Scientific Steering Committee (SSC) - Summary minutes of the plenary session of 16-17 April 1998

Annex 1: List of participants of the Scientific Steering Committee meeting of 16-17 April 1998

List of presence

Members of the SSC:

- Prof. Georges Bories
- Prof. Michael J. Gibney
- Prof. Philip James
- Prof. Keith H.Jones
- Prof. Werner Klein
- Prof. Ib Knudsen
- Prof. Robert Kroes
- Prof. Albert Osterhaus
- Prof. Gérard Pascal
- Prof. Marcel Vanbelle
- Prof. Martin Wierup
- Prof. Pierre. Le Neindre (replaced Prof. Garrido Abellán on 17/04/98 morning)
- Prof. Nicola. Loprieno (replaced Prof. Kemper on 17/04/98 morning)
- Prof. Marco Maroni (replaced Prof. Silva Fernandes on 16 & 17/04/98 morning)

Apologies:

- Prof. W.Bridges
- Prof. F.Garrido-Abellán
- Prof. Fritz H.Kemper
- Prof. A. Silva Fernandes

Participants from the Commission:

DGIII: L. Bansil, O.Rohte, J.-P. Feyaerts (16 April),J. Silva (16 April), K. Berend (17 April)

DG V C. Schatzl (17 April)

DGXII: M. Vidal (16 April)

DGXXIV: H.Reichenbach, J.J. Rateau, B. Carsin, T. Daskaleros, C.Deckart, W.De Klerck, C.Diez Ubierna, J.Kreysa, M. Lauridsen, G.Morrison, J.Moynagh, W. Penning, A.Van Elst, R. Vanhoorde, P.Vossen, M. Zampaglione.

Stagiaires: A. Matéo, A. Wilhelm

Annex 2: **Agenda of the Scientific Steering Committee (SSC) Meeting of 16-17 April 1998**

1. Welcome, apologies, introductory remarks

2. Approval of the agenda

3. Approval of the minutes of the meeting of 26-27 March 1998

4. Information by the Commission on the present state of affairs regarding the Commission policy on specified risk materials

5. Work plan for the SSC

5.1. Progress so far on multidisciplinary matters, not primarily related to TSE/BSE:
- the protection against the risk of infectious agents entering the human food or animal feed chains via raw animal material (for example as dead animals, condemned carcasses, sick animals, laboratory animals).
- Bovine Somatotropine
- Link between John's and Crohn' disease
- resistance to antibiotics.

5.2. Multidisciplinary matters relating to TSE/BSE
- Production systems and products, including environmental aspects;
- Safety of semen and embryos
- Human exposure risk, including SRMs and medicinal aspects;
- Geographical risk
- Monitoring
- Diagnosis tests of TSE in bovines

5.3. Other pending questions: source, allocation, schedule.
- The UK Date based export scheme.

6. Discussion and possible adoption of opinions
6.1 exposure limits to electromagnetic fields,

7. Organisational matters
Additional members for the TSE/BSE ad hoc group.

8. Co-ordination
8.1. Report of the Chairmen of the 8 Scientific Committees on issues treated or on the forthcoming agenda
8.2. Harmonisation of working procedures, in particular in relation to risk assessment methodologies.
8.3. The role of the Scientific Committees and the SSC in relation to risk assessment and risk management.
8.4. Definition of "acceptable" or "negligible" risk levels.

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

10. Any other business.
- Request by T.Roethe, Hannover, to follow some meetings of the SSC and other Scientific Committees as basis for a sociological study of the Commissions Scientific Advisory System in the context of a risk-society.

Annex 3: List of pending questions for the SSC (Update as on 17/04/98)

QUESTION	ORIGIN, DATE OF RECEPTION & DEADLINE	PROPOSED ATTRIBUTION	LEADING COMMITTEE, RAPPORTEUR & SECRETARY	EXPECTED DATE OF ADOPTION
I. Multidisciplinary matters, not related to TSEs				

QUESTION	ORIGIN, DATE OF RECEPTION & DEADLINE	PROPOSED ATTRIBUTION	LEADING COMMITTEE, RAPPORTEUR & SECRETARY	EXPECTED DATE OF ADOPTION
Possible human and animal risks related to the authorised commercialisation of recombinant Bovine Somatotropine in the E.U.	- Fischler and Bonino - 13.10.97 - June 1998		- SC-VHPH - R.Vanhoorde	July 1998
Possible links between Johne's disease and Crohn's disease.	- DGVI - June 1997 - no deadline	Garrido to report on progress	- SC-AHAW - J.Moynagh	
Genetically modified organisms (GMOs): requests for scientific advice on genetically modified plants	- Commission - Nov. 1998 - As soon as possible	Silva-Fernandes and Knudsen	- SC-Plants (M.Walsh) - SC-Food (P.Wagstaffe)	Permanent
Fallen stock: The protection against the risk of infectious agents or non conventional transmissible agents entering the human food or animal feed chains via raw animal material (for example as dead animals, condemned carcasses, sick animals, laboratory animals).	- SSC in its tallow and MBM opinions - March 1998 - Urgent	SCVPH lead, SCAHAW input	- SCVPH and SCAHAW	a.s.a.p.
Exposure limits to electromagnetic fields	- DGV - 01.98 - no deadline given	Klein to revise report	- Initial report: W.Klein - (P.Vossen) - SC-TEE: if needed	14/15-5-98
Resistance to antibiotics	- SSC - 03.98		- SSC: own WG - Jones - R.Vanhoorde	Nov. '98 First meeting: May '98
Quality, efficacy and harmlessness of non-conventional medicinal products	- DGV - 12.03.98 - urgent	Back to DG V clarification of question		
II. TSE/BSE matters: pending				
Production systems and products, incl. environmental aspects	-		**Vanbelle, Willeberg, Piva**	
- tallow, meat and bone meal, gelatine	- Commission - April 1997 - A.s.a.p.	Quantitative RA needed	- SSC - WG-HER - J.Kreysa	??
- Peptides and amino acids	- Commission - April 1997 - No deadline	G.Pascal to prepare report	- SSC - G.Pascal - P.Vossen	June '98
- Bi-calcium phosphate	- Commission - April 1997	MV to prepare report	- SSC - M.Vanbelle - P.Vossen	May 98

QUESTION	ORIGIN, DATE OF RECEPTION & DEADLINE	PROPOSED ATTRIBUTION	LEADING COMMITTEE, RAPPORTEUR & SECRETARY	EXPECTED DATE OF ADOPTION
	- No deadline			
- Organic fertilisers	- DGsVI + XXIV - 04-11/1997 - No deadline		- SSC - G.Piva / Bridges - P.Vossen	Next meeting: 18/05/98
Disposal of animals and animal tissues (SRM) assumed to carry a risk of being infected with BSE	- Various (EP, DGXI, DGVI, ….) - Various: 09.97-1.98 - No deadline	Riedinger, DE, to be added Merge with org. fertilizers	- SC-TEE - Bridges / Gibney - P.Vossen	June or July 1998
- Feeding of MBM to fur animals	- Commission: DGVI - November 1997 - No deadline given		- TSE/BSE-WG"Fur" - G.Piva - P.Vossen	Next meeting: 18/05/98
Semen and embryos: updated opinion	- Commission: - 9.01.98 - February 1998	To be finalised	- TSE/BSE - A.Somogyi - P.Vossen	June '98
Production systems and products, incl. environmental aspects (cont'd)	-		**Vanbelle, Willeberg, Piva**	
Animal-derived rennet: Need for carrying out a risk assessment and transmission studies	- DG VI - 15.07.97 - no deadline	A.O. to prepare report	- TSE/BSE - A.Osterhaus - P.Vossen	June '98 ?
Maternal transmission - Routes of infection, Risk assessment for these routes, Options to mitigate the risk from these routes	- DG VI - 15.07.97 - no deadline given	Add Pastoret to WG if WG needed	- TSE/BSE - A.Osterhaus - J.Kreysa	Sept.'98 ?.
Transfer of BSE to sheep: - Possibilities of transfer; Scrapie infectivity of peripheral nerves of sheep: implications in a BSE context	- DGVI and (indirect) FRG Government - 13.10.97 / 9.12.97 - no deadline	Members identified	- TSE/BSE - E.Vanoptenbosch - P.Vossen	First meeting 29/04/98
The guarantees provided by 'closed herds' as compared to 'BSE free regions'.	- DGIII - January 1998 - no deadline	Members identified	- TSE/BSE - E.Vanopten-bosch - P.Vossen	June 98
Organophosphates: review of the May 1997 opinion of the MDSC	- Various - 06-12.97 - no deadline	Meeting on 6/4/98	- TSE/BSE - E.Vanopden-bosch - P.Vossen	May 98
Intraspecies recycling of fish, pig and poultry waste (incl. fat) and meat	- DGVI & SEAC opinion of 03.12.97	Wierup to be asked to participate in	- SCVPH plus - SCAHAW plus SCAN	Sept '98 ?

QUESTION	ORIGIN, DATE OF RECEPTION & DEADLINE	PROPOSED ATTRIBUTION	LEADING COMMITTEE, RAPPORTEUR & SECRETARY	EXPECTED DATE OF ADOPTION
and bone meal and tallow. (See letter N° 03690 of DGVI of 21.01.98)	- 21.01.98 - no deadline	WG	- A.Osterhaus - R.Vanhoorde	
Acceptable minimum levels of cross-contamination in MBM.	- SSC opinion of 19-20.02.98	G.Piva should propose experts.	- TSE/BSE ad hoc group - Prof.G.Piva - P.Vossen	July '98 ?
Human exposure risk, including SRM and medicinal aspects	-		**P.James, P.Verger**	
Defining and listing of Specified Risk Materials	- Commission - October 1997 - 8-9.12.98	P.James will look into comments	- TSE/BSE – WG-HER - P.James - J.Kreysa	May '98 ?
Quantitative ranking of Specified Risk Materials according to their potential infectivity.	- SSC - 23.01.98 - a.s.a.p.	To be continued	- TSE/BSE – WG-HER - M.Gibney / P.James - J.Kreysa	preliminary 19-20.02.98 Final?
Safety of bovine blood and blood products.	- Various, - 08.97 – 01.98 - a.s.a.p.	P.J to monitor work on human blood	- TSE/BSE - P.James - J.Kreysa	Report June '98
Human exposure Risk : Assessment of the risk that humans are exposed to the BSE agent by consuming/using BSE animal derived materials and products.	- SSC - 26/27.03.98	New WG defined	- TSE/BSE ad hoc - P.Verger - J.Kreysa	First meeting: 29/04/98
Transmission of CJD via infected human blood; Risk quantification for CJD transmission via substances of human origin (Note: not to be restricted to nv-CJD)	- DG 24 & 3, Bonino - 7.11.97 + 14.01.98 - Asap	K.Jones to report to SSC	- SC-MPMD - K.Jones - A.Sanabria	June '98 ? Depends on SEAC
The use of specified risk materials for the manufacture of implantable medical devises	- DGIII - January 1998 - No deadline given	K.Jones to report to SSC	- SC-MPMD - K.Jones - A.Sanabria	??
Equivalency of alternative products for the use of intestine of animal origin for surgical sutures	- DGIII - January 1998 - No deadline given	K.Jones to report to SSC	- SC-MPMD - K.Jones - A.Sanabria	??
Geographical risk			**M.Gibney, E.Vanopten-bosch**	
TSE/BSE/Scrapie status of a country or region: - Risk assessment method(s) and	- Commission - 8-9.12.97 - 22-23.01.98	Work continued	- TSE/BSE-WG- - Sourcing - M.Gibney	Next meeting 7/5/98

QUESTION	ORIGIN, DATE OF RECEPTION & DEADLINE	PROPOSED ATTRIBUTION	LEADING COMMITTEE, RAPPORTEUR & SECRETARY	EXPECTED DATE OF ADOPTION
geographical aspects of the risk.			(WGSM) - J.Kreysa	
- Requests from EU-MS: SF, DK, SW, DE, IT, AT	- Governments - ?	Waiting		
- Request from Non-EU Countries: Norway, Canada, Argentina, USA	- Governments - ?	Waiting		
Monitoring			**A.Osterhaus, E.Vanopten-bosch**	
Monitoring of the validation of post-mortem BSE tests, not development of validation procedure.	- DGXXIV - February 1998	WG to be created	- TSE/BSE - Osterhaus - P.Vossen	First meeting in April ??
Monitoring of the research carried out by the Joint Research Centre on (a) the validation of a test to verify the heat treatment (20 minutes, 133°C) and (b) the detection of bovine material in meat and bone meals.	- SSC - Meeting of 16.10.97		- Vanopten-bosch - P.Vossen	permanent
TSE/BES matters: possibly upcoming questions				
Milk: review of the opinion of the Scientific Veterinary Committee of 1996 and of the MDSC of 1997	- Individuals, in letters to EP + Cabinet	P.Verger will follow lit. and report	- TSE/BSE ad-hoc	
Culling strategies: should herds where a clinical case was detected, but where it is clear that the animal was infected in another herd, be culled?	- Lux. government (generalised) - 15.01.98 - asap		- SC-AHAW ?	

Annex 4a: ANTI MICROBIAL RESISTANCE (Reflection paper by Dr.K.Jones)

Introduction

Following discussion on the subject of anti microbial resistance at the Scientific Steering Committee meeting on 26/27 March 1998, and the proposal to establish a new scientific committee, consideration was requested for key areas the committee might address, and a draft of a possible mandate.

Background

The introduction of penicillin into clinical practice in the 1940s made a significant contribution to the treatment of a wide range of infectious diseases in humans and

animals. The potential for micro-organisms to become resistant to antibiotics however was recognised early by the development of antibiotic resistant staphylococci - particularly those resistant to methicillin (the methicillin resistant staphylococcus aureus - MRSA).

Until recently the problem had been partially addressed by the development of a succession of new effective anti microbial chemotherapeutic agents. In recent years however there has been a significant slowing down in the rate of development of such agents, and at the same time, there has been rapid and extensive development of antimicrobial resistance.

Although there have been several important advances in the availability of antiviral and anti fungal agents, there have been no truly novel antibacterial drugs developed in more than 10 years. Increasing problems have therefore arisen in finding effective anti microbial chemotherapy for a number of major bacterial pathogens including methicillin resistant Staphylococcus aureus, vancomycin resistant enteroccoci, and multidrug resistant Mycobacterium tuberculosis. This has led to increasing difficulties in the management of a range of human and animal infections.

An important concern must be the cause for this rapid and widespread development of resistance. Although antimicrobial resistance to antibiotics might be expected to develop through a process of natural selection, it is considered (though not yet conclusively proven) that inappropriate use - both in human medicine and in animal husbandry - has been a major contributory factor. The precise mechanism for the development and transfer of resistance remains unidentified in most cases and considerable effort needs to be directed towards resolving the scientific basis of this problem. The concern amongst scientists however is sufficiently great for it to have been proposed that every administration of an antibiotic must be considered as an opportunity for the further development of antimicrobial resistance and this attitude needs to be registered with those who use antibiotics if the problems in clinical medicine are to be satisfactorily contained.

The problem of anti microbial resistance needs to be addressed urgently to ensure that best use is made of the antibiotics that currently remain effective. Failure to do so could have serious implications for the provision of healthcare in the future, by, for example, potentially limiting medical and surgical advances, lengthening and increasing the difficulty of post operative care and requiring the major provision of isolation facilities. Any strategy directed at human medicine needs to be comprehensive to ensure the preservation of current drug efficacy, to encompass re-education of practitioners and patients, and also to consider how encouragement might be given to the development of effective treatment alternatives.

Although anti microbial resistance has wide spread implications for current practice in clinical prescribing and for the treatment of disease in animals, a comprehensive assessment of the implications needs also to take account of the importance and impact of use of antibiotics in the treatment of animals destined to enter the human food chain, their use as growth promoters in veterinary practice and agriculture and the possible impact on human health of use of GMOs (as food both for humans and for animals destined for the human food chain). The new committee should be asked to take full account of all of these issues in fulfilling its remit.

The problem of anti-microbial resistant does not recognise national - nor indeed Community - boundaries and the international dimension of the problem needs to be

recognised taking account of initiatives underway in WHO and in third countries. Within the European Community itself there is a major body of scientific expertise, to which the proposed scientific committee will need access.

Because of the seriousness of it potential consequence, this issue of antibiotic resistance has been considered and debated widely by numerous academic, professional, industry and Government groups world-wide. Government bodies have considered the science, current issues and proposals for managing this problem, quite recently in Denmark, the UK, USA and Canada. Other countries have also shown concern and the WHO have studied the matter in depth and issued major reports, one as recently as this month. Several of these bodies have recently reported, some are about to report findings and recommendations, and a substantial body of information already exists across many scientific disciplines. This literature has not been comprehensively reviewed for this consideration.

Much of this evidence has, however, recently been reviewed by the Scientific Committee on Animal Nutrition (SCAN) at the request of the Commission, and the remainder needs to be assembled and analysed. An early task must therefore be to take stock across all disciplines and all scientific committees.

Proposal

The mandate of the scientific committee will need to be wide ranging, addressing all facets of the subject, including the extent of the problem, its aetiology in terms of scientific mechanisms and the relation of these to the practices of clinical medicine, animal husbandry and food production. It should also address the effects and implications of the continuing development of antimicrobial resistance, means of influencing its further progress and scientifically sound, practical advice on how to solve or ameliorate these problems.

As a first draft for discussion at the Scientific Steering Committee, I would propose the following mandate. The group should ***"Scientifically evaluate the current position regarding the prevalence and development of anti microbial resistance, examine its implications for human and animal health, particularly with regard to the development and management of infections. The group should evaluate factors contributing to the aetiology of the present situation, examine means of influencing or controlling the development of anti microbial resistance and make recommendations based on scientific evidence. It should also advise on the means of monitoring the outcome of measures which it might recommend, and consider the implications of its advice. It should evaluate scope for collaboration in resolving scientific issues, not only within, but also outwith, the European Community."***

Annex 4b:

BACKGROUND INFORMATION FOR A WORKING GROUP ON THE USE OF ANTI-MICROBIALS

(The text hereafter is not an official Commission position paper)

1. In the Communication on Consumer Health and Food Safety of 30 April 1997, the Commission indicated that recommendations for action could originate either from the results of scientific advice, risk analysis or control missions. It also specified that the Evaluation of Health Risks Unit was to fulfil a forward looking role for identifying potential or emerging hazards relating to consumer health and that any

Scientific Committee and the Scientific Steering Committee could draw the attention of the Commission to potential and emerging hazards in relation to consumer health.

2. The question of anti-microbial resistance falls under both criteria. The Evaluation of Health Risks Unit has become aware of a growing number of converging reports on increased anti-microbial resistance, in particular against some food-borne pathogens. Additionally, two scientific committees as well as the Scientific Steering Committee have discussed the matter recently:

- At its meeting of 18-19 September 1997, the Scientific Committee for Food drew the attention of the Commission "to the urgent need to give detailed consideration to the general question of anti-microbial resistance. Although the question had arisen in the context of risks of microbial resistance arising through food consumption, the problem was of relevance in other fields such as pharmaceuticals, animal nutrition and medicine." The Committee concluded that increasing anti-microbial resistance gave rise to potential risks to public health. It recognised the multi-disciplinary nature of the problem and suggested that it may be considered by the Scientific Steering Committee

- At its meeting of 22 December 1997, the Scientific Committee on Veterinary Measures relating to Public Health (SCVPH) recognised that the Scientific Committee for Animal Nutrition (SCAN) addresses the issue of feed additives. It was considered that this issue needs both an input from veterinary and from human medicine and that a series of scientific reports from international bodies were in the pipe-line. Therefore, the SCVPH concluded not to address the question of anti-microbial resistance immediately, but asked its Chairman to highlight the multi-disciplinary aspect of the problem to the SSC and to include an expert of the SCVPH in the SCAN working groups when discussing this question.

- At its meeting on 26-27 March 1998, the Scientific Steering Committee agreed on the establishment of a multi-disciplinary Working Group to examine all aspects related to the use of anti-microbials and the development of resistance. The Working Group shall comprise i.a. experts from the Scientific Committees with special competence in this field, as well as external experts in order to ensure coverage of the full range of areas concerned.

3. Anti-microbials are used for :

- prophylactic/therapeutic use in humans
- prophylactic/therapeutic use in animals
- improvement of feed efficiency in animals (growth promoters)
- phytosanitary use (e.g. in case of fire blight).

4. Medicinal products for human use

A medicinal product for human use must be authorised either centrally by the Commission (biotechnology and high technology medicinal products) or nationally by each Member State where it is to be placed on the market with a procedure for mutual recognition of national authorisations (Regulation Nr (EEC) 2309/93 and Directives 65/65/EEC and 75/319/EEC as amended). The authorisation specifies amongst others the therapeutic indications and the dosage. For centralised procedures, evaluations are carried out by the Committee for Proprietary Medicinal Products (CPMP) at the

European Agency for the Evaluation of Medicines (EMEA) and Community authorisations are delivered in accordance with a comitology procedure. Authorisations are valid for 5 years and are renewed upon request and submission of any new information gained during real use of the medicinal product.

5. Veterinary medicinal products

Veterinary medicinal products are also subject to marketing authorisation. In addition to biotechnology and high technology products, any new medicinal products which are intended primarily for use as a performance enhancer in order to promote growth of treated animals or to increase yields from treated animals are subject to the centralised authorisation procedure (Regulation Nr (EEC) 2309/93 and Directive 81/851/EEC as amended). Other veterinary medicinal products are authorised nationally with a mutual recognition procedure. Each authorisation specifies the animal species in which it may be used, the therapeutic indications, the dosage and the withdrawal period in food producing animals (time which must elapse between the last dose and slaughter). Maximum residue limits (MRLs) must be established for veterinary medicinal products for food-producing animals in accordance with Regulation (EEC) Nr 2377/90. The evaluation of applications for authorisation in the centralised procedure and MRL files is carried out by the Committee for Veterinary Medicinal Products (CVMP) at the EMEA. The Community authorisations and MRLs are adopted in accordance with a comitology procedure. Authorisations are valid for 5 years and are renewed upon request and submission of any new information gained during real use of the veterinary medicinal product.

6. Feed additives

6.1. The placing on the market of feed additives is regulated by Directive 70/524/EEC as amended. Antibiotics, coccidiostats and growth promoters authorised as feed additives before 1 January 1988 must be re-authorised following a full re-evaluation no later than 1 October 2003. Authorisations will be linked to named producers and shall be valid for 10 years.

For antibiotics, coccidiostats and growth promoters authorised after 31 December 1987 no scientific re-evaluation is foreseen. The new authorisations shall be granted no later than 1 October 1999 for a period of 10 years. The purpose of this new authorisation is to relate each substance to named producers.

6.2. Directive 70/524/EEC specifies that an additive shall be authorised at EU level only if:

- It has a favourable effect on the characteristics of those feedingstuffs or on livestock production when incorporated in such feedingstuffs;
- At the level permitted in feedingstuffs, it does not adversely affect human or animal health or the environment, nor harm the consumer by altering the characteristics of livestock products;
- Its presence in feedingstuffs can be controlled;
- At the level permitted in feedingstuffs, treatment or prevention of animal disease is excluded; this condition applies to all feed additives (including those listed in the annex to the Directive under the heading ‘antibiotics’) but does not apply to those listed as ‘coccidiostats and other medicinal products’;

- For serious reasons concerning human or animal health its use must not be restricted to medical or veterinary purposes (*quote from the Directive*).

Bacteria and other micro-organisms which are exposed to anti-microbials to which they are sensitive are either killed or their growth is suppressed. Spontaneous mutants which have a character which confers resistance to the anti-microbial will be selected and clones of such mutants can proliferate. Anti-microbials in feed additives are used at lower dosages than in therapy.

7. There is concern about increasing resistance of microbials to available treatment. The extent and trends of this resistance require further analysis. It has been suggested that the following factors could be involved:

- misuse and over-prescription of anti-microbials in human medicine
- bad compliance of patients with the prescribed treatment (e.g. using lower dosage or interrupting therapy as soon as symptoms disappear)
- use and misuse of anti-microbials in veterinary prophylaxis and therapy
- use of anti-microbials to improve feed efficiency in animals.

8. Until the 1970s, there was wide-spread belief that one could defeat anti-microbial resistance by constantly developing new molecules. However, most new anti-microbials are variations to existing ones and cross-resistance has appeared, which could wipe out the efficacy of classes of molecules rather than single substances. There is now considerable concern that the stock of natural anti-microbials that remain to be developed is running out.

ELEMENTS OF TERMS OF REFERENCE FOR A WORKING GROUP

ON THE USE OF ANTI-MICROBIALS

In addressing the question of the use of anti-microbials and the development of resistance, the Working Group is invited to address the direct and indirect risks and benefits of the use of anti-microbials in all areas concerned, i.e. in human and veterinary medicine (prophylactic and therapeutic use) and as feed additives. In particular the following elements should be considered:

- use/misuse in human and veterinary medicine
- nosocomial infections
- use/misuse as feed additives
- use/misuse for phytosanitary purposes
- prevention of zoonoses - food safety
- resistant/multi-resistant microbials
- microbial ecology (changes in normal microbial flora in particular environments e.g. in hospitals due to frequent use of disinfectants)
- identification of the factors involved in increase in anti-microbial resistance

- promotion of alternative preventive methods in human and veterinary medicine.

The Committee is asked to provide an opinion not later than 30 November 1998.

<u>Annex 5</u>: STATE OF PLAY ON PENDING PRODUCTS UNDER DIRECTIVE 90/220/EECAS OF 8 APRIL 1998

PRODUCT	COMPANY	USE	PRODUCT NOTIFICTION DETAILS
1. Swede rape tolerant to glufosinate ammonium From the United Kingdom (C/UK/95/M5/ 1)	**AgrEvo**	Handling in the environment during import, before and during storage and processing	• Received by the Commission: 03.05.96 • Deadline for objections: 21.07.96 • Submitted to SCP : 22.12.97 • Opinion by SCP : 10.02.98 • Opinion : Favourable • Regulatory Committee vote : Positive (18.03.98) • Commission Decision : Pending
1. Maize tolerant to glufosinate ammonium (T25) From France (C/F/95/12-07)	**AgrEvo**	As any other maize	• Received by the Commission: 24.05.96 • Deadline for objections: 11.08.96 • Submitted to SCP : 22.12.97 • Opinion by SCP : 10.02.98 • Opinion : Favourable • Regulatory Committee vote : Positive (18.03.98) • Commission Decision : Pending
1. Maize expressing the Bt *cryIA(b)* gene (MON 810) From France (C/F/95/12-02)	**Monsanto**	As any other maize	• Received by the Commission: 24.05.96 • Deadline for objections: 11.08.96 • Submitted to SCP : 22.12.97 • Opinion by SCP : 10.02.98 • Opinion : Favourable • Regulatory Committee vote : Positive (18.03.98) • Commission Decision : Pending
1. Maize	**Novartis**	Storage and	• Received by the

tolerant to glufosinate ammonium and expressing the Bt *cryIA(b)* gene From the United Kingdom (C/UK/96/M4/1)	**(formerly Northrup King)**	import for processing for food, feed and industrial uses	Commission: 25.11.96 • Deadline for objections: 21.03.97 • Submitted to SCP : 22.12.97 • Opinion by SCP : 10.02.98 • Opinion : Favourable • Regulatory Committee vote : Positive (18.03.98) • Commission Decision : Pending
1. Swede rape tolerant to glufosinate ammonium From Germany (C/DE/96/5)	**AgrEvo GmbH**	As any other swede rape	• Received by the Commission: 25.11.96 • Deadline for objections: 07.02.97 • Submitted to SCP : 10.02.98 • Status of SCP review : Request for additional information from the notifiers (18.03.98). Additional information submitted and is currently under review. An opinion is expected in the May 1998 or at the latest June 1998 SCP plenaries
1. Maize expressing the Bt *cryIA(b)* gene (MON 809) From France (C/F/95/12-01/B)	**Pioneer**	As any other maize	• Received by the Commission: 06.08.96 • Deadline for objections: 28.10.96 • Submitted to SCP : 10.02.98 • Status of SCP review : Request for additional information from the notifiers (18.03.98). Additional information submitted and is currently under review. An opinion is expected in the May 1998 or at the latest June 1998 SCP plenaries
1. Male sterile swede rape tolerant to gluphosinate	**Plant Genetic Systems**	As any other swede rape	• Received by the Commission: 16.01.97 • Deadline for objections: 30.03.97 • Submitted to SCP :

ammonium From Belgium (C/BE/96/01)			10.02.98 • Status of SCP review : Request for additional information from the notifiers (18.03.98). Additional information submitted and is currently under review. An opinion is expected in the May 1998 or at the latest June 1998 SCP plenaries
1. Cotton tolerant to herbicide From Spain (C/ES/97/01)	**Monsanto**	As any other cotton	• Received by the Commission : 24.11.97 • Deadline for objections : 13.02.98 • Submitted to SCP : 01.04.98 • Status : Currently under initial review by the GMO Working Group individual experts
1. Fodder beet tolerant to glyphosate From Denmark (C/DK/97/01)	**DLF-Trifolium, Monsanto and Danisco Seed**	Production of seeds and roots, animal feed	• Received by the Commission: 09.10.97 • Deadline for objections: 15.12.97 • Submitted to SCP : 01.04.98 • Status : Currently under initial review by the GMO Working Group individual experts
1. Potato with a change in starch composition From the Netherlands (C/NL/96/10)	**AVEBE**	As any other starch potato	• Received by the Commission: 24.07.97 • Deadline for objections: 26.09.97 • Not submitted to the SCP as of yet. Submission expected any time.
1. Tomato with reduced activity of the expression of the endogenous tomato fruit PG gene From Spain (C/ES/96/01)	**Zeneca**	As any other tomato	• Received by the Commission: 24.11.97 • Deadline for objections: 13.02.98 • Not submitted to the SCP as of yet. Submission expected any time.

1. Cotton expressing the Bt *cryIA(c)* gene From Spain (C/ES/96/02)	**Monsanto**	As any other cotton	• Received by the Commission: 24.11.97 • Deadline for objections: 13.02.98 • Not submitted to the SCP as of yet. Submission expected any time.
1. Male sterile chicory From the Netherlands (C/NL/94/25/ A)	**Bejo-Zaden BV**	Food and feed	• Received by the Commission: 20.09.96 • Deadline for objections: 25.11.96 • Suspended by the Dutch Competent Authority • Not submitted to the SCP. Submission status unclear at present.

Annex 6: Report from the Chairman of the Scientific Committee on Cosmetic and Non-Food Products, presented by Prof. N.Loprieno to the Plenary Session of 16-17 April of the Scientific Steering Committee.

A major activity of SC-CNFP is carried out by one of its Specific Working Parties (SWP), namely "Alternative to Animal Testing & Dossier". This SWP has the task to inform the SC-CNFP on the development of Alternative Methods to the use of Animal Models for the Safety Evaluation of Cosmetic Ingredients and Finished Products, according to the Sixth Amendment (Council Directive 93/35/EEC). The Amendment bans until June 2000 the use of animals in the sector of cosmetics and fixes January 2000 as dead-line for the Commission to present a proposal to the European Parliament about the fulfilment of the ban.

The Specific Working Party has been meeting in February 6th , on March 4th –5th , and 24th – 25th and has scheduled already two more meetings on April 20th – 21st and May 12th – 13th .

In its previous 3 meetings the SWP has met representatives of the European Cosmetic Industry, of the ECVAM (European Centre for the Validation of Alternative Methodologies of the European Commission), and representatives of DG III and DG XII.

It is possible to present today the state of the art of the achievements in the sector of "Alternatives" and the technical possibilities for introducing those new methodologies in the sector of safety evaluation of cosmetics.

There are three fields of activities in which conclusive results are possible in a short-term period of time:

1. Phototoxicity (Photo-irritation). This sector relates to all those cosmetic ingredients which adsorb UV light and might modify their molecule so as to present a toxicological potential for the consumer's health (due to their acquired reactivity with cells and genetic material). Presently there is no Animal Model defined in the OECD or EC guidelines for evaluation of this potential.

On the basis of two intensive research projects developed by European Commission (ECVAM) and European Cosmetic Industry (COLIPA), it has been possible to define an *in vitro* methodology, the so called *In Vitro Phototoxicity 3T3 cell Neutral Red Uptake* which is able to correctly identify phototoxic and non-phototoxic chemicals.

At the request of the SC-CNFP made in 1997, COLIPA has concluded a 3-Phase research project which applies this *in vitro* methodology to the testing of all the UV-filters already approved by the Cosmetic Directive (76/768/EEC). On these, an opinion of safety has been expressed by SC-CNFP.

The final result will be presented in 1998. It will than be possible to verify the adequacy of this methodology in the sector of the cosmetic safety testing.

To be mentioned also is that *in vitro* assays for testing UV adsorbing chemicals for their photomutagenic potential have been defined since 1990 by the SC-CNFP. These are currently being applied by the European Industry.

2. Percutaneous absorption. This issue interests all cosmetic ingredients, because it is able to inform the safety assessor about the real systemic exposure dose of the consumers, thus providing objective criteria for defining the safety margin.

At the present there are two draft guidelines at the OECD level (June 1996), for the evaluating the percutaneous adsorption of a chemical: one *in vivo* (a animal model) and one *in vitro*, which covers the cellular component. There is no agreement at the international level on these two draft guidelines because of the complexity and difficulty of the task.

COLIPA has presented to the Specific Working Party all scientific and technical information based on their continuous experience on the use of *in vitro* approach for evaluating the percutaneous absorption of cosmetic ingredients.

SC-CNFP has also evaluated different protocols and test results presented by COLIPA in their submission for inclusion in the positive lists of the 76/768/EEC Directive (Annex III, IV, VI, and VII) of different types of cosmetic ingredients, such as UV-filters, Preservatives, Colouring Agents and Hair Dyes.

Presently COLIPA is preparing the scientific basis of a series of protocols already developed for different cosmetic ingredients and is collecting the results of a series of tests developed on a wide number of chemicals.

ECVAM has also organised a workshop on percutaneous absorption and is participating to the present activity of comparing *in vitro* versus *in vivo* results.

It is generally expected that during 1998 it would be possible to conclude on different *in vitro* methodologies, as suitable and adequate procedures for defining the level of absorption.

The Specific Working Party wishes to continue the establishment of contacts with the scientific and technical experts from Cosmetic Industry in order to define a common basis for the acceptance of those new methodologies.

3. Human Testing. Already in 1997 the SC-CNFP declared that "*Experiments on man cannot replace those on animals*" and "*The purpose of experiments on humans is to confirm findings on safety and to verify the acceptability and efficacy of cosmetic products* (XXIV/1814/97)."

There is at the present no Commission position on human testing (XXIV/1285/98). There is a proposed OECD guideline for the "Acute Dermal Irritation Study in Human Volunteers", which contains a series of recommendations addressing the safety protection of the volunteers, ethical standards and other initial considerations (OECD: ENV/MC/CHEM/RD(98)1).

This problem has been already discussed with experts from COLIPA which have published two guidelines for the assessment of Skin Compatibility on Cosmetic Finished Products on Man (Food and Chemical Toxicology, 34 (1996) 651-660) and for the assessment of Skin Tolerance of Potentially Irritant Cosmetic Ingredients in Man (Food and Chemical Toxicology, 35 (1997) 1099-1106).

The Specific Working Party has decided to prepare a recommendation outlining the issue of human testing and to draft Guidelines on the use of human volunteers in the testing of potentially (cutaneous) irritant cosmetic ingredients, taking into account the ethical procedures approved in the European Union Member States for cosmetic products and their ingredients.

A conclusion dealing with cosmetic ingredients and cosmetic finished products would be reached on this issue during 1998,.

For all the other aspects of testing the toxicity (safety) of cosmetic ingredients and products, the possibility to substitute the animal models with alternative methods is presently still problematic, despite of an enormous number of ongoing research projects.

It has been decided that the Chairman of the SC-CNFP and the Chairman of the Specific Working Party "Alternative to Animal testing and Dossier" will visit two times per year ECVAM (Ispra, Italy) to become informed about the state of affairs and to discuss the results of the programs developed in the fulfilment of the Sixth Amendment.