NATIONAL REGULATORY CONFERENCE 2013
Regulatory Innovation Towards Transformation

Safety Assessment of Cosmetics

Mohd Helme Mohd Helan
SIRIM Berhad
May 8, 2013

Safety Assessment of Cosmetics

INTRODUCTION

ASEAN COSMETIC DIRECTIVE

INGREDIENTS (SUBSTANCES)

FINISHED PRODUCTS

TEST FACILITIES

Safety Assessment of Cosmetics

INTRODUCTION

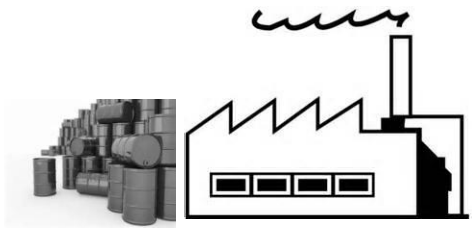
ASEAN COSMETIC DIRECTIVE

INGREDIENTS (SUBSTANCES)

FINISHED PRODUCTS

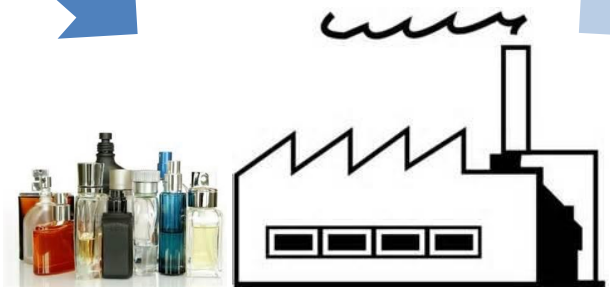
TEST FACILITIES

Introduction



Ingredients supplier

Safety Assessor



Manufacturer
Distributor

Test Facility

Regulatory Authority

Introduction

Risk Assessment

Hazard identification

Physical and chemical specifications
Toxicological properties
QSAR studies
Epidemiological studies
Clinical studies

Dose-response assessment

Relationship study between toxic response and exposure

Exposure assessment

Amount and frequency of human exposure to the substance

Introduction

Risk Assessment

- Hazard identification
- Dose-response assessment
- Exposure assessment
- Risk characterization

Calculation of probability the substance under investigation causes damage to human health and to what extent

Introduction

Risk Assessment

- Hazard identification
- Dose-response assessment
- Exposure assessment
- Risk characterization
- Risk management
- Risk communication

Based on WHO/UNEP/ILO (2001).
Approaches to Integrated Risk Assessment.

Safety Assessment of Cosmetics

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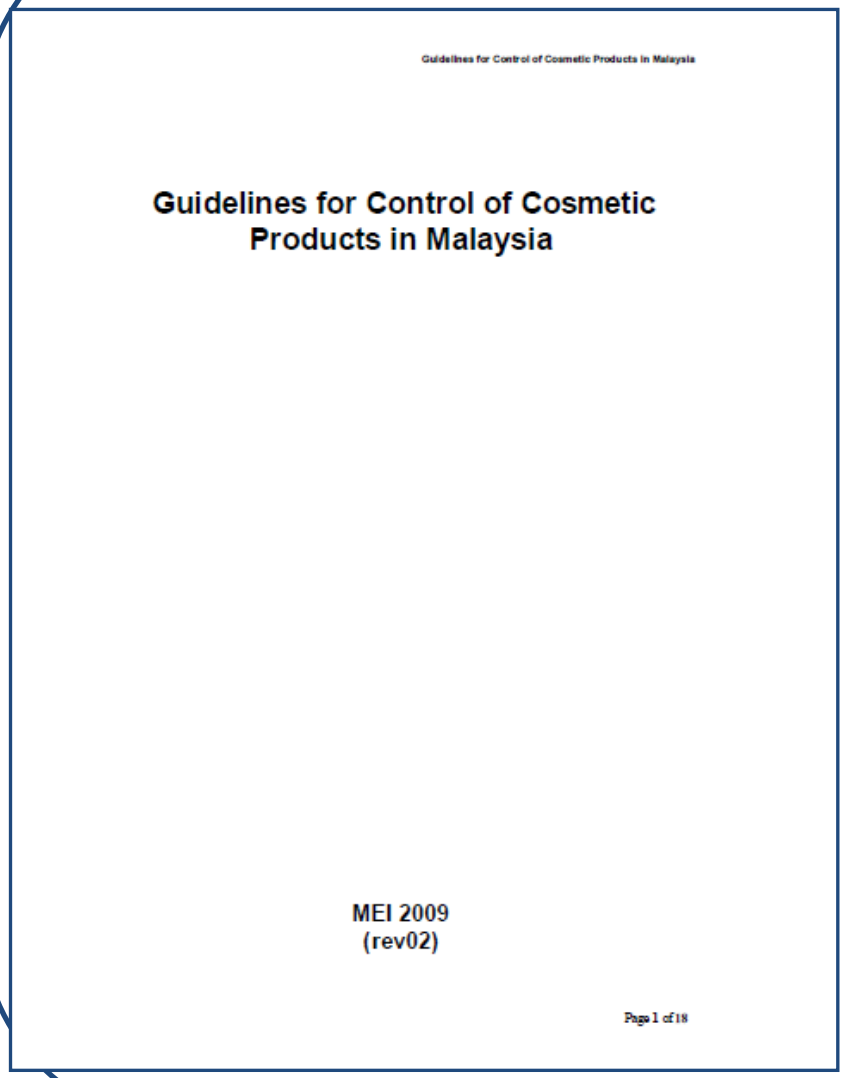
ASEAN Cosmetic Directive

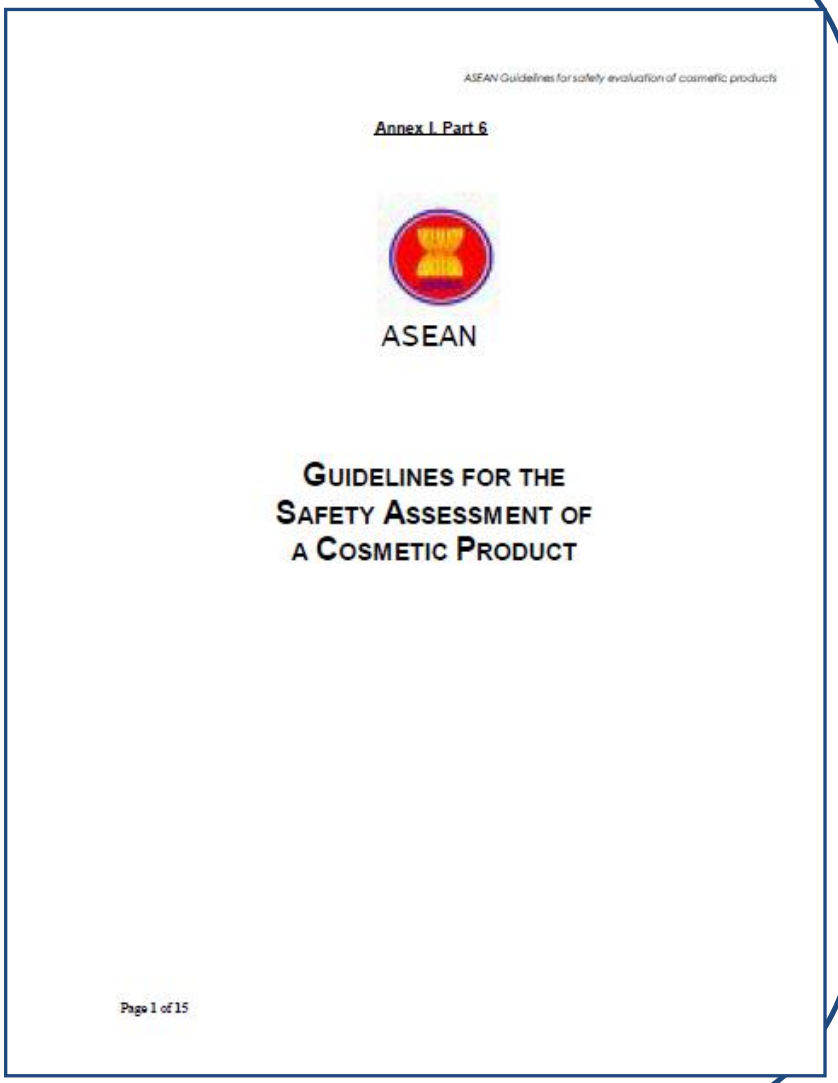


Guidelines for Control of Cosmetic Products in Malaysia

Guidelines for Control of Cosmetic Products in Malaysia

MEI 2009
(rev02)

Page 1 of 18



ASEAN Guidelines for safety evaluation of cosmetic products

Annex I, Part 6

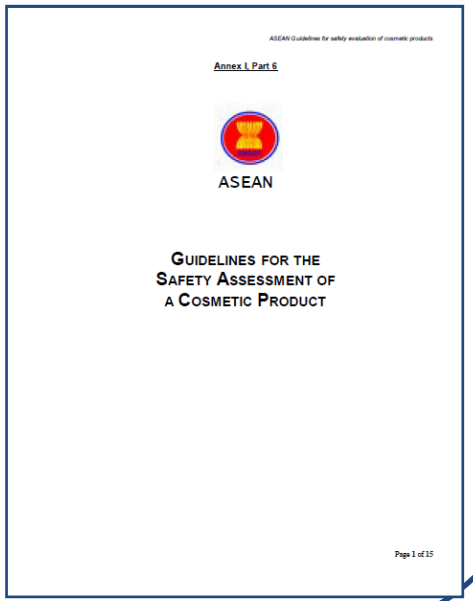
ASEAN

GUIDELINES FOR THE SAFETY ASSESSMENT OF A COSMETIC PRODUCT

Page 1 of 15

ASEAN Cosmetic Directive

Article 1: General Provisions
Article 2: Definition and Scope of Cosmetic Product
Article 3: Safety Requirements
Article 4: Ingredient Listings
Article 5: ASEAN Handbook of Cosmetic Ingredients
Article 6: Labeling
Article 7: Product Claims
Article 8: Product Information
Article 9: Methods of Analysis
Article 10: Institutional Arrangements
Article 11: Special Cases
Article 12: Implementation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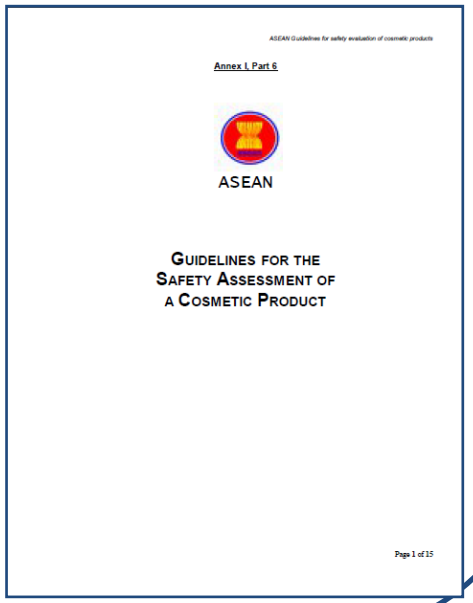
Article 12: Implementation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GUIDELINES FOR THE SAFETY ASSESSMENT OF A COSMETIC PRODUCT

Page 1 of 15

ASEAN Cosmetic Directive

Article 3: **Safety Requirements**

A cosmetic product placed on the market must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use, taking account, in particular, of the product's presentation, its labeling, instructions for its use and disposal, warning statements as well as any other indication or information provided by the manufacturer or his authorized agent or by any other person responsible for placing the product on the market.

ASEAN Cosmetic Directive

Article 8: **Product Information**

… assessment of the safety for human health of the

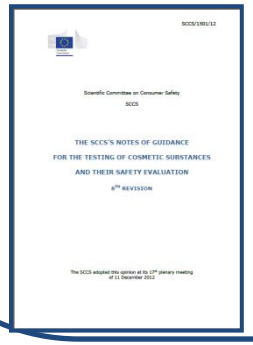
- finished product,
- its ingredients (or substances),
- its chemical structure and
- its level of exposure.

ASEAN Cosmetic Directive

Safety assessment
of cosmetic ingredients and products
remains a scientific exercise
that can only be performed
on a case-by case basis

ASEAN Cosmetic Directive

Generally,
major basis for safety evaluation
is provided
considering the toxicological profile
of its ingredients (substances)


SCCS/1491/12

Scientific Committee on Consumer Safety
SCCS

THE SCCS'S NOTES OF GUIDANCE
FOR THE TESTING OF COSMETIC SUBSTANCES
AND THEIR SAFETY EVALUATION
8TH REVISION

The SCCS adopted this opinion at its 13th plenary meeting
of 11 December 2012

"Safety of cosmetic products in the EU is based on the safety of the ingredients" (*SCCS Notes of Guidance, 8th Revision 2012*)

ASEAN Cosmetic Directive

As of March 11, 2013, the marketing ban will be enforced in Europe for cosmetics tested on animals. No chemical explicitly for use as a cosmetic ingredient should be tested on an animal after that date, anywhere in the world.

Regulation (EC) No 1223/2009 of the European Parliament and of the Council

ASEAN Cosmetic Directive

Issues

- Good Manufacturing Practice
- Ingredients (substances)
- Packaging
- Quality control (microbiology and chemical)
- Stability studies
- Labeling
- Product surveillance

Safety Assessment of Cosmetics

INTRODUCTION

ASEAN COSMETIC DIRECTIVE

INGREDIENTS (SUBSTANCES)

FINISHED PRODUCTS

TEST FACILITIES

Ingredients

- Mostly well-defined single chemical and often mixtures of chemicals
- Synthetic or natural origin (mineral, animal, botanical or derived from biotechnology)
- Fragrance
- Potential endocrine disruptors
- Carcinogenic, mutagenic or toxic to reproduction (CMR)
- Nanomaterials

Ingredients

ASEAN Cosmetic Directive

- Exclude ingredients in Annex II
- Restrictions laid down in Annex III
- Restrictions for colouring agents in Annex IV
- Restrictions for preservatives in Annex VI
- Restrictions for UV filters in Annex VII

Ingredients

…exclude,

- Incompatible toxicological data
- Insufficient toxicological data
- Not properly characterized

Ingredients

Physical and Chemical Specifications

- Chemical Identity
- Physical form
- Molecular weight
- Characterization and purity of chemical
- Characterization of the impurities/contaminants
- Solubility
- Partition coefficient (Log P_{ow})
- Additional specifications (flash point, liquid, solid, gases)
- Homogeneity and stability
- UV light absorption spectrum
- Isomer composition
- Functions and uses

Ingredients

Toxicological data

- Acute toxicity
- Corrosivity and Irritation (Skin and Eye)
- Skin sensitization
- Dermal/Percutaneous absorption
- Repeated dose toxicity
- Reproductive toxicity
- Mutagenicity/Genotoxicity
- Carcinogenicity
- Toxicokinetic studies
- Photo-induced toxicity
- Human data

Ingredients

Toxicological data

- Acute toxicity
- Corrosivity and Irritation (Skin and Eye)
- Skin sensitization
- Dermal/Percutaneous absorption
- Repeated dose toxicity
- Reproductive toxicity
- Mutagenicity/Genotoxicity
- Carcinogenicity
- Toxicokinetic studies
- Photo-induced toxicity
- Human data

Ingredients

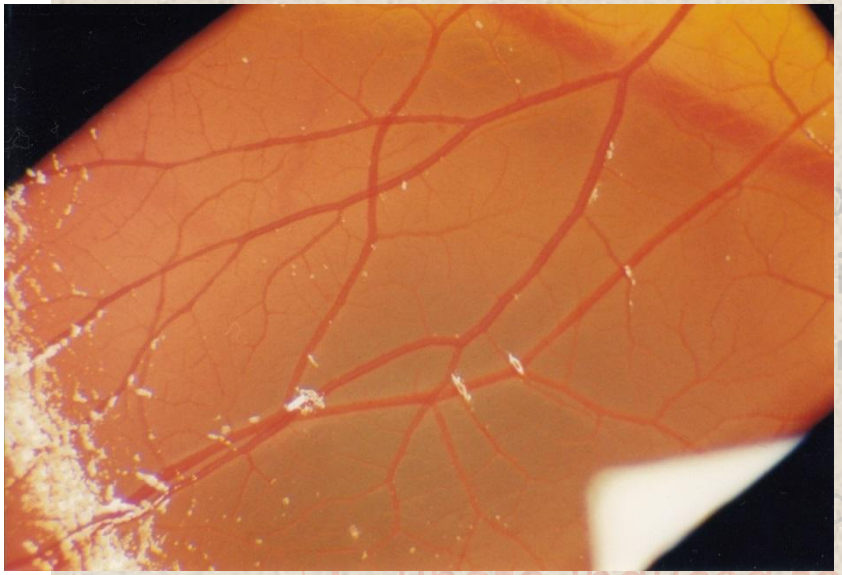
Toxicological data

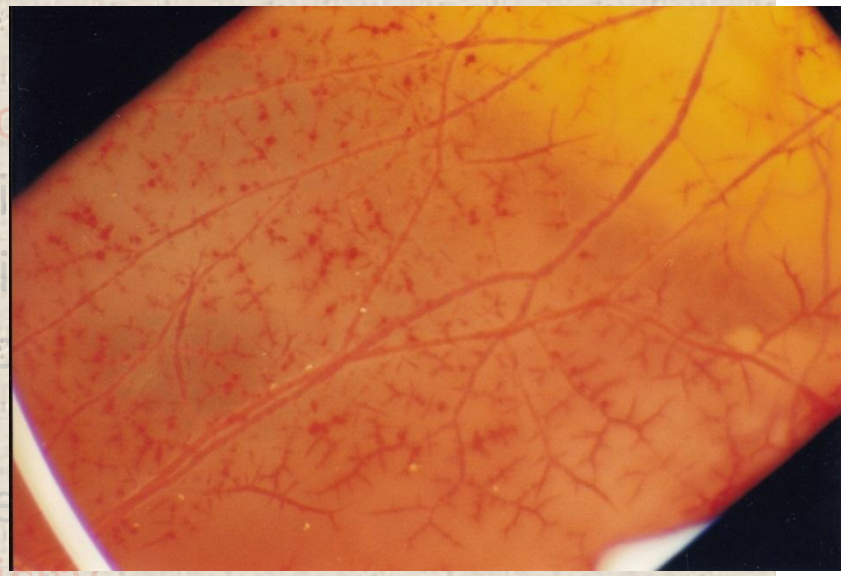
Skin Corrosion	OECD No 430 (2004) OECD No 431 (2004)
Skin Irritation	OECD No 439 (2010)
Skin Sensitization	Adverse Outcome Pathway (AOP) OECD No 168, Part 1 & 2 (2012)
Dermal Absorption	OECD No 428 (2004)
Photo-induced Toxicity	OECD No 432 (2004)

Ingredients

Toxicological data

Hen's Egg Test – ChorioAllantoic Membrane (HET-CAM)





0.1N NaOH

- ☑ Haemorrhage (bleedings)
- ☑ Vasclular lysis (blood vessel disintegration)
- ☐ Coagulation (protein denaturation)

Ingredients

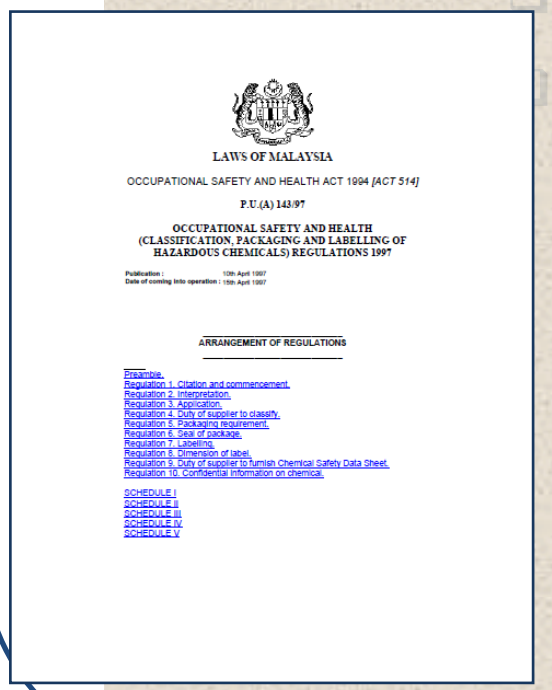
Toxicological data

- Safety Data Sheet (SDS)
- Internet
- Commercial data source

Ingredients

Toxicological data

- Safety Data Sheet (SDS)



LAWS OF MALAYSIA

OCCUPATIONAL SAFETY AND HEALTH ACT 1994 *[ACT 514]*

P.U.(A) 143/97

OCCUPATIONAL SAFETY AND HEALTH (CLASSIFICATION, PACKAGING AND LABELLING OF HAZARDOUS CHEMICALS) REGULATIONS 1997

Publication : 10th April 1997
Date of coming into operation : 15th April 1997

ARRANGEMENT OF REGULATIONS

Preamble.
Regulation 1. Citation and commencement.
Regulation 2. Interpretation.
Regulation 3. Application.
Regulation 4. Duty of supplier to classify.
Regulation 5. Packaging requirement.
Regulation 6. Seal of package.
Regulation 7. Labelling.
Regulation 8. Dimension of label.
Regulation 9. Duty of supplier to furnish Chemical Safety Data Sheet.
Regulation 10. Confidential information on chemical.

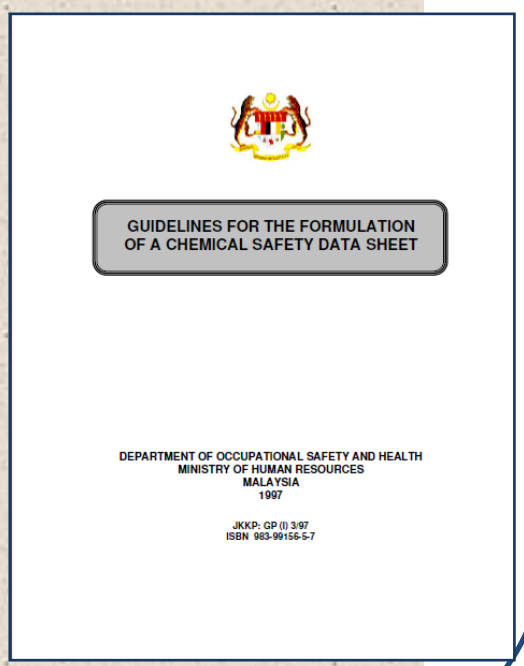
SCHEDULE I
SCHEDULE II
SCHEDULE III
SCHEDULE IV
SCHEDULE V

- Internet
- Commercial data source

Occupational Safety and Health Regulation

(Classification, Packaging and Labeling of Hazardous Chemical)
CLP Regulation 1997

(Chemical Classification, Labeling and Safety Data Sheets)
CLASS Regulation 201X



GUIDELINES FOR THE FORMULATION OF A CHEMICAL SAFETY DATA SHEET

DEPARTMENT OF OCCUPATIONAL SAFETY AND HEALTH
MINISTRY OF HUMAN RESOURCES
MALAYSIA
1997

JKKP: GP (I) 3/97
ISBN 983-99156-5-7

Ingredients

Toxicological data

- Safety Data Sheet (SDS)
- Internet
- Commercial database

Ingredients

Toxicological data

- Safety Data Sheet (SDS)
- Internet
- Commercial data source

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TEST FACILITIES

Finished Products

Safety assessment is to be performed by a qualified professional defined as the "Safety Assessor"

Finished Products

Safety Assessor

- Recognized competence & ethics
- Access to toxicological and analytical information
- Not involved with commercial aspect of product

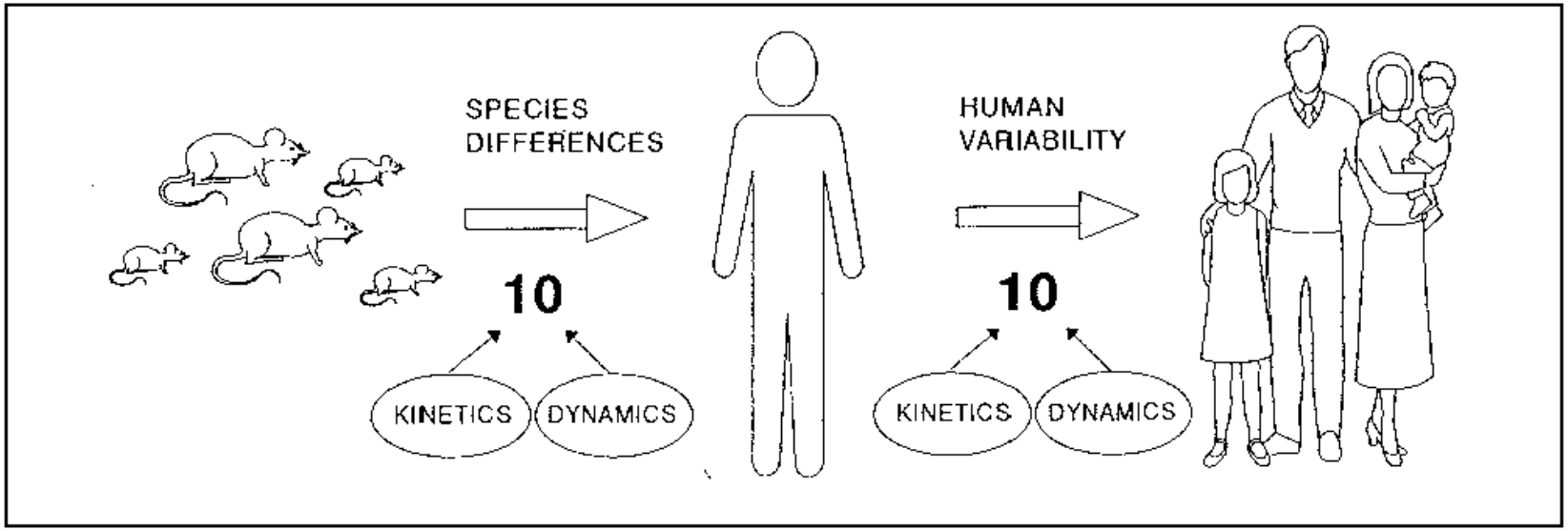
Finished Products

$$MoS = \frac{NO(A)EL}{SED}$$

MoS : Margin of Safety
NO(A)EL : No Observed (Adverse) Effect Level
SED : Systemic Exposure Dosage

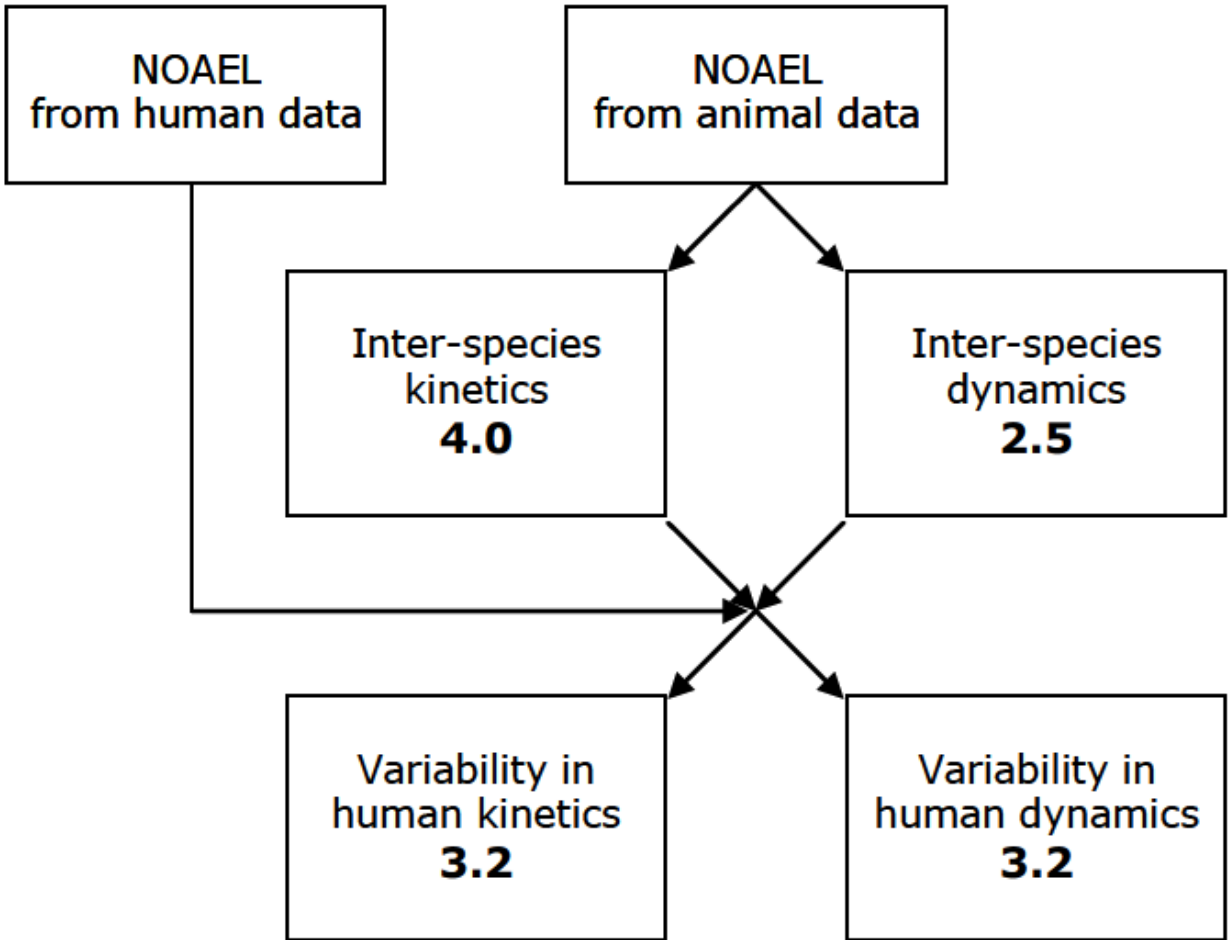
MoS > 100

Finished Products



"Safety of cosmetic products in the EU is based on the safety of the ingredients" (*SCCS Notes of Guidance, 8th Revision 2012*)

Finished Products



"Safety of cosmetic products in the EU is based on the safety of the ingredients" (*SCCS Notes of Guidance, 8th Revision 2012*)

Finished Products

$$\mathbf{SED} = \frac{\mathbf{DA_a}\ (\mu g/cm^2) \times 10^{-3}\ mg/\mu g \times \mathbf{SSA}\ (cm^2) \times \mathbf{F}\ (day^{-1})}{60\ kg}$$

SED (mg/kg bw/day)	Systemic Exposure Damage
DA_a (mg/cm^2)	Dermal Absorption reported as amount/cm2, resulting from an assay under in-use mimicking conditions
SSA (cm^2)	Skin Surface Area expected to be treated with the finished product
F (day^{-1})	Frequency of application of the finished product
60 kg	Default human body weight

Finished Products

Table 2: Mean exposed skin surface area per product type [Bremmer et al. 2005] and frequency of application per product type

Product type	Skin surface area involved (RIVM)		Frequency of application*
	Surface area (cm^2)	Parameters (if specified)	
Bathing, showering			
Shower gel	17500	total body area	*1.43/day*
Hand wash soap	860	area hands	10/day[2]
Bath oil, salts, etc.	16340	area body - area head	1/day
Hair care			
Shampoo	1440	area hands + 1/2 area head	1/day
Hair conditioner	1440	area hands + 1/2 area head	0.28/day
Hair styling products	1010	1/2 area hands + 1/2 area head	*1.14/day*
Semi-permanent hair dyes (and lotions)	580	1/2 area head	1/week (20 min.)
Oxidative/permanent hair dyes	580	1/2 area head	1/month (30 min.)
Skin care			
Body lotion	15670	area body - area head female	*2.28/day*
Face cream	565	1/2 area head female	*2.14/day*
Hand cream	860	area hands	2/day
Make-up			
Liquid foundation	565	1/2 area head female	1/day
Make-up remover	565	1/2 area head female	1/day
Eye shadow	24		2/day
Mascara	1.6		2/day
Eyeliner	3.2		2/day
Lipstick, lip salve	4.8[3]		*2/day*

* Frequency figures in *italics* correspond to the 90th percentile values of the 2005/2009 Colipa (now Cosmetics Europe) studies (see next paragraphs for details on these studies)

SCCS Notes of Guidance, 8th Revision 2012

Finished Products

$$SED = \mathbf{A}\ (mg/kg\ bw/day) \times \mathbf{C}\ (\%)/100 \times \mathbf{DA_p}\ (\%)/100$$

SED (mg/kg bw/day)	Systemic Exposure Damage
A (mg/cm^2)	Estimated daily exposure to a cosmetic product per kg body weight, based upon the amount applied and the frequency of application
C (%)	the Concentration of the substance under study in the finished product on the application site
DA_p (%)	Dermal Absoption expressed as a percentage of the test dose assumed to be applied in real-life conditions

Finished Products

Table 3: Estimated daily exposure levels for different cosmetic product types according to Colipa (Cosmetics Europe) data [SCCNFP/0321/00; Hall et al. 2007, 2011].

Product type	Estimated daily amount applied	Relative amount applied (mg/kg bw/day)	Retention factor [1]	Calculated daily exposure (g/day)	Calculated relative daily exposure (mg/kg bw/day)
Bathing, showering					
Shower gel	18.67 g	279.20	0.01	0.19	2.79
Hand wash soap [2]	20.00 g	-	0.01	0.20 [3]	3.33
Hair care					
Shampoo	10.46 g	150.49	0.01	0.11	1.51
Hair conditioner [2]	3.92 g	-	0.01	0.04	0.60
Hair styling products	4.00 g	57.40	0.1	0.40	5.74
Semi-permanent hair dyes (and lotions) [2]	35 ml (per application)	-	0.1	Not calculated	-
Oxidative/permanent hair dyes [2]	100 ml (per application)	-	0.1	Not calculated [4]	-
Skin care					
Body lotion	7.82 g	123.20	1.0	7.82	123.20
Face cream	1.54 g	24.14	1.0	1.54	24.14
Hand cream	2.16 g	32.70	1.0	2.16	32.70
Make-up					
Liquid foundation	0.51 g	7.90	1.0	0.51	7.90
Make-up remover [2]	5.00 g	-	0.1	0.50	8.33
Eye shadow [2]	0.02 g	-	1.0	0.02	0.33
Mascara [2]	0.025 g	-	1.0	0.025	0.42
Eyeliner [2]	0.005 g	-	1.0	0.005	0.08
Lipstick, lip salve	0.057 g	0.90	1.0	0.057	0.90
Deodorant					
Deodorant non-spray	1.50 g	22.08	1.0	1.50	22.08
Deodorant aerosol spray (ethanol-based) [5]	1.43 g	20.63	1.0	1.43	20.63
Deodorant spray (not ethanol-based)	0.69 g	10.00	1.0	0.69	10.00
Oral hygiene					
Toothpaste (adult)	2.75 g	43.29	0.05	0.138	2.16
Mouthwash	21.62 g	325.40	0.10	2.16	32.54

SCCS Notes of Guidance, 8th Revision 2012

Finished Products

Microbiology

	Category 1	Category 2
Cosmetic products	Products specifically intended for children under 3 years, to be used in the eye area on mucous membranes	Other products
Quantitative & qualitative limits* Total viable count for aerobic mesophyllic microorganisms	Should not exceed 10^2 cfu/g or 10^2 cfu/ml	Should not exceed 10^3 cfu/g or 10^3 cfu/ml
Quantitative & qualitative limits* *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans*	Must not be detectable in 1 g or 1 ml of a product (previously 0.5 g or ml)	Must not be detectable in 0.1 g or 0.1 ml of a product

*Based on Colipa 1997, McEwen et al. 2001, US FDA 2001

Safety Assessment of Cosmetics

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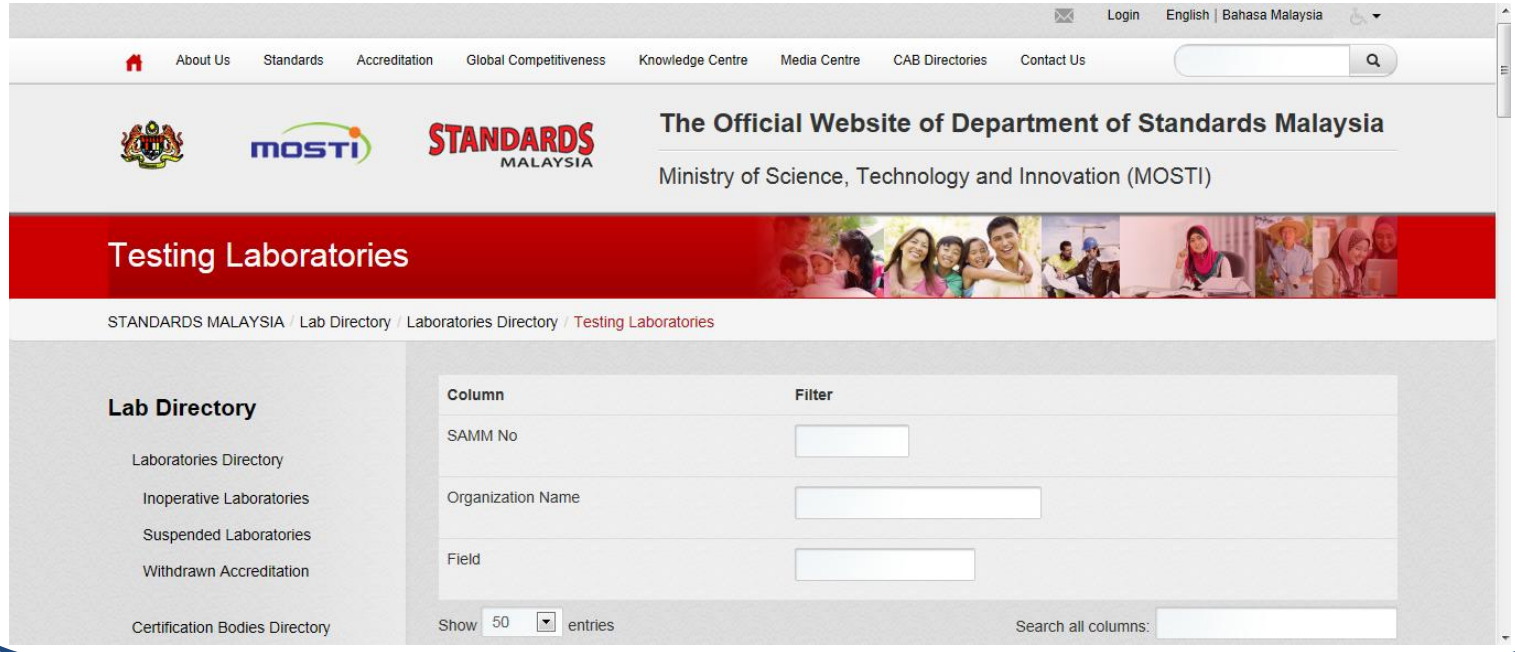
FINISHED PRODUCTS

TEST FACILITIES

Test Facilities

Skim Akreditasi Makmal Malaysia (SAMM)
MS ISO/IEC 17025: 2005

http://www.standardsmalaysia.gov.my/directory/testing-lab



Test Facilities

Skim Akreditasi Makmal Malaysia (SAMM)
MS ISO/IEC 17025: 2005

http://www.standardsmalaysia.gov.my/directory/testing-lab

Fields

Chemical
Biological
Microbiological
Toxicity

Test Facilities

Skim Akreditasi Makmal Malaysia (SAMM)
MS ISO/IEC 17025: 2005

http://www.standardsmalaysia.gov.my/directory/testing-lab

Total Active Testing Laboratories (as of 31 March 2013)

380

Fields	No of Entries
Chemical	286
Biological	48
Microbiological	58
Toxicity	2

Database search on 30 April 2013

Test Facilities

OECD GLP Compliant

bpfk	GOOD LABORATORY PRACTICE COMPLIANCE PROGRAM	Document No:	PKPB/300/105
	LIST OF GLP COMPLIANT TEST FACILITIES	Issue Date	1 July 2012
		Version	3
		Replace	Version 2
		Page	1 of 1

These Test Facilities are entered in the NPCB GLP Compliance Monitoring Program and shall be periodically inspected.

YEAR : **2012**

TEST FACILITY & ADDRESS	REGISTRATION NUMBER	SCOPE	AREA OF EXPERTISE	DATE OF CERTIFICATE	CONTACT PERSON
Environmental Technology Research Centre (ETRC), SIRIM Berhad 1, Persiaran Dato' Menteri, Seksyen 2, P.O.Box 7035, 40911 Shah Alam.	GLP 001	Pharmaceuticals Cosmetics Veterinary Drugs Food Additives	Mutagenicity	27 February 2012	Dr. Chan Sau Soon Tel: 03-55446564
Melaka Biotechnology Corporation Lot 7, MITC City, Hang Tuah Jaya, 75450 Ayer Keroh, MELAKA.	GLP 002	Pharmaceuticals Cosmetics Veterinary Drugs Food Additives	Mutagenicity	30 November 2011	Datin Nor Sabrina Mohd Noor Tel: 06-2313622
Info Kinetics Sdn Bhd Suite 126, Kompleks Eureka, Universiti Sains Malaysia, 11800 Minden, Pulau Pinang.	GLP 003	Pharmaceuticals Cosmetics Veterinary Drugs Food Additives	Analytical and Clinical Chemistry	7 May 2012	Dr. Lee Toong Chow Tel: 04-6589220

http://portal.bpfk.gov.my [30 April 2013]

Test Facilities

OECD GLP Compliant

LIST OF GLP COMPLIANT TEST FACILITIES (As of 1 September 2011)

NO.	TEST FACILITY ADDRESS & DETAILS	CONTACT PERSON	CATEGORY OF TEST ITEM*	AREA OF EXPERTISE*	RECOGNITION FROM	CERTIFICATE NO.
1.	**Acumen Scientific Sdn. Bhd.** Plot 256, Tingkat Perusahaan 5, kawasan Perindustrian Prai 2, 13600 Prai, Pulau Pinang, Malaysia. Tel: +604-3883777 Fax: +604-3987880 Email: inquiry@acumen.com.my/ liang-ming.yeow@acumen.com.my	Mr. Yeow Liang Ming	i-Pesticides	1-Physical-chemical testing	02-09-2010	GLP 001
2.	**Sumitomo Chemical Enviro-Agro Asia Pacific Sdn. Bhd.** Lot 62A, Persiaran Bunga Tanjung 1, Senawang Industrial Park, 70400 Seremban, Negeri Sembilan, Malaysia. Tel: +606-6793711 Fax: +606-6793698 Email: muneyserit@sumitomo-chem.com.my	Dr. Muney Serit	i-Pesticides	1-Physical-chemical testing	02-09-2010	GLP 002

Test Facilities

OECD GLP Compliant

NO.	TEST FACILITY ADDRESS & DETAILS	CONTACT PERSON	CATEGORY OF TEST ITEM	AREA OF EXPERTISE	RECOGNITION FROM	CERTIFICATE NO.
3.	**Toxicology Laboratory** Melaka Biotechnology Corporation Lot 7, MITC City, Hang Tuah Jaya, 75450 Ayer Keroh, Melaka. Malaysia. Tel: +606-2313622 Fax: +606-2323276 Email: haslan@mib.gov.my	Mr. Haslan Roslie	ii-Pesticides	3-Mutagenicity Testing	01-08-2011	GLP 003
4.	**Environment Technology Research Centre** SIRIM Berhad, 1, Persiaran Dato' Menteri, Section 2, P.O Box 7035, 40911 Shah Alam, Selangor. Malaysia. Tel: +603-5544 6564 Fax: +603-5544 6579 Email: sau.soon_chen@sirim.my	Dr. Chen Sau Soon	i-Industrial Chemicals ii-Pesticides	3-Mutagenicity Testing 4-Environmental Toxicity Studies on aquatic organisms 5-Studies on behaviour in water, soil and air	10-08-2011	GLP 004

*Note:

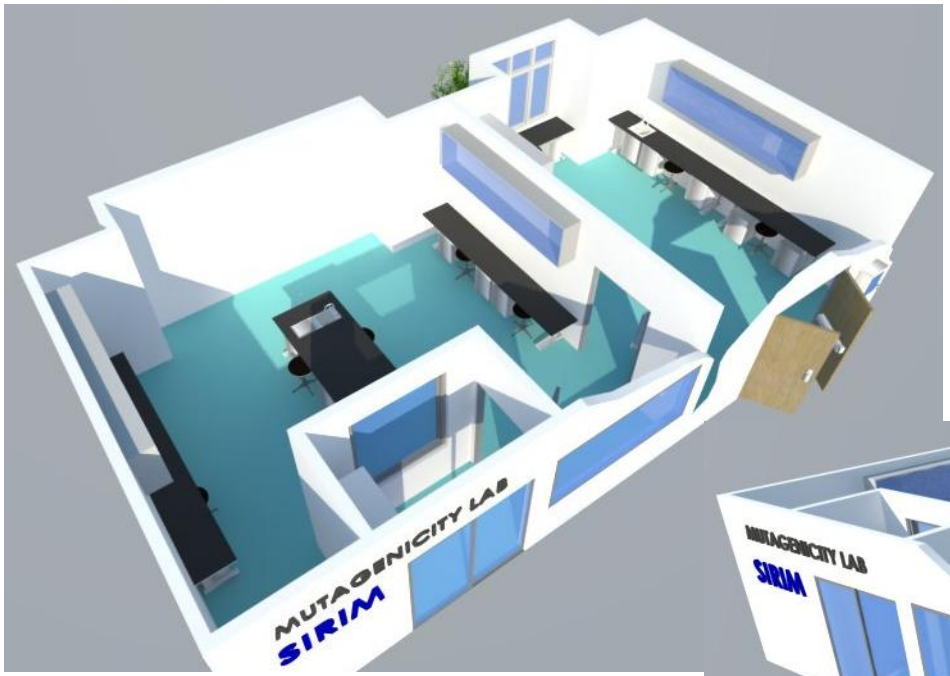
*** Category of Test Item**
Following code to be use:
- i- Industrial Chemicals
- ii- Pesticides
- iii- Feed Additives
- iv- Biotechnology (non-pharmaceutical products)

***Area of Expertise**
Following code to be use:
1- Physical-chemical testing
2- Toxicity Testing
3- Mutagenicity Testing
4- Environment Toxicity Studies on aquatic and terrestrial organisms
5- Studies on behaviour in water, soil, air; bioaccumulation
6- Residue studies
7- Studies on effect on Mesocosms and Natural Ecosystems
8- Analytical and clinical chemistry testing
9- Other studies: to specify

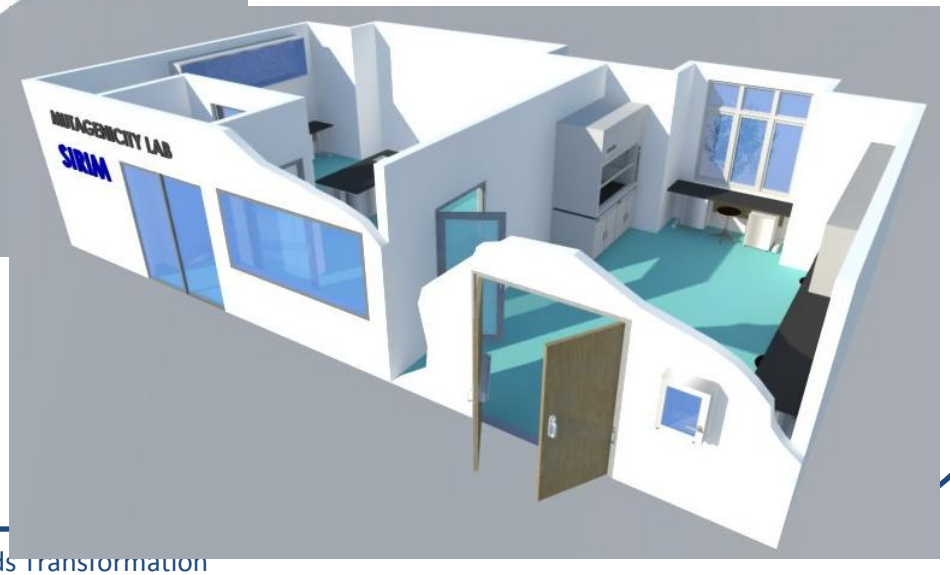
http://www.standardsmalayisa.gov.my [30 April 2013]

Test Facilities

OECD GLP Compliant



In Vitro Toxicity Laboratory
SIRIM Berhad



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