MALAYSIA'S NATIONAL PROJECT TO GATHER PRIMARY SAFETY DATA FOR NANO-BASED PRODUCTS IN THE LOCAL MARKET

KEMENTERIAN SAINS, TEKNOLOGI DAN INOVASI
MINISTRY OF SCIENCE, TECHNOLOGY AND INNOVATION

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MINISTRY OF SCIENCE, TECHNOLOGY AND INNOVATION

PROJECT ACTIVITIES

CHALLENGES

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PROJECT ACTIVITIES

1 Inventory and database construction

2 Nanosafety Testing

3 Nanosafety Management

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MINISTRY OF SCIENCE, TECHNOLOGY AND INNOVATION

PROJECT ACTIVITIES

1 **Inventory and database construction**

2 1.1 Local distribution and inventory listing

1.2 Nanosafety infrastructure and expertise

3 1.3 Construct database

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MINISTRY OF SCIENCE, TECHNOLOGY AND INNOVATION

PROJECT ACTIVITIES

1 **Inventory and database construction**

2

3

1.1 Local distribution and inventory listing

- Market study of nano-based products
- Product information, manufacturer, supplier, distributor, market size, nano-claims and availability
- Inventory listing and product classification
- Nanomaterial(s) used

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PROJECT ACTIVITIES

1 **Inventory and database construction**

2

3

1.1 Local distribution and inventory listing

Beilstein Journal of Nanotechnology
2015, *6*, pp 1769-1780

1814 consumer products
622 companies
32 countries

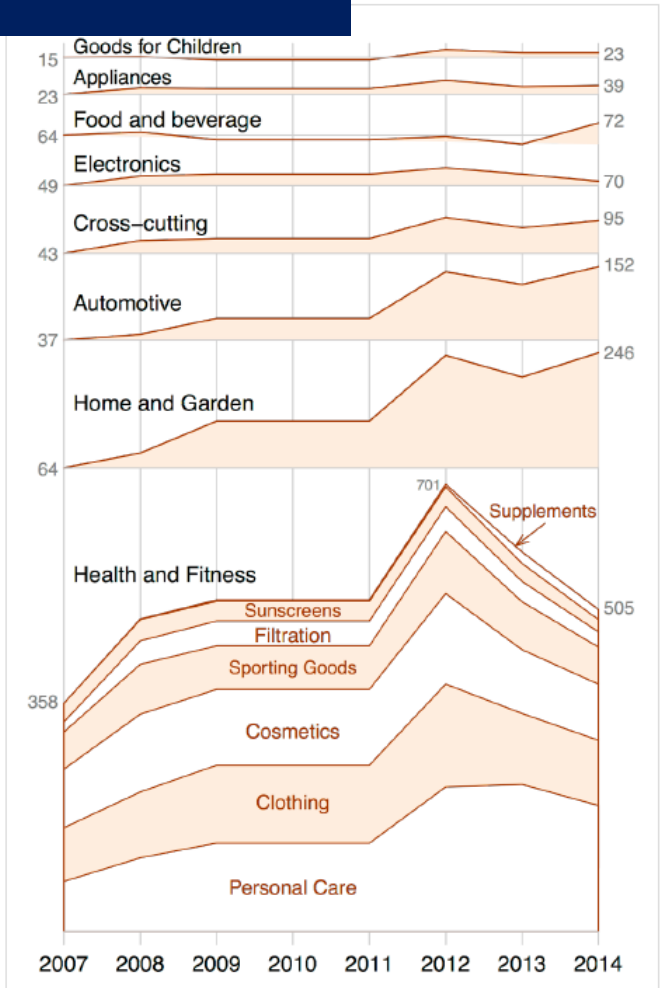

Figure 1: Number of available products over time (since 2007) in each major category and in the Health and Fitness subcategories.

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PROJECT ACTIVITIES

1 **Inventory and database construction**

2

3

1.1 Local distribution and inventory listing

Beilstein Journal of Nanotechnology
2015, *6*, pp 1769-1780

Health and Fitness
762 products
42% of total

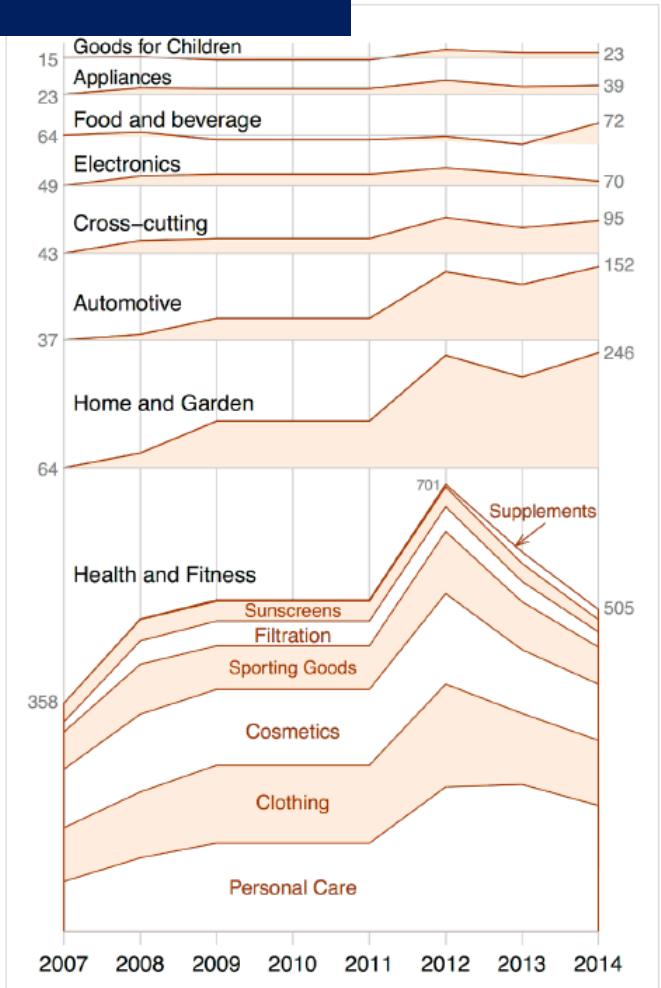

Figure 1: Number of available products over time (since 2007) in each major category and in the Health and Fitness subcategories.

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PROJECT ACTIVITIES

1 Inventory and database construction

1.1 Local distribution and inventory listing

2

3

- Food and agriculture;
- Energy and environment;
- Well-being, medical and health care; and
- Electronics, devices and system

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PROJECT ACTIVITIES

1 Inventory and database construction

1.2 Nanosafety infrastructure and expertise

2

3

- Survey on nano-based testing and infrastructure/facility
- List of equipment and expertise
- Local universities, research institutes and testing labs; both public and private
- Competency – laboratory accreditation and certification

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PROJECT ACTIVITIES

1 Inventory and database construction

1.3 Construct database

2

3

- Database from the output of Activity 1.1 and 1.2
- Database from Activities 2 and 3
- Accessible on-line for the public
- Database maintenance

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PROJECT ACTIVITIES

1

Nanosafety Testing

2

2.1 Review test methods and conduct toxicology studies

2.2 Environmental exposure and fate

3

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PROJECT ACTIVITIES

1

Nanosafety Testing

2

2.1 Review test methods and conduct toxicology studies

3

- Market study of nano-based products (Activity 1.1)
- 125 samples
- OECD Test Guidelines, ISO and other validated test procedures
  - Physical chemical properties
  - Toxicology
  - Ecotoxicology

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PROJECT ACTIVITIES

1

Nanosafety Testing

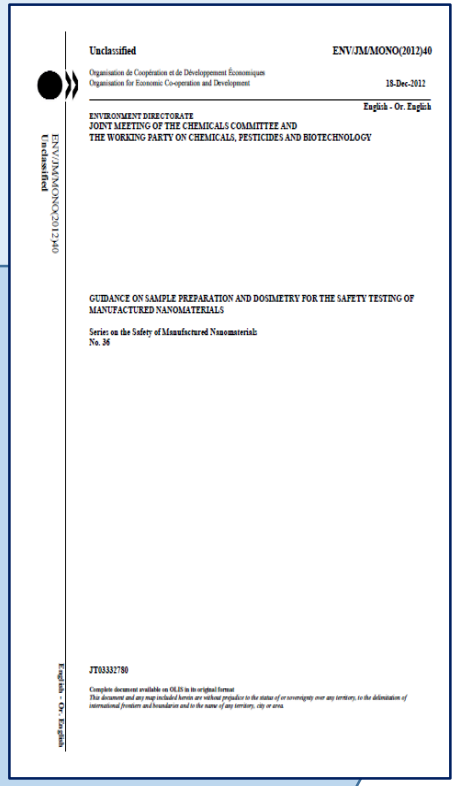
2

2.1 Review test methods and conduct toxicology studies

3

OECD Environment, Health & Safety Publications
Series on the Safety of Manufactured Nanomaterials

- ENV/JM/MONO(2016)7
- ENV/JM/MONO(2012)40
- ENV/JM/MONO(2014)34
- ENV/JM/MONO(2014)1



Unclassified ENV/JM/MONO(2012)40

Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development 18-Dec-2012

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND
THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

ENV/JM/MONO(2012)40
Unclassified

GUIDANCE ON SAMPLE PREPARATION AND DOSIMETRY FOR THE SAFETY TESTING OF MANUFACTURED NANOMATERIALS

Series on the Safety of Manufactured Nanomaterials
No. 36

JT03332780

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English - Or. English

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PROJECT ACTIVITIES

1

2

3

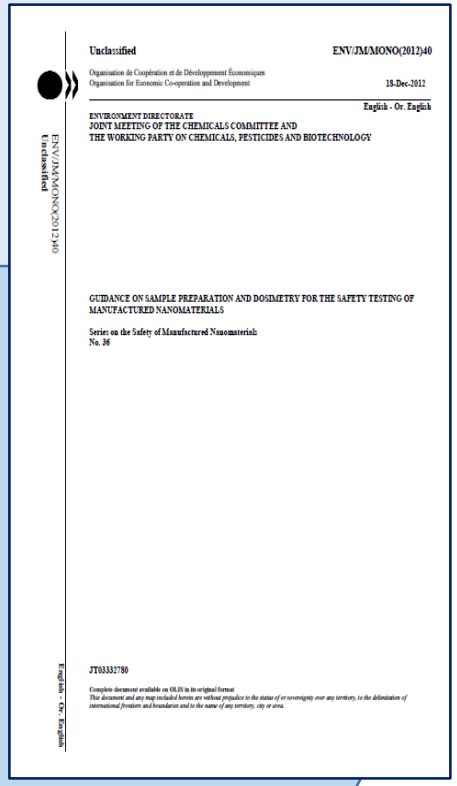
Nanosafety Testing

2.2 Environmental exposure and fate

- Biodegradation
- Bioaccumulation

OECD Environment, Health & Safety Publications
Series on the Safety of Manufactured Nanomaterials

❑ ENV/JM/MONO(2014)1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PROJECT ACTIVITIES

1

2

3

Nanosafety Management

3.1 Life cycle assessment

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PROJECT ACTIVITIES

1

2

3

Nanosafety Management

3.1 Life cycle assessment

Integration of Risk Assessment

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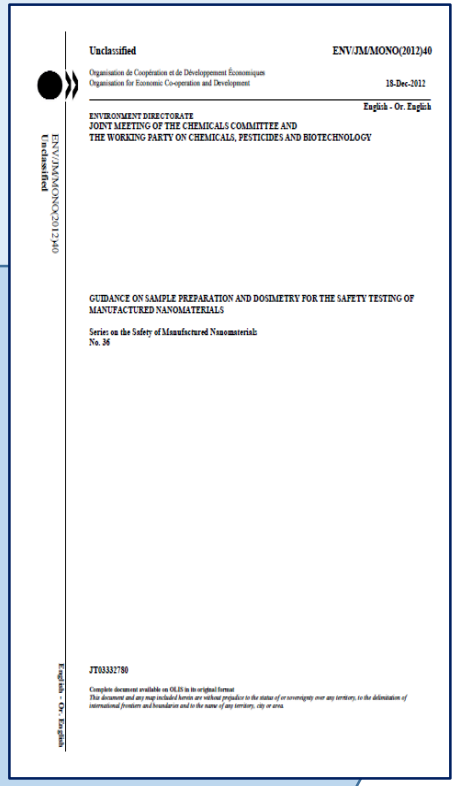
Series on the Safety of Manufactured Nanomaterials

- ENV/JM/MONO(2015)30
- ENV/JM/MONO(2016)63



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CHALLENGES

1 Hazard Identification

2

3

HAZARD CLASS	HAZARD CATEGORY			
Acute toxicity – oral	Cat. 1	Cat. 2	Cat. 3	Cat. 4
Acute toxicity – dermal	Cat. 1	Cat. 2	Cat. 3	Cat. 4
Acute toxicity – inhalation	Cat. 1	Cat. 2	Cat. 3	Cat. 4
Skin corrosion/irritation	Cat. 1A/1B/1C			Cat. 2
Serious eye damage/irritation	Cat. 1	Cat. 2		
Skin sensitization	Cat. 1			
Germ cell mutagenicity	Cat. 1A/1B		Cat. 2	
Carcinogenicity	Cat. 1A/1B		Cat. 2	

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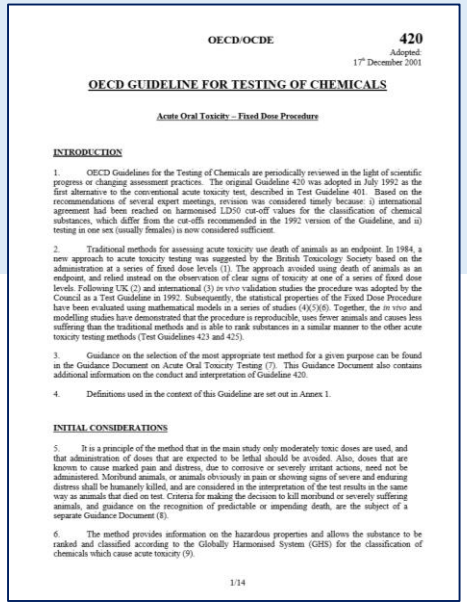
CHALLENGES

1 Hazard Identification

2

HAZARD CLASS	HAZARD CATEGORY			
Acute toxicity – oral	Cat. 1 5 mg/kg	Cat. 2 50 mg/kg	Cat. 3 300 mg/kg	Cat. 4 2000 mg/kg

3



OECD/OCDE 420
Adopted: 17th December 2001

OECD GUIDELINE FOR TESTING OF CHEMICALS

Acute Oral Toxicity – Fixed Dose Procedure

INTRODUCTION

1. OECD Guidelines for the Testing of Chemicals are periodically reviewed in the light of scientific progress or changing assessment practices. The original Guideline 420 was adopted in July 1992 as the first alternative to the conventional acute toxicity test, described in Test Guideline 401. Based on the recommendations of several expert meetings, revision was considered timely because: i) international agreement had been reached on harmonised LD50 cut-off values for the classification of chemical substances, which differ from the cut-offs recommended in the 1992 version of the Guideline, and ii) testing in one sex (usually females) is now considered sufficient.

2. Traditional methods for assessing acute toxicity use death of animals as an endpoint. In 1984, a new approach to acute toxicity testing was suggested by the British Toxicology Society based on the administration at a series of fixed dose levels (1). The approach avoided using death of animals as an endpoint, and relied instead on the observation of clear signs of toxicity at one of a series of fixed dose levels. Following UK (2) and international (3) *in vivo* validation studies the procedure was adopted by the Council as a Test Guideline in 1992. Subsequently, the statistical properties of the Fixed Dose Procedure have been evaluated using mathematical models in a series of studies (4)(5)(6). Together, the *in vivo* and modelling studies have demonstrated that the procedure is reproducible, uses fewer animals and causes less suffering than the traditional methods and is able to rank substances in a similar manner to the other acute toxicity testing methods (Test Guidelines 423 and 425).

3. Guidance on the selection of the most appropriate test method for a given purpose can be found in the Guidance Document on Acute Oral Toxicity Testing (7). This Guidance Document also contains additional information on the conduct and interpretation of Guideline 420.

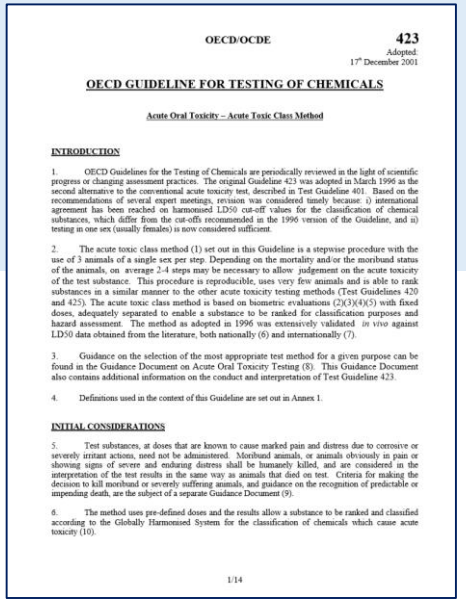
4. Definitions used in the context of this Guideline are set out in Annex 1.

INITIAL CONSIDERATIONS

5. It is a principle of the method that in the main study only moderately toxic doses are used, and that administration of doses that are expected to be lethal should be avoided. Also, doses that are known to cause marked pain and distress, due to corrosive or severely irritant actions, need not be administered. Moribund animals, or animals obviously in pain or showing signs of severe and enduring distress shall be humanely killed, and are considered in the interpretation of the test results in the same way as animals that died on test. Criteria for making the decision to kill moribund or severely suffering animals, and guidance on the recognition of predictable or impending death, are the subject of a separate Guidance Document (8).

6. The method provides information on the hazardous properties and allows the substance to be ranked and classified according to the Globally Harmonised System (GHS) for the classification of chemicals which cause acute toxicity (9).

1/14



OECD/OCDE 423
Adopted: 17th December 2001

OECD GUIDELINE FOR TESTING OF CHEMICALS

Acute Oral Toxicity – Acute Toxic Class Method

INTRODUCTION

1. OECD Guidelines for the Testing of Chemicals are periodically reviewed in the light of scientific progress or changing assessment practices. The original Guideline 423 was adopted in March 1996 as the second alternative to the conventional acute toxicity test, described in Test Guideline 401. Based on the recommendations of several expert meetings, revision was considered timely because: i) international agreement has been reached on harmonised LD50 cut-off values for the classification of chemical substances, which differ from the cut-offs recommended in the 1996 version of the Guideline, and ii) testing in one sex (usually females) is now considered sufficient.

2. The acute toxic class method (1) set out in this Guideline is a stepwise procedure with the use of 3 animals of a single sex per step. Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgement on the acute toxicity of the test substance. This procedure is reproducible, uses very few animals and is able to rank substances in a similar manner to the other acute toxicity testing methods (Test Guidelines 420 and 425). The acute toxic class method is based on biometric evaluations (2)(3)(4)(5) with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment. The method as adopted in 1996 was extensively validated *in vivo* against LD50 data obtained from the literature, both nationally (6) and internationally (7).

3. Guidance on the selection of the most appropriate test method for a given purpose can be found in the Guidance Document on Acute Oral Toxicity Testing (8). This Guidance Document also contains additional information on the conduct and interpretation of Test Guideline 423.

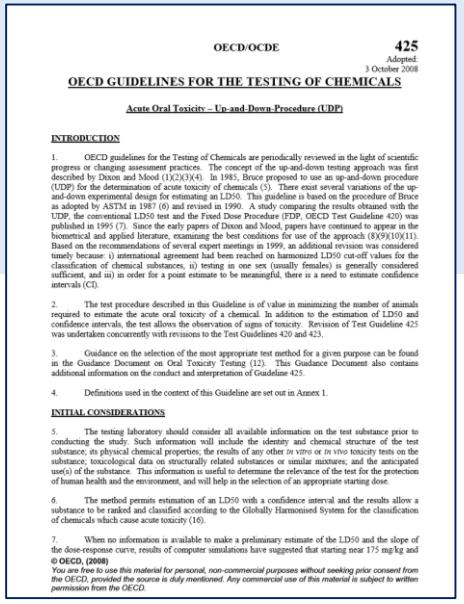
4. Definitions used in the context of this Guideline are set out in Annex 1.

INITIAL CONSIDERATIONS

5. Test substances, at doses that are known to cause marked pain and distress due to corrosive or severely irritant actions, need not be administered. Moribund animals, or animals obviously in pain or showing signs of severe and enduring distress shall be humanely killed, and are considered in the interpretation of the test results in the same way as animals that died on test. Criteria for making the decision to kill moribund or severely suffering animals, and guidance on the recognition of predictable or impending death, are the subject of a separate Guidance Document (9).

6. The method uses pre-defined doses and the results allow a substance to be ranked and classified according to the Globally Harmonised System for the classification of chemicals which cause acute toxicity (10).

1/14



OECD/OCDE 425
Adopted: 3 October 2008

OECD GUIDELINES FOR THE TESTING OF CHEMICALS

Acute Oral Toxicity – Up-and-Down-Procedure (UDP)

INTRODUCTION

1. OECD guidelines for the Testing of Chemicals are periodically reviewed in the light of scientific progress or changing assessment practices. The concept of the up-and-down testing approach was first described by Dixon and Mood (1)(2)(3)(4). In 1985, Bruce proposed to use an up-and-down procedure (UDP) for the determination of acute toxicity of chemicals (5). There exist several variations of the up-and-down experimental design for estimating an LD50. This guideline is based on the procedure of Bruce as adopted by ASTM in 1987 (6) and revised in 1990. A study comparing the results obtained with the UDP, the conventional LD50 test and the Fixed Dose Procedure (FDP, OECD Test Guideline 420) was published in 1995 (7). Since the early papers of Dixon and Mood, papers have continued to appear in the biometrical and applied literature, examining the best conditions for use of the approach (8)(9)(10)(11). Based on the recommendations of several expert meetings in 1999, an additional revision was considered timely because: i) international agreement had been reached on harmonized LD50 cut-off values for the classification of chemical substances, ii) testing in one sex (usually females) is generally considered sufficient, and iii) in order for a point estimate to be meaningful, there is a need to estimate confidence intervals (CI).

2. The test procedure described in this Guideline is of value in minimizing the number of animals required to estimate the acute oral toxicity of a chemical. In addition to the estimation of LD50 and confidence intervals, the test allows the observation of signs of toxicity. Revision of Test Guideline 425 was undertaken concurrently with revisions to the Test Guidelines 420 and 423.

3. Guidance on the selection of the most appropriate test method for a given purpose can be found in the Guidance Document on Oral Toxicity Testing (12). This Guidance Document also contains additional information on the conduct and interpretation of Guideline 425.

4. Definitions used in the context of this Guideline are set out in Annex 1.

INITIAL CONSIDERATIONS

5. The testing laboratory should consider all available information on the test substance prior to conducting the study. Such information will include the identity and chemical structure of the test substance; its physical chemical properties; the results of any other *in vitro* or *in vivo* toxicity tests on the substance; toxicological data on structurally related substances or similar mixtures; and the anticipated use(s) of the substance. This information is useful to determine the relevance of the test for the protection of human health and the environment, and will help in the selection of an appropriate starting dose.

6. The method permits estimation of an LD50 with a confidence interval and the results allow a substance to be ranked and classified according to the Globally Harmonised System for the classification of chemicals which cause acute toxicity (16).

7. When no information is available to make a preliminary estimate of the LD50 and the slope of the dose-response curve, results of computer simulations have suggested that starting near 175 mg/kg and

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CHALLENGES

1

Quality of Data

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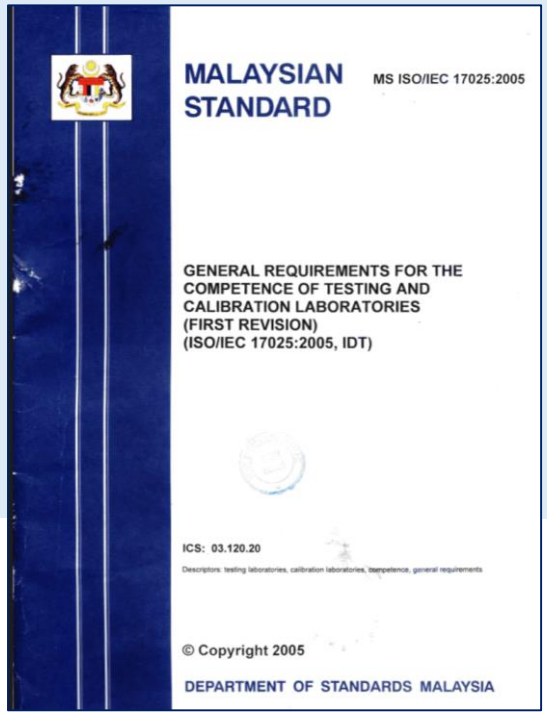
MALAYSIAN STANDARD

MS ISO/IEC 17025:2005

GENERAL REQUIREMENTS FOR THE COMPETENCE OF TESTING AND CALIBRATION LABORATORIES (FIRST REVISION) (ISO/IEC 17025:2005, IDT)

ICS: 03.120.20

Descriptors: testing laboratories, calibration laboratories, competence, general requirements

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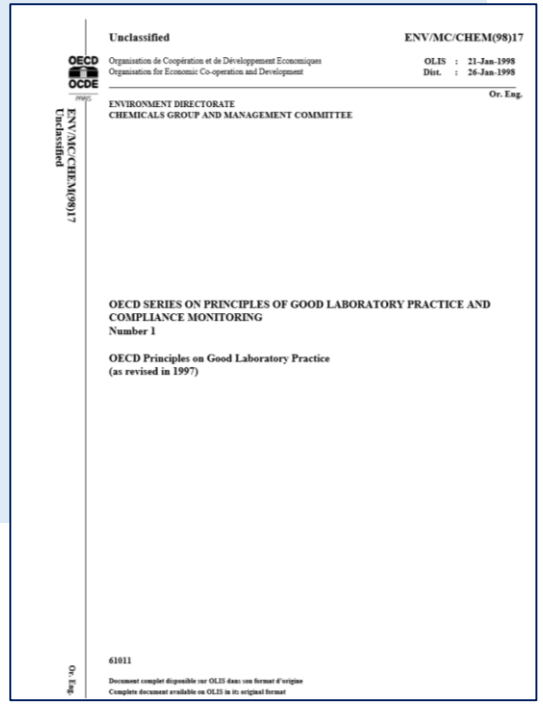
DEPARTMENT OF STANDARDS MALAYSIA

SAFETY DATA
ISO 17025 accreditation
OECD GLP certification


Unclassified ENV/MC/CHEM(98)17

Organisation de Coopération et de Développement Economiques
Organisation for Economic Co-operation and Development

OLIS : 21-Jan-1998
Dist. : 26-Jan-1998

Or. Eng.

ENVIRONMENT DIRECTORATE
CHEMICALS GROUP AND MANAGEMENT COMMITTEE

ENV/MC/CHEM(98)17
Unclassified

OECD SERIES ON PRINCIPLES OF GOOD LABORATORY PRACTICE AND COMPLIANCE MONITORING
Number 1

OECD Principles on Good Laboratory Practice
(as revised in 1997)

61011

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MINISTRY OF SCIENCE, TECHNOLOGY AND INNOVATION

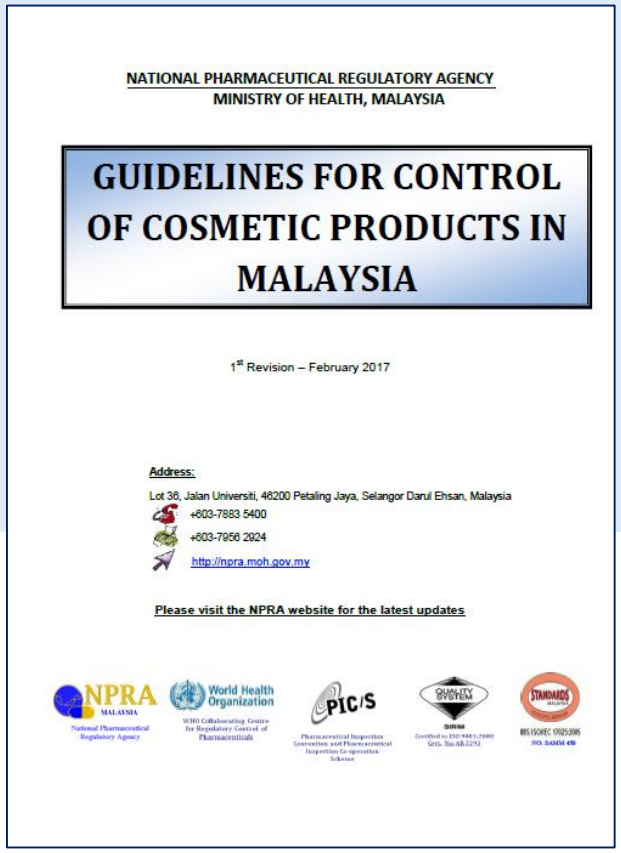
CHALLENGES

1

2

3

Regulatory



NATIONAL PHARMACEUTICAL REGULATORY AGENCY
MINISTRY OF HEALTH, MALAYSIA

GUIDELINES FOR CONTROL OF COSMETIC PRODUCTS IN MALAYSIA

1st Revision – February 2017

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Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor Darul Ehsan, Malaysia
+603-7883 5400
+603-7956 2924
http://npra.moh.gov.my

Please visit the NPRA website for the latest updates

ANNEX IV - Part 1
List of colouring agents allowed for use in cosmetic products

Colour index number: 77266 (nano)
Colour: Black

Annex VII
List of UV filters which cosmetic products may contain

Substance: Zinc oxide (nano)
Max. Authorized Conc.: 25%

Substance: Titanium dioxide (nano)
Max. Authorized Conc.: 25%

Substance: Tris-biphenyl triazine Tris-biphenyl triazine (nano)
Max. Authorized Conc.: 10%

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THANK YOU