IS THERE A "GOLD STANDARD" ?

CURRENT SITUATION

➢ **TESTING FOR SKIN SENSITISATION : INTEGRAL PART OF MOST "VERTICAL" EU LEGISLATIONS REQUIREMENTS**

- Chemicals
- Biocides
- Plant protection products
- Cosmetics
- Pharmaceuticals
- Detergents
- Food additives

➢ **SUBSTANCES MUST BE SAFE TO USE**
→ **ALTERNATIVE METHODS : SAME OR HIGHER LEVEL OF SAFETY**

➢ **USED FOR**
- HAZARD DETERMINATION

→ **CLASSIFICATION** } **- GHS (global harmonisation scheme), inc Cat 1A and 1B**
→ **LABELLING** } **- Critical to distinguish significantly sensitising substances from non-sensitising ones***

- RISK ASSESSMENT : RELATIVE POTENCY

**R43 : may cause sensitisation by skin contact*

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WHAT IS A "GOLD STANDARD" ?

IN DICTIONARIES :

Gold standard = Benchmark = point of reference - serving as a standard by which others may be measured or judged

Gold standard = test/dataset with 100% sensitivity and 100% specificity..... **not realistic**

... Evaluated against definition ... should be **interpreted in the context of** history, physical findings and other test results ...

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ACTUAL METHODOLOGY

IN VITRO TESTING

- SKIN PENETRATION **
- PEPTIDE REACTIVITY **
- DANGER SIGNALS **
- SURFACE MARKERS **

NON - INTACT IMMUNE SYSTEM

KEY COMPONENT(S) OF IMMUNE REACTION

→ 1 read-out : too simple

→ > 1 read-out : battery → STRATEGY

→ suitable for cosmetics

** Refinement*
Reduction

*** Replacement*

IN VIVO TESTING

IN MAN

HRIPT

IN ANIMAL

- BUEHLER
- GPMT
- LLNA*

INTACT IMMUNE SYSTEM

→ HRIPT, Buehler, GPMT :
1 subjective read-out,
ethical issues

→ LLNA :
1 objective read-out,
not for cosmetics after 2013

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IS THERE A "GOLD STANDARD" ?

QUESTIONS

- AGAINST WHICH TEST OR DATA SET SHOULD NEW *IN VITRO* TESTS BE VALIDATED ? **THUS WHAT IS THE "GOLD STANDARD"?**

VALIDATION AGAINST :

THINK OF :

Structural data, chemical reactivity (irritancy), epidermal bioavailability (aqueous/lipidic systems), guinea-pig results, clinical data, experimental human data, presence of impurities, vehicle used, interfering substances (coloration), quality of test (positive control e.g. hexyl-cinnamic aldehyde, mercaptobenzothiazole) etc.

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QUESTIONS

- **AGAINST WHICH TEST OR DATA SET SHOULD NEW *IN VITRO* TESTS BE VALIDATED ? THUS WHAT IS THE "GOLD STANDARD"?**

  VALIDATION AGAINST :

  - **Human data ? Clinical evidence ?**
  - **GPMT data ?**
  - **LLNA data ?**

  } **considered as being equivalent (LLNA : first choice !)**

- **WHAT ARGUMENTS AND SCIENTIFIC DATA ARE AVAILABLE : PRO AND CONS TO USE AS THE GOLD STANDARD**
  - **LLNA alone ?**
  - **Open choice of LLNA / GPMT ?**
  - **Weight of evidence approach ?**
    (data from all available sources advocated by GHS)

- **FOR MANY CHEMICALS ONLY DATA FROM LLNA ARE AVAILABLE; WHAT IS THEN A WEIGHT OF EVIDENCE APPROACH ?**

  e.g. Are data such as SAR, general information on chemical class, on impurities, monomeric residue amounts sufficient ?

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