

Minutes of the Scientific Steering Committee Meeting of 2-3 March 2000

1. Welcome, apologies, introductory remarks, declaration of interest in relation to the current agenda

Prof.Dr.Pascal welcomed the participants. He apologised, for the afternoon of 3 March, Prof.K.Jones and Prof.P.James. The list of participants is attached as annex 1.

Declarations of interest:

No member declared an interest in any of the items on the agenda of this specific meeting. In addition, Prof.W.Bridges, apologised for the previous meeting, completed and signed the "Annual Statement of Member's Interest and Declaration Concerning Confidentiality" (Annexes 1 and 2 to the Rules of Procedure of the SSC).

2. Approval of the agenda

The agenda was approved without changes. It is attached as annex 2.

3. Approval of the minutes of the meeting of 21-22 January 2000

The minutes of the meeting of 21-22 January 2000 were adopted without changes.

4. Multidisciplinary matters not relating to TSE/BSE

a. "Considerations for the evolution of scientific advice to address emerging health issues"

No further progress was made on this matter. The updated draft is being prepared, for discussion at a next SSC meeting (probably March or April 2000).

b. Harmonisation of risk assessment procedures

- Since the last SSC meeting, the working group on "Committee Guidelines" hold its second meeting on February 9, 2000. This activity progresses on two strands: review of presentation of risk assessments and development of guidelines. The preparation of various reports from other groups is following its course. All the contributions will be discussed during the next meeting of the working party on harmonisation of risk assessment procedures, scheduled on April 3, 2000. Due to time constraints, the overall progress made by this working group (except the issue discussed in item 2 hereafter) could not be further discussed in detail.

- Prof. Bridges presented the draft document on *Harmonisation of risk assessment working sub-group on the interface between risk assessors and risk managers*, prepared in the framework of the exercise on the harmonisation of risk assessment procedures. The document was very well received and considered to be a potential essential contribution to the new advisory system that as presently being debated and to contain already a number of suggestions to further improve the outputs of the present system. It was therefore proposed:

(i) to circulate for comments the draft document amongst the Commission Services that are concerned by scientific advice;

(ii) to invite all the scientific committees to comment on in and possibly provide further inputs. These could be channelled through the representative of each Committee in the plenary working group on Harmonisation of risk assessment procedures.

Prof .Kroes was further invited to already include the relevant parts of this paper, in his document integrating the SSC's comments on the Commissions White paper on Food Safety. (See also item 4.e hereafter).

c. Possibly emerging fields of concern with respect to health and consumer protection

The list attached as annex 3 to the minutes of the meeting of 21-22 January was further amended and discussed for a first time. The updated list figures in annex 3. This list should still be considered to be the result of a brainstorming. It is not ranked in terms of priority or in any other way. The SSC also stressed that it is in no way to be considered as list of priority public health concerns. Many other, and in many cases more important, public health and consumer protection issues do not figure on the list, for example because they are being addressed already, because they are not a "possibly emerging risk", because they are not within the mandate of the SSC, etc.

The SSC also stressed that this list is not a work programme for the following years, neither for the SSC nor for any other Committee. It rather aims to raise the awareness of the Commission and other Institutions on possible upcoming areas of concerns to on which the initiation of preparatory work could possibly be envisaged. (e.g., preparation of scientific dossiers, collection of data and information, etc.)

In terms of action, the SSC agreed that each item on the list would be clarified in a short explanatory note, which also provides a justification of why the item is on the list. These will be distributed and discussed at the next meeting. A work-distribution was agreed upon. Following that discussion, the list may be further amended and probably shortened.

d. White paper on Food Safety

The SSC had a first in-depth discussion on the *White Paper on Food Safety*. It was concluded that Professor Kroes would finalise, before the end of March 2000, a draft document containing the SSC comments on the White Paper. It will be discussed and possibly adopted at the SSC of 13-14 April 2000. This draft document will be based on:

- Comments from Profs Silano, Gibney and Kroes already received;
- Comments from Prof.Kundsen, prepared for the SCF;
- The Bridges document on the interaction/communication between the risk assessor and the risk manager during the preparation process for a scientific opinion;
- The discussions of the SSC of 2-3 March 2000, which emphasised on:
 - > The public health dimension of the European Food Safety Authority to be created and the need to include public health-related environmental aspects in its mandate.
 - > The impacts of the forthcoming enlargement of the EU to more than 20 Member States;
 - > risk communication;
 - > Links and co-operation between risk assessors and risk managers;
 - > TSE/BSE related advice: where and how?

In his draft document, Prof.Kroes should also make an attempt to sketch two alternative proposals: one towards a broad, integrated public health authority, not limited to food issues alone and one starting from the present White Paper scenario.

The chairmen of the Scientific Committees for Food, for Cosmetic and non-Food Products and for Plants announced that their respective committees were equally analysing the White Paper and preparing a document with comments for the attention of the Commission. It was proposed that also the 5 other Committees, if possible within their planning, would embark on a similar exercise.

e. Statement on the functioning of the EC's Scientific Committees

As requested at the SSC meeting of 21-22.01.00, the secretariat prepared a "Martyr draft" document on the functioning of the EC's Scientific Committees. Due to a lack of time, the document was not discussed. Prof. Wierup accepted to revise and amend the document and to prepare an updated draft for discussion at the next meeting. All members agreed to send their contributions *before 31 March 2000* to Prof. Wierup.

5. Multidisciplinary matters relating to TSE/BSE

5.1. Report by the chairman of the TSE/BSE ad-hoc group.

Prof. V. Silano, who chaired the last meeting of the TSE/BSE ad-hoc group, reported briefly on the meeting of the TSE/BSE ad hoc Group of 17 February 2000. All items addressed by the group are further dealt with in detail under point 5.2 of these minutes.

The planning of the preparation of a discussion paper on the hypothesis of "the 3rd route of transmission of BSE", in the light of the SSC opinion of 28-29 October 1999, was postponed, due to time constraints.

The discussion on the draft overall summary opinion on the geographical BSE risk in the European Union, was held under item 5.2.e.

5.2. Reports on specific issues

a. Safety of ruminant blood.

The working Group met for the third time on 16 February 2000. Progress is according to schedule and a draft opinion is still expected to be ready for discussion by the SSC at its meeting of April 2000.

b. Handling and storage of possibly BSE contaminated MBM.

This item was not discussed, due to a lack of time.

c. The safety of UK bone-in beef and of ruminant vertebral column for the production of gelatine and tallow (progress report).

This item was not discussed, due to a lack of time.

d. "Human Exposure Limit Line".

The report of the Working Group and the draft opinion prepared by the TSE/BSE *ad hoc* Group at its meeting of 17 February 2000, were discussed in detail and amended.

A preliminary opinion on *Oral exposure of humans to the BSE agent: infective dose and species barrier was adopted*. It is attached as Annex 4. It will be on Internet for public consultation until 31 March. Final adoption by the SSC is then expected for 13-14 April 2000, following possible further discussion by the TSE/BSE *ad hoc* Group at its meeting of 31 March 2000.

e. Geographical risk: finalised reports on the risk assessments of Member States and Third Countries (discussion on follow-up on the basis of a position paper to be prepared by the ad-hoc group).

The forthcoming geographical BSE risk opinion was discussed at length. Eventually, no opinions were adopted, only the following statement:

"In view of the cases of BSE continuing to occur in the EU, even in Member States that have not identified native cases in the past, the Scientific Steering Committee reminds that, in its efforts to define the possible implications of BSE on public health, it has repeatedly highlighted, in various opinions, the elements which contribute to the geographical BSE risk.

It is presently assessing the geographical BSE risk in the Member States and in a number of Third Countries, the preliminary results of which will be communicated to these countries in due time.

In view of both developments, the SSC wants to underline its earlier opinions indicating that the exclusion of Specified Risk Materials (SRMs) and fallen stock from the feed chain would reduce the risks of propagating the BSE agent, and that the exclusion of SRMs from the human food chain would reduce any possible BSE-risk for the consumer."

Prof. Silano was requested to update the overall opinion ("Avis chapeau") in light of discussions and of HELL opinion. Adopted is expected either at SSC of 13-14 April or together with the individual country reports. The individual country reports will be edited as drafts and each country will receive a copy of its own report for comments and additional information (if any), to be returned to the SSC secretariat before early May. These comments + the additional information possibly provided by the countries (covering period June 1999- May 2000) and the outcome of the most recent FVO inspections, will be included in updated country reports and discussed by the ad hoc Group at its meeting of 11 May 2000. The final discussion by the SSC will then be held at the SSC meeting of 25-26 May 2000.

f. TSE and culling (discussion). This item was not discussed, due to a lack of time.

g. Origin of BSE (progress report). This item was not discussed, due to a lack of time.

h. GME protocol on TSE inactivation

A copy of the comments made by Prof. Vanbelle and sent to GME (see item 5.2.d of the previous minutes), was made available for information to all the SSC members.

6. Organisational matters

- Transparency regarding the membership of working groups; guidelines.

This item was not discussed, due to a lack of time.

7. Co-ordination

a. Reports of the Chairmen of the 8 Scientific Committees.

The chairmen of all Scientific Committees provided written reports on the activities of their committees since the last SSC meeting (9-10 December 1999; see annex 7)

8. Information by the Commission services on matters related to consumer health

No information was provided by other Commission Services.

9. Any other business

No other business were discussed.

The meeting ended on Friday 21 January 2000, at 14h00.

The next meeting will be held in Brussels, on 13-14 April 2000, starting at 10h00.

Annex 1: List of participants of the Scientific Steering Committee meeting of 2-3 march 2000

Members of the SSC:

Prof. Georges Bories, Prof. James W. Bridges, Prof. Fulgencio Garrido Abellán, Prof. Michael Gibney, Prof. Anthony R. Hardy, Prof. Philip T. James (not present on 3 March 2000 afternoon), Prof. Keith H. Jones, Prof. Fritz H. Kemper, Prof. Werner Klein, Prof. Ib Knudsen, Prof. Robert Kroes, Prof. Albert Osterhaus, Prof. Gérard Pascal, Prof. Vittorio Silano, Prof. Marcel Vanbelle, Prof. Martin Wierup

Participants from the Commission:

DG ENV: B. Van Tongelen

DG SANCO: B. Carsin, J.J. Rateau, C. Berlingieri, G. Costa-David, W. de Klerck, C. Diez, F. Drion, M. Granero, J.L. Jouve, J. Kreysa, H. Opitz, W. Penning, E. Poudelet, J. Savio, A. Somogyi, A. Van Elst, J. Vergnettes, P. Vossen, A. Wilhelm

Annex 2: Agenda of the Scientific Steering Committee Meeting of 2-3 March 2000

1. Welcome, apologies, introductory remarks, declaration of interest
2. Approval of the agenda
3. Approval of the minutes of the meeting of 20-21 January 2000
4. Multidisciplinary matters:
 - a. "Considerations for the evolution of scientific advice to address emerging health issues" (progress report and discussion)
 - b. Possibly emerging fields of concern with respect to health and consumer protection (discussion)
 - c. Harmonisation of risk assessment procedures (progress report and discussion)
 - d. White paper on Food Safety (discussion)
 - e. Statement on the functioning of the EC's Scientific Committees (discussion)
5. Multidisciplinary matters relating to TSE/BSE
 - 5.1. Report by the chairman of the TSE/BSE ad-hoc group, including also the proposed planning for:
 - a discussion paper on the hypothesis of "the 3rd route of transmission of BSE", in the light of the SSC opinion of 28-29 October 1999;
 - an overall summary opinion on the geographical BSE risk in the European Union.

5.2. Reports on specific issues:

Production systems and products.

- a. Safety of ruminant blood (progress report)
- b. Handling and storage of possibly BSE contaminated MBM (progress report).
- c. The safety of UK bone-in beef and of ruminant vertebral column for the production of gelatine and tallow (progress report).

Human exposure risk

d. "Human Exposure Limit Line" (discussion and possible adoption of an opinion).

Geographical risk.

e. Geographical risk: finalised reports on the risk assessments of Member States and Third Countries (discussion on follow-up on the basis of a position paper to be prepared by the ad-hoc group).

f. TSE and culling (discussion).

g. Origin of BSE (progress report).

Other TSE/BSE related issues:

h. GME protocol on TSE inactivation

6. Organisational matters.

- Transparency regarding the membership of working groups; guidelines.

7. Co-ordination: Reports of the Chairmen of the 8 Scientific Committees.

8. Information by the Commission services on matters related to consumer health.

9. Any other business.

Annex 3:

Draft initial* list of possible fields for concern in the medium-term future

(Updated listing as on 3.03.00)

Factors predisposing for the emergence of infectious diseases:

- New viral diseases / prion diseases;
- Unexpected microbial diseases linked with (drinking) water;
- climatic change events: extreme weather events and results of increased temperatures;
- Xeno-transplantation;
- Upcoming diseases due to blood transfusion;
- Gene therapy; safety of vectors used in gene therapies
- Risk assessment of genetically modified viruses
- New infections because of antimicrobial resistance and/or because of increased virulence of agents.

Other fields:

- Macro-nutritional imbalance and its direct and indirect consequences for disease;
- (natural) toxin exacerbation (including, amongst others, mycotoxins and toxins in algae);
- Gene-therapy;
- Allergenicity (as yet unknown);
- Increase pressure to deliver quantitative estimates of risks involved with (unexpected) exposures to agents (chemical, biological and physical);
- New claims on supposed diseases (re cancer) due to cellular phones.
- Non communicable chronic diseases, causes and prevention: role of industrial chemical and chemical pollutants from food and environment.
- Environmental pollutants and endocrine disrupters and their interference with the immunosystem.
- Health hazards due to the recycling of toxic substances (for example when recycling animal waste);
- Scientific illiteracy as a possible (emerging) (individual and public) health hazard (including aspects such as risk

perception and risk communication).

Collateral issues needing further discussion:

- Implementing the sustainability principle across the various scientific committees; its implications for risk assessment and scientific advice.

* : This list should still be considered to be the result of a brainstorming. It is not ranked in terms of priority or in any other way. The SSC stresses that it is in no way to be considered as list of priority public health concerns. Many other, and in many cases more important, public health and consumer protection issues do not figure on the list, for example because they are being addressed already, because they are not a "possibly emerging risk", because they are not within the mandate of the SSC, etc.

Annex 4

Preliminary OPINION

ORAL EXPOSURE OF HUMANS TO THE BSE AGENT: INFECTIVE DOSE AND SPECIES BARRIER

Adopted by the Scientific Steering Committee

at its meeting of 2-3 March 2000

Text subject to further changes

THIS OPINION IS OPEN FOR PUBLIC COMMENTS
UNTIL 27 MARCH 2000

Comments can be sent to:

paul.vossen@ec.europa.eu

Please pay special attention to the SSC recommendation to the international scientific community to propose, during the present consultation, a "realistic" worst case scenario for the assessment of the possible residual risk in bovine derived products.

(Distributed separately, and available on Internet)

Annex 5: Reports from the secretariats of Scientific Committees on the major activities and milestones since the SSC meeting of 20-21 January 2000.

Scientific Committee for Plants

The SCP met on 28 January 2000. The Committee examined a number of draft opinions on genetically modified plants and plant protection product active substances. The following four opinions on plant protection products were adopted:

- Lambda cyhalothrin - dietary risk assessment, risk assessment for aquatic and beneficial organisms;
- Cyfluthrin and beta cyfluthrin - dietary risk assessment, ecotoxicological risk assessment;
- Pesticide residues - general criteria for the setting of acute reference doses for plant protection products.

Scientific Committee on Animal Nutrition (SCAN)

At its plenary of February, the Scientific Committee on Animal Nutrition adopted an opinion on the use of Bacillus in animal nutrition, which advises the Commission on the way to assess the production of toxin by the strains of Bacillus involved in certain products to be authorised as feed additives. The Committee adopted also a report on the assessment of the efficacy of micro-organisms used as feed additives. A similar report is also under preparation for enzymes. The rest of the Working groups continue their work and draft reports should be ready for the next plenary meeting (27-28 April).

Scientific Committee Veterinary Measures relating to Public Health

The Scientific Committee on Veterinary measures relating to Public Health adopted an opinion on the revision of ante- and post-mortem inspection procedures for an alternative inspection system for the slaughter of pigs at its plenary meeting of February. The working groups continue their work. Draft reports are expected for the next plenary meeting (11-12 April).

Scientific Committee on Animal Health and Animal Welfare

A. Meetings of the Subcommittee on Animal Welfare were held on 21.02.2000 and on 3.03.2000.

The document on **the WELFARE OF BROILER CHICKENS** prepared by the specific Working group, which had met for the final time on 1. and 2. February 2000 was on the agenda:

The very comprehensive draft prepared by the Working Group was thoroughly discussed. The Subcommittee requested some integrations in the document in particular concerning conclusions and recommendations. After the second meeting the Subcommittee accepted the revised draft. The document will be submitted for discussion and possible adoption to the Committee on Animal Health and Animal Welfare on 21.03.2000.

B. A Meeting of the Subcommittee on Animal Health was held on 22.02.2000

The document on *Possible links between Crohn's disease in man and paratuberculosis in animals* prepared by the specific Working group was on the agenda. The Subcommittee agreed on the structure and approved the document and a number of amendments were requested. The draft will be finalised and presented at the next Committee plenary (see above).

A number of new questions were put to the Committee on animal health matters. These concerned questions on Avian Influenza, Infectious Bovine Rhinotracheitis, Bluetongue and Infectious Salmon Anaemia, Contagious Bovine Pleuropneumonia.

C. Progress report of Working Groups:

0 - Inactivation of viruses in blood. The document is in preparation and will be discussed at the next Subcommittee.

- Working Groups on new questions:

1 The Welfare of Animals kept for fur production. This newly established WG will have its first meeting before the end of March.

2 The Welfare of Fattening Cattle. A group was set up and has not yet held its first meeting.

Scientific Committee for Toxicity, Ecotoxicity and the Environment

A. The 13th plenary meeting of the CSTE took place on the 4th of February 2000. In terms of progress made on the opinion requests to the CSTE and other CSTE initiatives the outcome was the following:

B. Dates for the CSTE plenary meetings for the year 2000 were agreed (pairs of dates are indicated as it is difficult to anticipate whether one or two day meetings will be needed later in the year - dates in brackets are provisional and two

day meetings will only take place in case of need): (10/11)April, 19/(20)June, 04/(05)September, 09/(10)October, 02/(03) November.

C. On the subject '*Terrestrial environment*' - '*Available scientific approaches to assess the potential effects and risks of chemicals on terrestrial ecosystems*' - A working group meeting took place on the 1st of March 2000. Several drafts on some of the different chapters of the report were discussed. Changes to these will be made before the next CSTEE plenary meeting (11th of April 2000) after which two more WG meetings should take place (before the June CSTEE plenary meeting) in view of possibly adopting the opinion/report then.

D. Regarding the opinion request on a *report from a study on Technical specifications for classification and presentation of ecological status of surface waters and a report from a study on technical specifications for monitoring of ecological status of surface waters*, there is no progress for the same reasons already highlighted in previous briefings for SSC minutes.

E. Evaluation of Technical s for Guidance (TNsG) in support of Directive 98/8/EC concerning the placing of biocidal products on the market - An opinion was finally adopted at the February 2000 CSTEE plenary meeting. In principle the CSTEE may be asked in the future about other documents to be produced in support of Directive 98/8 (Biocides).

F. Regarding the two outstanding opinion requests on '**lead**' [**(i)** a notification of the Danish authorities informing Commission services of their intention to ban lead in a significant number of applications and **(ii)** a general opinion request on hazards and risks posed by lead and its compounds to human health and the environment] a WG meeting took place on the 3rd of February 2000 but outstanding data on environmental effects prevented the Working Group from finalising the draft (on element **i**). Another working group meeting is scheduled for the 8th of March during which it is expected that the draft will be finalised, in which case an adoption by written procedure is foreseeable given the urgency of the matter for Commission services.

G. The opinion request mentioned in the previous briefing (four chemicals, with others to come, which have been risk assessed under Regulation 793/93 on existing substances: Nonylphenol (straight and branched chain) CAS 84852-15-3, 25154-52-3, Pentabromodiphenyl ether CAS No.32534-81-9, Octabromodiphenyl ether CAS No.32536-52-0 and Decabromodiphenyl ether CAS No.1163-19-5) have in the meantime been received by the CSTEE secretariat. As expected opinions on the environmental risk assessments of Nonylphenol and Pentabromodiphenyl were adopted at the February CSTEE plenary.

In the meantime other opinion requests on substances under Regulation 793/93 were submitted to the CSTEE for opinion (on the following chemicals): **(i)** 4,4'Methylenedianiline, **(ii)**1,4-Dichlorobenzene, **(iii)**Cumene and **(iv)**4-chloro-2-methylphenol, **(v)**Hydrogen fluoride, **(vi)**Dimethyl sulphate, **(vii)**Acrylaldehyde and **(viii)**Dioxane. 20 to 30 others are likely to be submitted in the near future making this an area of work that will keep the CSTEE significantly busy.

Because of the timeframe set by the requester Commission service for these substances, priority is being given to Hydrogen Fluoride, Acrylaldehyde, Dimethyl sulphate, 4,4- Methylenedianiline and Cumene and a WG meeting is scheduled for the 17th of March.

H. In regard to the ongoing subject of **environmental exposure assessment** progress has been limited. The plan to develop the report with the Environment Agency has failed due to lack of expertise and resources in the EA. The working group will integrate its activities with those of the new working sub-group of the Harmonisation of Risk assessment working party of the SSC.

I. Other opinion request were in the meantime submitted to the CSTEE on:

(i) Cadmium in fertilisers where a CSTEE opinion on a report on the subject of a "Programme of procedures for the assessment of risk to health and the environment from cadmium in fertilisers" has been requested (for adoption at the June CSTEE plenary meeting at the latest).

(ii) Methylene chloride where a CSTEE opinion of the CSTEE on risk assessments on Methylene chloride and certain chemicals in textiles has been requested. The CSTEE is to peer review the reports:

a) "Methylene chloride: Advantages and Drawbacks of Possible Market Restrictions in the EU" - TNO (Dr. Tukker & Ir. L.Ph. Simons - NL) report STB-99-53 Final - November 1999 and,

b) "Assessment of the Risks to Human Health Posed by Certain Chemicals in Textiles and of the Advantages and Drawbacks of Restrictions on their Marketing and Use" - Final Report - July 1999 - WS Atkins International Ltd (UK).

(iii) Still other possible opinion requests may be submitted in the near future on:

a) Relevant pesticides metabolites in drinking water

b) Construction products in contact with drinking water

c) Evaluation of active substances (in the context of the WFD)

d) Evaluation of chemical substances for endocrine disrupting potential/effects (in list of potential EDCs prepared by Commission services).

J. The next (14th) CSTEE plenary meeting is taking place on the 11th of April 2000.

Scientific Committee for Cosmetics and Non-Food Products

Five Working Party and one Plenary meeting took place, during which the following items were discussed :

A. Hair Dyes :

5 opinions were adopted during the plenary meeting of 17 February 2000. 2 dossiers were discussed during a WP meeting, of which one was addressed to the next plenary meeting of 3 May. Further data are required for the other one.

B. UV Filters :

S75 (coated Titanium dioxide) : Additional safety data were received which are being evaluated.

S74 : the Committee on Adaptation to Technical Progress (CATP) of the Annexes to Directive 76/768/EEC referred the opinion adopted on S74 back to the SCCNFP for some clarifications. The Committee drafted a reply which will be sent soon the DG ENTR.

C. Alternatives/Dossier :

An opinion on the predictive testing of potentially cutaneous sensitising cosmetic ingredients or mixtures of ingredients has been adopted. Animal and human assays are considered. Due to ethical questions concerning the risk for involved human volunteers and the limited scientific information available on this point, it is agreed that such predictive human sensitisation tests should not be carried out without a better understanding of the immunologic background and mechanism.

D. Preservatives, Colorants & Fragrances :

Opinions were adopted concerning the phenomenon of 'quenching' (a complete abrogation of the sensitising potential of a fragrance chemical by the presence of another specific fragrance chemical at defined ratios to the sensitising agent) and on the safety of tattoos. Although the safety of tattoos falls outside the classification of cosmetic products, the SCCNFP was requested to adopt an opinion as it may fall under the competence and the mandate for non-food products.

E. Inventory :

The draft update of the inventory of cosmetic ingredients has been received. It has been reviewed by the Working Party. Specific corrections have to be made before its adoption.

Scientific Committee for Medicinal Products and Medical Devices

A plenary meeting of the SC-MPMD took place on 16.2.2000. Two opinions were adopted:

- Opinion on Quality and Safety of Blood. (Doc. SANCO/SCMPMD/2000/0005 Final).
- Opinion on Update of the Opinion given by the Scientific Committee on Medicinal Products and Medical Devices on The Risk Quantification for CJD Transmission via Substances of Human Origin.

Other subjects such as "Xenotransplantation", "Latex" ad "Orphan Drugs" were discussed.