Direct Toxicological Assessment of Mixtures Causing Skin Irritation

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INTRODUCTION

In developed countries, 5-20% of the population suffers from contact dermatitis. Skin irritation is caused by mixtures of hazardous processing chemicals released from the clothing, footwear, bedding, cosmetics, toys, means of skin protection etc. These mixtures may contain hundreds of chemicals. Even minor fluctuations of initial ingredients and parameters of manufacturing technology can change the composition of the mixture. Many chemicals involved in the manufacturing process are present in the mixtures in residual quantities in concentrations below the detection level. There are additive and synergistic interactions between the chemicals. Although mixtures are generated, their composition is qualitatively and quantitatively not fully known. To assess the risk of skin irritation and offer an acceptable level of protection such mixtures must be tested directly.

METHODS AND MATERIALS

The Bull Spermatozoa Video Image Cytotoxicity Test was used to assess toxicity of various products. Test method work flow is presented in Table 1. Spermatozoa suspension motility measurement and toxicity index (I_t) calculation were performed by Videoimage Cytoxicity Analyzer (Fig. 1.) The test method has a short time duration of 2.5 hours and the ability to evaluate non-sterile extracts. The testing procedure is automated and mixture toxic effect is tracked in real-time. It is known that cytotoxicity and irritation test results are correlating closely. The test method is more sensitive and allows to quantify the risk of skin irritation. You can select products for people with increased sensitivity of the skin. Test method is 20 times faster and 25 times cheaper than other cytotoxic test methods. That eliminates severe limitations of whole mixture approach and makes it possible to test large volumes of product samples. To compare whole mixture and component based approaches thousands batches of finished products have been tested.

RESULTS

When the mixture contains residual amounts of chemicals at concentrations below the threshold for detection whole mixture testing has no alternative, component based approach simply gives a wrong result (Table 2). Typically about 3% of the production adopted by component based approach is rejected by whole mixture testing. Exception - medical gloves not treated with MPXX™ – a special batch cleaning technology. In this case, 96% of the products can cause skin irritation.

CONCLUSIONS

Whole mixture testing of raw materials and technological processes eliminates the possibility of toxic products. Application of the direct toxicological assessment of mixtures for several years has shown that it is an effective filter of products capable to cause skin irritation. The results obtained are closely correlated with the identified skin irritation among the population. The test method used is low cost, robust, proven and can be easily implemented on location.

Table 1. Bull spermatozoa video image cytotoxicity test work flow

Time, h:min	Procedure
00:00	Thaw one dose of bull spermatozoa suspension in glucose-citrate medium, 40 °C ↓
00:10	Prepare test-tubes containing 0,4 ml either of test sample or blank (glucose-citrate medium), 37 °C Per test-tube, add 0,1 ml of bull spermatozoa suspension, 37 °C Place samples into capillaries, 37 °C ↓
00:20	Measure bull spermatozoa suspension motility in 9,5 min interval, 37 °C ↓
02:50	Calculate toxicity index, and variation coefficients

Fig. 1. Videoimage cytotoxicity analyzer

Table 2. Medical gloves. Component based approach and whole mixture approach test results.

Component Based Approach					Whole Mixture Approach	
№	Type of Chemical Residue	Detection Limit (µg/g)	Result	Conc-lusion	I_t,%	Conc-lusion
1	Buthylated hydroxyanisole (BHA)	10	ND	EXTRACT IS NOT TOXIC	33,5	EXTRACT IS TOXIC
2	Buthylated hydroxytoluene (BHT)	10	ND			
3	Diphenyl Guanidine (DPG)	10	ND			
4	Diphenyl Thiourea (DPT)	10	ND			
5	Mercaptobenzothiazole (MBT)	10	ND			
6	Tetramethylthiuram disulphide (TMTD)	10	ND			
7	Zinc dibutyldithiocarbamate (ZDBC)	10	ND			
8	Zinc dimethyldithiocarbamate (ZDMC)	10	ND			
9	Zinc mercaptobenzimidazole (ZMBI)	10	ND			
10	Zinc mercaptobenzothiazole (ZMBT)	10	ND			
11	Zinc pentamethylenedithiocarbamate (ZPMC)	10	ND			
12	Zinc diethyldithiocarbamate (ZDEC)	2	ND			
13	Other chemical residues	-	ND			

ND - not detectable