SC JOHNSON'S CONSUMER PRODUCT HAZARD EVALUATION PROGRAM USING ALTERNATIVE ASSAYS

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ABSTRACT

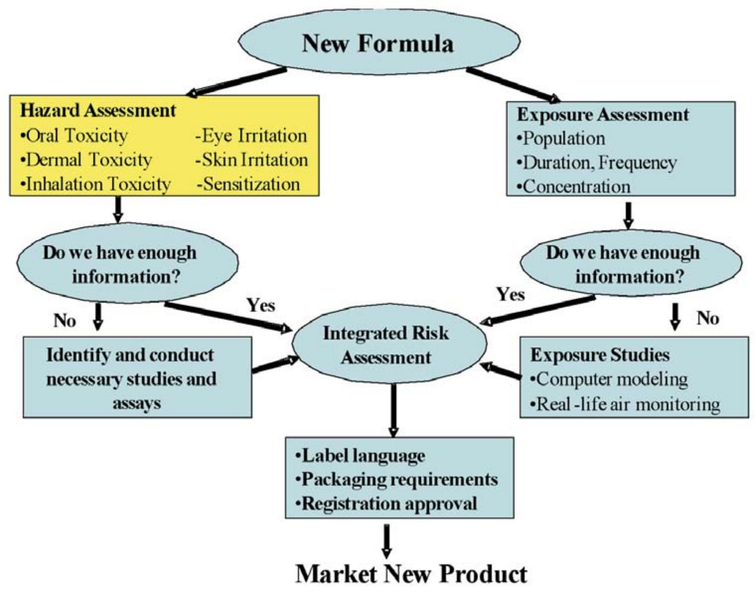
SC Johnson is a global consumer products company that manufactures a variety of household products that must be evaluated for human health hazards. For over 10 years, SC Johnson has conducted the necessary research to spearhead efforts to reduce the use of animals in the hazard assessment process. We routinely use alternative approaches such as the eye and skin irritation assays in a weight-of-evidence approach for hazard classification and labeling purposes for a variety of products. Assay choice and protocol considerations are defined so as to address possible modes of action on the target tissues. Specific benchmark formulations have been employed with each study to facilitate interpretation of the results. The Bovine Corneal Opacity and Permeability Assay (BCOP) has been used to assess ingredient synergies and the impact of various formulation components on the irritancy potential of the end-use products. The overall safety evaluation approach will be illustrated using two case studies. Alternative assays, especially the BCOP, are indispensable tools for assessing the potential irritancy of our products distributed worldwide while reducing the use of animals.

INTRODUCTION

The illustration above shows the breadth of products manufactured by SC Johnson (SCJ). With a corporate investment in alternative assays for over 10 years , SCJ has been able to launch many of these products without animal testing including air fresheners, personal care and most home cleaning products. Given this success with a wide range of household products, SCJ has helped establish a consortium of manufacturers to bring this same approach to the registration of antimicrobial cleaning products with the U.S. Environmental Protection Agency (EPA), see Poster P211.

Risk evaluation of consumer products involves a combination of inherent hazards and type and/or frequency of exposure. Because our products are formulated with well-characterized raw materials, the oral toxicity can be readily calculated. Dermal and inhalation toxicity are considered on a case-by-case basis as appropriate. In addition, for skin contact products, after a careful risk assessment is conducted human patch tests may be employed to assess allergenicity potential. This poster will deal primarily with the evaluation of eye and skin irritation. While the SCJ use of alternative assays is primarily for labeling decisions, alternative assays have also been found useful for optimizing formulations for mildness and understanding ingredient interactions.

GENERAL APPROACH TO NEW PRODUCT EVALUATION



SC Johnson uses alternative assays to evaluate eye and skin irritancy in a weight-of –evidence approach. In addition, the following evaluations are conducted as appropriate:

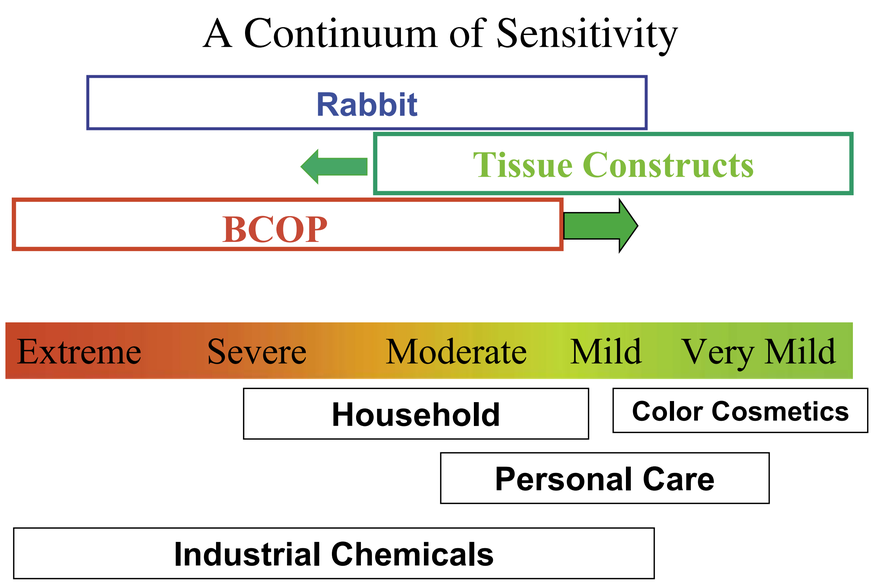
- Compare to previous *in vivo* / *in vitro* irritation studies conducted with similar products using our extensive database of over 1800 assays in various product categories.
- Research toxicology information on raw materials from published literature.
- Review of internal and external consumer experience with similar products.
- Conduct post-market surveillance.

ALTERNATIVE ASSAYS OF CHOICE FOR SC JOHNSON HAZARD EVALUATION

- Bovine Corneal Opacity and Permeability (BCOP) Assay
- Engineered human tissue constructs such as EpiOcular® and EpiDerm®
- Corrositex®
- Human patch and in-use tests to evaluate irritancy potency and allergenicity

BASIS FOR ASSAY CHOICE

The expected degree of irritancy and known chemical compatibilities for the tissue constructs drive test system and assay selection. Specific protocols may be selected to address specific modes of action as needed.



THE BCOP ASSAY - AN ASSAY OF CHOICE FOR EVALUATING HOUSEHOLD PRODUCTS

- Differentiates irritancy over a wide range.
- May be used to evaluate both aqueous and non-aqueous materials.
- Useful in assessing ingredient synergies.
- Useful in identifying formulation components that impact irritancy potential of end-use products.
- Addresses the major modes of action on the target tissue, i.e., membrane lysis, protein coagulation/denaturation, saponification, and alkylation/oxidative damage.

HOW DOES SC JOHNSON USE THE BCOP?

- To evaluate products including air fresheners, shave products, home cleaning products, insect repellents and raw materials.
- A series of standard protocols, developed over the past 10 years, is used to address the requirements of effectively evaluating our wide range of product classes.
- Concurrent controls are always used to assure the assay is performing as expected.
- Concurrent benchmarks are also employed.

IMPORTANCE OF BENCHMARKS

- SCJ has utilized concurrent benchmarks for over a decade (Ippolito et al., 1999).
- Benchmarks are critical to the successful use of *in vitro* alternative assays because they afford a point of comparison.
- Benchmarks should be chosen carefully based on:
  1. Chemical similarity to the test material
  2. Previously characterized behavior in the assay of choice
  3. Irritancy potential is well supported with data

HISTOLOGY IS A VALUABLE ADJUNCT TO THE BCOP ASSAY

- SCJ has been a corporate leader in emphasizing the use of histology in product hazard evaluation.
- Histological preparation and sectioning of the bovine cornea is a very helpful third endpoint in the BCOP.
- Histology provides valuable information concerning the depth and type of injury (See Poster P226 for illustrations of the usefulness of histology).

CASE I: ASSESSING INGREDIENT SYNERGY IN A BLEACH-CONTAINING CLEANER

The following table is an example of how SCJ used the BCOP Assay to evaluate bleach-containing cleaning products.

Composition Description	Exposure Time	Post-Exposure Time	*In Vitro* Score
Solution A: 1% NaOCl, standard bleach dilution (pH 12)	**5 minutes** 10 minutes 10 minutes	**4 hours** 4 hours 20 hours	**3.0** 13.7 28.0
Solution B: 0.5% citrate-buffered anionic surfactant (pH 6)	**5 minutes** 10 minutes 10 minutes	**4 hours** 4 hours 20 hours	**-2.1** -2.8 0.3
Solution C: 0.5% anionic surfactant with 0.25% NaOH (pH 13)	**5 minutes** 10 minutes	**4 hours** 4 hours	**7.5** 33.8
Solution D: 1% NaOCl, 0.5% anionic surfactant and 0.25% NaOH (pH 13) generic bleach cleaner	**5 minutes**	**4 hours**	**73.2**

- This table illustrates that the irritancy associated with individual components is not always additive. In the example above, the irritancy of Solution (Sol.) D greatly exceeded what was expected from its components, Solutions (Sols.) A and C.
- Note that a 5-minute exposure with Sols. A or C resulted in very low *In Vitro* Scores, but when combined as Sol. D, the *In Vitro* Score is quite high, showing that the combination was synergistic.
- Note the progressive damage over Post-Exposure time with Sol. A showing that the tissue damage from bleach solutions may not be immediately manifested (Maurer et al., 2001).
- Note the impact of the alkaline component in Sol. C compared with Sol. B, especially at the 10-minute exposure and the 4-hour Post-Exposure times.

CASE II: EFFECT OF SOLVENTS ON IRRITANCY OF AN INSECT REPELLENT

The following table illustrates how the BCOP Assay was used in a product development project at SCJ.

	Opacity	Permeability	BCOP Score	EPA *in vivo* Category
Repellent A (10% A.I.*, 88% ETOH, 2% other)	30.0	1.927	58.9	I
Repellent B (10% A.I., 90% BCAH**)	7.0	0.021	7.3	III
Repellent C (10% A.I., 50% volatile silicone, 40% ETOH)	45.7	2.532	83.6	I
Repellent D (10% A.I., 50% polymeric silicone, 40% ETOH	12.0	0.024	12.4	II

*A.I. = Active ingredient
**BCAH = Branched chain hydrocarbon

Judging irritancy potential solely on the basis of the irritancy of the active ingredient may be misguided. In the example above, all of the repellent formulations contained the same amount of active ingredient (A.I.), but the solvent vehicles were different resulting in dramatic differences in irritancy.

It is important to remember that the choice of vehicle can drive the irritancy potential because the vehicle may significantly alter the presentation and penetration of the A.I. to the target tissue.

CONCLUSIONS

- SC Johnson relies on alternative assays to make hazard evaluations and labeling decisions for a wide array of home and personal products.
- SC Johnson has developed an extensive database containing over 1800 *in vitro* studies on a variety of products, sparing thousands of animals.
- While labeling decisions are the most common use of alternative assays in the SC Johnson program, they have also been used to optimize formulations for mildness as part of the product development process and to evaluate ingredient interactions in mixtures.
- As part of an integrated weight-of-evidence approach to hazard evaluation, alternative assays for irritancy potential have enabled SC Johnson to greatly reduce the need for animal testing.
- The adoption of this approach to hazard evaluation for antimicrobial cleaning products will further reduce the need for animal testing.

REFERENCES

Ippolito, D.L., Connolly, P.L., Swanson, J.E., Lloyd, P.H., Raabe, H.A. and Manderfield, C.E. (1999). A longitudinal analysis of benchmark and control values in the BCOP Assay. **The Toxicologist** 48(1-S):337.

Maurer, J.K., Molai, A., Parker, R.D,, Li, L., Carr, G.J., Petroll, M.W., Cavanagh, D.H., and Jester, J.V. (2001). Pathology of ocular irritation with bleaching agents in the rabbit low-volume eye test. **Toxicological Pathology** 29(3):308-319.