



COUNCIL

C(2001)282  
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**Council**

**PROPOSAL FOR THE UPDATING OF THREE GUIDELINES AND THE DELETION OF ONE  
GUIDELINE FOR THE TESTING OF CHEMICALS**

(Note by the Secretary-General)

*This document is submitted to Council for approval under written procedure.*

English - Or. English

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1. Safety testing provides the scientific basis for the assessment of the risk chemical substances may pose to man and the environment and is therefore an important step in the overall chemical risk management process. The OECD Guidelines for Testing of Chemicals, which are the leading international standard for safety testing, are continuously reviewed and updated so that they remain in the forefront of science. New Guidelines are being introduced to improve risk management in Member countries and/or lead to a further reduction of animal use and improvements in animal welfare. Use of the OECD Guidelines will ensure that the data derived in the safety testing of chemicals are of high quality. Furthermore, the availability of internationally harmonised test methods allows both industry and governments to save money by avoiding duplicative work. As these harmonised methods are the cornerstone of the principle of Mutual Acceptance of Data, they also contribute to eliminating non-tariff barriers to trade.

2. The Council, in its Decision C(81)30(Final) of 12th May 1981 concerning the Mutual Acceptance of Data in the Assessment of Chemicals, instructed the previously named Management Committee of the Special Programme on the Control of Chemicals in conjunction with the Chemicals Group of the Environment Committee (renamed in 1998: Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology) to establish an updating mechanism to ensure that the Guidelines, which constitute an integral part of the afore-mentioned Decision, are modified from time to time as required through the revision of existing Guidelines or the development of new Guidelines.

3. Since 1981, ninety-three new or updated Guidelines have been adopted by the Council in twelve additional Council Decisions. The most recent adoption was that of four Guidelines on 22 January 2001 [C(2000)228/FINAL].

4. Three Guidelines (420, 423, 425) referred to in the draft Decision in Annex 1 to this document were endorsed by the 32<sup>nd</sup> Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, on 15<sup>th</sup> June 2001. Furthermore, the 32<sup>nd</sup> Joint Meeting approved the deletion of one Guideline 401 as this Guideline will become obsolete after the adoption of updated Guidelines 420, 423 and 425. These updated Guidelines are considered a major contribution to the improvement of animal welfare as well as a scientific advancement, thus ensuring that good science is maintained as the basis of sound safety assessment of chemicals.

5. The three updated Guidelines and the proposal for deletion of one Guideline were subsequently considered by the Environment Policy Committee which agreed, under written procedure on 22<sup>nd</sup> October 2001, to recommend their submission to Council with a view to adoption of the three updated Guidelines and the deletion of one obsolete Guideline. A concise chronology of the development of the three updated Guidelines together with consideration related to the deletion of Guideline 401 are set out in Annex 2.

6. The Secretary-General invites consequently the Council to adopt the following draft conclusions:

THE COUNCIL

- a) noted document C(2001)282;
- b) adopted the draft Decision supplementing the Decision of the Council concerning the Mutual Acceptance of Data in the Assessment of Chemicals [C(81)30(Final)], set out in Annex 1 to C(2001)282, and agreed to its declassification.

**ANNEX 1****DRAFT DECISION OF THE COUNCIL  
Supplementing the Decision of the Council concerning the Mutual Acceptance of Data in the  
Assessment of Chemicals**

THE COUNCIL,

Having regard to Article 5 a) of the Convention on the Organisation for Economic Co-operation and Development of 14<sup>th</sup> December 1960;

Having regard to the Decision of Council of 12<sup>th</sup> May 1981 concerning the Mutual Acceptance of Data in the Assessment of Chemicals [C(81)30(Final)];

On the proposal of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, approved by the Environment Policy Committee;

DECIDES to adopt the following Guidelines<sup>1</sup> which become an integral part of the Decision referred to above:

**Updated Guidelines**

**420:** “Acute Oral Toxicity: Fixed Dose Procedure”

**423:** “Acute Oral Toxicity: Acute Toxic Class Method”

**425:** “Acute Oral Toxicity: Up-and-Down Procedure”

DECIDES to delete the following Guideline, first adopted on 12<sup>th</sup> May 1981 and subsequently updated on 24<sup>th</sup> February 1987 and expel this Guideline from the Decision referred to above:

**Deletion of an Adopted Guideline:**

**401:** “Acute Oral Toxicity”

DECIDES the deletion of Guideline 401 to become effective on 17<sup>th</sup> December 2002, which is twelve months after the adoption of guidelines 420, 423 and 425 referred to above.

DECIDES that tests using Guideline 401 that are initiated before the effective date of deletion (13/12/2002) shall continue to be accepted under Decision C(81)30(Final).

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1. The texts of these Guidelines are available from the Environment Directorate as document ENV/EPOC(2001)17/REV1.

## ANNEX 2

**BRIEF CHRONOLOGY OF THE UPDATED GUIDELINES FOR THE TESTING OF CHEMICALS SUBMITTED TO COUNCIL FOR ADOPTION**

1. The revision of Guidelines 420 (Acute Oral Toxicity: Fixed Dose Procedure), 423 (Acute Oral Toxicity: Acute Toxic Class Method), and 425 (Acute Toxicity: Up and Down Procedure) has been discussed extensively in the last few years by the Working Group of National Co-ordinators of the Test Guidelines Programme (WNT) and the Joint Meeting in the context of the possible deletion of Test Guideline 401 (Acute Oral Toxicity).
2. The 28<sup>th</sup> Joint Meeting agreed to initiate the following three activities:
  - Development of a Guidance Document on Acute Oral Toxicity Testing, explaining possibilities and limitations of each of the three alternative methods and provide guidance on their use;
  - Development and circulation of a questionnaire on details and justification of the regulatory need for acute toxicity data; and
  - Arrangement for a Consultation Meeting of Experts on Acute Toxicity Testing to discuss the need to revise Test Guidelines 420, 423 and 425 in order to cover all current regulatory data needs in case TG 401 would be deleted.
3. In June 1999, the 29<sup>th</sup> Joint Meeting discussed progress made with these activities and debated the need for Guideline 401 to cover certain data needs. The 29<sup>th</sup> Joint Meeting agreed, in principle, that after completion of a thorough revision of Guidelines 420, 423 and 425 and the development of the Guidance Document, Guideline 401 would become obsolete and could be deleted. The 29<sup>th</sup> Joint Meeting drafted a detailed work plan and time schedule for the work needed in order to consider the deletion of TG 401.
4. In February 2000 the 30<sup>th</sup> Joint Meeting was brought up-to-date on the progress with the work. Taking into account that some unexpected issues (testing of mixtures, possible legal aspects) needed time to resolve, the Joint Meeting agreed to revise the earlier agreed time schedule of work and set new deadlines for the completion of the Guidelines revision and the Guidance Document development. The decision was made to convene a second Expert Consultation Meeting in August 2000 in Paris to discuss technical details of outstanding Guideline issues and reach consensus on all three guidelines and the Guidance Document.
5. The 31<sup>st</sup> Joint Meeting was brought up-to-date on the progress of the work and expressed its satisfaction with the full consensus reached at the 2<sup>nd</sup> Consultation Meeting of Experts. The 31<sup>st</sup> Joint Meeting requested the Secretariat to confirm Member countries' technical agreement on the proposals for the three updated Guidelines and the Guidance Document through one formal commenting round.
6. In October 2000, the proposals for updating Test Guidelines 420, 423, and 425 as agreed by the 2<sup>nd</sup> Expert Consultation Meeting in August 2000 were circulated to the WNT and national experts for review. Comments were received from 9 Member countries and industry. Based on these comments, the Secretariat revised the Guidelines and Guidance Document and, on 16<sup>th</sup> February 2001, circulated the newest revisions to National Co-ordinators for final approval with a deadline for response of 19<sup>th</sup> March 2001. By that date the National Co-ordinators agreed to the proposals.

7. The 32<sup>nd</sup> Joint Meeting agreed to some minor changes in all three Guideline proposals in order to harmonise fully elements common to these three Guidelines. Subsequently, the 32<sup>nd</sup> Joint Meeting endorsed the proposals for the updating of Guidelines 420, 423 and 425 and approved their submission to EPOC.

8. Following the 32<sup>nd</sup> Joint Meeting several editorial suggestions were received that would improve the comprehensibility of the guideline proposals. These have all been taken into account. In addition, following a review of the statistical evaluation procedure in draft Guideline 425 by the US Intergovernmental Co-ordinating Committee for the Validation of Alternative Methods (ICCVAM), a small number of technical corrections and clarifications have been made to this guideline.

9. The Guideline proposals were submitted by written procedure to EPOC, which agreed on 22<sup>nd</sup> October to submit them to Council recommending their adoption.

#### **DELETION OF TEST GUIDELINE 401**

10. The original Guideline 401 was part of the first set of Guidelines adopted by Council in May 1981. The Guideline was updated in February 1987. The reason for the revision was based on animal welfare concern. The original version of the Guideline was considered scientifically sound but avoidance of unnecessary animal suffering had never been truly considered in its design. As a result of the revision, the number of animals required for the test was reduced from 30 to 20 animals per test.

11. International concern about animal welfare in the life sciences in general and in regulatory risk assessment in particular continued to grow in the 1980s. This increased awareness of our (i.e. human) responsibility to protect animals resulted in increased pressure from society in many Member countries to make every effort possible to further reduce animal suffering. Consequently, efforts started to replace the still heavily criticised Guideline 401 by more animal friendly alternative methods. The three alternatives (Guidelines 420, 423 and 425) are now indeed able to replace Guideline 401 and, therefore, this Guideline should be deleted.

12. There is a need for test facilities and governments to familiarise with the revised alternative tests after their formal adoption by Council. This would require a phase-out period for Guideline 401 instead of an abrupt deletion. A phase-out period of one year was agreed by the 31<sup>st</sup> Joint Meeting and subsequently endorsed by EPOC as a reasonable period. Consequently, the phase-out period is defined by actual dates in the Council Decision, being one calendar year after the date of adoption of the updated Guidelines 420, 423, and 425.

13. It is recognised that the submission to the regulatory authorities of studies for the testing of chemical substances quite often happens only years after these studies have been conducted. In practice this means that tests, using Test Guideline 401, that have been conducted prior to the deletion of the Guideline may be submitted well after the date of its deletion. A similar situation occurs frequently for studies conducted in accordance with a previous version of an updated Guideline. If it can be shown that these studies were indeed initiated prior to the date of Adoption of the updated version, they should be accepted for purposes of assessment. Similarly, studies in accordance with Guideline 401 conducted before its deletion, will be accepted by regulatory authorities for purposes of hazard and risk assessment and other uses relating to protection of humans and the environment, if it can be demonstrated that these tests were indeed initiated before the date of deletion of the Guideline.

14. On the contrary, the provisions of the Council Decision on MAD will not be applicable to studies conducted in accordance with Guideline 401 but carried out after the date of its formal deletion. Thus,

regulatory authorities may determine that studies conducted in accordance with Guideline 401 but conducted after the date of its formal deletion need not be accepted in Member Countries for purposes of hazard and risk assessment and other uses relating to protection of man and the environment. It is well understood that the consequence of such 401 studies not being accepted under MAD is that the studies may need to be repeated, this time in accordance with any of the three alternative methods. This situation, however, is no different than that which can occur with other tests which do not follow OECD Test Guidelines.

15. In addition to the widespread use of OECD Guidelines in Member countries they are also frequently conducted, and used for regulatory assessments, in non-member countries. Therefore, non-member countries will be informed of the phasing-out of Guideline 401 and of the guidance concerning acceptance/non-acceptance of studies conducted before/after the phasing-out period.