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COUNCIL

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Council

PROPOSAL FOR THE ADOPTION OF NEW, UPDATED OR CORRECTED GUIDELINES FOR THE TESTING OF CHEMICALS

(Note by the Secretary-General)

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Background

1. The scientific basis for the assessment of risks chemical substances may pose to human health and the environment is provided by data on their safety. Therefore, testing is an important step in the overall chemical risk management process.

2. The OECD Guidelines for Testing of Chemicals are the international standard for non-clinical health and environmental safety testing of chemicals and chemical products. They are an integral part of the 1981 Council Decision on the Mutual Acceptance of Data (MAD) in the Assessment of Chemicals [C(81)30(Final)]. This Decision agreement guarantees that safety data developed in one member country using the OECD Test Guidelines and the OECD Principles of Good Laboratory Practice (GLP) will be accepted for regulatory purposes in another member country and need not be generated again. The 1989 Council Decision-Recommendation on Compliance with GLP [C(89)87(Final)] supplements this Decision, and the 1997 Council Decision on Adherence of Non-Member Countries [C(97)114/FINAL] opens the system up to non-members. Today Israel, Singapore, Slovenia and South Africa are full adherents to the three Council Acts; and Argentina, Brazil, India and Malaysia are provisional adherents.

3. The OECD Test Guidelines are a collection of over 130 internationally agreed test methods which are used by government, industry and independent laboratories to determine the safety of chemicals and chemical preparations, including pesticides, cosmetics and industrial chemicals. They cover tests for the physical-chemical properties of chemicals, human health effects, environmental effects, degradation and accumulation in the environment, biocide efficacy, and pesticide residue chemistry. It is expected that some specific Test Guidelines will also be needed for assessing manufactured nanomaterials, and OECD is currently undertaking steps to develop such methods. Test Guidelines are primarily used in regulatory safety testing and subsequent notification of chemicals and registration of, e.g., pesticides, medical and veterinary products, cosmetics, and food and feed additives. They should not be confused with data requirements, which are the prerogative of national authorities.

4. Test Guidelines can also be used for a variety of other purposes, including the selection/ranking of new chemicals and chemical products for further research and in toxicology research. Conformity to OECD Test Guidelines is often used as a commercial argument for selling products, such as detergents, which have been tested according these guidelines before they are placed on the market.

5. Test Guidelines are developed or updated to meet countries' regulatory needs and to keep pace with scientific progress in the area of hazard identification. Thus, an important part of the work on Test Guidelines is currently being dedicated to screening or testing chemicals for potential endocrine disrupting effects. Another priority issue for member countries is the development of methods using fewer or no laboratory animals. Certain Test Guidelines for determining important effects on human health, such as carcinogenicity and chronic toxicity, have recently been updated. Finally, cost-effectiveness of the test methods is considered during the process of any Test Guideline development or update.

6. Use of the OECD Test Guidelines will ensure that the data derived in the safety testing of chemicals are of high quality. Test Guidelines are developed and updated by using OECD-wide networks of National Coordinators and hundreds of national experts, which provides the opportunity for input from scientists from government, academia and industry throughout the course of their development.

7. **Furthermore, the availability of internationally harmonised test methods and the resulting Mutual Acceptance of Data allows both industry and governments to save money by avoiding duplicative testing [approximately EUR 145 million Euros per year according to *Cutting Costs in Chemicals Management* (OECD, 2010)]. As these harmonised methods are the cornerstone of the**

principle of Mutual Acceptance of Data, they also contribute to a large extent to eliminating non-tariff barriers to trade.

8. The Council, in its Decision C(81)30(Final) of 12 May 1981 concerning the Mutual Acceptance of Data in the Assessment of Chemicals, instructed the Management Committee of the Special Programme on the Control of Chemicals, in conjunction with the Chemicals Group of the Environment Committee (renamed in 1998 the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology), to establish an updating mechanism to ensure that the set of Test Guidelines, which constitutes an integral part of the aforementioned Decision, is modified from time to time as required through the update of existing Test Guidelines or the development of new Test Guidelines.

9. Since 1981, 138 new or updated Guidelines have been adopted by the Council in twenty-four Council Decisions. The most recent adoption was that of seventeen new, updated or corrected Test Guidelines on 7 September 2009 [C(2009)103].

10. The eleven draft new, updated or corrected Test Guidelines (TG 223, 233, 317, 487, 439, 442A, 442B, 209, 417, 429, and 437) referred to in the draft Decision in Annex I to this document were submitted to the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology (Joint Meeting) [ENV/JM(2010)24] and to the Environment Policy Committee (EPOC) [ENV/EPOC(2010)11] for endorsement under the written procedure by 15 June 2010.

11. The Joint Meeting and EPOC agreed to recommend the submission of the draft Test Guidelines to the Council with a view to their adoption.

12. A concise chronology of the development of the new, updated or corrected Test Guidelines is set out in Annex II to this document.

Proposed Action

13. In the light of the preceding, the Secretary-General invites the Council to adopt the following draft conclusions:

THE COUNCIL

a) noted document C(2010)97;

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 I to C(2010)97, and agreed to its declassification.

ANNEX I

DRAFT DECISION OF THE COUNCIL

Supplementing the Decision of the Council concerning the Mutual Acceptance of Data in the Assessment of Chemicals [C(81)30(Final)]

THE COUNCIL,

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

Having regard to the Decision of Council of 12 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, and approved by the Environment Policy Committee;

DECIDES to adopt the following Guidelines[*] which become an integral part of the Decision referred to above:

New Test Guidelines:

Section 2: Effects on Biotic Systems

223 Avian Acute Oral Toxicity Test
233 Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Water or Spiked Sediment

Section 3: Degradation and Bioaccumulation

317 Bioaccumulation in Terrestrial Oligochaetes

Section 4: Health Effects

487 *In Vitro* Mammalian Cell Micronucleus Test
439 *In Vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method
442A Skin Sensitization: Local Lymph Node Assay: DA
442B Skin Sensitization: Local Lymph Node Assay: BrdU-ELISA

[*] The texts of these Test Guidelines are available from the Environment Directorate as documents:

- ENV/JM(2010)25 including the draft new TG 487 and TG 439;
- ENV/JM(2010)26 including the draft new TG 223 and TG 233;
- ENV/JM(2010)27 including the draft new TG 442A and TG 442B;
- ENV/JM(2010)28 including the draft updated TG 417 and TG 429, as well as the correction to TG 437;
- ENV/JM(2009)29 including the draft new TG 317 and the updated TG 209.

Updated Test Guidelines:

Section 2: Effects on Biotic Systems

209 Activated Sludge, Respiration Inhibition Test (Carbon and Ammonium Oxidation)

Section 4: Health Effects

417 Toxicokinetics
429 Skin Sensitization: Local Lymph Node Assay

Corrected Test Guideline:

Section 4: Health Effect

437 Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants

ANNEX II

CONCISE HISTORY OF THE DRAFT NEW, UPDATED OR CORRECTED TEST GUIDELINES FOR WHICH ADOPTION IS REQUESTED

New Test Guidelines:

TG 223: Avian Acute Oral Toxicity Test

1. This draft Test Guideline is designed to estimate the acute oral toxicity of substances to birds. It provides three testing options: a limit dose test, and two sequential testing procedures. Sequential testing procedures were designed to minimise the numbers of birds used.

2. The project for developing this Test Guideline was included in the work plan of the Test Guidelines Programme (TGP) in 1999; it was led by the United Kingdom from 2007. The work actually started in May 2005, with an expert group meeting. The Working Group of National Coordinators of the Test Guidelines Programme (WNT) discussed the draft Test Guideline at its 2007 meeting, and sent written comments after the meeting. These comments were addressed, and the draft Test Guideline was revised at an expert meeting held in the United Kingdom in September 2007. A reading comprehension exercise and a simulation report were completed in 2008. A ring test was completed in 2009. In November 2009, the Secretariat requested comments from the WNT on the draft Test Guideline that had been further revised by the expert group. The final draft was prepared on the basis of the last comments received from the WNT, and it was submitted to the WNT, for approval, at its meeting held on 23-25 March 2010. At the meeting, the WNT agreed to a small additional change and approved the revised draft Test Guideline.

TG 233: Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Water or Spiked Sediment

3. This draft Test Guideline is designed to assess the effects of life-long exposure to chemicals on the freshwater dipteran *Chironomus* sp., fully covering the first generation and the early part of the second generation. Both water and sediment exposure scenarios are described in this Test Guideline. Part of the test method is already described in the existing TG 218 and TG 219 on the Sediment-Water Chironomid Toxicity Test, but this draft Test Guideline considers a significant addition of chironomid life stage.

4. The project for developing this Test Guideline was included in the TGP work plan in 2008; it was led by Germany. Upon recommendation from an expert group, a ring test was performed in 2008-2009. In November 2009, the Secretariat requested comments from the WNT on the draft Test Guideline. The final draft was prepared on the basis of the comments received from the WNT, and submitted to the WNT, for approval, at its March 2010 meeting. At the meeting, the WNT agreed to a few additional changes and approved the revised draft Test Guideline.

TG 317: Bioaccumulation in Terrestrial Oligochaetes

5. This draft Test Guideline is design to assess bioaccumulation in the soil. Terrestrial oligochaetes play an important role in the structure and function of the soil. This proposal is especially important for the evaluation of secondary poisoning in terrestrial food chains.

6. The project for developing this Test Guideline was included in the TGP work plan in 2008; it was led by Germany. The Secretariat requested comments from the WNT in March and November 2009. Revised drafts were prepared on the basis of the comments received from the WNT and the final draft was submitted to the WNT, for approval, at its March 2010 meeting. At the meeting, the WNT agreed to additional changes and approved the revised draft Test Guideline.

TG 487: *In Vitro* Mammalian Cell Micronucleus Test

7. This draft Test Guideline for a genotoxicity test is designed to detect the activity of clastogenic and aneugenic chemicals in cells that have undergone cell division during or after exposure to the test substance. Therefore, it provides a comprehensive basis for investigating chromosome damaging potential *in vitro.*

8. The project for developing this draft Test Guideline was included in the TGP work plan in 2002; it was led by the United Kingdom. The Secretariat requested comments from the WNT on a draft Test Guideline in June 2004. A retrospective validation was performed by the European Commission and the Secretariat requested comments from the WNT on a first revised draft in December 2006. An expert meeting, held in October 2007 in the United States, made further changes to the draft Test Guideline. The Secretariat requested comments from the WNT on a second revised draft in December 2007 and submitted a third revised draft, for approval, at its 2008 WNT meeting.

9. At the meeting, issues on the performance of the cytotoxicity measurement methods, included in the draft Test Guideline, were raised. There was a concern that two methods, if used, may underestimate the cytotoxicity and therefore underestimate the highest dose used in conducting the test. To resolve this issue, the United Kingdom agreed to lead a collaboration study to assess the performance of the two methods for assessing cytotoxicity. The WNT provisionally approved the draft Test Guideline, pending the outcome of the performance assessment. The report of the performance assessment, available in 2009, showed that the two methods could be included in the draft Test Guideline. The WNT finally approved the draft Test Guideline on 27 November 2009, by written procedure, with a minor change proposed by the Secretariat.

TG 439: *In Vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method

10. This draft Test Guideline provides an *in vitro* procedure that may be used for the hazard identification of irritant chemicals (substances and mixtures) in accordance with UN Globally Harmonized System of Classification and Labelling of Chemicals. It is based on the use of reconstructed human *epidermis*, which in its overall design closely mimics the biochemical and physiological properties of the upper parts of the human skin, *i.e.* the *epidermis*.

11. The project for developing this Test Guideline was included in the TGP work plan in 2008; it was led by the European Commission. The Secretariat requested comments from the WNT on successive drafts in June 2006, March 2009, September 2009 and December 2009. The draft Test Guideline was also discussed at two expert meetings held in Germany in October 2008, and in the United States in June 2009. Revised drafts were prepared on the basis of the comments received from the WNT and the final draft Test

Guideline was submitted to the WNT, for approval, at its March 2010 meeting. At the meeting, the WNT approved the draft Test Guideline.

TG 442A: Skin Sensitization: Local Lymph Node Assay: DA (LLNA:DA)
TG 442B: Skin Sensitization: Local Lymph Node Assay: BrdU-ELISA (LLNA: BrdU-ELISA)

12. These two draft new Test Guidelines differ from TG 429 (see below) insofar as they do not use radioisotopic elements to measure lymphocyte proliferation. This will allow the use of the assays in regions where the acquisition, use, or disposal of radioactivity is problematic. The LLNA: DA is a non-radioactive modification to the LLNA, which quantifies adenosine triphosphate content via bio-luminescence as an indicator of lymphocyte proliferation. The LLNA: BrdU-ELISA is a non-radioactive modification to the LLNA test method, which utilises non-radiolabelled 5-bromo-2-deoxyuridine (BrdU) in an ELISA-based test system to measure lymphocyte proliferation.

13. The projects, proposed by Japan, were introduced in the TGP work plan in 2009. The two draft new Test Guidelines and the draft updated TG 429 (see below) were developed in parallel. The Secretariat requested comments from the WNT on the three drafts in June 2009 and December 2009. An expert meeting, held in the United States in October 2009, addressed the comments raised by the WNT in the first commenting round. Revised drafts were prepared on the basis of the comments received from the WNT and the final drafts were submitted to the WNT, for approval, at its March 2010 meeting. At the meeting, the WNT agreed to a few additional changes and approved the three revised draft Test Guidelines.

Updated Test Guidelines:

TG 209: Activation Sludge, Respiration Inhibition test (carbon and /or ammonium oxidation)

14. TG 209 was originally adopted in 1984. Its update was proposed to meet regulatory needs of member countries and to reflect technical progress. The draft updated Test Guideline is designed to assess the effects of chemical substances on micro-organisms from waste-water treatment plants activated sludge (largely bacteria) by measuring their respiration rate (carbon and/or ammonium oxidation) as oxygen consumption. The results of the test may also serve as an indicator of suitable non-inhibitory concentrations of test substances to be used in biodegradability tests.

15. The project for updating this Test Guideline was included in the TGP work plan in 2007; it was led by the United Kingdom. Comments on the first draft were requested from the WNT in September 2009. The draft Test Guideline was revised on the basis of the comments received from the WNT and submitted to the WNT, for approval, at its March 2010 meeting. At the meeting, the WNT agreed to a few additional changes, and approved the revised draft Test Guideline.

TG 417: Toxicokinetics

16. TG 417 was originally adopted in 1984. Its update was proposed to meet regulatory needs of member countries and to reflect technical progress. The draft updated Test Guideline is designed to obtain adequate information on absorption, distribution, biotransformation (i.e. metabolism) and excretion of a test substance, to aid in relating concentration or dose to the observed toxicity, and to aid in understanding its mechanism of toxicity.

17. The project for updating this Test Guideline was included in the work plan of the TGP in 2000; it was led by the United States. The first draft of the updated TG 417 was submitted to an expert group in November 2006. Comments were addressed at an expert meeting held in the United States in June 2008. At

the meeting, the Expert Group agreed on the structure and general content of the draft Test Guideline. The Secretariat requested comments from the WNT on successive drafts in November 2008, June 2009, and December 2009. Revised drafts were prepared on the basis of the comments received from the WNT and the final draft was submitted to the WNT, for approval, at its March 2010 meeting.

18. At the meeting, the WNT agreed to a few additional changes and approved the draft Test Guideline, under the condition that a small group of interested countries would solve a pending technical issue concerning one paragraph of the draft Test Guideline. On 29 March 2010, the Secretariat organized a conference call and the pending issue was solved.

TG 429: Skin Sensitization: Local Lymph Node Assay (LLNA)

19. TG 429 was originally adopted in 2002. The draft updated Test Guideline includes a set of performance standards that can be used to evaluate the validation status of "me too" tests, i.e. new and/or modified test methods that are functionally and mechanistically similar to the LLNA. In addition, a reduced LLNA method, which could use up to 40% fewer animals, is also described as an option in this draft updated Test Guideline.

20. The project for updating this Test Guideline was included in the TGP work plan in 2009; it was led by the United States. The draft updated Test Guideline and the two draft new Test Guidelines (see above TG 442A and TG 442B) have been developed in parallel. The Secretariat requested comments from the WNT on the three drafts in June 2009 and December 2009. An expert meeting, held in the United States in October 2009, addressed the comments raised by the WNT in the first commenting round. Revised drafts were prepared on the basis of the comments received from the WNT and the final drafts were submitted to the WNT, for approval, at its March 2010 meeting. At the meeting, the WNT agreed to a few additional changes and approved the three revised draft Test Guidelines.

Corrected Test Guideline:

TG 437: Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants

21. TG 437 was adopted on 7 September 2009. A correction to paragraph 37 of this Test Guideline is needed. The correction is that it should be 1% sodium hydroxide or dimethylformamide, not 10% as in the adopted Test Guideline.