

Safety assessment and risk management of cosmetics.

SIMPLIFICATION OF COSMETICS DEVELOPMENT?



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Malmö, November 6. 2009.

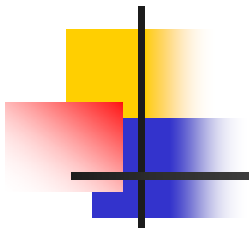
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A practical approach..

Presentation: Simplification.

1. Risk Management from the business managers point of view.
2. Aspects of fulfilling customers demands.
3. Manage and update current products!
4. Define your new product precisely from the start!
5. Selecting ingredients – and alternatives.
6. Calculating the opposite way in safety.
7. Safety assessment, finding relevant data.
8. Safety assessment used in marketing.
9. Special data needed for special purposes.



Risc Management of Cosmetics from a Management point of view. Basic demands, simple tools.

- For most Companies, the easiest customer to have is: A former customer.
- Therefore an important Risc Management point of view will be: How do we secure that customers..
 - ..are not disappointed by our products.
 - ..feel safe with our products
 - ..comes back to rebuy

Risc Management, A: customers?

"not disappointed"

A Quality statement

Adverse experience:

Unstable, miscoloured
with microorganisms,
Emballage problems

Positive experience:

Product improves xx.

Good acceptance,
easy to use..



"comes back"

A Personal action which proves customer
satisfaction. Study this group, and learn from it!

"feel safe"

A Personal experience

Adverse experience:

See negative statements
About products or related
in press or media.

Positive experience:

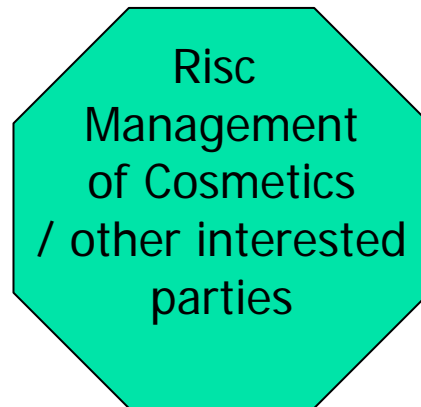
Allergic, Eco or Oec marking
Safety assessment statement

Risc Management

B: other interesting parties?

Legal affairs:
Cosmetic legislation:
Safety

Products, that
has not been
safety assessed
should not be
on the market.




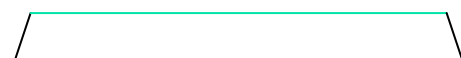
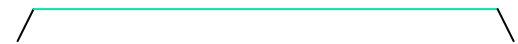
Stability

Microbiology
Packaging
PAO

The new Cosmetic decree will facilitate the process of demanding cosmetic products condemned and forcing draw back of products not fulfilling demands.

Basis: A stable and reliable product. Manage and update current products!

Ideally: Before finishing a product development:
Always perform +/- experiment tests in order to understand:

1. How broad your track is and to know the limits. 
1. How to broaden your track. 
2. How to adjust products. 
3. Understand whether you have developed your optimal product.



How to do +/- experiment tests – a simplified model

Formula	Standard	A+	A-	B+	B-	C+	C-	D+	D-
Water	60	66	54	60	60	60	60	60	60
Oil	30	30	30	33	27	30	30	30	30
Thickener	4	4	4	4	4	5	3	4	4
Emulsif.	5	5	5	5	5	5	5	6	4
Preserv.	1	1	1	1	1	1	1	1	1
Sum	100	106	94	103	97	101	99	101	99



Transfer from lab to production should be safe and reliable:

- What can go wrong:
- Heating and cooling processes and times.
- Stirring conditions and effect.
- Loss of ingredients/water compared to expectations from lab. Experiments.
- Physical processes after mixing: pumping, contact with package material, specific packaging related problems like: evaporation, incoming air, drying out....



Microbiology and packaging, PAO!

- From a consultants point of view:
- Relatively safe preservatives are becoming more and more popular – and widely used → more allergic reactions.
- Alternative preservative strategies have been extensively tested; but will always be of limited value.
- Understand that if you use preservatives not represented on the positive list, you are responsible for evaluating the risk/benefit balance: Risks in relation to humans and nature.
- Nearly all preservatives and the alternatives for self-preserving products are characterized by having good membrane penetrating properties – and many of them are irritants.
- They will normally be coactive as penetration enhancers.
- Preservation challenge testing should always be used as guidance for PAO.
- However also alternative strategies like packaging's with elegant closures and other means of reducing the risk for contact with consumers should be extensively considered.



SIMPLIFICATION OF COSMETICS DEVELOPMENT?

- The old proverb is also true for cosmetics development:
- Be sure to have the right tools before you start working!
- We have already looked at some relevant tools for the practical side of development and management.

- Now we will focus on development of new products!
- Without the right knowledge from the start of the development process you may waste a lot of time in your development process.

Information for a start:

In black:

safety information start:

Exact description of the expected outcome product:

Product type, market, **where to use**, **how to use**, **how much to use/day**, expected volume per year, price level, standards to fulfill, consumer expectancies to fulfill, label requirements to meet, **safety requirements to meet**, **special consumer demands (children, senzitized, professionals)**, how the product should be marketed...

Selecting ingredients – and alternatives: from your own database?

What I would like to know about my ingredients:

- INCI name, CAS-, Einecs-, Elincs- and REACH registration numbers, E-number and Max. tolerability, Molar weight and structure of molecule, Physical data: Wet density, flame- , melting- and boiling points, LogKow, Aerobic and Anaerobic biodegradability, Toxicity to Fish, Daphnia and Algae, Toxicity data to animals or human: LD50, TDLO and optimally NOAEL values, Dermal tox, Allergenicity, Photo tox, or other special toxic effects, Skin penetration, Cosmetic safety in general, Risc markings and possible risks of CMR- or Endocrine effects.
- - and the of sources of all relevant information.

No information is better than the source! – and for your safety assessment **data traceability is a demand!**



What is a safety assessment?

- A total overview of the product.
- Compliance with cosmetic directive?
- Label, Advertizing, marketing?
- All safety aspects including:
 - a. Effects on skin.
 - b. Systemic effects in the human body!
 - c. Evaluation of performed tests.
 - d. Checking for adverse effects.

Calculating the opposite way - from a NOAEL to accepted level of use. Example:

Body lotion, MoS=100, Skin penetration=100%

- How to calculate – from formula 2 in the SCCS Guide to Safety Assessment:
- $SED_i = (A_{Prod} \text{ mg/day} \times \text{Conc.}_i \% \times DA_i) / 60\text{kg}$
- $DA_i (\%) = \text{Dermal Absorption} / \text{Ingredient}$
- $\text{MoS} = \text{NOAEL} / \text{SED} \rightarrow \text{SED} = \text{NOAEL} / \text{MoS} \rightarrow$
- $\text{Conc.}_i = \text{NOAEL} \times 60\text{kg} / (A_{Prod} \text{ mg/day} \times DA_i)$
- $\text{Conc.}_i \% = \text{NOAEL} \times 60\text{kg} \times 100 / 8000 \times 1(100\%)$
 - if 8g=8.000 mg product is used pr day and 100% penetrates into the skin.
- $\text{Conc.}_i \% = 0,0075 \times \text{NOAEL} \text{ (value in mg/kg/day)}$

From a NOAEL to accepted level of use: SIMPLIFICATION for presentation purpose

NB: Accepted level if 100% penetrates the skin.

NB: These data are from public sources. You might be able to get improved data from qualified, cosmetic suppliers.

INCI	CAS no	NOAEL	Adult 60kg	Child 12kg	
Faktor to allowed concentration % stay on Body Lotion			X 0,0075	X 0,0015	
A	Panthenol	81-13-0	1000	7,5	1,5
B	Sorbitan stearate	1338-41-6	2500	18,75	3,75
C	Hexamethyl disiloxane	107-46-0	1	0,0075	0,0015
D	Dimethicone copolyol	64365-23-7	20	0,15	0,03
E	Laureth-9	3055-99-0	80	0,6	0,12
F	Glycerin	56-81-5	2000	15	3
G	Polyglyceryl-3 oleate	9007-48-1	1000	7,5	1,5
H	Urea	57-13-6	200	1,5	0,3
I	Aqua	7732-18-5			
J	Magnesium sulfate	7487-88-9	43	0,3225	0,0645
K	Sodium benzoate	532-32-1	1090	8,175	1,635
L	Phenoxyethanol	122-99-6	200	1,5	0,3

How to find tox data:

NB: Do not waste time on optimizing good data.
Use your time on problem areas.

- The optimal is to find general and public sources. Important examples are:
 - Hera Reports, IUCLID database.
 - Food safety documentation, JECFA.
 - Pay info: RTEC database and CIR reports,
 - Other possibilities are information from suppliers.
- However in these cases you should use the product, which data you are referring to. Quality of many products can differ depending on production process, cleaning- and purifying processes, additives, stabilizing- and preserving ingredients.



SCCP -> SCCS recommendations: How to choose and interpret data:

- *in vivo* tests using experimental animals,
- *in vitro* tests using validated or valid alternative methods,
- human data from clinical observations and compatibility tests in human volunteers,
- data from data banks, published literature, "in house" experience and data obtained
- from raw data suppliers, including QSAR structural alerts,
- relevant data on analogous compounds,



Ex. Analogue compounds

- Look at the chemistry: See: Epa, Dermwin
- Safety assessment understanding the chemistry performed by an experienced .. pharma, medicine, toxicology...

Example: Cancer

- Structural alerts for risk compounds:
- Cyclic compounds containing halogens: F, Cl, Br, J or N
- Ingredients containing N, S, F, Cl, Br, J, and ingredients having unsaturated bonds...

How to use Safety Assessment in marketing:



D: Premises/Conclusions:

D.1 Information on exposure:

Body Lotions are expected to be used all over the body.
Calculated use: $8 \times 1 \text{ grams / day} = 8 \text{ g/day}$.

D.2 Data sheet on the product is available.

D.3 Assessment of compliance with the EU Cosmetic Directive:

The product, labels and safety data sheet complies with
the EU Cosmetics Directive.

D.4 Acknowledgement of available information:

All needed information for this safety assessment has been available.



Example: Summary of the Safety Assessment:

E: Summary:

Extract of the Safety assessment on XX Body LOTION

E.1 Margin Of Safety:

According to the available data (see references*), the Margin Of Safety is > 100 for all ingredients and accordingly complies with the guidelines from SCCS.

E.2 Danger indication of ingredients:

According to the revised Cosmetic transparency act, customers are entitled to insight into the hazardous ingredients in a cosmetic formula.

The following ingredients in this formulation are regarded as hazardous according to the supplier or self evaluation.

Ingredient:	CAS	%	Danger Indication
Ceteareth-20	68439-49-6	0-1	Xn, R 22-41
Phenoxyethanol	122-99-6	0-1	Xn, R 22-41



Summary of the Safety Assessment

E.3 Perfume:

No perfume is present in this product.

E.4 Reports on adverse effects:

There have been no reports of adverse effects from this formula.
The product is very mild to the skin, see ref F.4.

E.5 Period After Opening, Microbiology:

This formula has been tested and accepted in accordance with the European Pharmacopoeia 6.0 2008: Microbiological quality of pharmaceutical preparations for topical application.

Criteria passed: A level by $\text{pH} < 6$.

It is a general experience that this test Criteria is advantageous for a safe production. It is also useful for accepting a long term PAO if wanted.

E.6 Stability experience:

This formula shows good stability data.

E.7 Evaluation of conducted testing of the final product:

Xx Lotion has been tested in the yyyy test and has been evaluated as mild*. See ref*.



Special data information

- For the Swedish Astma och Allergi Förbundet:
Scientific information on adverse effects/
allergic effects from ingredients.
- For Ecological labeling:
Demands on plant species, part of plant, grow
location and conditions, processes, amount of
raw material used for extraction.....
- Example: Excel file from <http://www.natrue-label.com/certification/application-for-certification/raw-material-documentation-files.html#c480>



Thank you for listening!

- SIMPLIFICATION OF COSMETICS DEVELOPMENT?
- SIMPLIFICATION is often a matter of using suitable tools and systematic work.
- 20 minutes..
- I prefer a 2 days workshop with your development team.