



La valutazione secondo SCCS NoG 12th

Parte I

Corso Valutatore della Sicurezza dei Prodotti Cosmetici

Nicola Lionetti

Responsabile Laboratorio Cosmetico

nicola.lionetti@labanalysis.it



Regolamento 1223/2009

.....

Regolamento 655/2013

Regolamento 1223/2009

■ Esplicitazioni:

Persona Responsabile (RP)

Good Manufacturing Practice (GMP)

Catena fornitura & Sorveglianza

Sicurezza Cosmetici

Verifica/Supporto ai claim

Safety Report

■ Art. 11 – La documentazione informativa contiene:

-
- relazione sulla sicurezza del prodotto cosmetico (CSR)

■ Art. 10 – CSR:

- garantito da PR
- aggiornata
- elaborata da persone qualificate

(farmacia, tossicologia, medicina o discipline simili, o corsi riconosciuti equivalenti dagli Stati Membri)

Safety Report

■ Art. 10 – CSR:

- La Commissione, in stretta cooperazione con tutte le parti interessate, adotta **linee guida** adeguate che consentano alle imprese, in particolare alle piccole e medie imprese, di ottemperare ai requisiti figuranti all'**Allegato I**.

Allegato I

COSMETIC PRODUCT SAFETY REPORT

La relazione sulla sicurezza dei prodotti cosmetici contiene, almeno, gli elementi seguenti:

PARTE A – Informazioni sulla sicurezza del prodotto cosmetico

PARTE B – Valutazione della sicurezza dei prodotti cosmetici

RISK ASSESSMENT



Cosmetico ???

Linee Guida

https://ec.europa.eu/growth/sectors/cosmetics/products/borderline-products_it

Guidance document on the demarcation between the **cosmetic products DIRECTIVE 76/768** and the **medicinal products DIRECTIVE 2001/83** as agreed between the commission services and the competent authorities of member states

FARMACO vs COSMETICO

Farmaco vs Cosmetico

“ripristinare, correggere, modificare funzioni fisiologiche”

1) Non include ingredienti cosmetici ...

... se non modificano significativamente il metabolismo e il suo funzionamento

***ECJ, C-1121/89 of 16.04.1991, “Upjohn”, ECR 1991 I-1703**

Linee Guida

MANUAL OF THE WORKING GROUP ON COSMETIC
PRODUCTS (SUB-GROUP ON
BORDERLINE PRODUCTS) ON THE SCOPE OF
APPLICATION OF THE COSMETICS
REGULATION (EC) NO 1223/2009 (ART. 2(1)(A))

VERSION 5.5 (2025)

“borderline-products”

Linee Guida

“borderline-products”

Prodotto per labbra ad effetto ‘plumping’
è un cosmetico?

soddisfa definizione Cosmetici

“applicato sulle labbra esclusivamente / principalmente per
modificarne l’aspetto”

... ma anche ricade nella definizione farmaci

“ripristinare, correggere, modificare funzioni fisiologiche...”

“Borderline-products”

Un prodotto per labbra ad effetto plumping è un cosmetico?

Conclusione

“Se il prodotto agisce per **infiammazione e/o irritazione (es. contenente capsaicina)**, l’induzione deliberata dell’effetto rigonfiante potrebbe essere percepita come una modifica significativa di una o più funzioni fisiologiche nelle labbra

⇒ **ricade nella definizione del farmaco”**

“Borderline-products”

Prodotto dopo-puntura è un cosmetico?

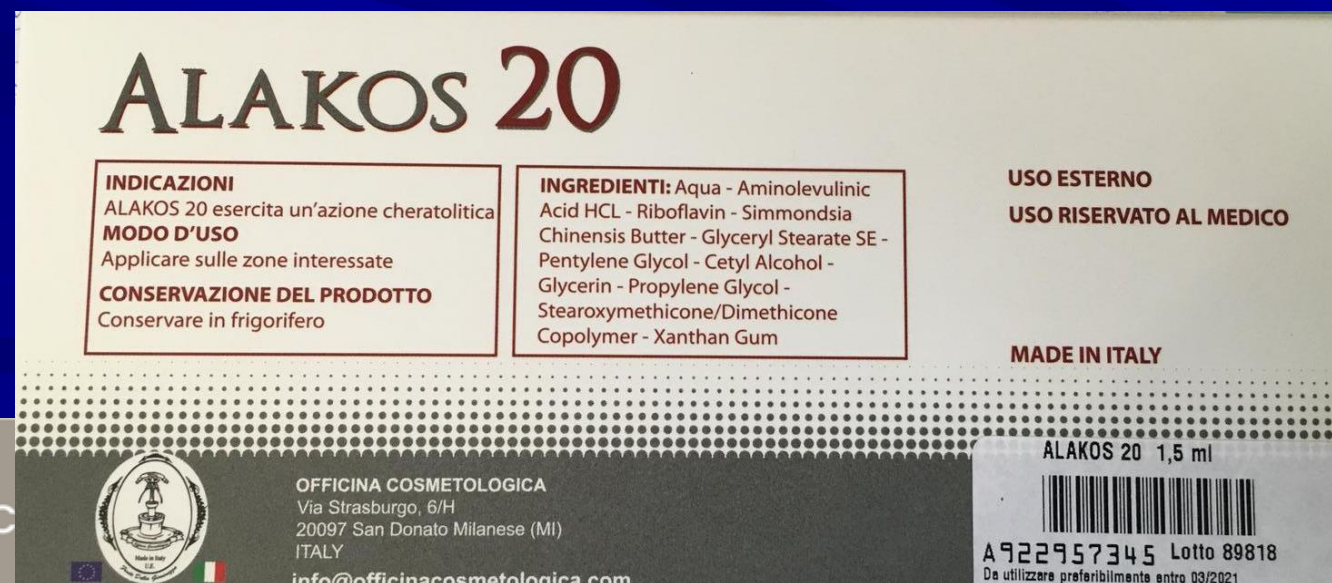
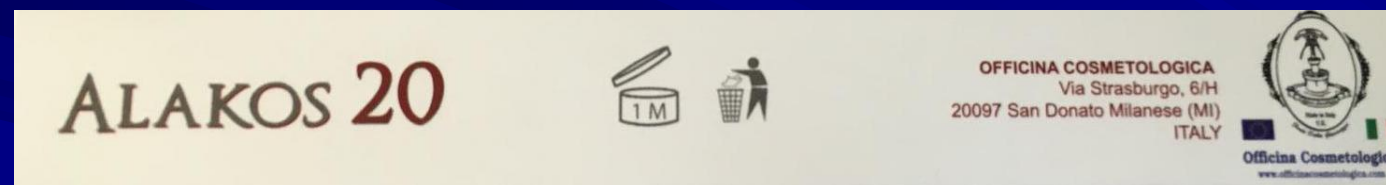
> **Presentazione del prodotto** (PROT. DGDFSC 73304-P- 14/10/2013)

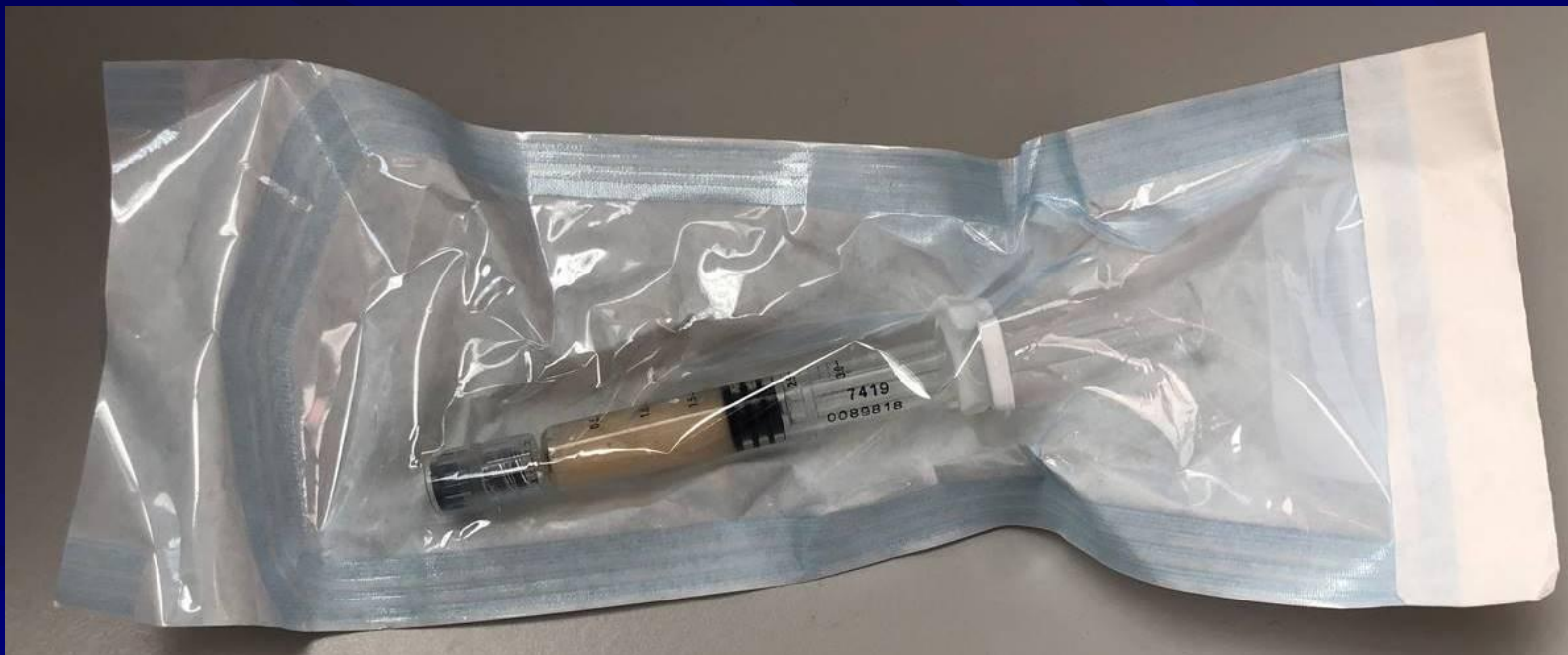
- lenitivo, rinfrescante, mitiga sensazione di fastidio → **OK**
- allevia dolore, infiammazione, gonfiore, ecc.) → **NO**
- Pittogrammi con immagine insetti → **OK**

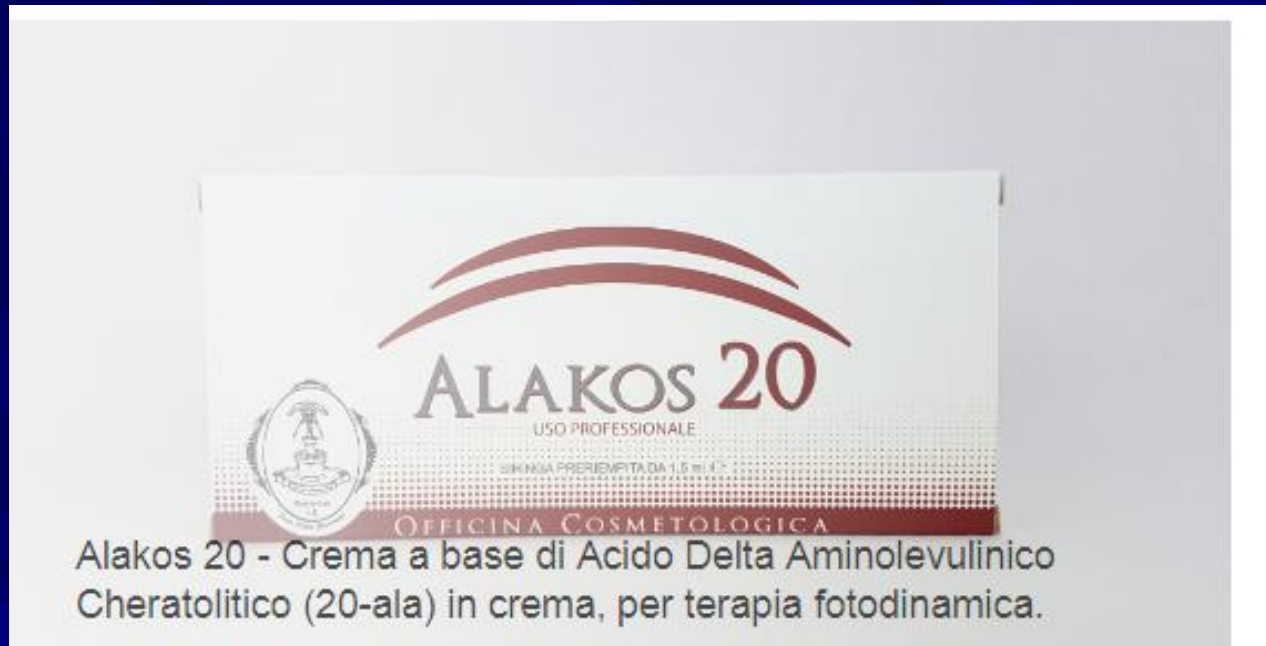
NO → prodotto insetto repellente o barriera/repellente

"Non utilizzare su cute lesa o con edemi/irritazioni" , "Non utilizzare su cute in stato patologico" , "Non utilizzare su cute abrasa" , "Non utilizzare in caso di processi infiammatori in corso"

Caso 1







Acido Aminolevulinico

CHE FACCIAMO?

Allegato I

PARTE A – Informazioni sulla sicurezza del prodotto

1. Composizione quantitativa e qualitativa
2. Caratteristiche chimico/fisiche e stabilità
3. Qualità microbiologica
4. Impurezze, tracce, informazioni materiale
imballaggio
5. Uso normale e ragionevolmente prevedibile

Allegato I

PARTE A – Informazioni sulla sicurezza del prodotto

6. Esposizione al prodotto cosmetico
7. Esposizione alle sostanze
8. Profilo tossicologico delle sostanze
9. Effetti indesiderabili & effetti indesiderabili gravi
10. Informazioni sul prodotto cosmetico

Allegato I

PARTE B – Valutazione della sicurezza del prodotto

1. Conclusioni della valutazione
2. Avvertenze/istruzioni per l'uso
3. Motivazione
4. Informazioni valutatore, approvazione parte B

Allegato I

PARTE A – Informazioni sulla sicurezza del prodotto

1. Composizione quantitativa e qualitativa
2. Caratteristiche chimico/fisiche e stabilità
3. Qualità microbiologica
- 4. Impurezze, tracce, informazioni materiale
imballaggio**
5. Uso normale e ragionevolmente prevedibile

Allegato I

4. Impurezze, tracce, informazioni materiale imballaggio

4.1 Purity of substances and mixtures

4.2 Evidence of the technical inevitability of the presence of traces of prohibited substances

4.3 Relevant characteristics of the packaging material, in particular purity and stability

Guidelines on Annex I

COMMISSION IMPLEMENTING DECISION
of 25 November 2013

on Guidelines on Annex I to Regulation (EC) No
1223/2009 of the European Parliament and of the
Council on cosmetic products
(2013/674/EU)

[http://ec.europa.eu/consumers/consumers_safety/
/cosmetics/legislation/](http://ec.europa.eu/consumers/consumers_safety/cosmetics/legislation/)

Guidelines on Annex I

3.4.3 Caratteristiche rilevanti del materiale del packaging

- Contatto diretto con il prodotto
- Dati di conformità con Food Contact Materials (migration)
- Esperienza con combinazioni formula/packaging simili
- Interazione tra prodotto & packaging
- Effetto barriera
- Composizione del packaging (+ additivi)
- Impurezze tecnicamente inevitabili

Esempio 1

Salviettina detergente per bambini

Schede Sicurezza/Tecnica della pack:

Incarto: Film Triplex Stampato Bianco Sandwich;

Materiale: PET 12 μ m – Adesivo – ALU 8 μ m – Adesivo – PE 75 μ m;

Schede Sicurezza/Tecnica del film:

Salvietta: Terpo 40 White Hydrophile

Materiale: 100% Polypropylene Fiber

Produttore dichiara: materiale idoneo al contatto con alimenti in ottemperanza al Reg (CE) n. 1935/2004 (Reg UE 10/2011)

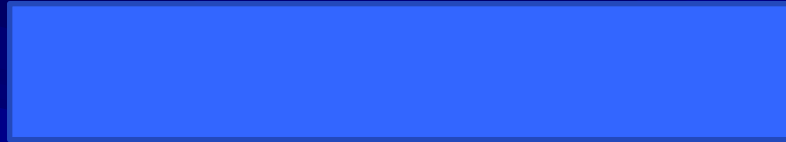
Esercizio 1a

Eyeshadow compatto in fondelli ricoperti di stagno in astucci plastica

Schede Sicurezza/Tecnica della plastica:

Acrylonitrile Butadiene Styrene (ABS) polymers > 98%

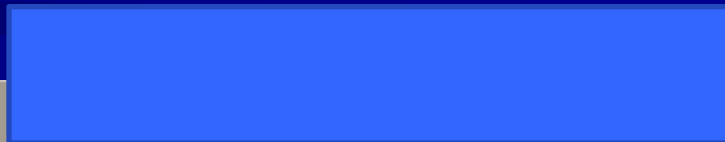
Styrene < 0,1% (Flam. Liq. 3, Acute Tox. 4, Eye Irrit. 2, Skin Irrit. 2)



Schede Sicurezza/Tecnica del fondello:

Nichel = 800 ppm

Arsenic = 200 ppm



Esercizio 1b

Gel lipofilo Intimo Lubrificante in flacone plastica (HDPE) laccato (ext)

Schede Sicurezza:

Può provocare sensibilizzazione per contatto con la pelle. Irritante per gli occhi e la pelle.

Classificazione : R 10 R 43 Xi ; R 36/38

RILEVANTE ?

Fornitore:

“..... are not formulated for direct food contact”

Allegato I

PARTE A – Informazioni sulla sicurezza del prodotto

6. Esposizione al prodotto cosmetico

7. Esposizione alle sostanze

8. Profilo tossicologico delle sostanze

9. Effetti indesiderabili & effetti indesiderabili gravi

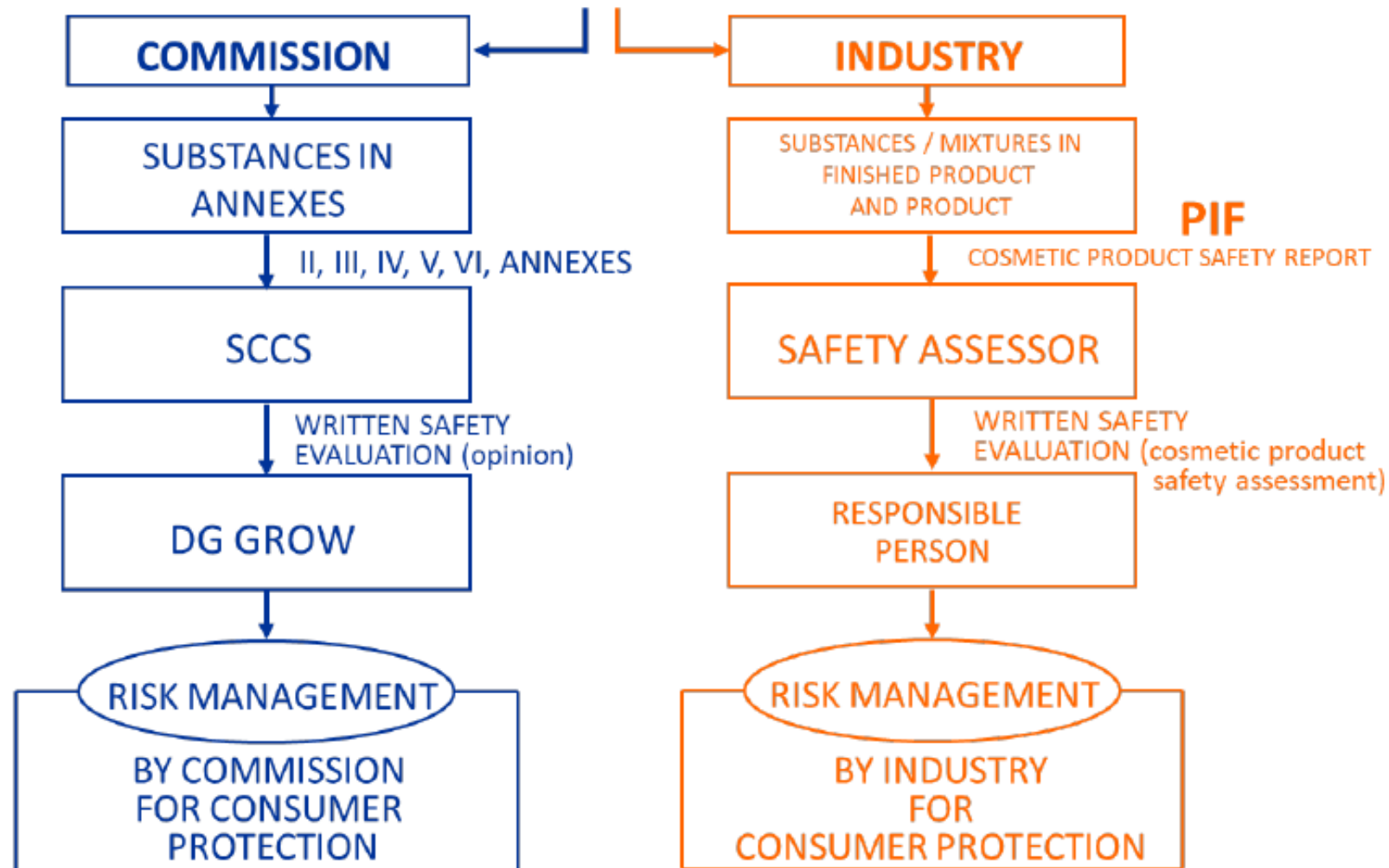
10. Informazioni sul prodotto cosmetico

**RISK ASSESSMENT
INGREDIENTI**

THE SCCS'S NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC SUBSTANCES AND THEIR SAFETY EVALUATION 12TH REVISION

The SCCS adopted this opinion at its plenary meeting of
May 2023

TWO CHANNELS ARE FUNCTIONAL IN THE SAFETY ASSESSMENT PROCESS



PIF: product information file.

Figure 1: Human health safety evaluation of cosmetic ingredients in the EU.

..... linee guida

Guidelines on Annex I

(2013/674/EU)

- 3.2.1 For UV absorbers, for instance, the absorption spectra should be provided.

THE SCCS'S NOTES OF GUIDANCE (7TH)

- 4-4.3 Challenge Testing.... is mandatory for all cosmetic products that, under normal conditions of storage and use, may deteriorate or form a risk to infect the consumer.

Punto 4-4.3

- 1) chemical identity;
 - 2) physical form;
 - 3) **molecular weight;**
 - 4) **characterisation and purity of the chemical including isomer composition;**
 - 5) **characterisation of the impurities or accompanying contaminants;**
 - 6) solubility;
 - 7) **partition coefficient ($\text{Log } P_{ow}$);**
 - 8) Vapour pressure (volatile liquids);
 - 9) Homogeneity and stability;
 - 10) Further physical and chemical properties if relevant for safety evaluation.
- 

Isopentyl 4 methoxycinnamate

Maximum absorption through the skin $DA_p =$

o/w: 0,4%

w/o: 2%

RISK ASSESSMENT PROCESS

PROCESSO DI VALUTAZIONE DEL RISCHIO

**1) IDENTIFICAZIONE
PERICOLO**

2) DOSE- RISPOSTA

**3) VALUTAZIONE
ESPOSIZIONE**

**CARATTERIZZAZIONE
RISCHIO**

**GESTIONE
RISCHIO**

**COMUNICAZIONE
RISCHIO**

PERICOLO $\neq$ RISCHIO

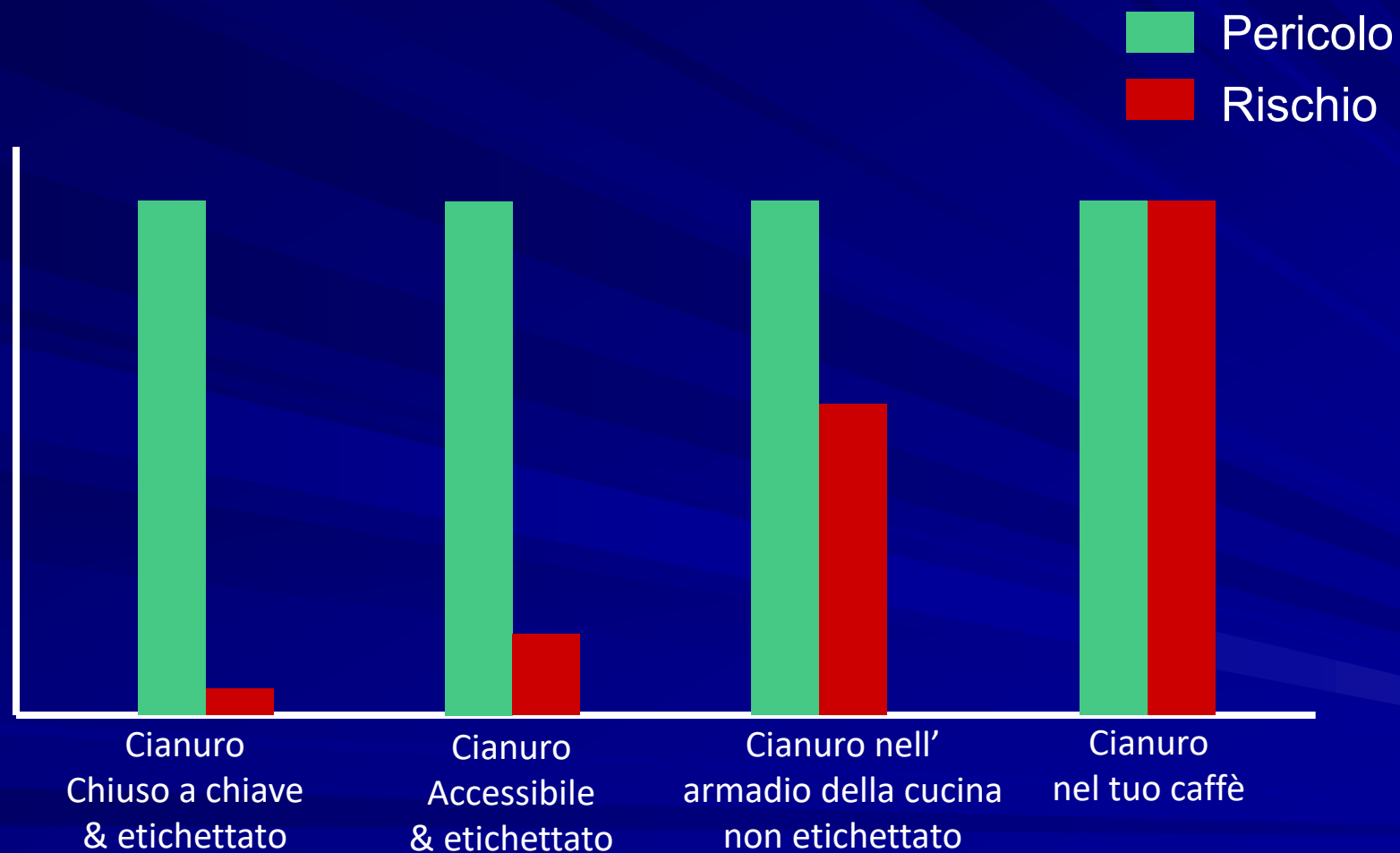
PERICOLO:

- POTERE DI CAUSARE DANNO
- PROPIETA' INTRINSECA
- NON E' RELAZIONATO alla DOSE o o alla ESPOSIZIONE

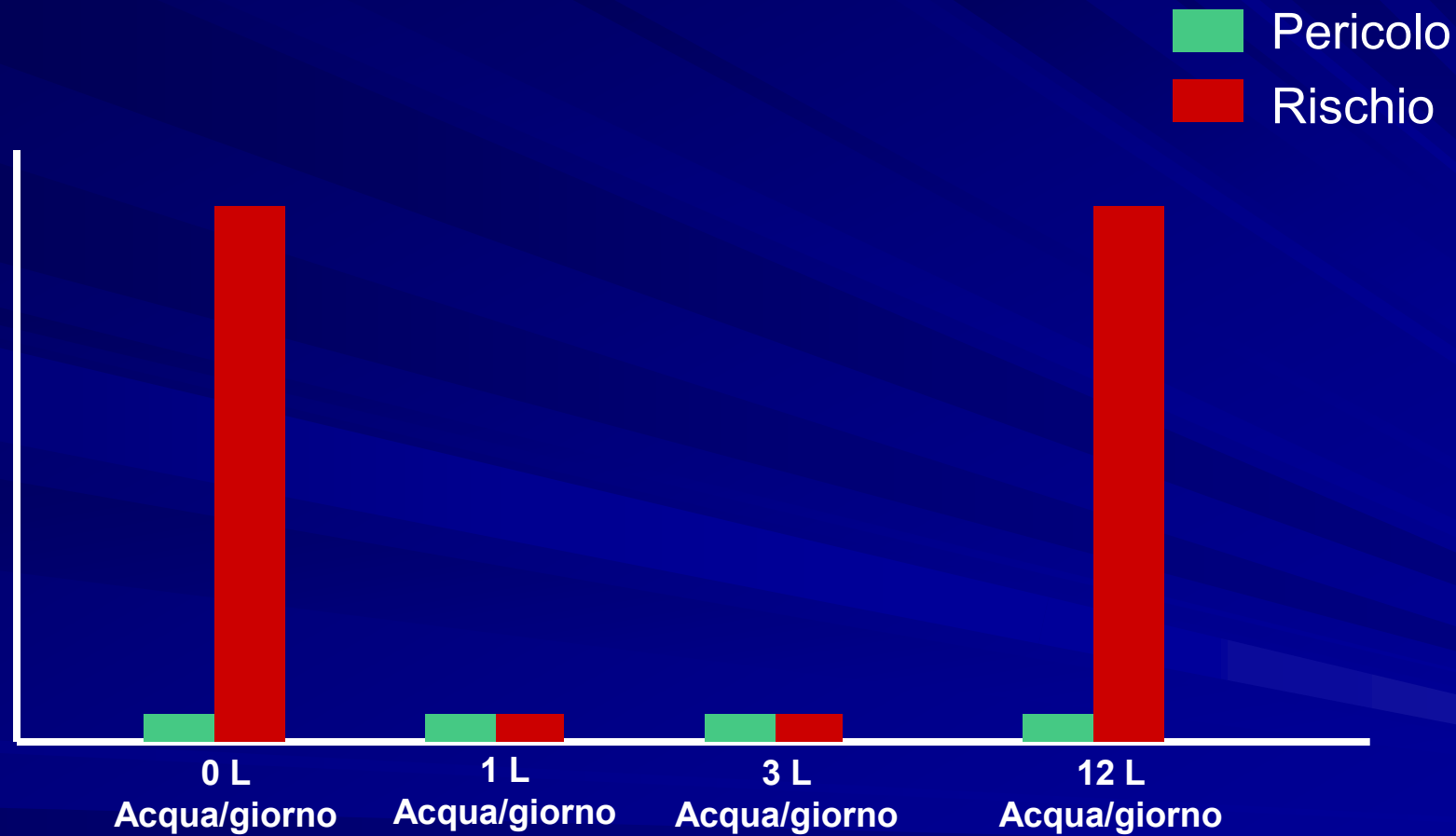
RISCHIO:

- PROBABILITA' DANNO
- RELAZIONATO all'ESPOSIZIONE
- CONSIDERARE SEVERITA' & NATURA del DANNO

RISCHIO POTENZIALE DI UNA SOSTANZA PERICOLOSA (CIANURO)



RISCHIO POTENZIALE DI UNA SOSTANZA NON PERICOLOSA (ACQUA)



PERICOLO $\neq$ RISCHIO

PERICOLO $\rightarrow$ DETERMINATO / MISURATO

RISCHIO $\rightarrow$

NON PUO' ESSERE MISURATO

E' UNA STIMA FATTA SEGUENDO REGOLE

PROCESSO DI VALUTAZIONE DEL RISCHIO

1) IDENTIFICAZIONE
PERICOLO

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RISCHIO

GESTIONE
RISCHIO

COMUNICAZIONE
RISCHIO

PROCESSO DI VALUTAZIONE DEL RISCHIO

1) IDENTIFICAZIONE PERICOLO



- Può X Causare un effetto avverso alla salute?
- Considerando

- Studi Epidemiologici
- Studi Clinici
- Studi IN-VIVO
- Studi IN-VITRO
- QSAR



**PROPRIETA'
INTRINSECHE**

3.5 DISCUSSION

Physicochemical properties

Exposure & Toxicokinetics

Toxicological Evaluation

Irritation and corrosivity

Skin sensitisation

Acute toxicity

Repeated dose toxicity

Reproductive toxicity

Mutagenicity / genotoxicity

Carcinogenicity

Photo-induced toxicity

Human data

Special investigation

PROCESSO DI VALUTAZIONE DEL RISCHIO

**1) IDENTIFICAZIONE
PERICOLO**

2) DOSE- RISPOSTA

**3) VALUTAZIONE
ESPOSIZIONE**

**CARATTERIZZAZIONE
RISCHIO**

**GESTIONE
RISCHIO**

**COMUNICAZIONE
RISCHIO**

PROCESSO DI VALUTAZIONE DEL RISCHIO

2) DOSE- RISPOSTA



- Qual è la relazione tra la DOSE & Incidenza/Severità degli effetti avversi?
- Qual è la DOSE necessaria a Causare Danno?
- NOAEL (**N**o **O**bserved **A**dverse **E**ffect **L**evel)

PROCESSO DI VALUTAZIONE DEL RISCHIO

NOAEL (No Observed Adverse Effect Level)

Dose massima somministrata di una sostanza che non provoca nessun cambiamento visibile nella morfologia, capacità funzionale, crescita di un organismo

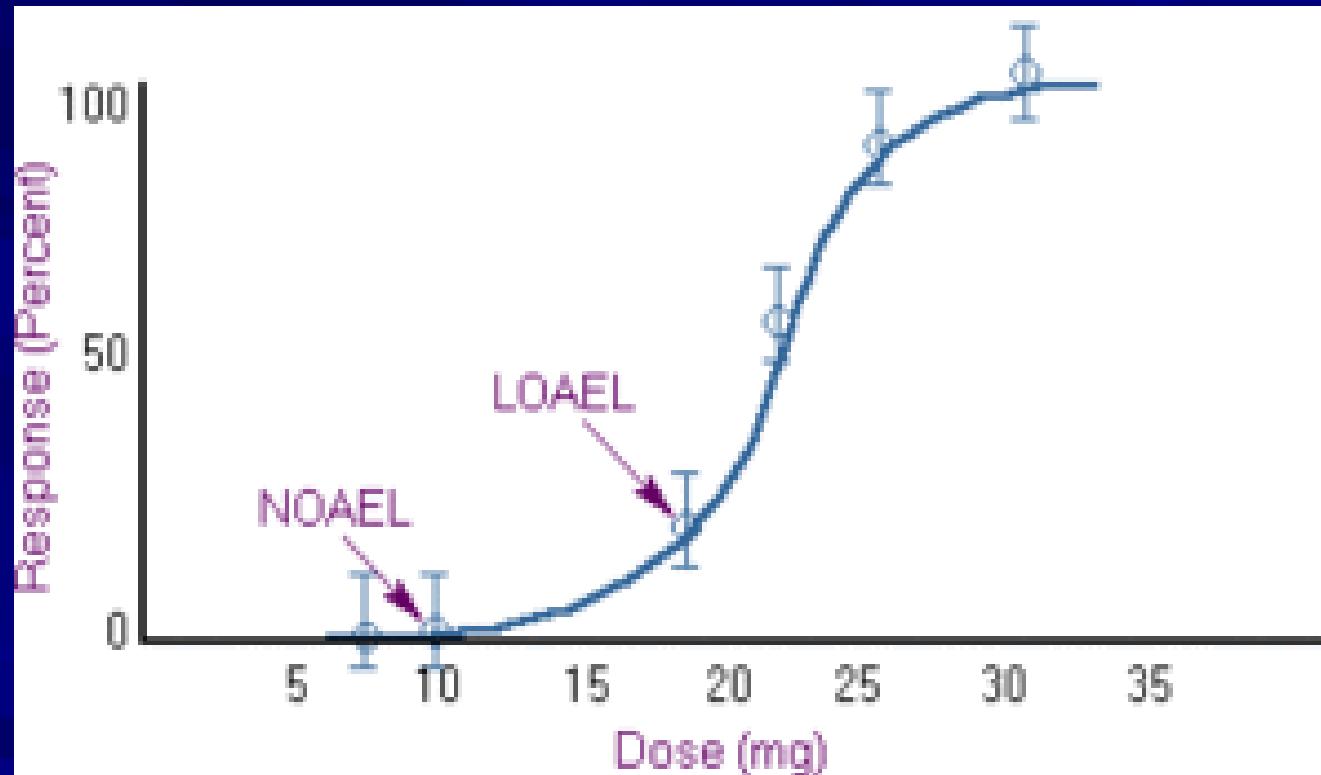
- Tossicità a lungo termine (90 giorni / 13 settimane)

NOAEL deve essere espresso in mg/kg bw/day

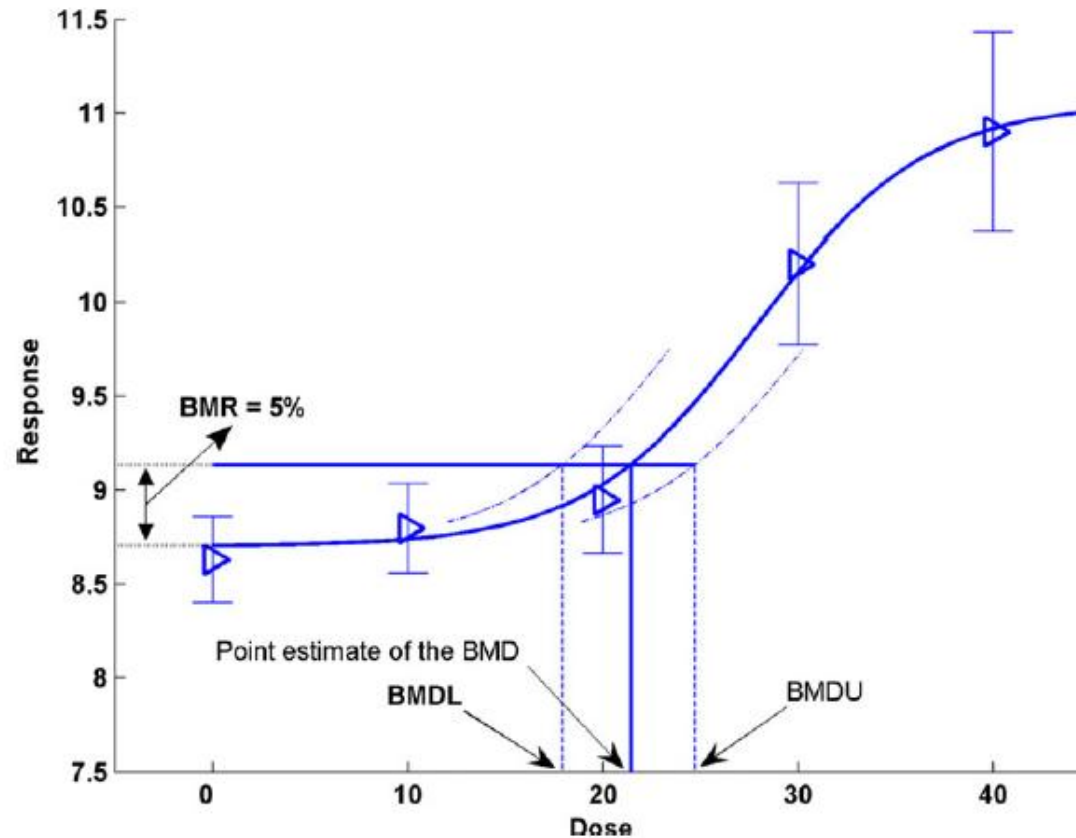
Repeated dose toxicity comprises the adverse general toxicological effects (excluding reproductive, genotoxic and carcinogenic effects) occurring as a result of repeated daily dosing with, or exposure to, a substance for a specific part of the expected lifespan of the test species.

NOAEL = No Observed Adverse Effect Level

LOAEL = Lowest Observed Adverse Effect Level



PROCESSO DI VALUTAZIONE DEL RISCHIO



[EFSA Journal 2017;15\(1\):4658](#)

Il più basso livello di confidenza del 95% legato alla BMDL è stato suggerito per rimpiazzare il NOAEL.



Introduction to benchmark dose methods and U.S. EPA's benchmark dose software (BMDS) version 2.1.1

J. Allen Davis^{a,*}, Jeffrey S. Gift^a, Q. Jay Zhao^b

^a U.S. Environmental Protection Agency, National Center for Environmental Assessment, Research Triangle Park, NC 27711, USA

^b U.S. Environmental Protection Agency, National Center for Environmental Assessment, Cincinnati, OH 45268, USA

Table 1

Advantages and limitations of the NOAEL and BMD methods.

BMD advantages

- Not limited to experimental doses
- Less dependent on dose spacing
- Appropriately accounts for variability and uncertainty resulting from study quality
- Takes into account the shape of the dose–response curve and other related information
- Corresponds to consistent response level and can be used to compare results across chemicals and studies
- Flexibility in determining biologically significant rates

BMD limitations

- Ability to estimate BMD may be limited by the format of data presented
- Time consuming
- More complicated decision making process

NOAEL limitations

- Highly dependent on dose selection
- Highly dependent on sample size
- Does not account for variability and uncertainty in the experimental results (e.g., does not account for study quality appropriately)
- Dose–response information (e.g., shape of dose–response curve) not taken into account
- Does not correspond to consistent response levels for comparisons across studies
- A LOAEL cannot be used to derive a NOAEL

NOAEL advantages

- Can be used when data is not amenable for BMD modeling
- Easy to derive
- Has been the standard method for deriving a POD for decades (e.g., is familiar to most risk assessors)

The following ***in vivo* repeated dose toxicity studies** with OECD guidelines are available:

1)

- Sub-acute oral toxicity (28 days) (EC B.7, OECD 407)
- Sub-acute dermal toxicity study (28 days) (EC B.9, OECD 410)
- Sub-acute inhalation toxicity study (28 days) (EC B.8, OECD 412)

2)

- Sub-chronic oral toxicity study: repeated dose 90-day oral toxicity study in rodents (EC B.26, OECD 408)
- Sub-chronic oral toxicity study: repeated dose 90-day oral toxicity study in non-rodents (EC B.27, OECD 409)
- Sub-chronic dermal toxicity study: repeated dose 90-day dermal toxicity study using rodent species (EC B.28, OECD 411)
- Sub-chronic inhalation toxicity study: repeated dose 90-day inhalation toxicity study using rodent species (EC B.29, OECD 413)

3)

- Chronic toxicity studies (primarily rodents) (EC B.30, OECD 452)
- Combined chronic toxicity/carcinogenicity studies (primarily rodents) (EC B.33, OECD 453)

Altri dati

- **TDI** (Tolerable Daily Intake)
- **ADI** (Acceptable Daily Intake)
- **DNEL** (Derived No Effect Level) ????????

corrispondenti al rapporto tra NOAEL o BMDL con fattori denominati Assessment Factors (sinonimo di UF e SF).

La dimensione di questi fattori è paragonabile al MOS

PROCESSO DI VALUTAZIONE DEL RISCHIO

ChemIDPlus Light — <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>

ChemIDPlus Advanced — <http://chem.sis.nlm.nih.gov/chemidplus/>

ToxNet — <http://toxnet.nlm.nih.gov/>

SCCS Opinion —
http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm

IPCS Inchem — <http://www.inchem.org/pages/jecfa.html>

NICNAS Australia — <http://www.nicnas.gov.au/chemical-information>

PROCESSO DI VALUTAZIONE DEL RISCHIO

Cosmetic Ingredient Review (CIR) Report — <http://www.cir-safety.org/ingredients>

ECHA Sostanze Registrate

— <http://echa.europa.eu/information-on-chemicals/registered-substances;jsessionid=9906DD56E71B9951024B8D5BD4815892.live1>

ECHA C&L Inventory database — <http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

International Journal of Toxicology — <http://ijt.sagepub.com/>

PROCESSO DI VALUTAZIONE DEL RISCHIO

1) IDENTIFICAZIONE
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RISCHIO

COMUNICAZIONE
RISCHIO

PROCESSO DI VALUTAZIONE DEL RISCHIO

3) VALUTAZIONE ESPOSIZIONE



Qual è la quantità & il tempo di
Esposizione?

Dosaggio

Esposizione Cutanea

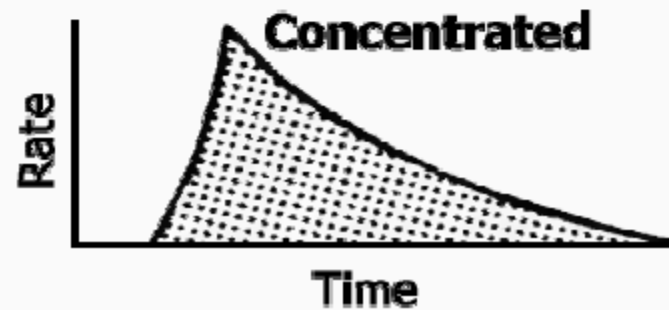
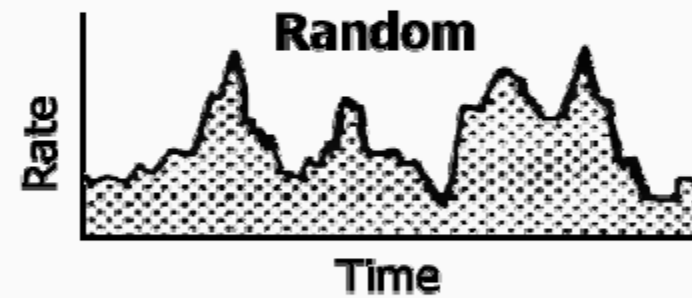
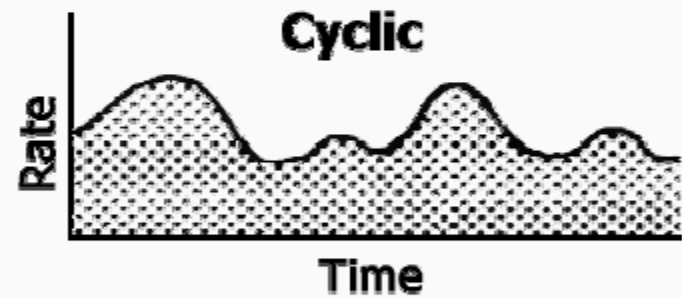
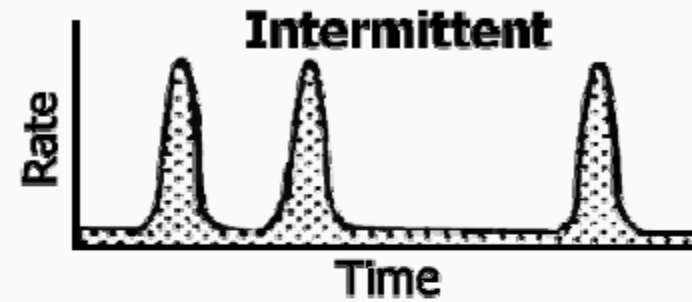
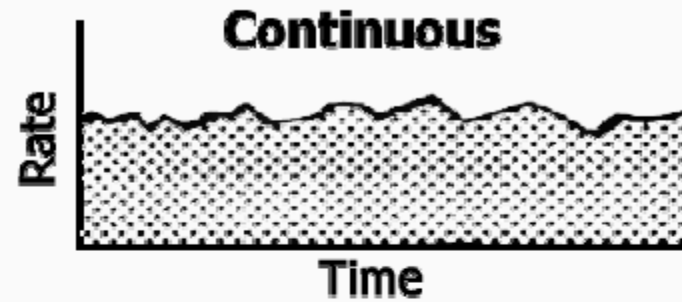
Exposure

Exposure Dosage di un ingrediente cosmetico

$\text{Exposure} = \text{Intensity} \times \text{Frequency} \times \text{Duration}$

Exposure = How much x How often x How long

MODELLI DI ESPOSIZIONE



Additional considerations:

- i. Some cosmetic substances are not used on a daily basis, although their NOAEL values have been obtained in studies after daily administration of the substances. Combining these NOAEL values with daily exposures therefore results in a clear overestimation of the risk. The comparison of a NOAEL resulting from a daily exposure study with the SED of a certain cosmetic ingredient is therefore accepted as a conservative estimate, even if it is only applied e.g. once per week or once per month. However, the daily amount for product categories with low frequencies of application may not be adjusted by the frequency (*i.e.* not divided by 30, if applied once per month), as justified by: "*The actual daily dose is independent of the exposure frequency. This means that if, for a certain scenario, worker or consumer exposure is only for a number of days per year, the exposure value is the actual dose on the exposure days, and not the daily dose averaged out (and thus divided!) over the whole year*" (ECHA, 2012a). This reasoning, however, may be changed for example in the case of hair dyes (e.g. oxidative hair dyes only once applied per month) and a MoS slightly below 100. One could consider a substance as being safe due to the occasional use and the built-in conservatism of assessment but only after expert judgement.

CALCOLO della DOSE di ESPOSIZIONE

Quantità applicata su cute/mucose:

- peso
- Peso per peso corporeo (ex: mg/kg bw)
- Peso per unità di superficie (ex: mg/cm² of skin)

Approccio caso per caso considerando:

- ❖ Tipologia di prodotto cosmetico
- ❖ Modalità d'applicazione
- ❖ Frequenza d'applicazione
- ❖ Tipo di consumatore (target group)
- ❖ Zona d'applicazione
- ❖ Tempo di contatto
- ❖ Concentrazione ingredienti
- ❖ Possibili usi sbagliati
- ❖ Packaging, produzione, etc

CALCOLO della DOSE di ESPOSIZIONE

Bambini → Differenza rapporto SSA/BW (0 → 10 anni):

2,3 nascita

1,8 a 6 mesi

1,6 a 12 mesi

1,5 a 5 anni

1,3 a 10 anni

Zona occhi e mucose

↑ assorbimento

Penetration enhancer (glicoli, etossilati, etc)

↑ assorbimento

CALCOLO DOSE ESPOSIZIONE GIORNALIERA SOSTANZA APPLICATA SU CUTE

$$E_{\text{Dermica}} = C \times Q \times F$$

Dove:

E_{Dermica} (g o mg/day): dose applicata disponibile x
assorbimento dermico / ingestione

C (% p/p): concentrazione sostanza

Q (g o mg/day): quantità prodotto applicata giornalmente

F : fattore di ritenzione/diluizione

Stime di esposizione a prodotti finiti

❖ Dati forniti da Cosmetics Europe (ex Colipa)

❖ 4 tipologie principali:

- Cura e igiene della bocca
- Occhi
- Leave-on
- Rinse-off

Fattore di ritenzione/diluizione

**Risciacquo e/o diluzione del prodotto
finito applicato su cute/mucose bagnata**

Ex: Dentifricio

Residui in contatto con la cute

Ex: Shampoo

IGIENE / CURA BOCCA

Prodotto	Quantità totale applicata (g)	Fattore di Ritenzione (%)	Esposizione giornaliera (g)
Dentifricio	2,75	5	0,14
Collutorio	21,62	10	2,16
Lipstick	0,057	100	0,06
Total			2,36

PRODOTTI OCCHI

Prodotto	Quantità totale applicata (g)	Fattore di Ritenzione (%)	Esposizione giornaliera (g)
Eye make-up	0,020	100	0,020
Fondotinta	0,51	100	0,51
Mascara	0,025	100	0,025
Eyeliner	0,005	100	0,005
Total			0,560

LEAVE-ON

Prodotto	Quantità totale applicata (g)	Fattore di Ritenzione (%)	Esposizione giornaliera (g)
Face cream	1,54	100	1,54
Hand cream	2,16	100	2,16
Body lotion	7,82	100	7,82
Deodorant non-spray	1,50	100	1,50
Hair styling	4,00	10	0,40
Total			13,42

RINSE-OFF

Prodotto	Quantità totale applicata (g)	Fattore di Ritenzione (%)	Esposizione giornaliera (g)
Make up remover	5,00	10	0,50
Hand wash soap	20,00	1	0,20
Shower gel	18,67	1	0,19
Shampoo	10,46	1	0,11
Hair conditioner	3,92	1	0,04
Total			1,04

Esposizione Giornaliera Massima

❖ Total oral hygiene products	2,36 g
❖ Total eye products	0,56 g
❖ Total leave on products	13,42 g
❖ Total rinse off products	1,04 g
Global Daily Exposure	≈17,4 g

Esposizione x inalazione

- Vapore
- Polvere
- Goccioline aerosol
- Particelle aerosol

Vapore

$$E_{\text{Inalabile}} = C \times Q \times F_{\text{evap}}$$

Da leggere....

Guide on Inhalation Safety Assessment for Spray Products

First Edition: June 2013

Corrections: November 2013

FEA - European Aerosol Federation

da leggere

...

Aerosol dispenser product type	Discharge rate [g/s]	Spray time [s]
Hairspray ^a	0.7	3 - 4
Antiperspirant/Deodorant Spray (90 th percentile)	0.8 ^c	1.4 ^d
Air freshener ^a	1.5 - 1.8	4 - 5
Furniture Polish ^a	1.8	2 - 3
All-purpose Cleaning Spray	1.2 ^e	24 ^e
Starch ^a	2.0	2 - 3
Carpet Cleaner ^a	2.0	20 - 30
Oven Cleaner ^a	2.0	10 - 15
Flying Insect Killer ^b	1.5	10
Crawling Insect Killer ^b	1.5	60- 90
De-icer ^a	2.5	15 - 20
Paints ^a	0.8	30 - 40

Table 3: Discharge rates (including propellants and solvents) and spray times for aerosol applications
(^a) BAMA, 2008; ^b) Bremmer *et al.*, 2006c; ^c) Bremmer *et al.*, 2006a;
^d) Steiling *et al.*, 2012; ^e) Weerdesteijn *et al.*, 1999)

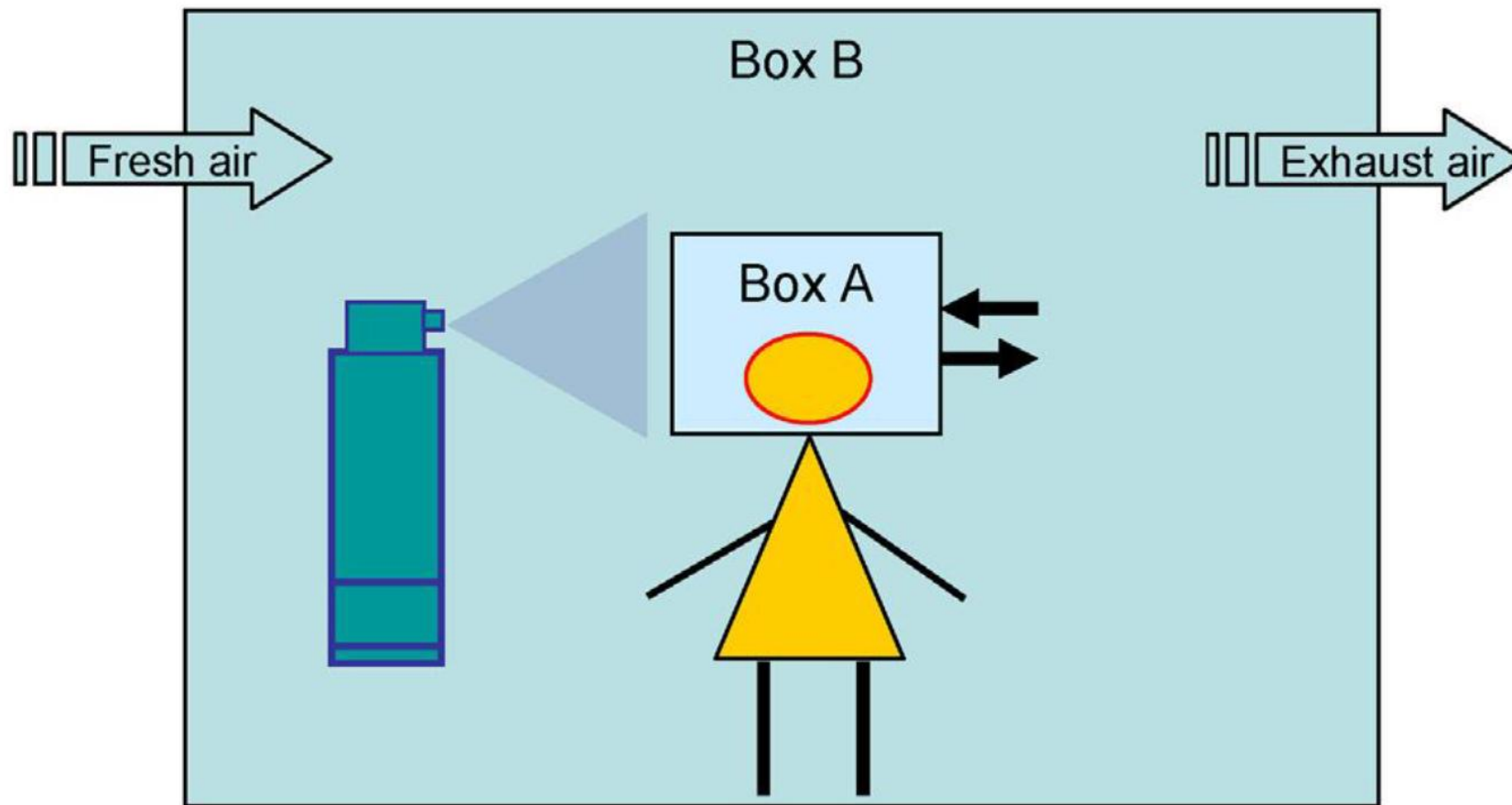
Da leggere....

.....da Pag.60

Scientific Committee on Consumer Safety SCCS OPINION ON decamethylcyclopentasiloxane (cyclopentasiloxane, D5) in cosmetic products

The SCCS adopted this Opinion at its 9th plenary
meeting on 25 March 2015

Esposizione x inalazione



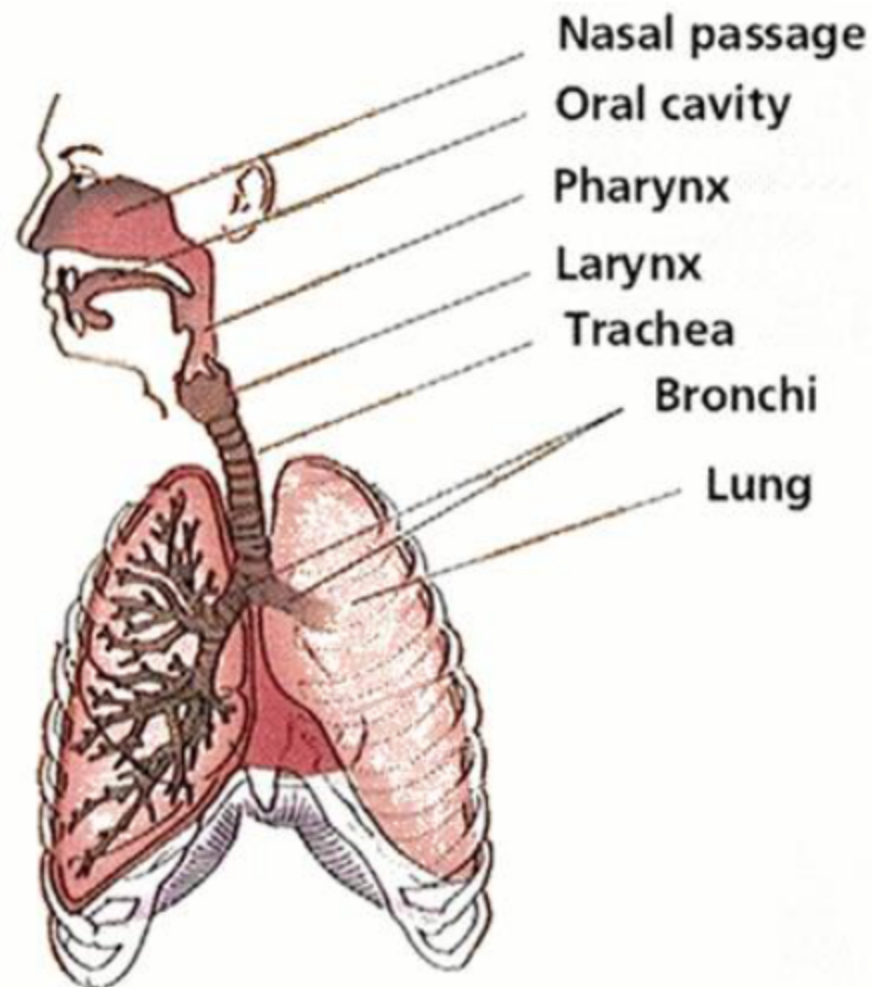
Esposizione x inalazione

- BOX 1 = 1000 L = 1 m³
- BOX 2 = 10000 L = 10 m³
- Equilibrio Immediato
- No ricambio d'aria

Valore espresso = mg o g/m³

Esposizione x inalazione

- Vapore
- Polvere
- Goccioline aerosol
- Particelle aerosol



Nasopharyngeal region

Deposition: impaction, diffusion
 Clearance: mucociliary, sneezing/blowing
 Pathology: inflammation, cancer, ulceration
 Targeted by: $>30\ \mu\text{m}$ particles
 highly reactive, water soluble gas,
 “inhalable fraction”

Tracheobronchial region

Deposition: impaction, sedimentation, diffusion
 Clearance: mucociliary, coughing
 Pathology: obstruction, irritation, cancer, ulceration
 Targeted by: $10\text{--}30\ \mu\text{m}$ particles, $200\ \mu\text{m}$ fibres,
 “thoracic fraction”

Pulmonary region (parenchyma)

Deposition: sedimentation, diffusion
 Clearance: phagocytosis, solubilisation, interstitial
 Pathology: inflammation, fibrosis, cancer, oedema, emphysema
 Targeted by: $<10\ \mu\text{m}$ particles, $10\text{--}12\ \mu\text{m}$ fibres
 less reactive/water soluble gas,
 “respirable fraction”

Figure 1: The human respiratory tract

Esposizione x inalazione

- Inalabile (naso e bocca) $\leq 100 \mu\text{m}$;
- Toracica (laringe) $\cong 11,64 \mu\text{m}$;
- Respirabile (alveoli) $\cong 4,25 \mu\text{m}$;

Misure dimensioni particella

Esposizione x inalazione

Misure dimensioni particella



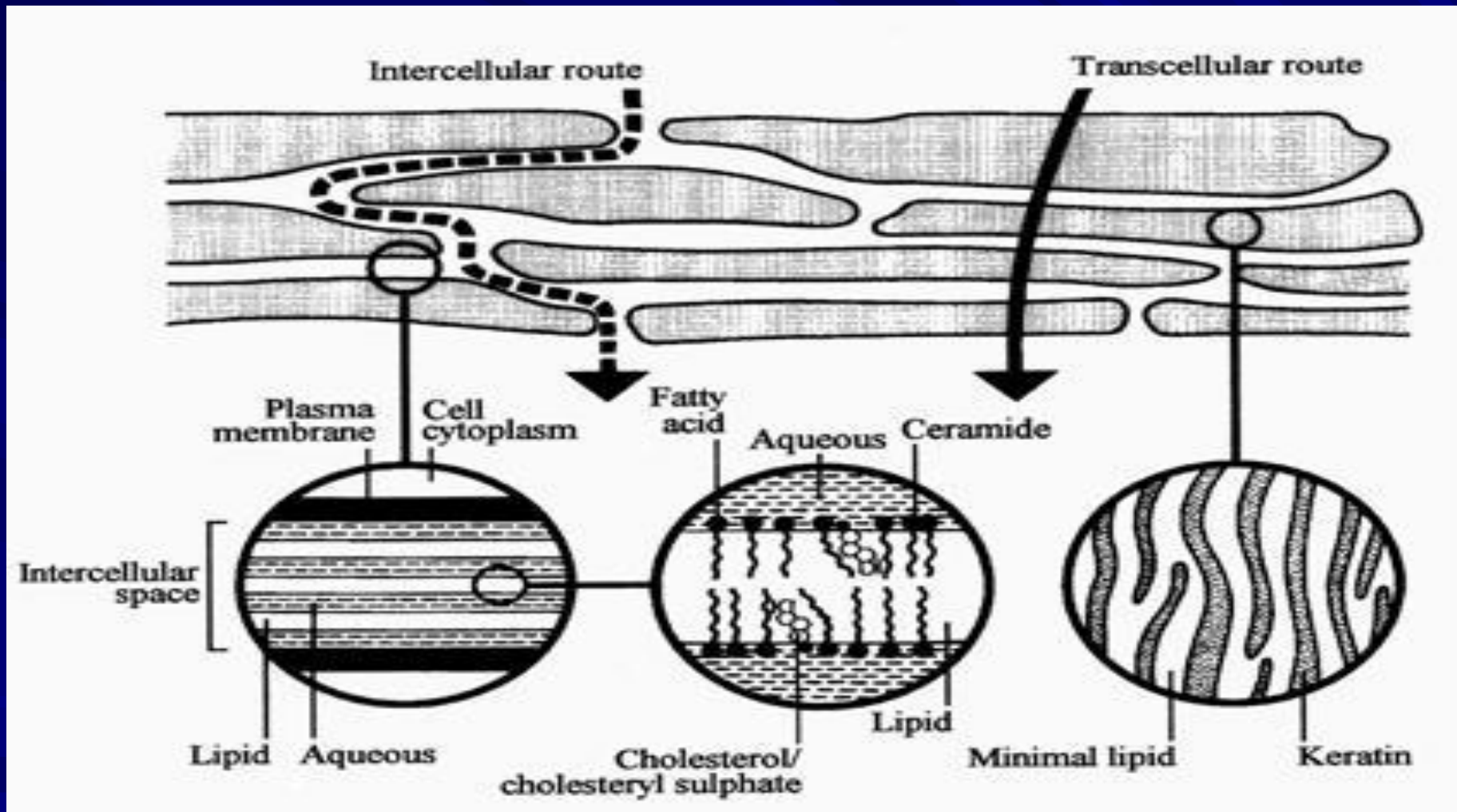
Considerando evaporazione

ASSORBIMENTO CUTANEO

Esposizione cutanea: quantità di sostanza in contatto con unità superficie cutanea per un definito periodo di tempo

Assorbimento Cutaneo: passaggio di una sostanza attraverso la cute

VIE DI PENETRAZIONE

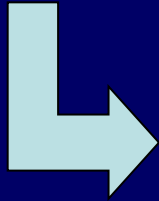


Assorbimento cutaneo: variabili

- **Struttura cutanea**
- **Proprietà chimico-fisiche penetrante**
- **Veicolo**
- **Dosaggio / Concentrazione**

Proprietà chimico-fisiche del penetrante

$$J = \frac{DK(c_V - c_R)}{h} = k_p(c_V - c_R)$$



$$J = k_p \Delta C = \frac{KD}{L} \Delta C$$

D = Coefficiente di Diffusione (dimensioni/PM, carica)

K = Coefficiente di Ripartizione (polarità)

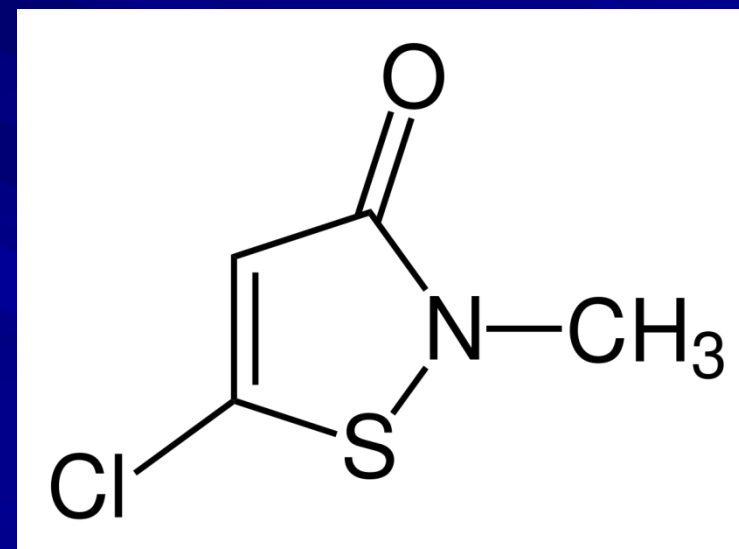
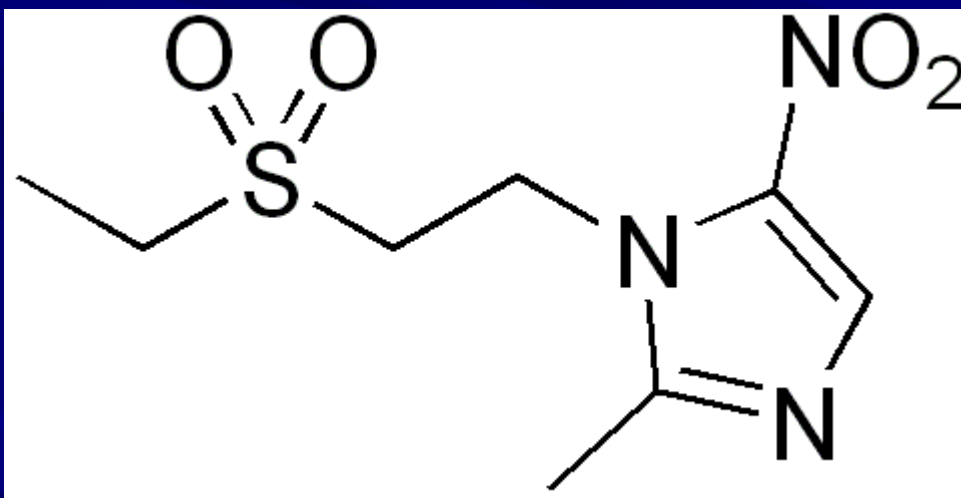
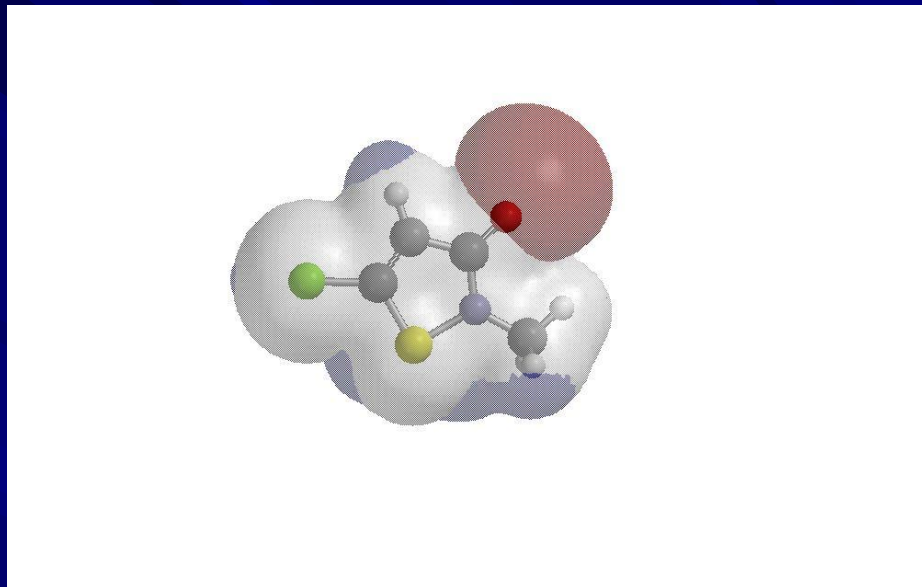
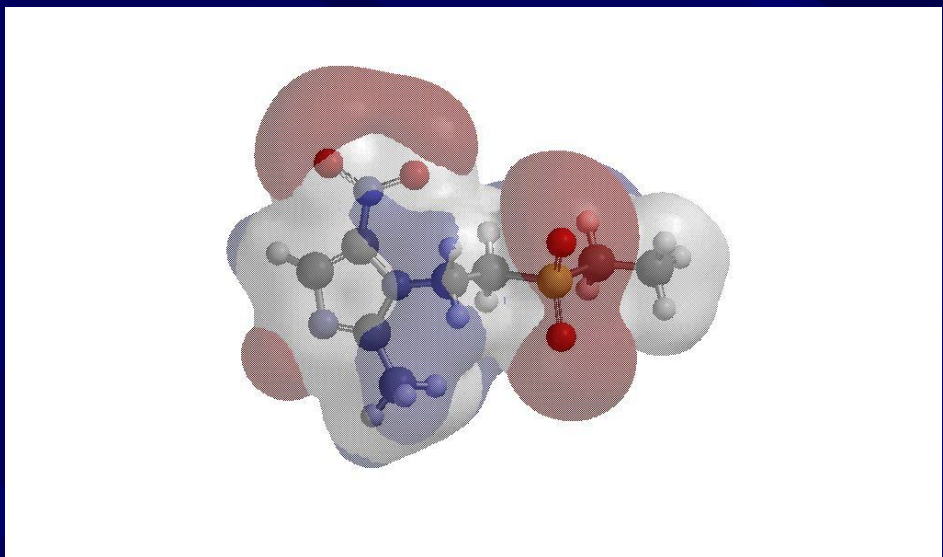
K_p = Coefficiente di Permeabilità

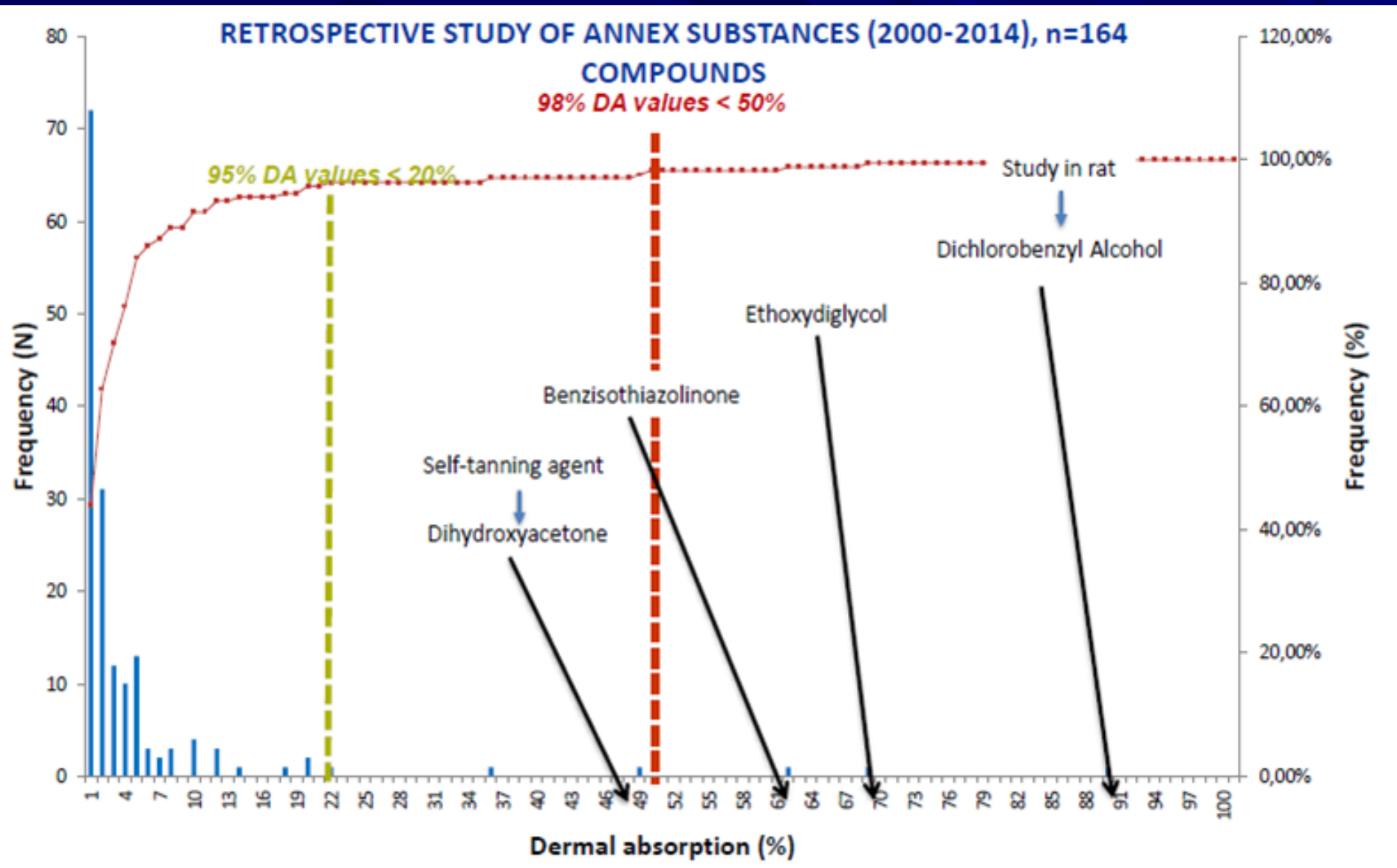
$$\log k_p \text{ (cm/sec)} = - 6.3 + 0.71 \cdot \log K_{\text{Oct/Acqua}} - 0.0061 \text{PM}$$

ASSORBIMENTO CUTANEO

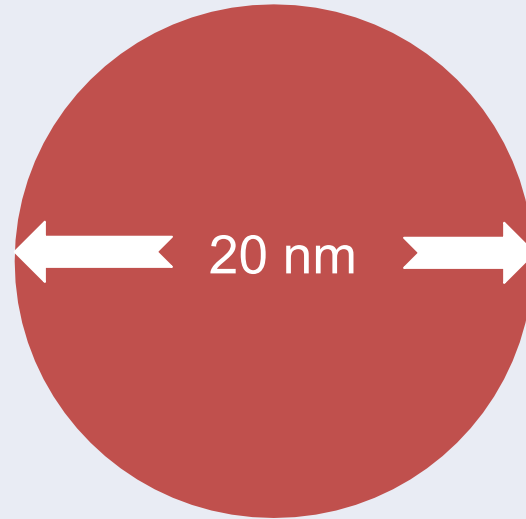
A retrospective study of the Annex (to Cosmetic Regulation) substances present in the opinions (2000-2014) of the SCCS and its predecessors has shown that the cosmetic ingredients characterised by the following physicochemical properties,

- MW > 500 Da,
- High degree of ionisation,
- Log Pow ≤ -1 or ≥ 4 ,
- Topological polar surface area $> 120 \text{ \AA}^2$,
- Melting point $> 200^\circ\text{C}$,





Size of Common UV Filters

UV Filter Categories	Molecular Weight	Size Molecule / Particle Diameter		
PBSA, EHMC	< 300 Da	< 1 nm		
EHT, BEMT	> 500 Da	> 1 nm		
Polysilicone-15 (Polymer)	6000 Da	3 nm		
MBBT, TBPT Microfine organic particles, partially "Nano"	>3'000'000 Da (= smallest particles)	20-500 nm		
Which UV filters will penetrate into the skin most probably?				
For UV Filters <i>Nano means</i>		BIG !		

ASSORBIMENTO CUTANEO

- ❖ Quantità assoluta di una sostanza che penetra la cute dopo un certo periodo ($\mu\text{g}/\text{cm}^2$)
- ❖ Espresso come percentuale %

SED

Quantità attesa nel flusso sanguigno

$$\text{SED} = \text{mg}/\underline{\text{kg bw}}/\text{day}$$

Media → body weight = 60 kg (comunemente accettata)

CALCOLO (SED)

$$SED = E_{\text{prodotto}} \times \frac{C}{100} \times \frac{DA_p}{100}$$

SED (mg/kg bw/day) = Dose di esposizione sistemica

E_{prodotto} (mg/kg bw/day) = Expos/day stimata/kg BW

C (%) = Concentrazione sostanza

DAp (%) = Assorbimento cutaneo

CALCOLO DOSE ESPOSIZIONE GIORNALIERA SOSTANZA APPLICATA SU CUTE (I)

$$E_{\text{Dermica}} = C \times Q \times F$$

Dove:

E_{Dermica} (g o mg/day): dose applicata disponibile x
assorbimento dermico / ingestione

C (% p/p): concentrazione sostanza

Q (g o mg/day): quantità prodotto applicata giornalmente

F : fattore di ritenzione/diluizione

CALCOLO (SED)

$$SED = E_{dermica} \times \frac{1}{BW} \times \frac{DA_p}{100}$$

SED (mg/kg bw/day) = Dose di esposizione sistemica

$E_{dermica}$ (mg/day) = Expos/day stimata

BW (Kg) = peso corporeo 60 Kg (adulto)

D_{ap} (%) = Assorbimento cutaneo

Example 2a

- **SPF 50+ - Sunscreen Product**
- **Body**
- **Leave-on = 100% Retention**
- **Children 6+ months**

Label

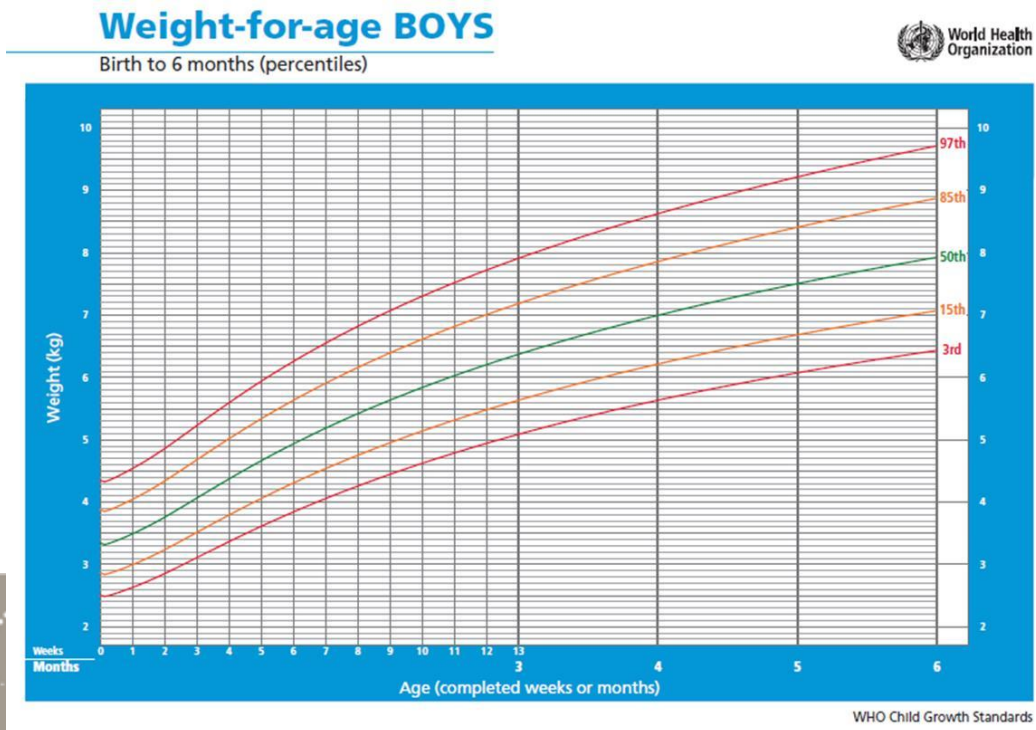
Apply evenly 20 minutes before sun exposure. The amount of product applied is essential for good protection. Apply to face, neck and décolleté. For the child, 0.50 mg/cm^2 is required. In particular, this corresponds to:

- a) 3 full teaspoon for children over 3 years old;
- b) 2 full teaspoon for children between 1 and 3 years;
- c) 1 full teaspoon for children between 6 months and 1 year;

..... For the adult, apply 2 mg/cm^2 or about 36 g (six teaspoons). Reapply every 2 hours, especially after swimming or excessive sweating.

Product Exposure

- **SCCS** → $\approx 18\text{g}$ ($0.5\text{mg}/\text{cm}^2 \times 17500\text{cm}^2 \times 2 \text{ applications}/\text{day}$)
- **SSA/BW** = 1.8 (6 months)
- **WHO** → 8 Kg (6 months – http://www.who.int/childgrowth/standards/chts_wfa_boys_p/en/)



$$= 18 \text{ g}/60 \text{ Kg} \times 1.8 \text{ (factor)} \times 8\text{Kg} =$$

4.3 g/day

[pag 16 of SCCS/1446/11](#)

Children Exposure

RIVM report 320005005/2007

Non-food products: How to assess children's exposure?

J.G.M. van Engelen, L.C.H. Prud'homme de Lodder

Appendix Table 3: Default values for body surface area and surface area by body part

Age	Default value Body surface area ^{a)} (m ²)	Default values Surface area by body part ^{b)} (m ²)							
		Head	Trunk	Arms & hands	Arms	Hands	Legs & Feet	Legs	Feet
3 mo	0.31	0.061	0.100	0.053	0.037	0.016	0.094	0.072	0.022
10.5 mo	0.44	0.077	0.149	0.077	0.055	0.023	0.134	0.103	0.031
3.5 yrs	0.64	0.090	0.214	0.122	0.088	0.035	0.214	0.170	0.045
6.5 yrs	0.84	0.105	0.281	0.164	0.118	0.046	0.291	0.230	0.061
13.5 yrs	1.40	0.132	0.459	0.280	0.200	0.080	0.529	0.424	0.105

^{a)} Source: Bremmer et al. (2006a)

^{b)} Calculated from percentages given by Bremmer et al. (2006a)

en
s and Integrated Risk Assessment
en@rivm.nl

IVM report 320005001/ 2004 in which
d. Appendix 3 contains default values
sess the exposure for children.

This investigation has been performed by order and for the account of the Ministry of Health, Welfare and Sports (VWS), within the framework of project 320005.

For **sunscreen lotion**, an amount of **18.0 g/day** is used in the MoS calculation. It is used as a standard exposure value in the safety evaluation carried out by the SCCS **but is not meant as a recommended amount to be applied by the consumer** (SCCNFP/0321/02). To reach a comparable level as indicated by the Sun Protection Factor (SPF), sunscreen products have to be applied in quantities similar to the ones used for SPF testing, *i.e.* 2 mg/cm² (total amount of approx. 36 grams) for the body of an average adult person (2006/647/EC). The quantity of 2 mg/cm², however, is the amount necessary to obtain reproducible SPF results under laboratory conditions. It is higher than the amount usually applied by consumers.

This observation has been reported frequently: when consumers use their own sun products (lotions, alcoholic solutions, gels, creams, sprays,...) and apply the products on the whole body surface, values for use of products between 0.5 - 1.3 mg/cm² have been found (Stenberg *et al.*, 1985; Bech-Thomsen *et al.*, 1993; Diney, 1996; Gottlieb *et al.*, 1997; Autier *et al.*, 2001 and 2007). The values seem to depend on the study protocol used, the location on the body measured and several other factors. More recent publications still come to comparable values in the range of 0.39-1 mg/cm² (Danish Protection Agency No. 151, 2016, Ficheux *et al.*, 2016a, Gomez-Berrada *et al.*, 2017). When the product is applied only to the face, then the amount applied might be higher than 2 mg/cm² (Gomez-Berrada *et al.*, 2017). The amount used by the SCCS in safety calculations reflects actual consumer use and takes the whole body area (17500 cm²) into account. The average exposed skin area of sunscreen users according to the recent report of the Danish authorities is 14,700 cm².

The use of 18g/d sunscreen corresponds with the values reported by Biesterbos *et al.* (Biesterbos *et al.*, 2013), who found a mean use amount of 9.2 g/application, derived on the basis of pictures. If two applications are considered, this is about 18 g/d. Unpublished data by von Goetz (von Goetz, 2018) from a small-scale pilot study with weighing also provided a



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Food and Chemical Toxicology 45 (2007) 2097–2108



www.elsevier.com/locate/foodchemtox

Review

European consumer exposure to cosmetic products, a framework for conducting population exposure assessments

B. Hall ^{a,*}, S. Tozer ^b, B. Safford ^c, M. Coroama ^d, W. Steiling ^e,
M.C. Leneveu-Duchemin ^f, C. McNamara ^g, M. Gibney ^h

^a *L'Oréal, Worldwide Safety Evaluation, River Plaza 25-29 quai Aulagnier, 92600 Asnières-sur-Seine, France*

^b *Procter & Gamble, Central Product Safety, P&G Technical Centres Ltd., Whitehall Lane, Egham, Surrey TW20 9NW, UK*

^c *Unilever, Safety and Environmental Assurance Centre, Colworth Park, Sharnbrook, Beds MK44 1LQ, UK*

^d *Colipa, Avenue Hermann-Debroux 15A, B-1160 Brussels, Belgium*

^e *Henkel KGaA, Corporate SHE and Product Safety-Human Safety Assessment, Henkelstr. 67, 40191 Dusseldorf, Germany*

^f *Beiersdorf AG, Unnastrasse 48, 20245 Hamburg, Germany*

^g *CREMe Software Ltd., Innovation Centre, Trinity College, Dublin 2, Ireland*

^h *Agriculture and Food Centre, Food Science and Veterinary Medicine, University College Dublin, Belfield, Dublin 4, Ireland*

Received 31 January 2007; accepted 1 June 2007

Diaper Area ??



Scientific Committee on Consumer Safety

SCCS

OPINION ON Parabens

Updated request for a scientific opinion on propyl- and butylparaben

COLIPA n° P82

SCCS/1514/13 - Scientific Committee on Consumer Safety SCCS - OPINION ON Parabens

- 12 According to this data, the following quantities of products are used daily for children:
- 13 - for leave-on products:
- 14 0.063 g/d for body care leave-on products,
- 15 1.34 g/d for leave-on products for nappy area,
- 16 0.55 g/d for wipes for nappy area
- 17 - for rinse-off products:
- 18 1 g/d for rinse-off products for body care
- 19 2.4 g/d for rinse-off products for nappy area,

Ingredienti

Alcohol Denat. 5% (Diethyl Phthalate 3% v/v)

Alcohol 4.98%

Diethyl Phthalate 0,02%



Opinion concerning Diethyl Phthalate (SCCNFP/0411/01, final)

Maximum dermal absorption through the skin = 5 %

$$\frac{\text{SED} = 4,30 \text{ g} \times 0,02\% \text{ (I)} \times 5,0\% \text{ (DA)}}{8 \text{ Kg}} = \underline{5,4 \times 10^{-6} \text{ g/Kg bw/d}}$$

CALCOLO (SED) ALTERNATIVO

$$\text{SED} = \frac{\text{DA}_a (\mu\text{g}/\text{cm}^2) \times 10^{-3} \times \text{SSA} (\text{cm}^2) \times F (\text{day}^{-1})}{60 \text{ kg bw}}$$

(mg/kg bw/day)

$\text{DA}_a (\mu\text{g}/\text{cm}^2)$ = “Dermal Absorption” come quantità ($\mu\text{g}/\text{cm}^2$)

$\text{SSA} (\text{cm}^2)$ = Superficie cutanea (prevista) in contatto con prodotto

$F (\text{day}^{-1})$ = Frequenza d'applicazione

Esposizione x inalazione

- Vapore
- Polvere
- Goccioline aerosol
- Particelle aerosol

CALCOLO (SED)

$$SED_{inh} = E_{prodotto} \times \frac{C}{100} \times f_{evap}$$

$$SED_{inh} = E_{inalabile} \times \frac{1}{BW}$$

CALCOLO (SED)

$$SED_{inh} = E_{prodotto} \times \frac{C}{100} \times f_{evap}$$

Modello 2-BOX

$$SED_{inh} = (a_{inh-1} + a_{inh-2}) \times f_{ret} \times f_{resp} \times f_{appl} / bw$$

CALCOLO (SED)

$$SED_{inh} = E_{prodotto} \times \frac{C}{100} \times f_{evap}$$

$$SED_{inh} = (a_{inh-1} + a_{inh-2}) \times f_{ret} \times f_{resp} \times f_{appl} / bw$$

$$a_{inh-1, inh-2} = a_{expo} \times r_{inh} \times t_{1,2} / V_{1,2}$$

$$a_{expo} = a_{product} \times C_{product} \times f_{air}$$

CALCOLO (SED)

$$SED_{inh} = (a_{inh-1} + a_{inh-2}) \times f_{ret} \times f_{resp} \times f_{appl} / bw$$



$$a_{inh-1, inh-2} = a_{expo} \times r_{inh} \times t_{1,2} / V_{1,2}$$



$$a_{expo} = a_{product} \times C_{product} \times f_{air}$$

CALCOLO (SED)

$a_{inh-1, inh-2}$ (mg): quantità potenzialmente inalabile nei box

f_{ret} : fattore ritenzione sostanza nei polmoni ($\cong 75\%$)

f_{resp} : frazione respirabile (misurata sperimentalmente);

f_{appl} (day-1): frequenza di applicazione

$t_{1,2}$ (min): durata di esposizione nei 2 Box

$V_{1,2}$ (L): volume dei Box (Box1 = 1 m³ - Box2 = 10 m³);

CALCOLO (SED)

a_{expo} (mg): quantità di sostanza disponibile all'inalazione

r_{inh} (L/min): velocità di inalazione (≈ 13 L/min);

a_{product} (g): quantità di prodotto erogata

C_{product} (mg/g): concentrazione ingrediente **(compreso propellente)**

f_{air} : frazione aereo-veicolata

SOLARE – APPENDIX 11

Parameter	Parameter description	Propellant spray	Pump spray	Unit	Reference
a_{product}^*	amount per application* air-borne fraction of spray	9	9	g/application	SCCS, NoG
f_{air}	mist Box 1 (Near-field around the head)*	1	0.2	fraction	Bremmer et al, 2006
V_1^*		1000	1000	L	SCCS, Octocrylene
t_1^*	duration of exposure in Box 1 (near field)*	2	2	min	SCCS, Octocrylene
r_{inh}	inhalation rate Box 2 (Far-field, e.g. bathroom)*	13**	13**	L/min	US-EPA 2011
V_2^*		10000	10000	L	SCCS, Octocrylene
t_2^*	duration of exposure in Box 2 (far field)*	10	10	min	SCCS, Octocrylene
f_{resp}	respirable fraction	<i>experimental data</i>	<i>experimental data</i>	fraction	
f_{ret}	substance retention fraction in the lungs (25% exhaled)	0.75	0.75	fraction	Rothe et al., 2011
f_{appl}^*	frequency of application*	2	2	per day	SCCS, NoG
bw	bodyweight	60	60	kg	SCCS, NoG

STICK ANTITRASPIRANTE – ESEMPIO 2b

Product type:	LEAVE ON PRODUCT
Application area:	Axillae
Possible route of absorption:	Cutaneous
Average quantity per application:	1.50 g/day (Deodorant non-spray – 11 th SCCS Revision)
Retention Factor:	100 %
Body weight (adult)	60 Kg
Product Exposure (mg/Kg bw/day) = $1.50 \text{ g} \times 1000 \text{ mg} \times 100\% / 60 \text{ Kg} \cong 25 \text{ mg/kg bw / day}$ This quantity can be considered either for acute or for chronic toxicity evaluations	

DIMETHICONE = 23.65 %

DIMETHICONE inhaled/day = $1500 \text{ mg} \times 23.65\% / 10 \text{ m}^3 \cong 35,5 \text{ mg/m}^3$

* volume (10 m³) as standard parameter for BOX-2 (SCCS, 11th revision).

PROCESSO DI VALUTAZIONE DEL RISCHIO

**1) IDENTIFICAZIONE
PERICOLO**

2) DOSE- RISPOSTA

**3) VALUTAZIONE
ESPOSIZIONE**

**CARATTERIZZAZIONE
RISCHIO**

**GESTIONE
RISCHIO**

**COMUNICAZIONE
RISCHIO**

PROCESSO DI VALUTAZIONE DEL RISCHIO

CARATTERIZZAZIONE RISCHIO

- Dati su INGREDIENTI

Irritazione, Sensibilizzazione, etc..... &

NOAEL, BMDL



Calcolo MoS

CALCOLO DEL MARGINE DI SICUREZZA (MoS)

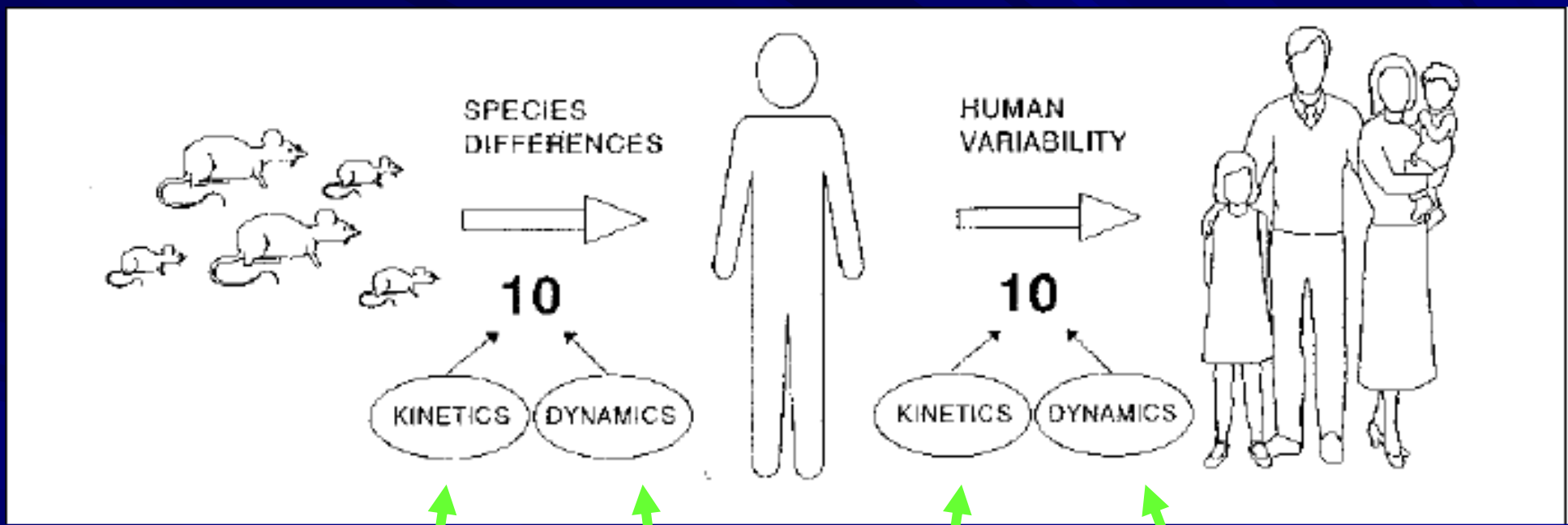
$$\text{Margin of safety} = \frac{\text{POD}_{\text{sys}} \text{ (mg/ Kg bw/ day)}}{\text{SED (mg/ kg bw/ day)}}$$



$$\text{MoS} \geq 100$$

Risk characterisation usually involves an expert followed by calculation of an uncertainty factor or 'margin of safety' (MoS). This calculation depends on the systemic exposure to the substance and its toxicological parameters.

L'omissione di questo step deve essere accuratamente giustificata.



4.0

2.5

3.2

3.2

Esempio 3

DEHP in solare bambini

Opinion concerning Diethyl Phthalate (SCCNFP/0411/01, final)

NOAEL = 150 mg/kg bw/d from a sub-chronic oral toxicity study in rats: “toxic signs after 16 weeks of exposure of DEP in the diet consisted of an increase in relative liver weight (without significant abnormal histological findings) in females at concentrations at 1 % and 5 % and in a lesser extent at 0.2 % (corresponding to 150 mg/kg body weight/day).

$$\text{MoS} = \frac{\text{NOAEL}}{\text{SED}} = \frac{0,15 \text{ g/Kg bw/d}}{5,4 \times 10^{-6} \text{ g/Kg bw/d}} = 2,8 \times 10^4$$

Esempio 4

crema bambini

Camphor = 4.6%

NOEL = 250 mg/kg/day (13 settimane – US EPA)

Dermal Absorption = n.d.

$$\text{SED} = \frac{3,90 \text{ g} \times 4,6\%}{8 \text{ Kg}} = \underline{\underline{2,2 \times 10^{-2} \text{ g}}}$$

$$\text{MoS} = \frac{\text{NOAEL}}{\text{SED}} = \frac{0,25 \text{ g/Kg bw/d}}{2,2 \times 10^{-2} \text{ g/Kg bw/d}} = \underline{\underline{11}}$$

ASSENZA NOAEL

1) LOAEL = Lowest Observed Adverse Effect Level →
→ Fattore addizionale = 3 (1-10)

2) Studio su 28 giorni →
→ Fattore addizionale = 3

Esempio 5

solare bambini

Dibutyl Adipate = 15%

NOEL = 1000 mg/kg/day (28 giorni - CIR; OECD-SIDS)

Dermal Absorption < 2% (BASF-2011 Rep. No C1100693-0)

$$\text{SED} = \frac{4,30 \text{ g} \times 15\% (I) \times 2\% (DA)}{8 \text{ Kg}} = \underline{1,6 \times 10^{-3} \text{ g}}$$

$$\text{MoS} = \frac{\text{NOAEL}}{\text{SED}} = \frac{0,33 \text{ g/Kg bw/d}}{1,6 \times 10^{-3} \text{ g/Kg bw/d}} > \text{205}$$

Esercizio 2a

Solare Bambini = 0+

Caprylyl Glycol = 0,5%

NOEL = 300 mg/kg/day (28 giorni – I. j. T 2012)

Dermal Absorption $\cong$ 90%



STICK ANTITRASPIRANTE – Esercizio 2b

Product type:	LEAVE ON PRODUCT
Application area:	Axillae
Possible route of absorption:	Cutaneous
Average quantity per application:	1.50 g/day (Deodorant non-spray – 11 th SCCS Revision)
Retention Factor:	100 %
Body weight (adult)	60 Kg
Product Exposure (mg/Kg bw/day) = $1.50 \text{ g} \times 1000 \text{ mg} \times 100\% / 60 \text{ Kg} \cong 25 \text{ mg/kg bw / day}$ This quantity can be considered either for acute or for chronic toxicity evaluations	

DIMETHICONE = 23.65 %

NOAEC $\geq$ 400 ppm - Dimethicone 2 cst

OECD 413 (Subchronic Inhalation Toxicity 90-Day Study)

STICK ANTITRASPIRANTE

DIMETHICONE inhaled/day = $1500 \text{ mg} \times 23.65\% / 10 \text{ m}^3 \cong 36 \text{ mg/m}^3$

* volume (10 m^3) as standard parameter for BOX-2 (SCCS, 12th revision).

NOAEC $\geq 400 \text{ ppm}$ - Dimethicone 2 cst, OECD Guideline 413;

Concentration (ppm) = $24.45 \times \text{concentration (mg/m}^3) / \text{molecular weight}$

Concentration (ppm) = $24.45 \times 36 \text{ mg/m}^3 / 384.84 \text{ g/mol} = 2,3 \text{ ppm}$

MW = 384.84 for Dodecamethylpentasiloxane (Sigmar-Aldrich)

24.45 = volume occupied by one mole of gas (1 atmosphere, 25 ° C)

MoS = $400 \text{ ppm} / 2.3 \text{ ppm} \cong 174$

ASSENZA DATI

.... An example where this could apply would be the presence of a substance in the cosmetic product at a low level, with the expected (worst case) exposure levels being below the appropriate threshold of toxicological concern (TTC) values....

SCCS, SCHER and SCENIHR, Opinion on Use of the Threshold of Toxicological Concern (TTC) Approach for Human Safety Assessment of Chemical Substances with focus on Cosmetics and Consumer Products, SCCP/1171/08.

Opinion on Use of the
Threshold of Toxicological
Concern (TTC) Approach for
Human Safety Assessment of
Chemical Substances with
focus on Cosmetics and
Consumer Products,
SCCP/1171/08

$$1,5 \mu\text{g/person/d} =$$

$$0,025 \mu\text{g/kg bw/d}$$

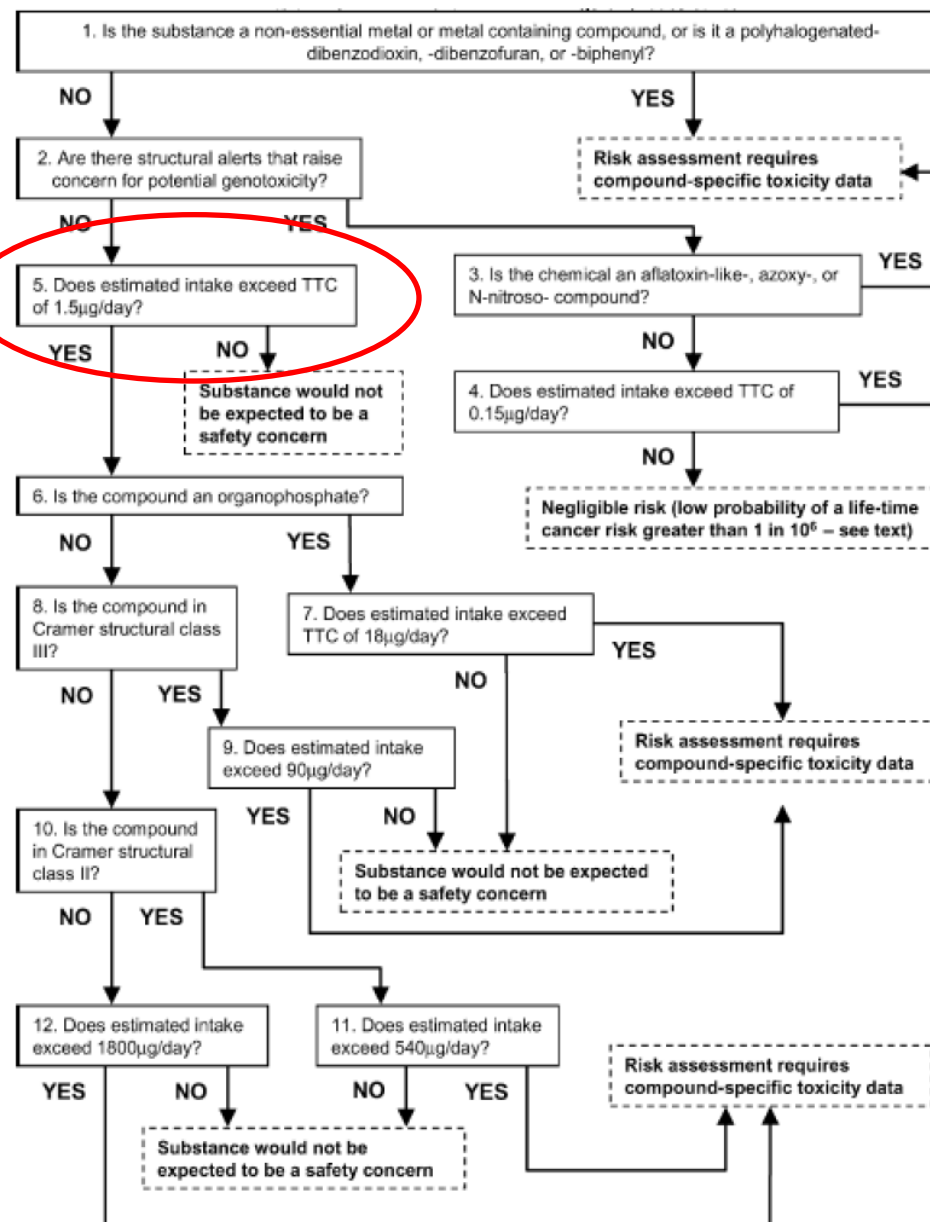
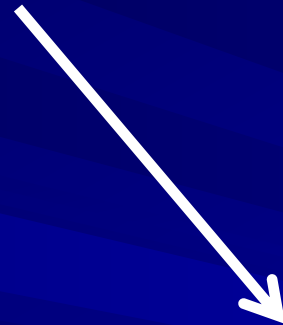


Figure 1: The TTC decision tree suggested by the ILSI Europe Expert group (Kroes et al., 2004).

ASSENZA DATI

..... Another example could be the inclusion of food materials for which a much higher innocuous ingestion level is known....

- Polimeri o $\uparrow$ MW
- Similitudine strutturale
- QSAR



DA = 10% sostanze con MW > 500 Da

Basic criteria for the in vitro assessment of dermal absorption of cosmetic ingredients SCCS/1358/10

Esempio 7

- Ombretto
- Contorno occhi
- Leave-on = 100% ritenzione
- Adulto
- CI 77510 (10 ppm ioni cianuro) = 10%

SCCS → 0,02 g/giorno

$$\text{SED} = \frac{0,02 \text{ g/d} \times 10\%}{60 \text{ Kg}} = \underline{3,3 \times 10^{-5} \text{ g/Kg bw/d}}$$

Esempio 7

Ioni cianuro $\rightarrow 10 \text{ mg/kg}$



$$3,3 \times 10^{-5} \text{ g} \rightarrow 3,3 \times 10^{-10} \text{ g} =$$

$$= 3,3 \times 10^{-2} \text{ ng} < 1,5 \text{ } \mu\text{g/kg}$$

Esempio 8

- 1) chemical identity;
- 2) physical form;
- 3) molecular weight;
- 4) characterisation and purity of the chemical;**
- 5) characterisation of the impurities or accompanying contaminants;**
- 6) solubility;
- 7) partition coefficient ($\text{Log } P_{ow}$);
- 8) additional relevant physical and chemical specifications;
- 9) homogeneity and stability;
- 10) UV-VIS-absorption spectrum;
- 11) isomer composition;
- 12) function and uses.

Esempio 8

- Fard
- Viso
- Leave-on = 100% ritenzione
- Adulto
- RM 1 → Talco (<10 ppm Nichel) = 56%
- RM 2 → Talco (<200 ppm Nichel) = 2%

$$\text{Exp} = 10 \text{ ppm} \times 56\% + 200 \text{ ppm} \times 2\% = \underline{9,6 \text{ ppm}}$$

Obiettivo 4. Livelli di tracce di metalli

Manca una regolamentazione sulle concentrazioni considerate «tracce tollerabili»

mg/Kg	Germania ^a	Canada ^b	ISS ^c
As	5	3	1
Cd	5	3	5
Co			5
Cr III			5
Cr VI			1
Hg	1	3	1
Ni			10
Pb	20	10	20
Sb	10	5	10

a) Bundesinstitut für Risikobewertung (BfR), 2006 "Kosmetische Mittel: BfR empfiehlt Schwermetallgehalte über Reinheitsanforderungen der Ausgangsstoffe zu regeln", Stellungnahme Nr. 025/2006 des BfR vom 05. April 2006. Web site:

http://www.bfr.bund.de/cm/343/kosmetische_mittel_bfr_empfiehl_schwermetallgehalte_ueber.pdf

b) Health Canada. Guidelines for Canadian Drinking Water Quality: Guideline Technical Document - Arsenic. May 2006; Health Canada. (2009). Draft Guidance on Heavy Metal Impurities in Cosmetics. http://www.hc-sc.gc.ca/cps-spc/legislation/consultation/_cosmet/metal-metiaux-consult-eng.php

c) ISS documento n° SGT 43/09 19721 FARM-CHF22 (prot. 03/07/2009-0034194) – Proposta di limiti ammissibili per alcuni elementi tossici inquinanti nei prodotti cosmetici.

ISS documento n° SGT 80/09 17930 FARM-CHF 22 (prot. 16/09/2009-0045187) – Oggetto: violazione art. 7 della legge 11.10.86 n. 713. Parere tecnico su concentrazione di cromo trivalente

Limite dermatologico per Ni, Cr e Co: 1 mg/kg *

* D A. Basketter, G. Angelini, A. Ingber, P. S. Kern And T. Menne'. Nickel, chromium and cobalt in consumer products: revisiting safe levels in the new millennium, Contact Dermatitis 2003; 49: 1-7

ANNOUNCEMENTS AND REPORTS

Technically avoidable heavy metal contents in cosmetic products

Table 1 In future, heavy metal contents in cosmetic products exceeding the following values are considered as technically avoidable

Element	Cosmetic products in general (mg/kg)	Toothpaste (mg/kg)
Lead (Pb)	2.0 ^a	0.5
Cadmium (Cd)	0.1	0.1
Mercury (Hg)	0.1	0.1
Arsenic (As)	0.5 ^b	0.5
Antimony (Sb)	0.5	0.5

^a For the products make-up powder, rouge, eye shadow, eye liner, kajal, as well as theater, fan or carnival make-up: 5 mg/kg

^b For theater, fan or carnival make-up: 2.5 mg/kg

Esempio 9

- Balsamo
- Capelli e cuoio capelluto
- Rinse-off = 1% ritenzione
- Adulto
- Fenossietanolo = 0,3% → (Phenol 0,1%)
- Allegato V, n° 29 = max 1%

$$\text{SED} = \frac{0,04 \text{ g/d} \times 0,3\% \times 0,1\%}{60 \text{ Kg}} = \underline{2,0 \times 10^{-6} \text{ mg/Kg bw/d}}$$

ECHA = applicazione 0,9 mg/Kg bw/day considerata sicura (NOAEL dermico di 260 mg/Kg bw/day)

Esempio 10

- Shampoo
- Capelli e cuoio capelluto
- Rinse-off = 1% ritenzione
- Adulto
- SLES = 11% → 1,4 Diossano $\leq$ 30 ppm/m.a.

$$\text{Exp} = 30 \text{ ppm} \times 11\% = \underline{\underline{3,3 \text{ ppm}}}$$

FDA prodotti cosmetici detergenti contenenti da 1,4 a 23 ppm (media di 7,4 ppm) sono considerati sicuri

PROCESSO DI VALUTAZIONE DEL RISCHIO

**1) IDENTIFICAZIONE
PERICOLO**

2) DOSE- RISPOSTA

**3) VALUTAZIONE
ESPOSIZIONE**

**CARATTERIZZAZIONE
RISCHIO**

**GESTIONE
RISCHIO**

**COMUNICAZIONE
RISCHIO**

PROCESSO DI VALUTAZIONE DEL RISCHIO

GESTIONE RISCHIO

- Restrizioni:
Concentrazione di un ingredienti
Frequenza o quantità applicata
- Autorizzazione senza limiti & restrizioni
- No vendita/Ritiro dal mercato

PROCESSO DI VALUTAZIONE DEL RISCHIO

1) IDENTIFICAZIONE
PERICOLO

2) DOSE- RISPOSTA

3) VALUTAZIONE
ESPOSIZIONE

CARATTERIZZAZIONE
RISCHIO

GESTIONE
RISCHIO

COMUNICAZIONE
RISCHIO

PROCESSO DI VALUTAZIONE DEL RISCHIO

COMUNICAZIONE RISCHIO

- Avvertenze in etichetta
 - evitare contatto con occhi/mucose
 - non applicare su pelle irritata
 - non superare la dose indicata
 - etc

COSMETIC SAFETY REPORT

Include

- Informazioni ingredienti, produzione, packaging, contaminazioni chimiche & microbiologiche....
- Quantificare esposizione
- Quantificare e valutare I RISCHI



Combinazione di tutti questi parametri



GRAZIE

NICOLA LIONETTI

nicola.lionetti@labanalysis.it