continued from previous page

A *New TG 431* for an *in vitro* skin corrosion test (employing reconstituted human skin, namely, the EPISKIN™ and EpiDerm™ models): an EU initiative as a result of the ECVAM validation study, for which consensus was also reached in the autumn of 2001.

A *New TG 432* for the 3T3 NRU phototoxicity test: an EU initiative as a result of the ECVAM/COLIPA validation study, for which consensus was also reached at the autumn 2001 meeting.

Some formal steps still remain for these test guidelines for alternative methods, but they are now well on the way to acceptance at the OECD level, and therefore to worldwide application.

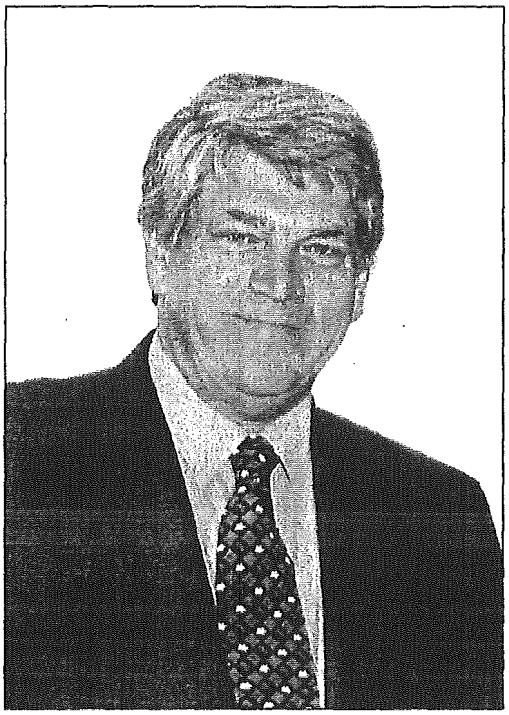
The May meeting was the first time that a consortium of animal welfare organisations (ICAPO) had participated in such an OECD meeting. It is reported that their presence and interventions were welcomed by the official delegates, and that they raised the question of the three *in vitro* tests for embryotoxicity, recently endorsed as scientifically valid by the ESAC.

Only those who are aware of OECD procedures, and have been involved in the protracted discussions which have led to these recent successes, will be able to fully appreciate their significance or understand how grateful those committed to alternatives should be to all concerned (not least to those in the OECD Secretariat).

However, this is not a time to be complacent for, significant though these steps may be, they are small in relation to the length and difficulty of the journey on which we have embarked. The EU Chemicals Policy and demands for tests for so-called endocrine disruptors are merely two examples of the many challenges that must be faced.

A report on *Alternative (Non-animal) Methods for Chemicals Testing: Current Status and Future Prospects*,[2] prepared by ECVAM and the ECVAM Working Group on Chemicals, has been published as a supplement to FRAME's journal *ATLA*, and the *Proceedings of the ECVAM Status Seminar*, held at Ispra in June 2002, will be published as a supplement to *ATLA*, later this year.

Professor Balls will be devoting more time to his voluntary work at FRAME, with his former colleagues at ECVAM, and with FRAME's network of collaborators in industry, academia and government, to contribute to the development and validation of alternative methods, and to the improvement of the regulatory process, so that chemicals and products of various kinds, including medicines, vaccines, medical devices, cosmetics, household products and agricultural products, can be manufactured, transported and used more economically and more safely, while the current reliance on animal test procedures is progressively reduced.



MB CBE

All at FRAME are delighted that Professor Michael Balls (Chairman of the Trustees of FRAME) was awarded the CBE in the Queen's Birthday Honours List, for services to humane animal research. This award coincides with Michael's retirement from ECVAM, where he has been Head of Unit since its inception in 1993. This is a fitting tribute to his tireless research and campaigning in support of the Three Rs and the use of alternative methods.

[1] Worth, A.P. & Balls, M. (2001). The role of ECVAM in promoting the regulatory acceptance of alternative methods in the European Union. *ATLA* **29**, 525–535.

[2] Worth, A.P. & Balls, M., eds (2002). Alternative (non-animal) methods for chemicals testing: current status and future prospects. A report prepared by ECVAM and the ECVAM Working Group in Chemicals. *ATLA* **30**, Suppl. 1, 125pp.

ONLINE VERSIONS OF THE *INVITTOX* DATABASE AND ECVAM WORKSHOP REPORTS

The ERGATT/FRAME/ECVAM *INVITTOX* database of *In Vitro* Techniques in Toxicology is now available through the World Wide Web at http://www.invittox.com/. Registration, which is free of charge, is required. The same site will also host online versions of all the ECVAM workshop reports, which first appeared in *ATLA*.

SCCNFP/0546/02, final

THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS INTENDED FOR CONSUMERS

MEMORANDUM

CONCERNING

THE ACTUAL STATUS OF ALTERNATIVE METHODS TO THE USE OF ANIMALS IN THE SAFETY TESTING OF COSMETIC INGREDIENTS

adopted by the SCCNFP during the 20th plenary meeting
of 4 June 2002

1. Introduction

One of the major mandates of the SCCNFP, defined by the Commission (DG XXIV/1890/98, 20 May 1998), is to act as a resource of scientific expertise to the European Commission with regard to the development of alternative methods. As such the SCCNFP advises the European Commission on the status of alternative methods to animal testing of cosmetics on an on-going basis and particularly, in accordance with Art. 4,1(i) of Council Directive 76/768/EEC, amended by Council Directive 93/85/EEC.

In particular, the Commission has requested the SCCNFP to assess the possibility to replace safety data obtained on the basis of animal tests with data obtained using alternative methods and to indicate those end-points for which no alternative methods are yet available (doc. n° 16831 of 11 August 1998).
The SCCNFP therefore closely follows the scientific developments of alternative methods by academia, industry and public institutions and this in a broader context in order to identify the alternative methods that are applicable to the safety evaluation of cosmetic ingredients and finished products. Also scientific discussion meetings are organised with ECVAM and COLIPA scientists to evaluate the results of pre-validation and validation studies and their applicability to the cosmetics sector.

For the moment, the number of validated alternative methods, fitting into the 3Rs concept of Russell and Burch (Reduction, Replacement, Refinement) (1) and available for the practical application in regulatory testing and risk assessment of cosmetic ingredients is limited.
According to the "Notes of Guidance for Testing of Cosmetic Ingredients for their Safety Evaluation" (SCCNFP/0321/00 Final), the specific toxicity studies necessary for the safety evaluation of cosmetic ingredients include acute toxicity, percutaneous absorption, skin irritation, eye irritation, skin sensitisation and photosensitisation, subchronic toxicity, mutagenicity/genotoxicity, phototoxicity/photoirritation, photomutagenicity/ photogenotoxicity, human data, toxicokinetics and metabolism data, long-term toxicity and carcinogenicity.

Only for some of these areas, appropriate alternatives currently exist and these are present in different stages of development :

- formally validated tests accepted by SCCNFP;
- tests equivalent to formally validated tests and accepted by SCCNFP;
- tests under validation, not yet completed or not successful (not accepted by SCCNFP).

In a number of specific toxicological fields of key importance for the safety evaluation of cosmetic ingredients appropriately validated alternative tests are lacking. These include in particular subchronic toxicity, long-term toxicity, carcinogenicity and toxicokinetics. For the field of photomutagenicity/photogenotoxicity the *in vitro* methodology is quite well developed.

The existing techniques will not be discussed here but in another part of the SCCNFP Notes of Guidance in which the new testing strategy, in particular for testing of hair dye cosmetic ingredients (SCCNFP/0566/02, 17 April 2002), is being presented.

2. Formally validated 3R methods accepted by the SCCNFP

Formally validated methods are those alternatives that have followed the validation process, as set up by ECVAM and the independent ECVAM Scientific Advisory Committee (ESAC) , including test development, prevalidation (informal interlaboratory study), validation (formal interlaboratory study with coded substances), independent assessment and progression toward regulatory acceptance (2).
These methods are based on a so-called prediction model, an algorithm for converting the results obtained into a statement about the *in vivo* toxicity under study (3).
Currently 5 formally validated 3R methods exist that have been also accepted by the SCCNFP: 4 corrosivity tests and 1 phototoxicity test.

2.1. Skin Corrosivity

- The rat skin transcutaneous electrical resistance (TER) assay, using excised rat skin as a test system and its electrical resistance as an endpoint, has been endorsed by ESAC (31 March 1998; http://www.iivs.org/news/ratskin.html) (4)
The method is taken up in Annex V method B.40 of the Dangerous Substances Directive (Directive 67/548/EEC), thereby making its use for chemicals mandatory.
The Draft New OECD Guideline 430 (March 2002) on *in Vitro* Skin Corrosion: TER is still under consideration by the OECD Member States.

- EPISKIN™ and EpiDerm™, two commercialised human skin models consisting of reconstructed human epidermal equivalent using cell viability (MTT-test) as an endpoint, have been endorsed by ESAC (31 March 1998 and 14-15 March 2000, respectively); http://www.iivs.org/news/ratskin.html) (4) (5)
These methods are taken up in Annex V of the Dangerous Substances Directive 67/548/EEC and are mandatory for skin corrosion testing of chemicals in the EU.
The Draft New OECD Guideline 431 (March 2002) on *In Vitro* Skin Corrosion: Human Skin Model Test still is under consideration by the OECD Member States.

- Corrositex™ is a commercial system of reconstituted collagen matrix taking colour or physical change in indicator as an endpoint. The model was prevalidated and validated by ECVAM-funded studies and had an unacceptably high underprediction rate. Consequently, it was endorsed by ECVAM only for skin corrosion testing of acids, bases and derivatives.
It has not been taken up in the Dangerous Substances Directive. The Revised Draft Updated OECD Guideline 404 (June 2001) on Acute Dermal Irritation/Corrosion is still under consideration by the OECD Member States.

2.2. Phototoxicity

The 3T3 neutral red uptake (3T3 NRU) test for phototoxic potential uses 3T3 fibroblasts and UV-A irradiation.
It has been endorsed by ESAC (1-2 October 1997; http://www.iivs.org/news/3t3.html) and a statement on its use for the particular purpose of testing UV-filters has been issued (7).

The 3T3 NRU test is taken up in Annex V, method B41 of the Dangerous Substances Directive 67/548/EEC making it mandatory for chemical testing of phototoxic potential.
The Draft New OECD Guideline 432 (March 2002), namely Draft Proposal for a New Guideline: 432 *In Vitro* 3T3 NRU Phototoxicity test is still under consideration by the OECD Member States.

3. 3R methods equivalent to formally validated tests and accepted by the SCCNFP

These 3R methods have been accepted by ESAC as being equivalent to formally validated tests. They include a test for skin sensitisation, the murine local lymph node assay (LLNA), and an *in vitro* percutaneous absorption test.

3.1. Skin Sensitisation : LLNA

The murine local lymph node assay is a refinement test, thus still an *in vivo* test on mice, providing reduction of the number of animals used and refinement in the methodology in comparison with the traditional guinea pig-based methods (guinea pig maximisation test and the Buehler test). It is more rapid, quantitative and objective.
In principle, the assay evaluates the extent to which a chemical contact allergen stimulates the proliferation of lymphocytes in lymph nodes draining the site of chemical application. A chemical is regarded as a skin sensitiser if it induces a stimulation of ≥ 3 fold that found in vehicle treated controls.
The LLNA has been formally validated in the USA and has been endorsed as scientifically valid by ESAC (14-15 March 2000;
http://iccvam.niehs.nik.gov/methods/llnadocs/llna_val.htm) (8)
It forms the basis of the Draft Revised New OECD Guideline 429 on Skin Sensitisation: Local Lymph Node Assay (June 2001).

3.2. Percutaneous Absorption

The *in vitro* methodology for percutaneous absorption testing is based on the use of Franz-cells. It measures the diffusion of substances across excised human or pig skin, which may be of full or partial thickness. In the case of non-viable skin only diffusion can be measured. When fresh skin is used both, diffusion and skin metabolism, can be assessed. This methodology has not been formally validated, but the cosmetic and the pesticides industry have provided the necessary in use data to create confidence in the methodology. There is now the Draft OECD Test Guideline 428 on Skin Absorption: *in Vitro* Method (9) and a Draft OECD Guidance Document for the Conduct of Skin Absorption Studies (10). Both, are still under consideration by the OECD Member States.
The SCCNP has accepted the *in vitro* methodology to evaluate percutaneous absorption of cosmetic ingredients (20 January 1999) and has defined an additional set of basic criteria for cosmetic ingredients (23 June 1999) (SCCNFP/0167/99 Final).

4. 3R methods under validation (not yet completed or not successful)

A number of alternative methods exist that either have not yet been taken completely through the formal validation process or were not successful in this respect.
To the former category belong embryotoxicity tests, and acute lethal toxicity tests; to the latter eye and skin irritation testing.

4.1 Embryotoxicity tests

Since the field of developmental toxicity is very complex, it is expected that the various stages cannot be mimiced using one alternative method.
Embryotoxicity has been studied separately and so far three embryotoxicity tests have been formally prevalidated and validated. In addition, a prediction model has been developed to classify the chemicals into non, weak/moderate, strong embryotoxic substances.
The existing alternative tests consist of the whole embryo culture (WEC), the micromass (MM) test and the embryotoxic stem cell test (EST).
The last two tests were considered scientifically valid by ESAC (16-17 October 2001) for distinguishing into the 3 just mentioned categories of embryotoxicity whereas the WEC test was considered scientifically valid for identifying strong embryotoxic chemicals. The ESAC statements will now be published and the areas of application defined (ESAC meeting 3 June 2002).
The 3 alternative embryotoxicity tests have not yet discussed within the SCCNFP.

4.2. Acute lethal toxicity

Reduction and refinement alternatives of the LD_{50} method have been accepted at the OECD and EU level. These are :

- Acute Oral Toxicity – Fixed Dose Method, Updated OECD Guideline 420 (20 December 2001) and B.1bis in Annex V to Directive 67/458/EEC;
- Acute Oral Toxicity – Acute Toxic Class Method, Updated OECD Guideline 423 (20 December 2001) and B.1tris in Annex V to Directive 67/458/EEC;
- Acute Oral Toxicity – Up- and Down Procedure, Updated OECD Guideline 425 (20 December 2001) not yet an equivalent in Annex V to Directive 67/458/EEC.
- Currently, a formal validated replacement alternative for acute lethal toxicity does not yet exist. A validation study of a basal cytotoxicity test will be soon initiated by ICCVAM and ECVAM principally based on the mass of data generated before by FRAME, MEIC and the Halle and Gores Registry of Cytotoxicity (11-26).

4.3. Eye irritation tests

A list of alternative methods has been compiled by ECVAM (table 1) (27) providing a good overview (28-38). These methods are in different stages of development but it has been shown by all the validation exercises run until now that it is not possible to formally establish the scientific validity of a single or more replacement tests, applicable across the full range of eye irritation potency (39). It is generally considered that a battery of alternative tests is required for the

assessment of eye irritation since there are multiple mechanisms of eye irritation. These tests should model then the different mechanisms and provide complementary results.
Generally spoken the BCOP-test (bovine cornea opacity-permeability test) seems good for neutral organics and the RBC (red blood cell) and NRU (neutral red uptake) tests for surfactants. For alcohols and esters no good methodologies are yet available (39).
According to the strategy proposed by the OECD, new chemicals can be classified as irritating to the eye on the basis of a tiered testing strategy including structure-activity relationships, physicochemical tests and *in vitro* tests. Animal testing is then only necessary as a last confirmation step of negative results (6). Consequently, this strategy critically depends on the availability of one or more scientifically validated *in vitro* tests for inclusion in this strategy. However, currently these are not available.

4.4. Irritation tests

Also alternative tests for skin irritation (Table 2) belong to the category of tests for which a lot of prevalidation efforts have been done (40). However, these were not leading to a successful outcome of starting a formal validation study.

5. Lacking domains of alternative methods

For biokinetic endpoints, besides the *in vitro* percutaneous absorption test mentioned before, not much is yet in a sufficient state to be taken up in validation. For biotransformation a selection of methodology and prevalidation of computer-based approaches and *in vitro* culture tests remain to be done.
For the important and large area of target organ toxicity and systemic toxicity a lot of development work is necessary. For neurotoxicity some relevant data exist and a tiered approach on the sequential assessment of basal cytotoxicity and neurospecific endpoints is recommended by ECVAM (27). However, it must be noted that until today no single *in vitro* method for neurotoxicity has been formally validated.
Also in several other areas not many tests are available that can currently be used in regulatory testing. Strategies are being proposed by ECVAM for nephrotoxicity testing and a study is running on the identification of possible *in vitro* endpoints. For the other organs no specific methods are yet available (27). As already mentioned, for repeat-dose toxicity testing, no generally accepted alternative methods are available for replacing chronic testing in animals, although this is an important issue in the safety evaluation of cosmetics consuming a large number of animals.
An ECVAM workshop on novel, advanced *in vitro* methods for long-term testing was held in 1999 and the report was recently published (41). Several models exist for long-term testing in liver, kidney and central nervous system, but no validation is yet been done.
For genotoxicity and carcinogenicity, *in vitro* mutagenicity tests are quite well developed as far a genototoxic compounds are concerned. Tests for detecting non-genotoxic carcinogens is another issue. As long as these do not exist, *in vivo* rodent studies will remain necessary.
For reproductive toxicity, 3 embryotoxicity methods have been endorsed by ESAC (see before), but these are only a small part of the tests needed in reproductive toxicity testing, which usually is performed *in vivo* and consumes much animals.

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Table1: *in vitro* methods for eye irritation

Method	Test system	Endpoint	Reference
Bovine corneal opacity and permeability (BCOP) test	Excised cornea from the bovine eye	Opacity and permeability of the cornea	28
Hen's egg test-chorioallantoic membrane (HET-CAM)	Hen's egg	Damage to chicken chorioallantoic membrane	29
Chorioallantoic membrane-trypan blue staining (CAM-TBS)	Hen's egg	Damage to chicken chorioallantoic membrane	30
Isolated rabbit eye (IRE) test	Isolated rabbit eye	Corneal swelling, corneal opacity and fluorescein retention	31
Isolated chicken eye (ICE) test	Isolated chicken eye	Corneal swelling, corneal opacity and fluorescein retention	32
Fluorescein leakage (FL) test	Madin-Darby Canine Kidney (MDCK) cells	Damage caused to the tight junctions in MDCK monolayers	33
Neutral red uptake (NRU) test	3T3-L1 cells	Cell viability	34
Neutral red release (NRR) test	Rabbit corneal fibroblasts or mouse embryonic fibroblasts or normal human epidermal keratinocytes	Damage to the cell membrane	35
Red blood cell (RBC) haemolysis test	RBCs from calf blood samples	Damage to cytoplasmic membrane (haemolysis) in combination with damage of liberated cellular proteins (denaturation)	36
Agarose Diffusion Method	L929 mouse fibroblast cells	Cell death	37
EpiOcular™	Reconstituted human corneal epithelium	Cell viability, release of inflammatory mediators; permeability (MTT, IL-1, IL-1α, PGE2, LDH, and sodium fluorescein permeability)	38

From ECVAM report April 2002

Table 2 : *in vitro* methods for skin irritation

Method	Test system	Endpoint	Applicability	Formal Status
EPISKIN™human skin model (commercial system)	reconstructed human epidermal equivalent	Cell viability (MTT reduction assay)	general; a few materials may interfere with MTT reduction	Protocol modification and prevalidation (validation study under discussion)
Epi<<<Derm™human skin model (commercial system)	reconstructed human epidermal equivalent	Cell viability (MTT reduction assay)	general; a few materials may interfere with MTT reduction	Protocol modification and prevalidation (validation study under discussion)
Pig ear test	pig ear	Trans-epidermal water loss (TEWL)	general	Further development necessary
Mouse skin integrity function test (SIFT)	excised mouse skin	TEWL and electrical resistance	general; a few materials may interfere with either TEWL or ER determination	Protocol modification and prevalidation (validation study under discussion)

From ECVAM report April 2002

to the timing limitations imposed by the review and funding cycle.

Name of Committee: Center for Scientific Review Special Emphasis Panel, Immunologic Mechanisms of PDT Therapy.

Date: August 5, 2002.

Time: 2 p.m. to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: NIH, Rockledge 2, Bethesda, MD 20892, (Telephone Conference Call).

Contact Person: Sharon K. Pulfer, PhD, Scientific Review Administrator, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 4140, MSC 7804, Bethesda, MD 20892, (301) 435–1767.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: Center for Scientific Review Special Emphasis Panel, ZRG1 GRM 08.

Date: August 6, 2002.

Time: 9:30 a.m. to 10 a.m.

Agenda: To review and evaluate grant applications.

Place: NIH, Rockledge 2, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Jo Pelham, BA, Scientific Review Administrator, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 4102, MSC 7814, Bethesda, MD 20892, (301) 435–1786.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: Center for Scientific Review Special Emphasis Panel, Experimental Therapeutics.

Date: August 6, 2002.

Time: 11:30 a.m. to 12:30 p.m.

Agenda: To review and evaluate grant applications.

Place: NIH, Rockledge 2, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Sharon K. Pulfer, PhD, Scientific Review Administrator, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 4140, MSC 7804, Bethesda, MD 20892, (301) 435–1767.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: Center for Scientific Review Special Emphasis Panel, Placebo Effect RFA.

Date: August 7, 2002.

Time: 9 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn, 8120 Wisconsin Avenue, Bethesda, MD 20814.

Contact Person: J. Scott Osborne, PhD, Scientific Review Administrator, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 4114, MSC 7816, Bethesda, MD 20892, (301) 435–1782.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine, 93.306; 93.333, Clinical Research, 93.333, 93.337, 93.393–93.396, 93.837–93.844, 93.846–93.878, 93.892, 93.893, National Institutes of Health, HHS)

Dated: July 24, 2002.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 02–19264 Filed 7–30–02; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Center for Scientific Review Special Emphasis Panel, F05 Fellowship.

Date: July 25, 2002.[1]

Time: 7 a.m. to 8 a.m.

Agenda: To review and evaluate grant applications.

Place: St. Gregory Hotel & Suites, 2033 M Street, NW., Washington, DC 20036.

Contact Person: Randolph Addison, PhD, Scientific Review Administrator, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 5144, MSC 7840, Bethesda, MD 20892, (301) 435–1025, *addison@csr.nih.gov.*

[1] Editorial Note: This document was received at the Office of the Federal Register on July 25, 2002.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: Center for Scientific Review Special Emphasis Panel, Neurotechnology Development Special Emphasis Panel.

Date: July 26, 2002.

Time: 1 p.m. to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: NIH, Rockledge 2, Bethesda, MD 20892, (Telephone Conference Call).

Contact Person: Carole L. Jelsema, PhD, Scientific Review Administrator and Chief, MDCN Scientific Review Group, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 5210, MSC 7850, Bethesda, MD 20892, (301) 435–1248, *jelsemac@csr.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine, 93.306; 93.333, Clinical Research, 93.333, 93.337, 93.393–93.396, 93.837–93.844, 93.846–93.878, 93.892, 93.893, National Institutes of Health, HHS)

Dated: July 24, 2002.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 02–19269 Filed 7–30–02; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institute of Environmental Health Sciences; National Toxicology Program; Availability of the Report, Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Evaluation of EPISKIN™, EpiDerm™ (EPI–200), and the Rat Skin Transcutaneous Electrical Resistance (TER) Assay: *In Vitro* Test Methods for Assessing the Dermal Corrosivity Potential of Chemicals

Summary

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) announces the availability of the report entitled, "ICCVAM Evaluation of EPISKIN™, EpiDerm™ (EPI–200), and the Rat Skin Transcutaneous Electrical Resistance (TER) Assay: *In Vitro* Test Methods for Assessing the Dermal Corrosivity Potential of Chemicals," NIH Publication 02–4502. The report contains test method summary reports,

protocols, and the ICCVAM's final recommendations on the three methods.

Availability of Report

The report is available electronically (PDF and HTML) on the NICEATM/ICCVAM Web site at *http://iccvam.niehs.nih.gov.* A limited number of printed reports are available. To receive a printed report, please contact the NICEATM at P.O. Box 12233, MD EC–17, Research Triangle Park, NC 27709, phone: 919–541–2384, fax: 919–541–0947, or *niceatm@niehs.nih.gov.*

Background

ICCVAM initiated evaluation of the validation status of three in vitro test methods for assessing the dermal corrosivity potential of chemicals and chemical mixtures in 2001. The test methods are EPISKIN™ (EPISKIN SNC, Lyon, France), EpiDerm™ (EPI–200) (MatTek, Ashland, MA), and the Rat Skin TER assay. The European Centre for the Validation of Alternative Methods (ECVAM) conducted validation studies on the three test methods. The ECVAM Scientific Advisory Committee and the European Commission's Scientific Committee for Cosmetic Products and Non-food Products subsequently reviewed and recommended the methods for regulatory acceptance. The NICEATM prepared a background review document (BRD) summarizing available data and prior reviews for the three corrosivity test methods. ICCVAM considered this compendium of information and concluded that further evaluation by an independent scientific peer review panel was not necessary. The BRD and proposed ICCVAM recommendations on the test methods were made available for public comment in a **Federal Register** notice (Vol. 66, No. 189, pp. 49685–49686; Sept. 28, 2001). All public comments received were posted on the ICCVAM/NICEATM Web site (*http://iccvam.niehs.nih.gov*) and considered by ICCVAM prior to finalizing its test recommendations.

Based on an evaluation of the ECVAM validation studies and all other available data, the ICCVAM recommends that EPISKIN™, EpiDerm™ (EPI–200), and the Rat Skin TER assay can be used to assess the dermal corrosivity potential of chemicals and chemical mixtures in a weight-of-evidence approach using an integrated testing scheme for dermal irritation/corrosion. In this approach, positive *in vitro* corrosivity responses will not generally require further testing and the results can be used for classification and labeling without the need for animal testing. Accordingly, these methods provide for the replacement of animal use when positive results are obtained.

In accordance with Public Law 106–545, the ICCVAM test recommendations will be forwarded to Federal agencies for their consideration and appropriate action. Agency responses to ICCVAM test recommendations will be made available on the ICCVAM/NICEATM Web site (*http://iccvam.niehs.nih.gov*). Inquiries or comments about the report should be addressed to: Dr. William S. Stokes, Director, NICEATM, NIEHS, P.O. Box 12233, MD EC–17, Research Triangle Park, NC 27709; e-mail: *niceatm@niehs.nih.gov;* fax: 919–541–0947; tel. 919–541–2384.

Dated: July 22, 2002.

Samuel Wilson,

Deputy Director, National Institute of Environmental Health Sciences.

[FR Doc. 02–19261 Filed 7–30–02; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

[Docket No. FR–4739–N–33]

Notice of Proposed Information Collection: Comment Request; Section 202 Supportive Housing for the Elderly

AGENCY: Office of the Assistant Secretary for Housing-Federal Housing Commissioner, HUD.

ACTION: Notice.

SUMMARY: The proposed information collection requirement described below will be submitted to the Office of Management and Budget (OMB) for review, as required by the Paperwork Reduction Act. The Department is soliciting public comments on the subject proposal.

DATES: *Comments Due Date:* September 30, 2002.

ADDRESSES: Interested persons are invited to submit comments regarding this proposal. Comments should refer to the proposal by name and/or OMB Control Number and should be sent to: Wayne Eddins, Reports Management Officer, Department of Housing and Urban Development, 451 7th Street, SW., L'Enfant Plaza Building, Room 8003, Washington, DC 20410.

FOR FURTHER INFORMATION CONTACT: Willie Spearmon, Director, Office of Housing Assistance and Grant Administration, Department of Housing and Urban Development, 451 7th Street, SW., Washington, DC 20410, telephone (202) 708–3000 (this is not a toll free number) for copies of the proposed forms and other available information.

SUPPLEMENTARY INFORMATION: The Department is submitting the proposed information collection to OMB for review, as required by the Paperwork Reduction Act of 1995 (44 U.S.C. Chapter 35, as amended).

This Notice is soliciting comments from members of the public and affected agencies concerning the proposed collection of information to: (1) Evaluate whether the proposed collection is necessary for the proper performance of the functions of the agency, including whether the information will have practical utility; (2) Evaluate the accuracy of the agency's estimate of the burden of the proposed collection of information; (3) Enhance the quality, utility, and clarity of the information to be collected; and (4) Minimize the burden of the collection of information on those who are to respond; including the use of appropriate automated collection techniques or other forms of information technology, *e.g.,* permitting electronic submission of responses.

This Notice also lists the following information:

Title of Proposal: Section 202 Supportive Housing for the Elderly.

OMB Control Number, if applicable: 2502–0267.

Description of the need for the information and proposed use: This information is required in connection with the application submission requirements for the Section 202 Supportive Housing Program for the elderly. The information is necessary to assist HUD in determining applicant eligibility and capacity to develop housing for the elderly within statutory and program criteria.

Agency form numers, if applicable: HUD–92015–CA, HUD–92041, HUD–92042, HUD–50070, HUD–50071, HUD–2880, HUD–2990, HUD–2991, HUD–2992, SF–424, SF–LLL.

Estimation of the total numbers of hours needed to prepare the information collection including number of respondents, frequency of response, and hours of response: The estimated total number of hours needed to prepare the information collection is 15,960, the number of respondents is 400 generating approximately 400 annual responses, the frequency of response is on occasion, and the estimated time needed to prepare the response varies from 20 minutes to 22 hours.

Status of the proposed information collection: Extension of a currently approved collection.

Authority: The Paperwork Reduction Act of 1955, 44 U.S.C., Chapter 35, as amended.

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TOILETRIES, FRAGRANCES AND SKIN CARE

THE NEWS THIS WEEK Vol. 23, No. 31 August 5, 2002

Kao John Frieda Buy To Establish U.S. Mass Hair Care Foothold

- **John Frieda hair color plans included in expansion strategy under Kao**, according to Japanese beauty giant. Acquisition agreement announced Aug. 1 would provide Kao with foothold into U.S. mass market hair care category. Company also will use $160 mil. John Frieda business as vehicle for bringing existing hair care technology to the U.S. Kao's $450 mil. planned purchase is in line with strategy to build North American presence 5

- **Revlon turnaround strategy under CEO Jack Stahl calls for return to color cosmetics** innovation, company says during analyst meeting in New York City Aug. 1. Building on existing cost-cutting efforts, Revlon is entering new phase focused on top-line growth and improved marketing initiatives, Stahl states. Exec predicts 10%-12% revenue growth in long term, but does not plan to provide short-term guidance 4

- **Revlon North American Q2 sales trend up at $217 mil.**, boosted by new products, company reports to analysts Aug. 1. However, international sales fell 8.4% due to impact of foreign exchange, softness in Venezuela, Argentina, leading to 2.4% decline in consolidated net sales of ongoing operations. Firm recorded $35.4 mil. net loss from continuing business, excluding restructuring, consolidation costs 5

Coty Celine Dion Scent Aims For Titanic Impact In 2003

- **Coty Celine Dion fragrance will be positioned as premium-priced mass market offering** aimed at widespread competition from prestige fragrances sold at mass, Coty Beauty Americas President Thoreux says. Singer's premier fragrance, which is slated to debut in first half of 2003, initially will be sold at retailers such as J.C. Penney, Sears, Kohl's in the U.S., exec notes. Line will later roll out to broader mass market distribution 3

- ***Speedo Protek* developed as first "serious sports toiletries" brand**, manufacturer Knowledge Merchandising, Inc. says. Products in the 19-SKU line are formulated to protect against damage from chlorine, salt and UVA/UVB rays and are targeted to active men and women. Line is debuting in 2,000 UK doors and is expected to enter 30 countries, including the U.S., in time for 2004 Summer Olympics 7

- **Unilever Prestige to introduce fifth scent under *Valentino* in December**; ***Valentino Gold*** will bow exclusively in Nordstrom doors. Fragrance among a series of second half launches planned by Unilever's North American home and personal care division, which experienced a 2.6% sales decline during Q2. Worldwide personal care sales advance 7%, boosted by 11% gain in mass market skin, hair and deodorant sales, firm says 6

- **Estee Lauder *So Ingenious* powder foundation extended with liquid makeup, loose powder**, which can be used alone or in combination with one another, the company says. Launching in September, So Ingenious extensions are formulated with the same proprietary ***QuadraColor*** technology used in the original formula 6

"The Rose Sheet" (ISSN 1530-1222) is published weekly (except the week of Christmas) by F-D-C Reports, Inc., 5550 Friendship Blvd., Suite One, Chevy Chase, MD 20815-7278. The annual subscription rate is (1) $800 or (2) $440 for additional copies mailed in the same envelope with $800 subscription. Cole Palmer Werble, President. Periodicals Postage paid at Bethesda, MD and at additional mailing offices. POSTMASTER: Send address changes to "The Rose Sheet", 5550 Friendship Blvd., Suite One, Chevy Chase, MD 20815-7278.

- **ICCVAM review of three dermal corrosivity test methods is being forwarded to federal** agencies for review and action, the National Toxicology Program's National Institute of Environmental Health Sciences says. Review was conducted under newly implemented expedited process, relying on validation studies already evaluated in Europe. ICCVAM recommends the three methods be used in a "weight of evidence approach using an integrated testing scheme" 8

- **Sunscreen ingredient name change requirement one-year delay requested, CTFA, CHPA** say in July 26 petition for stay of FDA technical amendment. Groups warn agency that current Sept. 1 deadline for amending names of four ingredients would disrupt supply chain. Relabeling of affected products is "a major undertaking that cannot be accomplished in a few months," associations maintain 7

- **Cinnamaldehyde, dipropylene glycol show "no evidence" of carcinogenicity** in two-year rodent feeding studies conducted by the National Toxicology Program, according to recently-released draft reports. Cinnamaldehyde nominated for testing by FDA based on its widespread use as flavor, fragrance ingredient. Dipropylene glycol testing proposed by the National Cancer Institute due to its suspected broad consumer, occupational exposure. Reports to be reviewed by NTP subcommittee at Sept. 5 meeting 8

- **Unilever *Suave for Men* mark for hair care products published July 30** for third-party review by the Patent & Trademark Office in its official weekly gazette; Trademark Review 9

Marketing In Brief

Prescriptives: Estee Lauder division launches print ad campaign spotlighting new logo and "Custom Beauty" tagline. First ad, breaking in August books, supports Super Line Preventor, while four future adds will support additional products in the Prescriptives lineup. Ads feature full body shots of different models beside life-size products; each ad uses a model of a different ethnicity in an attempt to appeal to the "global woman," according to company. New products debuting in September under Prescriptives include Powderful Adjustable Coverage Pressed Powder ($28) and Camouflage Kit Full Coverage Concealer ($27)....

Clarins: ***Baldessarini Hugo Boss*** men's fragrance, based on fashion line of same name, to debut exclusively in Saks Fifth Avenue New York City beginning in October, Parisian firm says. Targeting men ages 35-60, fragrance is characterized as "very distinctive scent, yet with broad appeal," Clarins maintains. Baldessarini contains notes of tangerine, bitter orange, clove buds, cumin seeds, patchouli and fir balsam. Scent collection includes eau de cologne (75 mL for $53), edc "prestige" refillable product (50 ml for $89) and refill (50 mL for $42) as well as aftershave, shower gel and deodorant stick....

La Prairie: Cellular Anti-Wrinkle Firming Serum will be added to Swiss firm's anti-aging lineup in October. Serum combines time-release retinol complex with vitamins C and E, green tea and coenzyme Q10 for wrinkle fighting and "superior" antioxidant protection, La Prairie claims. Cellular complex works to "energize and nourish skin," while chapparal works to "instill radiance enhancing properties," company says. Product will be sixth member of La Prairie's Swiss Cellular De-Agers line of treatment serums, which launched in September 2001 ("The Rose Sheet" May 21, 2001, p. 8). Like existing products, new serum will retail for $150 and will be available in select department stores worldwide....

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Cinnamaldehyde Shows "No Evidence" Of Carcinogenicity In NTP Studies

Flavor and fragrance ingredient cinnamaldehyde showed "no evidence" of carcinogenic activity in rodent studies conducted by the National Toxicology Program, according to a recently-released draft report of findings.

In two-year feeding studies in F344/N rats and B6C3F1 mice, trans-cinnamaldehyde was not linked to any neoplastic or nonneoplastic effects at doses of 1,000, 2,100 or 4,100 ppm, the draft states.

Cinnamaldehyde is used primarily as a cinnamon flavoring for food and beverages and to impart a cinnamon scent in medical products, fragrances and cosmetics.

Because of its potential for skin sensitization, the Research Institute for Fragrance Materials has recommended it be used in personal fragrances in equal amounts with either dilimone or eugenol to quench irritation, the group said.

FDA nominated trans-cinnmaldehyde for testing based on its widespread use as a flavor and fragrance ingredient and its structural similarity to cinnamyl anthranilate and 3,4,5-trimethoxy cinnamaldehyde, two known rodent carcinogens, the report notes.

A separate NTP draft report on dipropylene glycol likewise found no evidence the chemical causes cancer in F344/N rats or B6C3f1 mice. The conclusion was based on a two-year study involving administration of dipropylene glycol via drinking water at levels ranging from 2,500 to 40,000 ppm.

Dipropylene glycol is found mainly in plasticizers and polyester resins but also is a component of cosmetics and fragrances, the report notes. The Cosmetic Ingredient Review designated the ingredient "safe as used" in cosmetics in a 1985 final report.

The National Cancer Institute nominated the chemical for testing based on its high production volume and suspected widespread consumer and occupational exposure.

The two reports are scheduled to be reviewed by the NTP Board of Scientific Counselor's Technical Review Subcommittee at a Sept. 5 meeting in Research Triangle Park, N.C. ("The Rose Sheet" July 22, 2002, In Brief). Also scheduled for consideration is a draft report on the toxicology and carcinogenesis of urethane and ethanol. Final versions of the documents will be issued pending approval by the board. ♦♦

ICCVAM Dermal Corrosivity Test Review Completed Under Expedited Process

The Interagency Coordinating Committee on the Validation of Alternative Methods has released final recommendations accepting three animal alternative methods to test dermal corrosivity under a newly-implemented expedited review process, the National Toxicology Program's National Institute of Environmental Health Sciences said.

The expedited review of the ***EpiDerm***, ***EPISKIN*** and Rat Skin Transcutaneous Electrical Resistance corrosivity tests was initiated following their endorsement by the European Centre for the Validation of Alternative Methods Scientific Advisory Committee.

"The experience gained during this review will facilitate future ICCVAM consideration of ECVAM-validated and ESAC-endorsed methods," ICCVAM said in a July 31 *Federal Register* notice. "This process enhances the likelihood of international harmonization and provides an opportunity to develop concordant recommendations between the United States and the European Union where feasible," ICCVAM added.

By using the ECVAM validation studies and ESAC reviews of the three test methods, ICCVAM was able to review the assays while bypassing the independent scientific peer review panel process.

Working with the European Union in this way "minimizes or avoids duplication of effort and avoids needless delays in achieving mutual endorsement and acceptance of scientifically validated methods," ICCVAM explained.

In the final report, ICCVAM recommends that MatTek's EpiDerm, L'Oréal's EPISKIN and the Rat Skin TER assay can be used to test dermal corrosivity in a "weight-of evidence approach using an integrated testing scheme."

In this approach, the test methods generally can replace animal tests when positive *in vitro* corrosivity results occur. However, *in vivo* dermal corrosion/irritation testing would follow negative *in vitro* responses. Similar recommendations were included in the draft report published in September ("The Rose Sheet" Oct. 15, 2001, p. 8)

ICCVAM's recommendations are now being forwarded to federal agencies for review and action. ♦♦

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM): A Review of the ICCVAM Test Method Evaluation Process and Current International Collaborations with the European Centre for the Validation of Alternative Methods (ECVAM)

William S. Stokes,[1] Leonard M. Schechtman[2] and Richard N. Hill[3]

[1]National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods, Environmental Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, 27709, USA; [2]National Center for Toxicological Research, Food and Drug Administration, Rockville, MD 20857, USA; [3]Office of Prevention, Pesticides, and Toxic Substances, US Environmental Protection Agency, Washington, DC 20460, USA

Summary — Over the last decade, national authorities in the USA and Europe have launched initiatives to validate new and improved toxicological test methods. In the USA, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), and its supporting National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), were established by the Federal Government to work with test developers and Federal agencies to facilitate the validation, review, and adoption of new scientifically sound test methods, including alternatives that can reduce, refine, and replace animal use. In Europe, the European Centre for the Validation of Alternative Methods (ECVAM) was established to conduct validation studies on alternative test methods. Despite differences in organisational structure and processes, both organisations seek to achieve the adoption and use of alternative test methods. Accordingly, both have adopted similar validation and regulatory acceptance criteria. Collaborations and processes have also evolved to facilitate the international adoption of new test methods recommended by ECVAM and ICCVAM. These collaborations involve the sharing of expertise and data for test-method workshops and independent scientific peer reviews, and the adoption of processes to expedite the consideration of test methods already reviewed by the other organisation. More recently, NICEATM and ECVAM initiated a joint international validation study on *in vitro* methods for assessing acute systemic toxicity. These collaborations are expected to contribute to accelerated international adoption of harmonised new test methods that will support improved public health and provide for reduced and more-humane use of laboratory animals.

Key words: *alternative method, animal welfare, ECVAM, ICCVAM, NICEATM, regulatory acceptance, validation.*

Introduction

Concerns about animal welfare and difficulties in achieving the regulatory acceptance of alternative test methods have led to related new legislation and government initiatives in both Europe and the USA during the past 20 years (1–5). The European Commission responded by establishing the European Centre for the Evaluation of Alternative Methods (ECVAM) in 1991, to coordinate the validation of alternative test methods at the European Union (EU) level (1). In the USA, an *ad hoc* Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) was established in 1994 to develop an interagency process for achieving the regulatory acceptance of alternative testing methods (2, 6). This was followed in 1997 by the establishment of a standing ICCVAM to coordinate the interagency evaluation of new test methods, and the establishment of a National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) to provide operational support for ICCVAM (6).

ICCVAM and ECVAM subsequently implemented programmes and activities to facilitate the development, validation, regulatory acceptance, and implementation of new alternative test methods. Because ICCVAM and ECVAM were established in response to different legislative mandates, different organisa-

Address for correspondence: Dr W.S. Stokes, National Institute of Environmental Health Sciences, Mail Code EC-17, P.O. Box 12233, Research Triangle Park, NC 27709, USA.

tional structures and processes have evolved. Despite these differences, both organisations seek to achieve the adoption of new test methods that will reduce, refine and replace (by causing less pain and distress) the use of animals in testing, and that will support continued or improved protection of human health and the environment. Because of this shared goal, useful and productive collaborations have developed between ICCVAM and ECVAM.

This paper will first provide an overview of the ICCVAM and NICEATM and their test-method evaluation process, followed by a discussion of past and current collaborations with ECVAM. Opportunities for future collaborations are discussed in a separate paper in this issue of *ATLA* (7).

The Background and History of ICCVAM and NICEATM

The *NIH Revitalization Act* of 1993, *Public Law (P.L.) 103-43* (8), directed the National Institute of Environmental Health Sciences (NIEHS) to establish criteria for the validation and regulatory acceptance of alternative testing methods, and to develop a process by which scientifically valid alternative methods could become accepted for regulatory use. The law also directed the NIEHS to develop and validate alternative toxicological testing methods that could reduce or eliminate the use of animals in acute and chronic toxicity testing.

The *ad hoc* ICCVAM

The Director of the NIEHS established an *ad hoc* ICCVAM in September 1994, to develop a report responsive to the requirements in *P.L. 103-43*. The *ad hoc* ICCVAM comprised representatives from the 15 US government agencies that are now represented on ICCVAM (Table 1). The Committee sought broad input from stakeholders, including industry, academia, animal welfare organisations, and the international community, including ECVAM and other European centres such as the Fund for the Replacement of Animals in Medical Experiments (FRAME), the National German Center for Documentation and Validation of Alternatives to Animal Experiments (ZEBET), and the Netherlands Center for Alternatives (NCA). The *ad hoc* ICCVAM recognised the existence of many European publications that were helpful to the committee in accomplishing its charge. A draft report was discussed at an ICCVAM international workshop in Alexandria, VA, USA, in December 1995. A final report, *Validation and Regulatory Acceptance of Toxicological Test Methods,* was published in 1997 (9). The report describes validation and acceptance criteria and processes for new and revised test methods. The principles embodied in these criteria are based on good science and the need to ensure that the use of new test methods provides equivalent or better protection than previous testing strategies.

The Establishment of a Standing ICCVAM

A standing ICCVAM was established in 1997 to evaluate new test methods of interest to Federal agencies and to coordinate cross-agency dialogue on issues regarding test method development, validation, acceptance, and national/international harmonisation (6, 9). ICCVAM was also established to provide a mechanism for interagency communication with non-government organisations throughout the process of test method development and validation. ICCVAM is staffed by scientists from various Federal agencies, who contribute outside their regular duties, and by support staff from NICEATM. Over 40 designated representatives from the 15 Federal agencies participate on the committee. Representatives serve as points of contact and identify individuals with particular expertise from their agencies to serve on specific test-method working groups.

The *ICCVAM Authorization Act* of 2000

The *ICCVAM Authorization Act* of 2000, *Public Law 106-545* (10), established ICCVAM as a perma-

Table 1: Member Agencies of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)

Consumer Product Safety Commission
Department of Defense
Department of Energy
Department of Health and Human Services
Agency for Toxic Substances and Disease Registry
Food and Drug Administration
National Institute for Occupational Safety and Health
National Institutes of Health, Office of the Director
National Cancer Institute
National Institute of Environmental Health Sciences
National Library of Medicine
Department of the Interior
Department of Labor
Occupational Safety and Health Administration
Department of Transportation
US Department of Agriculture
Environmental Protection Agency

nent interagency committee composed of the heads or their designated representatives from the 15 Federal agencies that originally agreed to participate on the *ad hoc* ICCVAM (Table 1). The law specified the purposes and duties of ICCVAM (Tables 2 and 3).

NICEATM

The NIEHS established NICEATM to support ICCVAM and its activities (6, 11, 12). NICEATM is part of the Environmental Toxicology Program, Division of Intramural Research, NIEHS, located at Research Triangle Park, NC, USA. NICEATM Office provides committee management and support for the three operating components of NICEATM: ICCVAM, Peer Review and Expert Panels, and the Scientific Advisory Committee.

The ICCVAM Scientific Advisory Committee

An Advisory Committee on Alternative Toxicological Methods (ACATM) was established in 1997 to provide ICCVAM and NICEATM with constructive advice from knowledgeable scientists outside of government (12). The Committee, which was composed of professionals from academia, industry, animal welfare groups, and other organisations, provided advice on the activities and priorities of NICEATM and ICCVAM and on ways to foster partnership activities and interactions among interested parties. The Committee operated in accordance with the *Federal Advisory Committee Act* (FACA; 13), and met twice yearly in public session. The ACATM was re-chartered in 2002 as the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM; 14), in accordance with the *ICCVAM Authorization Act* (10). The SACATM provides advice to ICCVAM and NICEATM on ICCVAM activities (10). The SACATM also operates in accordance with the FACA, with meetings open to the public, and the opportunity for the public to make comments at meetings. Requirements for representation on the SACATM are specified by law and the SACATM Charter (10, 14). There are 15 voting members, and ICCVAM agency representatives serve as *ex officio* non-voting members.

Table 2: Purposes of ICCVAM (10)

Increase the efficiency and effectiveness of Federal agency test method review.
Eliminate unnecessary duplicative efforts and share experiences between Federal regulatory agencies.
Optimise utilisation of scientific expertise outside the Federal Government.
Ensure that new and revised test methods are validated to meet the needs of Federal agencies.
Reduce, refine or replace the use of animals in testing where feasible.

The ICCVAM Test Method Evaluation Process

The primary function of ICCVAM is to evaluate new, revised, and alternative test methods, and to provide test recommendations to Federal agencies (10). Test methods for which there are completed validation studies can be submitted to ICCVAM for consideration. If accepted for review, an independent scientific peer-review panel is usually convened to evaluate the validation status of the test method. Based on the results of this independent evaluation, ICCVAM develops and forwards recommendations to Federal agencies about the potential usefulness and limitations of the test method.

Table 3: Duties of ICCVAM (10)

Consider petitions from the public for review and evaluation of new and revised test methods for which there is evidence of scientific validity.
Coordinate the technical review and evaluation of new and revised test methods of interagency interest.
Submit ICCVAM test recommendations to each appropriate Federal agency.
Facilitate and provide guidance on validation criteria and processes.
Facilitate: — acceptance of scientifically valid test methods — awareness of accepted methods — interagency and international harmonisation of test protocols that encourage the reduction, refinement and replacement of animal test methods
Make ICCVAM final test recommendations and agency responses available to the public.
Prepare reports on the progress of this Act and make these available to the public.