Finally he informed the committee of his upcoming participation in a meeting in Madrid, organised under the auspices of the Spanish presidency of the EU, where he will be asked to present the CSTEE opinion. He will be accompanied by Dr. José Tarazona then.

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5. Presentation of the research project B6-7920/98000025 on Endocrine disrupters by representative(s) of RIVM (NL)

Dr Piet Wester made a presentation of the status quo on the RIVM research project on EDCs being financed under contract B6-7920/98/00025. He presented the update of their project on endocrine disrupters in fish the aims of which are basically: 1) the development of a Partial Life Cycle study in Zebrafish; 2) the development of a reference histology atlas and 3) The assessment of impact on reproduction / population by EDCs. During the presentation were highlighted aspects on endpoints in this model (PLC study) which are: i) Reproduction parameters; ii) Toxicological pathology; iii) Immunohistochemical vitellogenin analysis.

On these endpoints, the key findings were, after gynogenic exposure: i) Reduced frequency of oviposition with accumulation of eggs and egg debris in the ovary and oviduct; ii) Inhibition of spermatogenesis; iii) Feminisation of juvenile males; iv) induction of vitellogenin expression in both sexes; vitellogenin accumulates in intra- and extravascular body fluids; v) Transgenerational mortality (exposure of F0 and F1 induces mortality in F2; this is a dose-dependent effect with up to 100% mortality); vi) All histological estrogenic effects are reversible.

After androgenic exposure: i) Methyltestosteron induced estrogenic effects (induction of vitellogenin expression), probably after aromatisation of the molecule. Methyltestosteron has a relative estrogenic potency of approximately 0.025. ii) The non-aromatisable 17alfa-dihydromethyltestosteron accelerates sperm maturation; the employed exposure time of three weeks may be too short to uncover functional effects on sperm fertility because of the relative long maturation time of sperm; iii) 17alfa-dihydromethyltestosteron also has limited estrogenic activity (receptor interaction? limited aromatisation?).

After antithyroid (propylthiouracyl, goitrogen) exposure: i) No effects on general and reproduction parameters (max. conc. 1 g / L); ii) Limited effect on larval development; iii) Clear induction of goiter (from 10 mg/L onwards).

The interlaboratory differences, after completion of the histological analysis for other laboratories and comparison with their findings with those of competing laboratories, seem to show that they vary between material from different sources, *i.e.* i) No intersexuality was observed in the RIVM zebrafish stock, although this was seen in specimen from other laboratories; ii) Findings from other laboratories suggest that male differentiation in juvenile zebrafish may be preceded at least in part by initial female differentiation; furthermore, the time frame of sexual differentiation may vary between laboratories. These findings were considered to be strain dependent variations.

On behalf of the CSTEE the committee chairman congratulated Dr Wester and his team for his work and wished in success in the final stages of the project. He also expressed the committee's wish of being kept informed about its outcome.

6. Regulation 793/93 on Existing substances (ESR):

A. Status reports/opinions (Human Health and/or Environment) on:

Opinions were adopted on the following substances and sections:

a) *Cyclohexane* (HH and Env)

b) *Dodmac* (Env)

c) *Bis(2-ethylhexyl)phthalate (DEHP)* (HH and Env)

d) *3,4-dichloroanyline* (Env)

e) *Naphthalene* (HH)

f) *Ethyl acetoacetate* (HH)

g*) Trichloroethylene* (HH and Env)

Opinions are available in:

http://europa.eu.int/comm/food/fs/sc/sct/outcome_en.html

h) *Tetrachloroethylene* (Env)

A draft was presented by the CSTEE *rapporteur* but its adoption postponed for the next CSTEE plenary.

i) *Bis(pentabromophenyl)ether* (HH and Env)

The CSTEE *rapporteur* for both sections provided the CSTEE with his first impressions on the RAR. One committee member undertook to provide a contribution in view of allowing for a possibly final draft text to be presented at the occasion of the next plenary.

j) *Methyl acetate* (HH and Env)

The discussion on this chemical was postponed till the next plenary.

B. State of play regarding other substances evaluated under the ESR

7. Input of the CSTEE into the revision of the 'Technical Guidance Document' in support of Regulation 793/93 – (Please check the drafts in the e-mail.)

Status reports/opinions of subgroups on:

1. *'Environmental exposure'*

2. *'Marine risk assessment'*

3. *'Environmental effects assessment'*

4. *'Human health exposure assessment'*

5. *'Human Health effects assessment'*

The 'chairs' responsible for the various subsections of the TGD presented the drafts under their respective co-ordination. Given the perceived need to change them in the light of some last minute views/comments the decision was taken to postpone the adoption. This should now take place by written procedure the deadline for which was set for 25 January 2002. Before then the CSTEE secretariat will co-ordinate with the 'chairs' the finalisation and distribution of final versions of the various sections which will include the changes felt needed today. It was also judged convenient that the format of the opinions on the various subsections should to the extent possible be harmonised. Finally the view was also expressed that an 'extra' document/opinion of the CSTEE summarising some general aspects of the TGD should also be worked out and adopted. A committee member took up this task.

8. *Member States' assessments of the risk to health and the environment from cadmium in fertilisers*

The committee acknowledged the documentation package made available. The composition of the working group was reminded and further additions to it considered in

view of filing in some possible knowledge gaps. The decision was taken to hold a working group meeting on 23 January 2002 where some progress is to be expected, including the production of a first draft.

9. Emerging issues identified by the SSC and for which the CSTEE is the 'lead' committee:

a) *Endocrine disruption (Human health)*

The committee was informed by the working group chairman about the outcome of the working group meeting held the day before and where, apart from the progress/conclusions on the CSTEE WG activity proper and the decision to hold a working group meeting on 26 June 2002, there was also a presentation made by representatives of companies BKH and WRc on studies they had undertook at DG ENVs request, following the CSTEE opinion of 5 September 2000 and the EC Communication of 14 June 2001 [Twelve substances have been contracted to WRc-NSF (UK) and 435 contracted to BKH (NL)]. In particular, there seemed to be two items worth exploring: (i) the evaluation of data on ED - so-called weight of evidence and (ii) the methodology by which to take a "second cut" of data from 435 substances.

<u>The following were the main features of the WRc study:</u>

- Twelve substances assessed: 9 industrial chemicals with endocrine disruptions effects or potential endocrine disrupting effects without current regulatory measures and 1 synthetic and 2 natural oestrogenic hormones .
- Framework will be developed for the categorisation and prioritisation of substances for regulatory action. Represents a stage between the initial identification of candidate substances of concern and the implementation of any regulatory action. Framework is criteria-based, but expert judgement is required:
    1. Collection and collation of relevant exposure and exposure and effects (endocrine and non-endocrine mediated) data as required
    2. Assessment of the relevance and validity of the data against defined criteria (definitive, indicative, low significance, unusable)
    3. Evaluation of the significance of the data and identification of a robust data-set
    4. Assessment of the regulatory implications of the data set (weight of evidence, effects occur at lower doses than those causing general effects, exposure)
- Summary of significant endocrine disrupting effects data: Matrix of target groups and a) laboratory studies, b) epidemiological studies and c) mechanistic studies
- Comparison endocrine disrupting and general toxicological data: Matrix of type of data (range, lowest value) and NOAELs for target groups
- Issues to be addressed: a) synergism and b) limited knowledge of invertebrate endocrine systems and test methods to test for effects in such systems
- Project should be completed within 3 months (middle of May 2002)

<u>And the BKH study had the following ones:</u>

- Gathering information on 435 chemicals listed in the EC report of 14 June 2001 with insufficient data (based on the BKH report)
- Review of the history of former study

- Mentioned suggestions for improvement (developments of validated methods, dose-response/potency considerations, quantification of exposure, cut-off points for production volume and persistence criteria to be extended, development of a transparent system for evaluation, development of inclusion and exclusion criteria)
- Revised set-up of methodology (revised flow-chart incorporating CSTEE comments) results in 3 categories: a) Not HPV/not persistent/no exposure, b) HPV and/or persistent and/or exposure, c) no data
- Screening criteria for evaluation of ED-related effects: Relevance effect parameter, test reliability, dose-response, ED potency, ED SAR, comparisons to general toxicity
- Evaluation criteria: Category 1) At least one study providing evidence of ED in an intact organism. Not a formal weight of evidence approach. Category 2) Potential for endocrine disruption based on in vitro studies etc. Category 3) No scientific basis for inclusion in list or no data
- Evaluation of exposure concern to human and wildlife: a) Expected high exposure concern, b) expected medium exposure concern, c) expected low exposure concern. EUSES, producer/use organisation information, data from risk assessments
- Project should be completed within 6 months (ends middle of August)

The working group had found the presentations very useful, noting that the previous criticisms of the CSTEE had been thoroughly addressed. A number of specific questions and comments had been given to the presenters. The CSTEE concurred with the position of the working group. It is expected that the CSTEE will be asked for opinions on the final reports when they become available.

b) ***Indoor climate***

Since the working group meeting scheduled for 8 January had to be dropped in favour of a meeting of the TGD working group it was felt that another one needed to be scheduled but no date could be agreed. In the meantime the working group chairman is to provide a new background document.

10. *Environmental impact evaluation of Alkaline processes used for animal by-product treatment*

The committee was informed by the its chairman that this activity was now under the responsibility of the SSC. This subject will in principle be given a follow up according to the chairman's recommendations as expressed in the minutes of the previous CSTEE (7 December 2001) plenary meeting. The CSTEE will be kept informed on developments in this area.

11. Feedback from the relevant services of the Commission on the follow up to the opinions adopted previously by the CSTEE

None reached the CSTEE secretariat and none was provided at the plenary.

12. Strategies for dealing with additional opinion requests submitted by other DGs of the Commission, if any

No new submissions reached the CSTEE secretariat either.

13. Participation of the CSTEE in activities/working groups of other scientific committees of the Commission

The SCAN Secretary introduced a question on the SCAN agenda which related to the re-evaluation of 9 medicinal substances having a coccidiostat effect and currently authorised as feed additives under Council Directive 70/524/EEC. The re-evaluation process is about to start and covers several areas including impact on the environment. SCAN divided the evaluation exercise in four groups, one of them being dedicated to ecotoxicity.

Expertise of the CSTEE would be useful. Therefore the SCAN Secretary expressed the wish of SCAN to involve some CSTEE experts in that group. The CSTEE requested some clarifications on the kind of molecules under assessment and the scientific profile needed, agreed in principle to participate and nominated two of its members for the SCAN working group. Other experts could be identified later, namely nominees from Profs. K. V. Leeuwen, C. Janssen and P. Calow.

The SCAN secretary also informed that the molecules for evaluation are the following:

- Decoquinate (DECCOX®)
- Halofuginone (STENOROL®)
- Lasalocid sodium (AVATEC 15%®)
- Monensin sodium (ELANCOBAN®)
- Narasin (MONTEBAN®)
- Salinomycin sodium (SACOX 120 micro-Granulate®)
- Robenidine hydrochloride (CYCOSTAT 66G®)
- Nicarbazin (KOFFOGRAN®)
- Amprolium (Amprol Mix □)

14. Update on the latest meetings of the Scientific Steering Committee on matters of interest to the CSTEE

a) Harmonisation of Risk Assessment Task Force and Working groups

b) Cross committee's collaboration

The CSTEE chairman informed the committee about the latest developments on topics in the agenda of the SSC.

15. Arrangements for the following (30th) plenary meeting of the CSTEE and scheduling of CSTEE plenary meetings for the 2nd half of 2002

Committee members were reminded of the dates decided at the 28th plenary for CSTEE plenary meetings during the 1st half of 2002 and which were:

30th CSTEE plenary – 22 February 2002
31st CSTEE plenary – 8 April 2002
32nd CSTEE plenary – 22 May 2002
33rd CSTEE plenary –27 June 2002

The next CSTEE plenary was thus confirmed for 22 February 2002 but for lack of time no dates for CSTEE plenary meetings for the 2nd half of 2002 could be set.

16. Any other business

The committee were informed about enforcement by DG BUDGET of new rules regarding experts' bank details in order to proceed with the necessary reimbursements.

Without any other business the meeting was closed.

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SCIENTIFIC COMMITTEE ON
TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)
29th PLENARY MEETING

9 January 2002, all day, starting at 10H00 in Centre Albert Borschette, rue Froissart 36, B-1040 Brussels

- Final AGENDA -

1. **Welcoming address, apologies for absence, declarations of interest**

2. **Adoption of the draft agenda**

3. **Approval of the draft minutes of the 27th and 28th CSTEE plenary meetings**

4. **Health effects of Radio Frequency and Electromagnetic fields** – recommendations of the CSTEE for research – **status report**

5. **Presentation of the research project B6-7920/98000025 on Endocrine disrupters by representative(s) of RIVM (NL)**

6. **Regulation 793/93 on Existing substances (ESR):**
   A. Status reports/opinions (Human Health and/or Environment) on:

   a) *Cyclohexane* (HH and Env) - for opinion
   b) *Dodmac* (Env) - for opinion
   c) *Bis(2-ethylhexyl)phthalate (DEHP)* (HH and Env) - for opinion
   d) *3,4-dichloroanyline* (HH and Env) - for opinion
   e) *N-Vinyl pyrrolidone* (HH) – for opinion
   f) *Naphthalene* (HH and Env) - for opinion
   g) *Ethyl acetoacetate* (HH and Env) - for opinion
   h) *Trichloroethylene* (HH and Env) - for opinion
   i) *Tetrachloroethylene* (Env) - for opinion
   j) *Bis(pentabromophenyl)ether* (HH and Env) - presentation of RAR and 1st discussion
   k) *Methyl acetate* (HH and Env) - presentation of RAR and 1st discussion

   B. State of play regarding other substances evaluated under the ESR

7. **Input of the CSTEE into the revision of the 'Technical Guidance Document' in support of Regulation 793/93 - Status reports/opinions of subgroups on:**
    1. ***'Environmental exposure'***
    2. ***'Marine risk assessment'***
    3. ***'Environmental effects assessment'***
    4. ***'Human health exposure assessment'***
    5. ***'Human Health effects assessment'.***

8. ***Member States' assessments of the risk to health and the environment from cadmium in fertilisers*** **– progress report**

9. **Emerging issues identified by the SSC and for which the CSTEE is the 'lead' committee:**
    a) *Endocrine disruption (Human health)* **- progress report**
    b) ***Indoor climate***

10. ***Environmental impact evaluation of Alkaline processes used for animal by-product treatment*** **- progress report**

11. **Feedback from the relevant services of the Commission on the follow up to the opinions adopted previously by the CSTEE**

12. **Strategies for dealing with additional opinion requests submitted by other DGs of the Commission, if any**

13. **Participation of the CSTEE in activities/working groups of other scientific committees of the Commission**

14. **Update on the latest meetings of the Scientific Steering Committee on matters of interest to the CSTEE**
    a) Harmonisation of Risk Assessment Task Force and Working groups
    b) Cross committee's collaboration

15. **Arrangements for the following (30th) plenary meeting of the CSTEE and scheduling of CSTEE plenary meetings for the 2nd half of 2002**

16. **Any other business**

SCIENTIFIC COMMITTEE ON
TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)

29th PLENARY MEETING

9 January 2002, 10H00

Brussels, Belgium

LIST OF PARTICIPANTS

CSTEE:
Prof. James BRIDGES, Prof. Peter CALOW, Prof. CANTELLI-FORTI, Prof. Wolfgang DEKANT, Prof. Erik DYBING, Prof. Helmut A. GREIM, Prof. Colin JANSSON, Prof. Bo JANSSON, Dr. Claude LAMBRE, Dr. José V. TARAZONA, Prof. Benedetto TERRACINI, Prof. Janneche UTNE SKARE, Prof. Cornelis VAN LEEUWEN, Prof. Katarina VICTORIN, Prof. Marco VIGHI, Prof. Joseph VOS.

EUROPEAN COMMISSION:

HEALTH AND CONSUMER PROTECTION DG:
Messrs. Jorge COSTA-DAVID and Eric THEVENARD. Mrs A. WILHELM

ENTERPRISE DG:
Messrs. Philipe BRUNERIE and S. PICKERING

JOINT RESEARCH CENTRE (ISPRA):
Mrs. Kirsten VORMAN