Expert workshops and expert panel meetings are convened to consider test methods for which adequate validation studies have not yet been conducted or completed. Expert panels may:

1. evaluate the interim validation status of methods;
2. evaluate proposed validation studies;
3. develop recommendations for research, development, and validation studies needed to further characterise or improve the usefulness of test methods;
4. evaluate the adequacy of current methods for assessing specific toxicities and the potential for enhanced accuracy with proposed methods; and
5. recommend testing areas in need of improved or new methods.

Federal agencies and other funding sources can then use this information to establish priorities for appropriate research, development and validation efforts.

Test Method Submissions

ICCVAM has prepared test method submission guidelines to assist test developers in the planning of development and validation activities (15). The guidelines also outline the information necessary to address ICCVAM validation and acceptance criteria. Test developers are encouraged to communicate with ICCVAM throughout test development and validation, in order to maximise the likelihood that sufficient and appropriate information will be generated for agencies to adequately assess the usefulness of a test method. ICCVAM can also serve as a means of obtaining interagency comments on proposed validation study designs and protocols. Following the completion of appropriate validation studies, the sponsor submits all the available information, data and supporting documentation to ICCVAM in accordance with the ICCVAM Submission Guidelines (Figure 1; 10). Sponsors must describe the extent to which each of the specified validation and acceptance criteria have been addressed (4). The submission must contain sufficient information for an independent, scientific, peer-review panel to assess the validation status of the method, and for agencies to assess its acceptability for providing useful information for hazard or risk assessment. NICEATM reviews submissions for completeness, and requests additional information, as necessary. ICCVAM then determines whether the method is appropriate and applicable for further evaluation, and the priority that the test method should have for review.

ICCVAM Interagency Working Groups

Once a decision is made to review a test method and resources are available, an ICCVAM Interagency Working Group is organised to collaborate with NICEATM to carry out the technical evaluation of the test method (Figure 1). Working Groups are composed of government scientists recommended by ICCVAM member agencies. Working Groups assess the completeness of submissions, and may request additional information or analyses deemed necessary to make decisions about methods. They recommend expert scientists to serve on peer-review panels and prepare questions that should be addressed by review panels. Finally, Working Group members develop draft test method recommendations for consideration by ICCVAM, based on the peer-review panel assessment.

Independent Scientific Peer-review Panels

When adequate information and data are available for a test method, and the method has been accepted for ICCVAM evaluation, an independent peer-review panel is convened. The panel is charged with developing conclusions about the validation status of the proposed test method, including its usefulness for generating information for specific human health and/or ecological risk-assessment purposes (Figure 1). The panel consists of experts from the USA and abroad, who are knowledgeable in the field, and who do not have conflicts of interest that could influence the outcome of the evaluation.

In assessing the validation status of a method, peer-review panels are asked to consider all available information and to evaluate the extent to which the ICCVAM validation and acceptance criteria have been addressed. The panel compares the performance of the test method with that of the current reference method, and develops conclusions and recommendations with regard to the usefulness of the test method, and its advantages and limitations. From a scientific perspective, the panel addresses how and when the new test method might substitute for, or replace, existing methods or approaches, or how the method might serve as a component of a testing battery or tiered testing approach.

Where applicable, peer-review panels are also asked to evaluate the extent to which test methods consider and incorporate alternatives that can reduce, refine or replace animal use. This is important when proposed test methods involve the use of animals, as US laws, regulations and policies require scientists to consider alternative methods and approaches before they use animals in research and testing procedures (4, 16). These include the 1985 *Amendment to the Animal*

Welfare Act (17), implemented as regulations in 1989 (18), and the *Health Research Extension Act* of 1985 (19), which was implemented by the Public Health Service Policy on the Humane Care and Use of Laboratory Animals in 1986 (20).

A critical aspect of ICCVAM evaluations is the transparency of the process (2, 9). To that end, it is crucial that all interested parties have the opportunity to provide comments on proposed test methods. Accordingly, test method submissions are made available to the public for comment before peer-review meetings are held. Meetings are conducted in open public session, and opportunity for comment is provided during meetings. Peer-review panel reports are made available to the public.

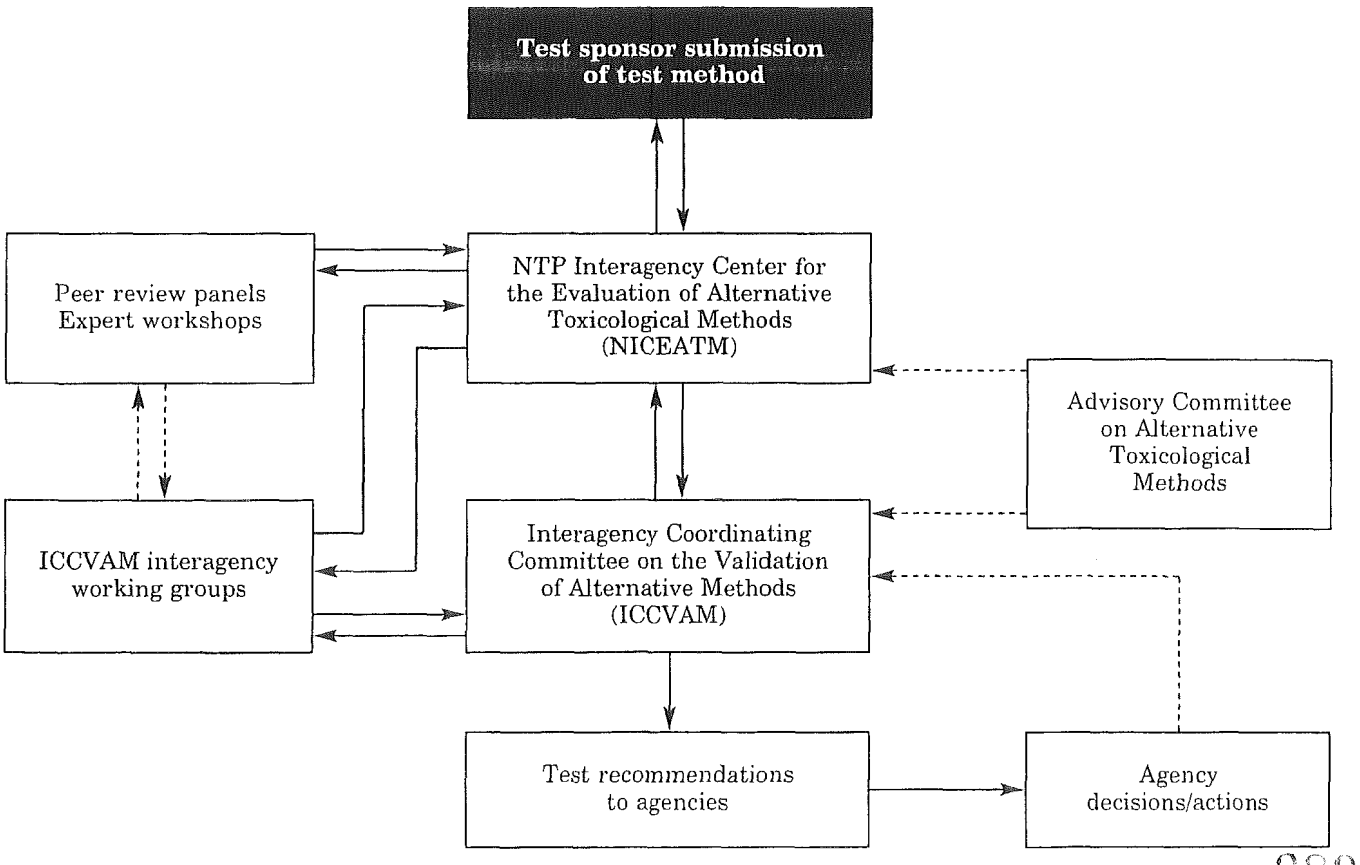
ICCVAM Test Recommendations

ICCVAM neither approves nor accepts a test method for regulatory purposes. Rather, the Committee reviews the scientific peer-review panel report and public comments, and develops test method recommendations with regard to potential usefulness, limitations and applicability to Federal testing requirements. The test method submission, peer-review panel report, public comments, and ICCVAM test method recommendations are combined into an ICCVAM Test Method Evaluation Report which is forwarded to Federal agencies for their consideration (Figure 1). All reports are publicly available at no charge on the ICCVAM/NICEATM Web site in a readily downloadable format.

Regulatory Agency Consideration of ICCVAM Recommendations

In accordance with *P.L. 106-545*, agencies are required to review ICCVAM test recommendations and to notify ICCVAM of their findings within 180 days. Each Federal agency considers the ICCVAM recommendations and determines the regulatory acceptability of the method for the agency's needs, i.e. whether the test method can be used in assessing the hazards or risks associated with the agents that come within their purview, and whether the method complies with their statutory mandates (Figure 1). Each Federal agency communicates its decisions about when and how test methods can be used to meet agency testing requirements. ICCVAM is required to make both Federal agency responses and ICCVAM recommendations available to the public.

Figure 1: ICCVAM test method evaluation process



The Implementation of New Test Recommendations

Implementing newly accepted test methods requires the education and training of potential users and regulatory scientists in the performance of test method procedures and the interpretation of results (9). Thus, adequate and appropriate training is important to agencies, testing laboratories, industry, and the public, to ensure that test methods are performed properly. ICCVAM has collaborated with the International Life Sciences Institute (ILSI) and Federal agencies to organise training workshops for two types of test method, the local lymph node assay (21–25) and *in vivo* and *in vitro* methods for acute oral toxicity testing (26–30). The value and success of these educational workshops is demonstrated by the recommendation of faculty and participants at both workshops (which included many international scientists) that training workshops should be convened for all future test methods recommended by ICCVAM.

Comparison of ICCVAM and NICEATM with ECVAM

A comparison of ICCVAM and NICEATM with ECVAM reveals both similarities and differences in their organisational structures and functions. The structure and functions of ECVAM have recently been reviewed (1), and therefore will only be briefly discussed in this section.

ICCVAM is an interagency committee composed of representatives from 15 Federal agencies, whereas NICEATM is the operational component that provides committee management and scientific support services for ICCVAM. NICEATM and ECVAM are similar in that both are components of government health research organisations. ECVAM is located in the Institute for Health & Consumer Protection at the EC's Joint Research Centre, whereas NICEATM is a component of the National Institutes of Health.

The ECVAM Scientific Advisory Committee (ESAC) has similarities to both the ICCVAM and SACATM. The ESAC is composed of representatives from the European Commission and the 15 EU Member States, as well as industry, academia, and animal welfare organisations. Operationally, the ESAC performs some functions similar to those performed by ICCVAM, the SACATM, and ICCVAM scientific peer-review panels. For example, the ESAC reviews the scientific validity of test methods, a function which is performed in the USA by ICCVAM's independent peer-review panels. As with ICCVAM, the ESAC also develops statements endorsing the validity of methods, which are then forwarded to governmental regulatory agencies for acceptance consideration. Both ICCVAM and the ESAC are charged with promoting the acceptance of validated methods. Finally, the ESAC provides scientific advice to ECVAM, which is similar to the SACATM's role in providing advice to ICCVAM and NICEATM.

The main function of ECVAM is to coordinate the validation of alternative methods at the EU level (1). Within the USA, the NIEHS is charged with this function (8), although other Federal agencies may also undertake validation studies relevant to their needs, such as the EPA's validation of its Endocrine Disruptor Screening and Testing Program. Finally, ECVAM has intramural research laboratories and extramural contract programmes to conduct test method research, development, prevalidation and validation studies. Although NICEATM does not have resources for research and development, activities of this nature are currently conducted elsewhere within the NIEHS intramural research programme and by means of extramurally funded grants.

ICCVAM and ECVAM Collaborations

US interactions with ECVAM began before ICCVAM was formally established. For example, both US and ECVAM and other European scientists planned and participated in the 1993 Interagency Regulatory Alternatives Group (IRAG) Workshop on Eye Irritation Testing: Practical Applications of Non-Whole Animal Alternatives (31), and the first World Congress on Alternatives and Animal Use in the Life Sciences (32). Subsequent collaborations with ICCVAM have been established in three areas: workshops and expert peer reviews, expedited consideration of test methods evaluated by the other organisation, and a joint NICEATM–ECVAM validation study.

ICCVAM–ECVAM Workshop and Expert Panel Collaborations

ICCVAM and ECVAM have collaborated to ensure the participation of highly qualified scientists in their respective workshops and expert meetings. For example, scientists from ECVAM, the ESAC, and the EU were among the invited experts for the *ad hoc* ICCVAM International Workshop on Validation and Regulatory Acceptance of Alternative Toxicological Methods in 1995 (9). Following the establishment of the standing ICCVAM in 1997, the Committee has regularly involved ECVAM and/or EU scientists in its workshops and expert review meetings (23, 29, 33, 34). ICCVAM solicits nominations of scientists for expert panels and solicits information and data on test methods that will be evaluated. ECVAM is informed of these requests and helps to disseminate notices to European scientists and organisations. When detailed test method background review documents and submissions are made available to the

public, ECVAM is likewise notified and asked to disseminate this information to interested stakeholders for their comments.

ICCVAM also invites the international community to participate in implementation and training workshops. In a like manner, ECVAM has invited experts from the ICCVAM and other US government and non-government organisations to participate in several of its workshops. The first ICCVAM participation was in a 1995 workshop entitled, *The Three Rs: The Way Forward* (35). ECVAM workshops have subsequently provided invaluable state-of-the-science summaries and focused recommendations on various types of test methods and related issues. Many of the workshop reports have served as key references for ICCVAM workshops and expert scientific review meetings.

ICCVAM Procedures for Consideration of Test Methods Endorsed by ECVAM

ICCVAM recognised that it would be inefficient and duplicative to conduct its own in-depth peer review for test methods that have undergone independent validation and review by ECVAM and the ESAC. Accordingly, ICCVAM developed an expedited process (7, 36, 37) for the consideration of test methods that have undergone validation and which have been endorsed by ECVAM and accepted by the EU. The process involves an assessment of the test method by an ICCVAM Working Group and ICCVAM, followed by the development of proposed ICCVAM test recommendations if there is no substantive disagreement with the ECVAM assessment. Other outcomes are possible, such as the specification of certain test parameters or qualifiers that may be necessary to meet the regulatory testing requirements of affected agencies. A *Federal Register* notice is then published, requesting public comments on the proposed recommendations and supporting test-method materials. ICCVAM reviews the public comments, and, if no major issues are identified, finalises its test recommendations and forwards them to the US Federal agencies for acceptance decisions. If major issues were to be identified as a result of the public comment process, ICCVAM would determine an appropriate approach for resolution, such as convening an independent scientific review panel.

This expedited review process should accelerate the interagency consideration of test methods evaluated by ECVAM, and reduce or eliminate delays in recommending useful test methods to Federal agencies. Compared with the normal independent peer-review process, the expedited process is expected to reduce the review time by at least 9–12 months.

ICCVAM Review of ECVAM-validated *In Vitro* Corrosivity Methods

The first test methods to undergo expedited review by ICCVAM were three alternative *in vitro* test methods for assessing skin corrosivity — EpiDerm™, EPISKIN™, and the rat skin transcutaneous electrical resistance (TER) assay (36, 37). ECVAM previously completed validation studies on these methods, and they had been reviewed and endorsed by the ESAC and accepted by the EU (38). A background review document and proposed ICCVAM recommendations for these three methods were made available for public comment in a *Federal Register* notice (36). Public comments were received and considered by the ICCVAM. No major issues were identified, and the ICCVAM adopted final test recommendations (37) later forwarded to Federal agencies for their consideration in 2002.

ECVAM Evaluation of ICCVAM Recommended Test Methods

ECVAM has established procedures similar to the ICCVAM expedited process for consideration of test methods evaluated by ICCVAM (1). The ESAC reviews ICCVAM test method evaluation reports and recommendations, and then develops and publishes statements regarding their scientific validity. These statements are then forwarded to appropriate offices within the EC for regulatory acceptance decisions (1). The first ICCVAM-evaluated test method reviewed and endorsed by the ESAC was the local lymph node assay for assessing dermal hypersensitivity, in 2000 (39). The ESAC also reviewed and endorsed the CORROSITEX® assay for dermal corrosivity, in 2001 (40).

This reciprocal consideration by ICCVAM and ECVAM of one another's evaluations has contributed to greater efficiency and international harmonisation and has paved the way for future cooperative efforts (7).

The NICEATM–ECVAM Joint Validation Study on *In Vitro* Methods for Assessing Acute Systemic Toxicity

NICEATM and ECVAM have initiated the planning and design of a joint validation study to evaluate the usefulness of two *in vitro* cytotoxicity assays for estimating the acute oral systemic toxicity potentials of chemicals. The validation study was recommended by expert participants at an ICCVAM/NICEATM International Workshop on *In Vitro* Methods for Assessing Acute Systemic Toxicity (29). The participants recommended that two *in vitro* cytotoxicity methods should be further evaluated to determine their utility for predicting rodent

and human acute systemic toxicity. These recommendations were based in part on published evaluations of *in vitro* methods by the Multicenter Evaluation of *In Vitro* Cytotoxicity (MEIC) Programme and a comparison of *in vivo* and *in vitro* data for 347 chemicals in the Register of Cytotoxicity (RC; 41, 42). Based on the RC results, Horst Spielmann and his colleagues at ZEBET subsequently proposed that cytotoxicity methods could be useful for predicting starting doses for *in vivo* acute oral toxicity studies, thereby reducing the number of animals necessary for such determinations (43). Following the workshop, a guidance document describing how *in vitro* methods can be used to estimate the starting dose for animal acute toxicity studies was prepared by Rodger Curren (Institute for In Vitro Sciences), Julia Fentem (Unilever), and Manfred Liebsch (ZEBET; 30).

The validation study will evaluate the relevance and reproducibility of two neutral red uptake assays described in the guidance document, i.e. one involving a rodent cell line (murine 3T3 cells), and the other employing a human cell type (normal human epidermal keratinocytes). Seventy-two coded chemicals, representing 12 chemicals from each of the five globally harmonised hazard classification categories and twelve chemicals that do not require a hazard classification (44), will be tested in each of three laboratories (45). Major objectives of this validation study are to evaluate the extent to which *in vitro* basal cytotoxicity assays can predict human and *in vivo* rodent acute lethality and to determine the extent to which animal use can be reduced and refined when such *in vitro* information is used to estimate starting doses for *in vivo* studies. The study will also provide important baseline cytotoxicity data that can be used as the basis for development and validation of additional *in vitro* assays necessary to characterise the toxicity of outlier chemicals not accurately predicted by basal cytotoxicity assays.

Conclusions

Despite differences in organisational structure and processes, both ECVAM and ICCVAM seek to achieve the adoption and use of alternative test methods. Collaborations and reciprocal processes have evolved to enhance the international consideration and adoption of new test methods recommended by ECVAM or ICCVAM. These collaborations involve the sharing of expertise and data for test method workshops and independent scientific peer reviews, and the use of expedited processes for the consideration of test methods previously reviewed in the USA or the EU. More recently, ECVAM and the NICEATM have initiated a joint international validation study on *in vitro* methods for assessing acute systemic toxicity. These initiatives provide increased efficiency, avoid duplicative efforts, accelerate test method consideration and adoption, and facilitate international harmonisation. Such collaborations provide a foundation for future coordination of efforts. This, in turn, will facilitate the validation and acceptance of alternative test methods that will benefit animal welfare through the reduction, replacement, and more-humane use of laboratory animals, while providing for the protection of human health and the environment.

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ECVAM–ICCVAM: Prospects for Future Collaboration

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Summary — The level and complexity of testing for hazard and risk assessment of marketed products and environmental agents has increased substantially over time, resulting in the use of greater numbers of both animals and humans for testing. Today, industry and regulatory bodies worldwide face increasing pressures to demonstrate responsible utilisation of laboratory animals, to limit their use, and to employ alternative non-animal tests. Institutions have also been established to identify, encourage the development of, conduct research on, and validate new, improved, and surrogate test methods that will reduce and replace animal use. Two such organisations are ECVAM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). As the evolutionary changes occurring in the field of toxicology result in an unprecedented increase in the introduction of alternative methodologies, these will strain the capacities of such alternative-methods institutions. That realisation is causing a shift in thinking and is creating an impetus to seek approaches by which to collaborate and develop more-efficient operational procedures for the validation and regulatory acceptance of alternative methods. Similarities in objectives, functions, scientific standards, and commitment to the principles of validation and animal welfare support the value of a cooperative arrangement between ECVAM and ICCVAM, to minimise duplication of effort, maximise productivity, and influence the international adoption of alternative tests. Opportunities for ECVAM–ICCVAM collaboration are discussed, which illustrate the feasibility and potential benefits of such a partnership.

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

Introduction

Over the course of the twentieth century in the United States and Europe, regulation of the production and use of consumer products and environmental agents has resulted in an unprecedented and progressive increase in regulatory surveillance and compliance practices. Such practices have been applied to the manufacture of such materials, their pre-market testing and post-marketing oversight, and their environmental impact. Factors such as these have brought about a significant expansion in regulatory agency standards and requirements that promote human and animal health, and help to assure product quality, safety and effectiveness, protection of the environment, and industry accountability. In response to the promulgation of regulatory requirements set forth by appropriate governing bodies, industry has had to generate information and data that demonstrate responsiveness to their legal and ethical obligations to protect the public and the environment. As a consequence, the manner by which products are evaluated and approved for use has been significantly affected, and has evolved to a point that has resulted in a dramatic increase in the extent of animal and human testing, leading to a significant protraction of product reviews, which have progressed from superficial, often perfunctory "considerations" to careful in-depth evaluations.

Against this backdrop of prevailing governances and statutes, attention to, and regard for, animal welfare has emerged as a result of both social concern and directives established by national and international authorities. These have brought about the establishment of centres of excellence in the European Union and in the United States, and subsequently in other countries, to address both scientific issues and animal welfare concerns regarding testing methodologies. Two such principal organisations are ECVAM (http://ecvam-sis.jrc.it) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM; http://iccvam.niehs.nih.gov).

ICCVAM, together with its operational/administrative centre, the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), operates under the auspices of the National Institute of Environmental Health Sciences (NIEHS). ECVAM is a European Commission activity supported by 15 European Union Member States, and receives advice from a scientific advisory committee composed of representatives from these 15 countries and from industry, academia and animal welfare organisations. ICCVAM consists of representatives of the 15 member US Federal agencies which carry out public health and environmental research and regulatory functions. A historical

account of ICCVAM/NICEATM and its processes is available in this issue of *ATLA* (1); ECVAM's activities have been similarly described (2). A comparison of these organisations, which follows later, will demonstrate the existence of sufficient similarities and consistencies that would argue for broad interaction and cooperation of such "alternative-methods institutions" on the basis of their similar objectives and complementary approaches toward the achievement of those objectives.

The Challenges and the Opportunities

Previously accepted thinking argued a mutual exclusivity of the scientific practices that help to advance human and environmental safety, and the humane and ethical aspects of animal health and welfare. In fact, due largely to organisations such as ECVAM and ICCVAM/NICEATM, and other institutions and programmes dedicated to the advancement of animal use alternatives (for example, FRAME, ZEBET, Johns Hopkins University Center for Alternatives to Animal Testing (CAAT), the Institute for In Vitro Science (IIVS) and the Netherlands Centre for Alternatives (NCA), it has come to be recognised that these factors need not be mutually exclusive, but rather can co-exist in a way that serves both causes. To support both interests, the challenge and responsibilities faced by the regulatory authorities become multifaceted. To fulfill their regulatory mandate to protect the public and the environment, it is incumbent upon agencies to make use of the best scientific methods available, to encourage appropriate validation[1] of methods, and to ensure the relevance[2] and reliability[3] of those methods used for hazard/safety/risk assessment purposes (3). To comply with national animal-welfare regulations and policies, those agencies are also obliged to be sensitive and responsive to animal welfare principles that encourage the refinement, reduction and replacement (the Three Rs) of animal use in research and testing (4, 5). ECVAM and ICCVAM/NICEATM support both regulatory objectives by espousing the Three Rs and promoting the general principles of validation as prerequisites for recommending the regulatory use of methods.

The challenge to uphold these principles rests not only with the government authorities, but also with industry. As emerging science, new technologies, and high-throughput methodologies affect chemical discovery, development, formulation, and reformulation (such as in the case of drugs and pesticide products), and yield greater numbers of potentially useful chemical candidates and products, toxicological practices will be vigorously challenged to keep up with the testing demands imposed. These demands, created by today's ever-accelerating technological progress, can be viewed as opportunities that will translate into the need to: a) develop new, reliable, rapid, and economical test methods; b) refine current methods that employ animals, so as to alleviate pain and distress or reduce the numbers of animals used; c) employ alternative non-animal test methods as high-capacity screening tools and/or definitive safety assessments; and d) standardise and validate such methods to encourage their use.

This is exemplified by the new molecular technologies that are revolutionising the field of toxicology. The "-omics" technologies such as genomics and proteomics are being aggressively investigated in many institutions worldwide, including certain US government centres of excellence, such as those established at the FDA National Center for Toxicological Research (http://publicdev.nctr.fda.gov/index.html) and the NIEHS National Center for Toxicogenomics (http://niehs.nih.gov/nct).

Toxicogenomics is one such area that holds promise for future non-animal alternative methods. As a new scientific discipline that combines such emerging technologies as genomics, proteomics, metabonomics, and bioinformatics, it holds the potential for providing high-throughput methods for use in toxicology, to investigate disease susceptibility and risk, and to identify and characterise mechanisms of action of known and suspected toxicants. Toxicogenomics will provide an opportunity to redefine models that are more mechanistically related to the human. Another encouraging area is the use of biomarkers as predictive models for toxicity induced *in vivo* (6). The discovery of reliable biomarkers predictive of human toxicity could result in significant reduction, refinement or replacement of animal use in toxicity testing. However, for all the promise such fields offer, they will ultimately need to move beyond being research tools, and find purpose in the practical application of their various sub-disciplines. Their ultimate value and utility with respect to assessing human and environmental safety will best be decided by multi-factorial validation of one or more of their component sub-disciplines, to achieve acceptance by both industry and the regulator, and ultimate implementation for regulatory purposes.

[1]*Validation:* the process by which the *reliability* and *relevance* of a test method are established with regard to its proposed use.
[2]*Relevance*: the extent to which a test method will correctly predict or measure the biological effect of interest.
[3]*Reliability*: a measure of the extent to which a test can be performed reproducibly within and among laboratories and over time.

In the face of all of these challenges and opportunities, ECVAM and ICCVAM/NICEATM will themselves be faced with their own challenges and opportunities in response to public needs and expectations, their growing obligations, and the rate at which those obligations will be encountered. ECVAM's charge will be to: a) respond with ever-increasing commitments of its monetary and personnel resources; b) prioritise and re-prioritise its validation efforts as need and consequence dictate; c) conduct greater numbers of prevalidation and validation studies; d) perform significantly more methods evaluations; e) administer more workshops, seminars, symposia, etc. to explore, educate and inform; and f) forward more and more recommendations to the ECVAM Scientific Advisory Committee (ESAC) and relevant authoritative bodies. ICCVAM/NICEATM's charge will be to: a) respond with careful prioritisation of increasing demands on its current limited resources; b) identify funding to support its research and development goals; c) heighten its pursuit of prevalidation/validation efforts; d) prioritise nominated methods for review on the basis of need and importance, scientific utility, regulatory applicability, and responsiveness to the Three Rs; e) coordinate more committee evaluations of methods (i.e. by expert working groups, peer-review panels) to determine their validation status and facilitate further studies as necessary; f) conduct more workshops, seminars, and public forums to investigate prospective alternative methods, and to educate and train end-users and regulators; and g) expand its reporting obligations to inform member agencies, the public and the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM), thereby ensuring programme transparency.

This forthcoming escalation in activity by ECVAM and ICCVAM/NICEATM will also affect the regulatory arena. Regulatory authorities will need to allocate additional resources (manpower, time, funding) from sources already over-committed and directed elsewhere. They will be faced with the need to consider more and more new, improved or alternative methods judged to be reliable and relevant, and that could potentially supplement or supplant current methods for regulatory purposes. Where feasible, appropriate and scientifically justifiable, they will also need to promote acceptance and implementation of such methods and encourage their use for regulatory purposes. Notwithstanding all of these considerations, the governing authorities will need to remain obligated to uphold their regulatory responsibilities by maintaining the highest scientific standards that ensure product safety and efficacy and protection of the environment, while being responsive to the principles established by ECVAM/ICCVAM and to animal welfare issues.

Although regulated industry will similarly be affected by these challenges and opportunities, they will realise certain advantages from this anticipated scientific revolution and the expansion of ECVAM/ICCVAM responsibilities. Such potential benefits to industry include: a) the availability of dependable, rapid, economical alternative test methods; b) cost savings that result from the use of alternative methods that reduce or replace animals otherwise employed for safety testing; c) the employment of dependable high-throughput screening methods; d) the identification of new, reliable molecular biomarkers of toxicity with human relevance; e) improved high-throughput approaches to facilitate chemical discovery efforts (for example, drugs, environmental compounds); and f) more-rapid and more-reliable test methods for the identification of potentially useful/safe chemical analogues and new molecular entities. Still, as with all the other sectors, industry will need to live up to its own responsibility to employ the best and most dependable, validated technologies that provide assurance of product safety and efficacy and protection of the environment, while abiding by animal welfare practices and principles.

Looking for the Solution: The Need for Change

Considering all the potential ramifications of the prospective opportunities that emerge from the challenges and responsibilities described, and which broadly affect the public, industrial, and regulatory spheres, it is apparent that currently employed toxicological practices will be unable to keep up with the demands imposed. Additionally, in the absence of necessary adjustments, reprioritisation, redirected resources, new financial and personnel commitments, etc., the validation and endorsement process may well be impeded. This dilemma will be further exacerbated as ICCVAM faces growing numbers of submissions and external pressures, and ECVAM contends with its own increasing commitments. To enrich the scientific base of alternative methods upon which it can draw, and thereby enhance the impact of its activities, ICCVAM will need to expand its current committee strategy as a passive recipient of methods for validation assessment submitted by test developers and sponsors, to become a more active petitioner of methods. It is envisaged that the role of ICCVAM/NICEATM could grow to: a) include proactive solicitation of candidate, scientifically credible, new/revised/alternative testing initiatives that are both potentially useful for hazard/risk assessment and responsive to the Three Rs; b) identify opportunities for providing seed money to research institutions (for example, federal, state and private) to stimulate and support directed research on method development and validation; and c) provide funding and oversight to complete research and validation

activities for promising test methods already under development. Such funding initiatives would serve to motivate and guide the progression of promising methods beyond development to a stage that could help ensure their practical application for regulatory purposes. Historically, ECVAM has been an important patron of such efforts and engages in its own research and development of alternative non-animal test methods (7) and, with ICCVAM backing and NIEHS funding, NICEATM has embarked on the similar sponsorship of appropriate activities (1).

A key strategy, which will aid in addressing these issues and the need to reform the current autonomous practices of similar organisations, will come from the establishment of alliances between international sister organisations such as ECVAM and ICCVAM/NICEATM (8). Such an association will provide opportunities to exploit missions, visions, goals, and duties held in common by such organisations. It would take advantage of cooperation in order to influence the international harmonisation and acceptance of mutually endorsed validated methods. It would allow for ECVAM–ICCVAM/NICEATM collaborative research and development efforts. Finally, it would provide opportunities for mutual agreement on test method prioritisation for validation, partnerships in validation efforts, co-sponsorship of extramural prevalidation/validation activities, coordination of submissions to the OECD, and the leveraging of resources to operate more efficiently and synergistically. Synergism is defined as "the simultaneous action of separate agents [entities] which, together, have a greater total effect than the sum of their individual effects" (9). Thus, the level of global recognition and influence attributed to ECVAM and ICCVAM can only be enhanced by an operational alliance, characterised by the complementarity of their respective technical and organisational abilities, particular areas of scientific expertise, and national and international regulatory

Table 1: The missions of ECVAM and ICCVAM

ECVAM	ICCVAM
To play a leading role at the European level in the independent evaluation of the relevance and reliability of tests for specific purposes, through research on advanced methods and new test development and validation	To coordinate interagency issues at the US Federal level on test method development, validation, scientific peer review, and regulatory acceptance, and to promote national and international harmonisation and adoption of methods

Table 2: ECVAM's duties

To coordinate the validation of alternative test methods at the European level
To act as a focal point for the exchange of information on the development of alternative test methods
To set up, maintain and manage a database on alternative procedures
To promote dialogue between legislators, industries, biomedical scientists, consumer organisations and animal welfare groups, with a view to the development, validation and international recognition of alternative methods
To help expand the role of the European Commission Joint Research Centre in prenormative research

Table 3: ICCVAM's duties

To promote scientific validation and regulatory acceptance of new/improved alternative test methods
To coordinate review/evaluation of new/revised alternative test methods of interagency interest (convening Expert Working Groups and Peer Review Panels)
To facilitate and provide guidance on test method development, the validation process, validation criteria, regulatory acceptance criteria and submission requirements
To provide recommendations to Federal agencies on the validation status of test methods and their regulatory suitability
To facilitate interagency regulatory acceptance and promote international harmonisation and adoption of scientifically validated test methods
To facilitate awareness of accepted test methods (end-users, regulators) through notifications and workshops

Table 4: The roles of ECVAM and ICCVAM in method progression

ECVAM	ICCVAM
Research and development (intramural, collaborative; supporting role)	Research and development (convey test needs)
Prevalidation (primary role)	Prevalidation (guidance)
Validation (primary role)	**Validation** (ICCVAM guidance; NICEATM administration of studies)
Sponsorship, managements; independent assessment (for example, ESAC); recommendations	**Independent assessment** (NICEATM/EWG preliminary review; independent PRP review)
Formal recommendations made by ESAC	ICCVAM recommendations made to Federal agencies
Regulatory acceptance (supporting role)	Regulatory acceptance and implementation

ESAC = ECVAM Scientific Advisory Committee; EWG = Expert Working Group; NICEATM = National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods; PRP = Peer Review Panel.

Bold typeface indicates the primary roles of each organisation.

influence. Some initial interactions and collaborations that have paved the way for a future ECVAM–ICCVAM consortium are described elsewhere in this supplement to *ATLA* (1).

Comparisons of ECVAM and ICCVAM

The prospects for the success of future collaborations of ECVAM and ICCVAM are made evident by a comparison of the two organisations.

Missions, duties and roles of ECVAM and ICCVAM

The respective missions of ECVAM and ICCVAM are described in Table 1. Broadly, the efforts of both organisations are directed at: identifying new, revised, improved, alternative methods; determining their attendant validation status; and promoting and guiding their validation for prospective regulatory use. ECVAM participates directly in the research aspects of test development and validation (2), whereas ICCVAM serves more of a coordinating role for methods evaluation within the regulatory community (3, 10). Despite these broad differences, a closer examination of the actual duties performed by these two bodies (Tables 2 and 3) shows considerable similarities. Thus, at a functional level, the distinctions between ECVAM and ICCVAM lessen and their likenesses become more apparent. The similarities in their roles with respect to the shepherding of test methods from the development stage through to the recommendation stage preceding regulatory acceptance (Table 4) further illustrate their operational congruity. Although the emphasis of certain aspects of their respective roles may differ, both ECVAM and ICCVAM, on the whole, perform corresponding functions. For example, whereas ECVAM has primary roles in prevalidation and validation efforts, ICCVAM's primary role rests with evaluation of the validation status of test methods, including the conduct of independent scientific assessment (see Table 4). In the end, both organisations offer recommendations to their respective governing bodies regarding the technical acceptability and validity of a method, with an eye toward regulatory adoption. Recognising that the ECVAM and ICCVAM processes are dynamic ones, continually evolving and improving, even as they are being employed, the minor variations in emphasis could blur even further as the level of interaction of the two organisations increases.

Roles of the scientific advisory committees of ECVAM and ICCVAM

The ESAC and the SACATM, created to provide advice to ECVAM and ICCVAM, respectively, share many similarities (Table 5). The ESAC makes formal recommendations regarding validation, application and acceptance of methods based upon the scientific recommendations that it receives from ECVAM and others (2). The SACATM offers its advice and guidance to ICCVAM and its operational centre, NICEATM, as well as to the Director of the NIEHS regarding ICCVAM/NICEATM scientific and administrative activities (11–13). That function is independent of the scientific recommendations made by ICCVAM itself to Federal agencies regarding the sci-

Table 5: The roles of the ESAC and the SACATM

ESAC	SACATM
Advise ECVAM on development, validation and acceptance of alternative methods	Advise Director of NIEHS, ICCVAM, and NICEATM on statutory mandated ECVAM functions and NICEATM activities; for example, evaluation of alternative methods, harmonisation of test protocols, validation of alternative methods, ICCVAM test recommendations, priorities and opportunites for alternative methods
Promote the activities of ECVAM in EU Member States	
Promote acceptance of validated methods by EU Member States through formal recommendations on the scientific validity of methods and statements regarding their applicability for a particular purpose	

ESAC = ECVAM Scientific Advisory Committee; NICEATM = National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods; NIEHS = National Institute of Environmental Health Sciences; SACATM = Scientific Advisory Committee on Alternative Toxicological Methods.

entific validity of a given method. Despite this primary operational difference, the overall roles of the ESAC and the SACATM are sufficiently alike to be considered closely comparable.

Expedited review processes

Recognising that both ECVAM and ICCVAM may, at times, be faced with evaluating the same methods, and that such duplicated efforts would be redundant, time-consuming, and an inefficient use of technical expertise, and would delay international harmonisation and concurrence, ICCVAM developed an "expedited review process" (1, 14, 15). The adoption of this process by ICCVAM was an explicit acknowledgment of the scientific proficiency of its counterpart organisation, and clearly communicated its interest in collaborating on validation assessments for the purpose of reducing the time and duplicated effort otherwise encountered with autonomous reviews. ECVAM has likewise developed a similar expedited review process that closely parallels that of ICCVAM (2). Table 6 outlines the current ECVAM and ICCVAM processes for reciprocal consideration of methods evaluated by one another. In both cases, one or the other organisation is the primary

Table 6: Reciprocal consideration of ECVAM- and ICCVAM-evaluated methods: expedited review processes[a]

ECVAM	ICCVAM
Critical review of ICCVAM report by ECVAM and ESAC — release of formal statement of endorsement — endorsement circulated and published	Critical review of ECVAM report by ICCVAM Expert Working Group — public comments sought by publication of evaluation and draft ICCVAM recommendations in *Federal Register* — ICCVAM final recommendations forwarded to Federal agencies
Reviewed by other expert committees and Commission services — for example, specific Directorates General	Agencies consider ICCVAM recommendations and respond as to acceptance of recommendations
Commission informs EU Competent Authorities	Implementation — integration into regulatory testing scheme — guidances, guidelines, testing requirements updated
Regulations updated	— notification of regulators and end-users

ESAC = ECVAM Scientific Advisory Committee.

[a]*A method deemed scientifically validated for a specific purpose by one or other organisation undergoes an abbreviated evaluation by its counterpart.*

reviewing body of a method submitted for evaluation. Upon completion of the validation assessment by the primary institute, the secondary body critically reviews all of the validation study data and supporting information, the evaluation report and the resulting recommendations. Mutual recognition of the validation status of a method results in the recommendations being forwarded to the appropriate regulatory authorities for their consideration, adoption, and implementation (see Table 6). These expedited review processes have already helped to pave the way for future similar efforts that can potentially reduce the time and effort invested in the evaluation of the validation status of methods ultimately required from more than a single alternative-methods institution, and has identified an area of shared interest to ECVAM and ICCVAM that can help render their respective validation processes more efficient.

Future ECVAM–ICCVAM Collaboration Opportunities

The similarities and consistencies between ECVAM and ICCVAM and their processes, as well as their shared fundamental interests in the refinement, reduction and replacement of animal use in testing and research, will serve as a practical basis for the anticipated future collaborations, reciprocal solicited involvement, and sharing of validation-related experiences and activities. Table 7 summarises the areas (some of which were described earlier) in which this kind of ECVAM–ICCVAM association has had some successes, and that can serve as a foundation upon which to build and strengthen future partnerships. One of these is the combined effort to achieve mutual recognition of the validation status of a given scientifically validated method, and the subsequent joint nomination of the method, together with its standardised protocol, to the OECD Chemicals Testing Programme, for generation of a harmonised OECD test guideline that would ensure worldwide adoption of the method. Thus, ECVAM and ICCVAM would serve in their identified and recognised roles (see Tables 2–4) and the OECD would do its part in international guideline development. In effect, under this arrangement, a three-way association would be established (8), which would be respectful of each other's mission, role, strengths, and position in the prevalidation/validation assessment and harmonised guideline development processes.

Experience has demonstrated that a successful ECVAM–ICCVAM partnership is best achieved through open communication and collaboration, instituted upon initiation of a validation effort, where each institution can provide input and each can gain a better understanding of the respective scientific and regulatory perspectives as they relate to a given method undergoing evaluation. Such a practice provides the greatest opportunities for accord and mutual endorsement of methods, such that proposals forwarded to OECD, as described above, carry the scientific backing of both alternative-methods institutions.

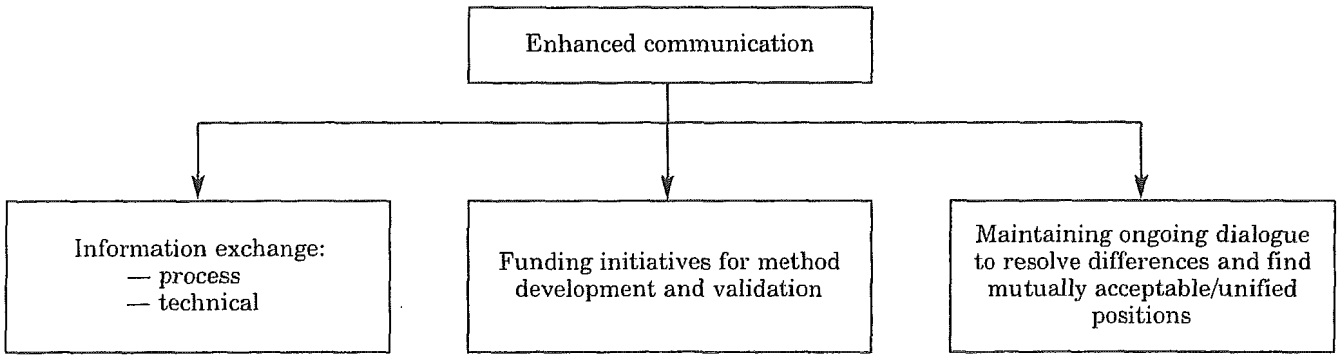
Less efficient, though still productive, are practices that involve sharing of information between ECVAM and ICCVAM after an initial evaluation by the primary reviewing body (as is done for the expedited reciprocal review process). This interactive practice allows for opportunities to resolve differences (philosophical, scientific, data interpretation, etc.) that might otherwise undermine the influence and advantages of joint nominations to OECD. The least productive practices are those in which the two alternative methods institutions conduct their activi-

Table 7: Similarities/consistency: the basis for future ECVAM–ICCVAM collaboration opportunities

Partnering to identify commonality in validation evaluation process
Harmonising the respective processes to limit/avoid duplicative efforts
Defining a reciprocal **streamlined (expedited) evaluation process**
Conjoint nomination of mutually endorsed scientifically validated methods to the **OECD**
Formalising of a process for the **mutual recognition and acceptance** of validation procedures and endorsed validated methods for specific purposes/applications
Seeking ways to achieve more the **more-timely and more-efficient implementation** of validated alternative methods

ICCVAM = Interagency Coordinating Committee on the Validation of Alternative Methods; OECD = Organization for Economic Cooperation and Development.

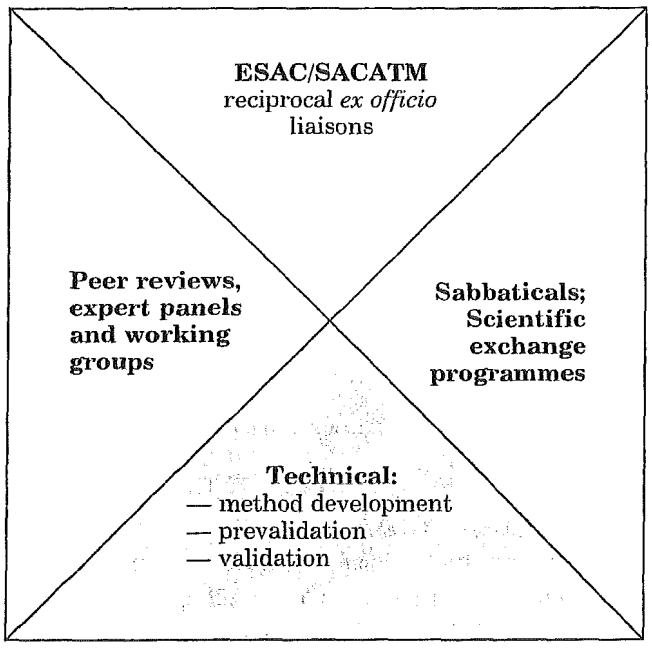
Figure 1: Opportunities for collaboration: enhanced communication



ties independently of one another, are non-communicative (or only minimally so), and operate autonomously. Under these circumstances, there would be reduced likelihood of cooperation and agreement, and noticeable redundancy in effort.

Thus, the way forward, and the way toward the mutually beneficial achievement of valid replacements, reduction, and refinements of animal test methods, is that which pursues unencumbered and forthright communications and interactions between ECVAM and ICCVAM. This is best exemplified by the various collaboration opportunities available that can underpin the future successes sought by both organisations. Figures 1–3 illustrate several such opportunities. Enhanced communication (Figure 1) can take the form of open exchange of information, both in terms of the processes used to implement the respective programmes and the technical aspects of method development and prevalidation/validation endeavours (general principles as well as test method-specific efforts). Cooperative strategies can be shared for appropriating extramural funding for research and development that yield candidate test methods, and for the validation of those methods in anticipation of regulatory use. Of critical importance in such a partnership is the need to establish and maintain an uninterrupted dialogue, so that issues of disparity, including differences in legal and regulatory requirements, can be identified, discussed and resolved by mutual understanding, negotiation and/or compromise.

Figure 2: Opportunities for collaboration: cross-fertilisation of expertise



ESAC = ECVAM Scientific Advisory Committee; SACATM = Scientific Advisory Committee on Alternative Toxicological Methods.

Other opportunities for collaboration become available through cross-fertilisation of expertise (Figure 2), wherein there exists reciprocal participation of scientists on different ECVAM and ICCVAM functions. For example, *ex officio* liaisons could be exchanged for the respective scientific advisory committees (ECVAM's ESAC and ICCVAM's SACATM). Such liaisons would provide mutually beneficial exchange of insights and advice, based upon experiences and activities in the respective organisations. Scientists from each organisation could also participate in expert working groups that focused on specific scientific areas of test methods, as well as in peer-review panels to provide independent evaluations of ECVAM and ICCVAM recommendations. Technical experts with experience in the development, prevalidation, and validation of alternative non-animal assays could provide their expertise, as necessary. Reciprocal sabbaticals and similar exchange programmes could provide opportunities for education and scientific collaboration in all areas of alternatives testing, method assessment, and regulatory implementation.

Further opportunities for future collaboration could take the form of: a) joint ECVAM–ICCVAM workshops, seminars, and study sections; and b) cooperative method-development and validation efforts (Figure 3). Such efforts would further foster the harmonisation and standardisation of test methods and institutional processes. Symposia that addressed relevant alternative toxicological methodologies and examined the validation status of tests with potential regulatory applicability could be jointly sponsored, and would pave the way toward mutual endorsement. Such symposia could also provide a forum for ECVAM and ICCVAM to examine and discuss scientific issues and test methods of common interest and potential regulatory utility, such as the newly emerging technologies, high-throughput screening methods, toxicogenomics, and other revolutionary toxicological sub-disciplines. On the acceptance of a validated test method, jointly held training workshops could serve to educate, inform, and train end-users and regulators regarding the scientific basis of the method, how the test is conducted, its applications, data interpretation, and case studies.

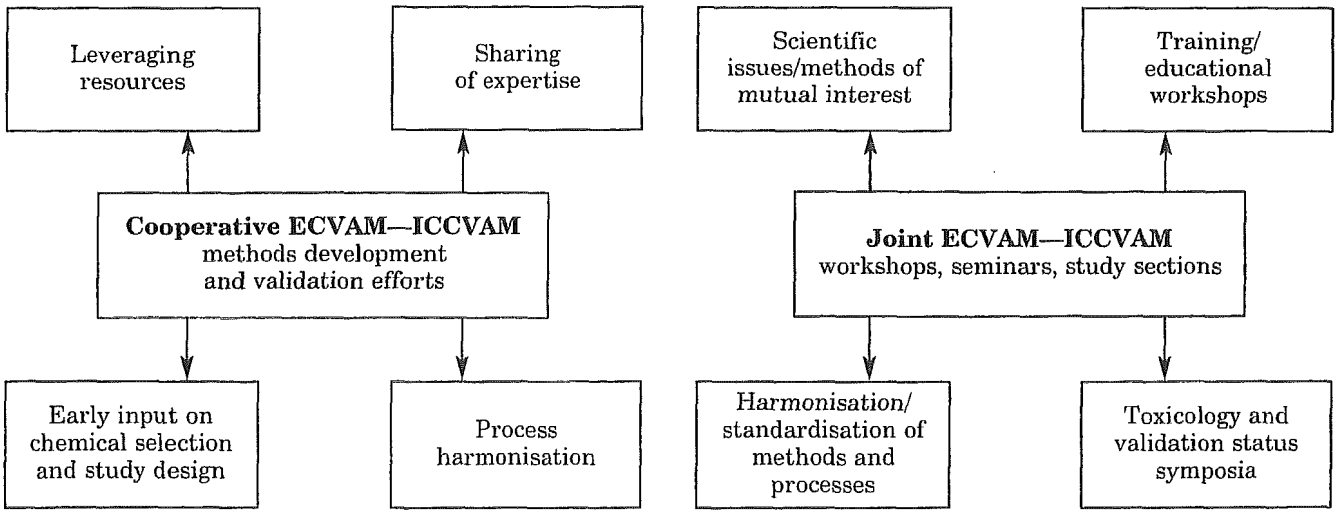
Regarding test method development and validation efforts (Figure 3), there exist several areas for potential cooperation and partnership. These could develop through: a) exploitation of ECVAM and ICCVAM/NICEATM resources, as well as utilisation of outside expertise; b) having direct and early input on study design, chemical selection for validation efforts, establishing mutually agreed criteria for test method evaluation, and setting minimum performance standards for methods that come under review; and c) striving toward process harmonisation in order to minimise redundancy, expedite the validation and acceptance processes, and provide a unified position on validation matters.

With all that is at stake, and all the opportunities available to satisfy regulatory responsibilities, industry objectives, and public concerns, it would appear that any progress toward an ECVAM–ICCVAM partnership would provide the greatest opportunity for success in promoting the use of validated alternative test methods and altering the present animal testing paradigm. An earnest commitment to that goal on the part of these prototypical organisations and their respective governing authorities will help to ensure that success.

Conclusion

ECVAM and ICCVAM are independent organisations that share similar and overlapping objectives. In an era of limited and dwindling resources, the advantages of partnership are many, and such an alliance would allow for improved efficiency and greater productivity for both organisations, with the added benefit of enhanced domestic and international regard and influence. Co-sponsored test method development and prevalidation/validation efforts and conjoint test recommendations, would carry the weight of two prestigious organisations speaking with one voice. The global influence of such an association would have a significant impact on the standardisation of protocols, the harmonisation of testing strategies, and the worldwide adoption of ECVAM–ICCVAM-recommended alternative methods that

Figure 3: Opportunities for collaboration: test means of development, validation and education



ECVAM = European Centre for the Validation of Alternative Methods; ICCVAM = Interagency Coordinating Committee on the Validation of Alternative Methods.

would refine, reduce or replace animal use in research and testing. The resulting collaborative model would be one that takes advantage of the strengths and expertise of each organisation. The interdigitation of two such distinct but parallel entities having similar aims and purposes could serve as the basis for an international science-based matrix of alternative methods institutes capable of influencing the direction and process of research, development, and validation assessment of alternative methodologies. The time is right, and the leaders of both ECVAM and ICCVAM are poised and receptive to such collaboration.

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TOILETRIES, FRAGRANCES AND SKIN CARE

THE NEWS THIS WEEK

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AHA "Sunburn Alert" Labeling Advised By FDA

- **Alpha hydroxy acid labeling draft guide includes "Sunburn Alert" warning statement,** applies to all AHA-containing products formulated for topical use. FDA publishes long-anticipated guidance in Dec. 2 *Federal Register*. Wording and scope of proposed warning differs somewhat from earlier CTFA proposal, which advised "Sun Alert" preface, pushed for statement to be applicable only to AHA-containing products sold as exfoliants 4

- **AHA labeling guidance is interim step as FDA reviews additional data** on ingredient's impact on skin sensitivity to the sun, agency explains. Proposal is being issued as guidance rather than regulation pending results of NTP long-term study of alpha hydroxy acids, agency adds. Additional agency action may be taken based on results of the study, effectiveness of final guidance 3

- ***Garnier Fructis* shampoos, conditioners expected to energize "sleepy" hair care category** with U.S. launch planned in February, L'Oréal projects. Fructis will broaden Garnier's presence in the U.S. hair care market, where the brand currently is known for its *Nutrisse* and *Lumia* hair color lines. Fructis lineup comprises 11 "fortifying" SKUs including six shampoos, four conditioners and one deep conditioner 5

- **Colgate-Palmolive *Lady Speed Stick Naturals* taps into natural products segment,** company says. Antiperspirant formula features 50% skin conditioners combined with wetness protection, Colgate claims. Three variants – Soothing with Aloe, Conditioning with Vitamin E and Moisturizing with Silk Extracts – will debut in January backed by $10 mil. marketing spend. Campaign will include print ads, high-value FSIs, ethnic promotions 5

- **Elizabeth Arden targeting drug chains for open-sell retail expansion,** which is fueling firm's mass market sales, CEO Beattie says during third quarter earnings call Dec. 4. Mass market sales advance 14% during the period, while mid-tier, prestige sales fall 12% and 7%, respectively. Net sales improve 10% to $314.8 mil., and earnings grow 12.9% to $37.2 mil. 6

Jil Sander, Kenzo Forecast Sunny Retail Environment For Fragrance Revivals

- ***Jil Sander Sun Men* debuts in March as "outdoorsy, everyday" offering,** U.S. distributor Gary Farn says. Targeting ages 18-30, scent is second men's offering in the designer portfolio. Women's counterpart also will be relaunched in the U.S., with cleaner, more modern logo, firm adds. Both fragrances will be supported with vial, blotter card sampling, as well as ads in retailer catalogs 8

- ***Kenzo Parfum d'Eté* relaunch in March will feature new packaging, bottle, juice,** Givenchy says. Premiering in select Nordstrom, Sephora doors, fragrance is being repositioned using *Flower by Kenzo* as a model. *Jungle Elephant* fragrance also will be reintroduced in January with new name, *Kenzo Jungle*, and new packaging 8

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In Brief

Animal testing alternatives: Pilot project on alternative methods to animal testing recommended by cosmetics industry group at TransAtlantic Business Dialogue conference in Chicago Nov. 8-9. Group calls for "alignment and/or mutual recognition of the criteria" used to validate alternative methods by the U.S. ICCVAM and European ECVAM. Proposal also recommends exchange of information at an early stage, mutual acceptance of alternative methods validated by the two scientific boards and coordination of research into alternative methods, according to the conference report. Pilot program recommended based on EU's move towards banning cosmetics tested on animals as part of the Seventh Amendment to the Cosmetics Directive. Ban should be monitored as early warning candidate for possible trade dispute, expert group adds. Sunscreen testing, ingredient labeling harmonization also discussed....

Emission standards: Cosmetic caps would be regulated under proposed rule for National Emission Standards for Hazardous Air Pollutants: Surface Coating of Plastic Parts and Products, FDA announces in Dec. 4 *Federal Register* notice. Proposed rule would require plastic parts and products surface coating operations to meet hazardous air pollutants emission standards "reflecting the application of the maximum achievable control technology," FDA says. Standards are expected to reduce HAP emissions in this category by 80%, agency states. Comments will be accepted until Feb. 3....

N.Y. VOC reg: New York Department of Environmental Conservation revised consumer products rule regulating volatile organic compounds is in line with Ozone Transport Commission model. Published in November, rule will regulate VOC content limits for products including antiperspirants, nail polish remover, hairspray, hair mousses, hair styling aids. Revised rule sets VOC content limits for aerosol antiperspirants at 40% rather than previously recommended 0%. Rule is effective Jan. 1, 2005. Cosmetics, Toiletry and Fragrance Association supports OTC model and is lobbying 12 Northeastern states and District of Columbia to adopt the rule in place of other VOC regulations. OTC model rule, adopted in 2001, sets Jan. 1, 2005 effective date ("The Rose Sheet" April 2, 2001, p. 9)....

CTFA adds B2B service: Cosmetic, Toiletry and Fragrance Association will launch Business Opportunities Web site Jan. 1 to provide business-to-business opportunity for exporters, importers, suppliers, agents, buyers and distributors in the personal care industry. Site is intended for "serious-minded" users only, so ads will be reviewed for out-of-date and misleading information, CTFA states. Ads will be posted on the site for three months at a fee – $250 for the first 50 words for members and $350 for non-members....

Listerine* sales:** Listerine ***PocketPaks retail sales exceeded $175 mil. in first year with more than 200 mil. of the oral care strips sold, Pfizer Consumer Healthcare says. Introduction is credited with reinvigorating the 120-year-old brand. Backed with a $40 mil. ad campaign, PocketPaks were expected to exceed $100 mil. in first year sales when they launched in October 2001 ("The Rose Sheet" Oct. 15, 2001, Marketing In Brief)....

Prescriptives hires King: Cosmetics entrepreneur Poppy King appointed VP-creative marketing of the Estee Lauder division effective Dec. 2, Prescriptives announces. In the new position, King will work with the Prescriptives team to create unique color concepts, company says. King started her own cosmetics line in 1992 in Australia at the age of 18 and most recently served as CEO of her company, Poppy Industries. King's line entered U.S. distribution in Barneys in 1993....

Purebeauty appointments: Beauty retailer makes several appointments aimed at expanding the Encino, Calif.-based chain. Trader Joe's Corporate Comptroller Al Calvanico appointed CFO, effective immediately, firm announces Dec. 2. Exec, who is credited with long-history of increasing revenue growth for retail concepts, will oversee accounting, finance and information technology departments. Allison O'Connor appointed VP-merchandising, joining firm from plant and garden retailer Poppybox. Walt Disney Corporate Marketing Manager Mike Kraus will serve as corporate director of marketing, overseeing development and positioning of the brand, advertising and marketing promotions....

Nordstrom free-standing spa: Seattle-based retailer plans to open first free-standing day spa this spring in Chicago, company says. The 3,500-square-foot spa will offer services as well as private label botanical and aromatherapeutic skin care products for the face and body, according to Nordstrom. Retailer currently operates nine Nordstrom Spa doors within department stores in locations such as San Francisco, Seattle, Atlanta and Scottsdale....

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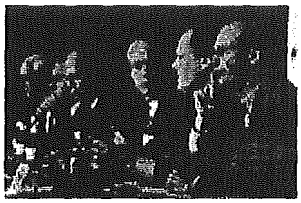

TABD Chicago CEO Conference press conference, from left, Danish Undersecretary for Foreign Affairs Niels Henriks Sliben, European Commissioner for Enterprise and Information Society Erkki Liikanen, 2002 U.S. TABD Chairman Phil Condit, 2002 EU TABD Chairman Sir Charles Masefield, Undersecretary of Commerce for Trade Grant Aldonas, and European Commissioner for Trade Pascal Lamy."

TABD EU Chairman Sir Charles Masefield addresses the TABD Press Conference

TABD CEO Press Conference

2002 EU TABD Chairman Sir Charles Masefield, Undersecretary of Commerce for Trade Grant Aldonas and European Commissioner for Trade Pascal Lamy at the final press conference