PS 1554 L'ORéAL COMMITMENT IN THE DEVELOPMENT, EVALUATION, AND VALIDATION OF SCREENING AND TESTING APPROACHES CONTRIBUTING TO THE 3RS.

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Dissemination of advances on alternative methods represents a step to promote alternatives to animal testing in line with the EU Cosmetics Directive. Over the past decade there have been great efforts in the industry or academic laboratories to develop alternative methods either in silico or in vitro that would comply with regulatory constraints. The implementation is still limited given that it is a great challenge to replace historical approaches by good and well predictive in vitro tests. L'Oréal has, based on these principles, developed test methods to screen and test potential effects on chemicals. We have focused initially on approaches for skin irritation, since this is an important endpoint for chemicals used in Cosmetics. A peer review on various aspects of alternative techniques was performed at all stages of the research and development with a focus on in vitro methods improvement of chemicals selection (screening) as well as quality testing. Following the development of the screening test, we have implemented some protocols (i.e. EpiSkin and SkinEthic RHE) for pre-validation and validation processes according to ECVAM's recommendations. To ensure quality and objectivity, experts from international committees oversee the content. Details of the approach will be presented for both skin corrosion and irritation with a set of 20 reference chemicals. Moreover, the poster described the practical approaches developed by L'Oréal in the areas of eye irritation (SkinEthic HCE defined with 90 chemicals), skin sensitization (MUSST assay optimized with 50 chemicals), phototoxicity and genotoxicity. By participating actively in relevant forums, L'Oréal and other industries continue to promote the development of new tools and methodologies as well as favor the acceptance of in vitro alternatives by authorities.

PS 1555 TOXICITY OF SMALL 50CC ENGINE EMISSIONS ON ORGANOTYPIC CULTURES OF RAT LUNG TISSUE: 2-STROKE, 4-STROKE ENGINES AND LUBE OIL (LO) QUALITY IMPACTS.

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Emissions small scooters is becoming a major health concern in Asia, Africa and in European cities. We aim to compare the impacts on the toxicity profiles according to engine technology, exhaust after-treatment and LO quality.
One 4-stroke and two 2-stroke scooters (50 cc bore) were run on dynamic benches EC47 cycle. Emissions were continuously monitored, sampled and hot-diluted prior being delivered to organotypic cultures of lung tissue under Air/liquid conditions for 3 hours. Lung tissue was evaluated for viability (ATP), anti-oxydant defenses (GSH, Catalase, SOD, GST, GPx, and GRED activity levels) and inflammation (TNFalpha secretion). 4-stroke engine had a moderate impact on lung tissue ATP, induced a marked GSH depletion and increased GPx activity. 2-strokes engine impacts varied according to after-treatment technology and LO. Low oxidation catalysis and mineral oil were found to be the worse situation inducing a marked ATP and GSH depletions, decreased activity of both Mn and Cu/ZnSOD and a decrease in TNF alpha secretion. High oxidation catalysis and semi-synthetic LO was found to be the best situation with only minor impacts on the above listed endpoints. Measurements of CO, NO, NO2, HC, and particulate matter (PM) showed that under warm engine conditions, 2-stroke engine with high oxidation catalysis and semi-synthetic LO was the least emitting situation for CO, HC and PM. 4-stroke engine proved to have intermediate emissions levels for CO, HC and PM. 2-stroke engine with low oxidation catalysis and mineral LO was found to be the worse situation for HC and PM. In conclusion : Emissions from small scooters may have detrimental impacts on lung tissue which may be highly reduced by the use of an oxidation catalyst and high quality LO. Suitable recently designed after-treatment strategies allow a very efficient reduction of 2-stroke engine emissions and toxic potential leading to an even lesser impact than for the 4stroke commercially available engine emissions.

PS 1556 HISTORY OF SAFE USE OF CRY1C PROTEIN.

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Plants expressing insecticidal Bt proteins (δ-endotoxin) are called Bt protected plants and are important in modern agriculture. These plants provide protection from insect pests and reduce the use of chemical pesticides. Due to high specificity of their mode of action, Cry proteins are not toxic to non-target organisms including insects, animals and human beings. We have examined the history of safe use of Cry1C protein and assessed its safety concern based on review of available literature which contains data from biosafety studies. In-silico homology search did not show similarity of Cry1C protein to known allergen or toxins. Sequence search did reveal 50% homology with other Cry1 proteins, especially to Cry1Ab, Cry1Ac and Cry1F which have been used in many commercial biopesticides and Bt crops. In-vitro study using simulated gastric fluid demonstrated that Cry1C protein was readily degraded at pH 1.2, and in heat stability study completely degraded at 100°C. In addition, animal feeding studies and allergenicity studies with plant products expressing Cry1C protein did not show treatment related effect. In conclusion, there is a reasonable certainty of no harm in inclusion of Cry1C protein in human food or animal feed.

PS 1557 LOCAL AND SYSTEMIC TOXICITY OF IMPLANTED ACCELERATOR-FREE POLYCHLOROPRENE-TYPE AND LATEX SURGICAL GLOVE MATERIAL.

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Asthma from latex gloves has prompted marketing of non-latex gloves including synthetic polyisoprene and polychloroprene surgical gloves. We have recently reported the presence of dihydroabietic (DHA) acid in these gloves, a compound that is extremely toxic in fish, but uninvestigated in mammals. Potential toxicity of DHA in surgical gloves is a concern because of potential exposure of patient tissues to DHA during extensive surgical procedures. Therefore, we investigated the hypothesis that the subcutaneous implantation of DHA containing polychloroprene gloves causes local and systemic toxicity. Mice (6/group) were subcutaneously implanted with 200 mg each of a polychloroprene glove or of a latex glove or 9 mg DHA, or underwent sham surgery, and were sacrificed 24 hr post-exposure. Implants were recovered for DHA analysis and tissues were processed for semi-quantitative histopathology. Latex caused multifocal and coalescent, moderate to marked necrosis of myofibers at the implantation site in all mice (pathology score, 7.16 ± 0.16; p=0.0048) and mild to moderate suppurative inflammation (5.66 ± 0.42; p=0.0048). The polychloroprene caused multifocal, mild to moderate, necrosis and mild inflammation in 3 of 6 mice. In the tissues beneath the implantation site (the epaxial myofibers and the adjacent fascia), significant changes were observed that varied by tissue and glove material. In peripheral blood, latex increased polymorphonuclear cells (37% ± 0.01; p<0.0001) and decreased lymphocytes (61% ± 0.01; p<0.0001) compared to sham controls. In bone marrow cytology, polychloroprene material decreased the myeloid to erythroid ratio (p=0.0767) and decreased the mature pool of myeloid cells in bone marrow sections. These results suggest the need for additional studies of local cytotoxicity and systemic hematotoxicity of surgical glove components.

PS 1558 DETAILED CHEMICAL COMPARISONS OF NEW AND OLD SERIES REFERENCE SMOKELESS TOBACCO PRODUCTS (STP).

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Some health experts recommend that smokers, who refuse to quit or refuse to use nicotine replacement therapies, switch to low TSNA smokeless tobacco products (STP). US-style moist snuff is the most popular STP, but has attracted criticism because of toxicological concerns. Use of *in vitro* assays (e.g., Ames; Rickert et al., Regul. Toxicol. Pharmacol. 2009 53:121-33)) to assess STP toxicity was of limited utility in distinguishing product types and brands within a type; and use of the *in vitro* mammalian GreenScreen HC assay (GADD45a-GFP reporter hosted in TK6 cells) (Lauterbach et al., Toxicol. Sci. 2010 114(1-S):2590) did not yield data that correlated with levels of known genotoxicants in the old series reference STP. However, the genotoxicity may stem from other sources such as sugar-amine reaction products as indicated by detailed GC-MS analyses of the STP. A new series of reference STP has just been released, and the moist snuff (CRP2 replaces 2S3), dry snuff (CRP3 replaces 1S2),and chewing tobacco (CRP4 replaces 2S1) products use the same recipes as did the earlier samples. While the routine analytical data on the new products are similar to those of the old, the detailed analytical data (GC-MS analyses (BSTFA/DMF extract of STP) were performed on an Agilent 6890 GC coupled with an Agilent 5972 MS with DB-5MS capillary GC column (25 m X 0.50 ?m film thickness and 0.25 mm ID)) was used. Our research shows differences in sugars, organic acids, and marker compounds for sugar-amine reaction products. Our findings indicate that toxicological properties of the new reference STP and

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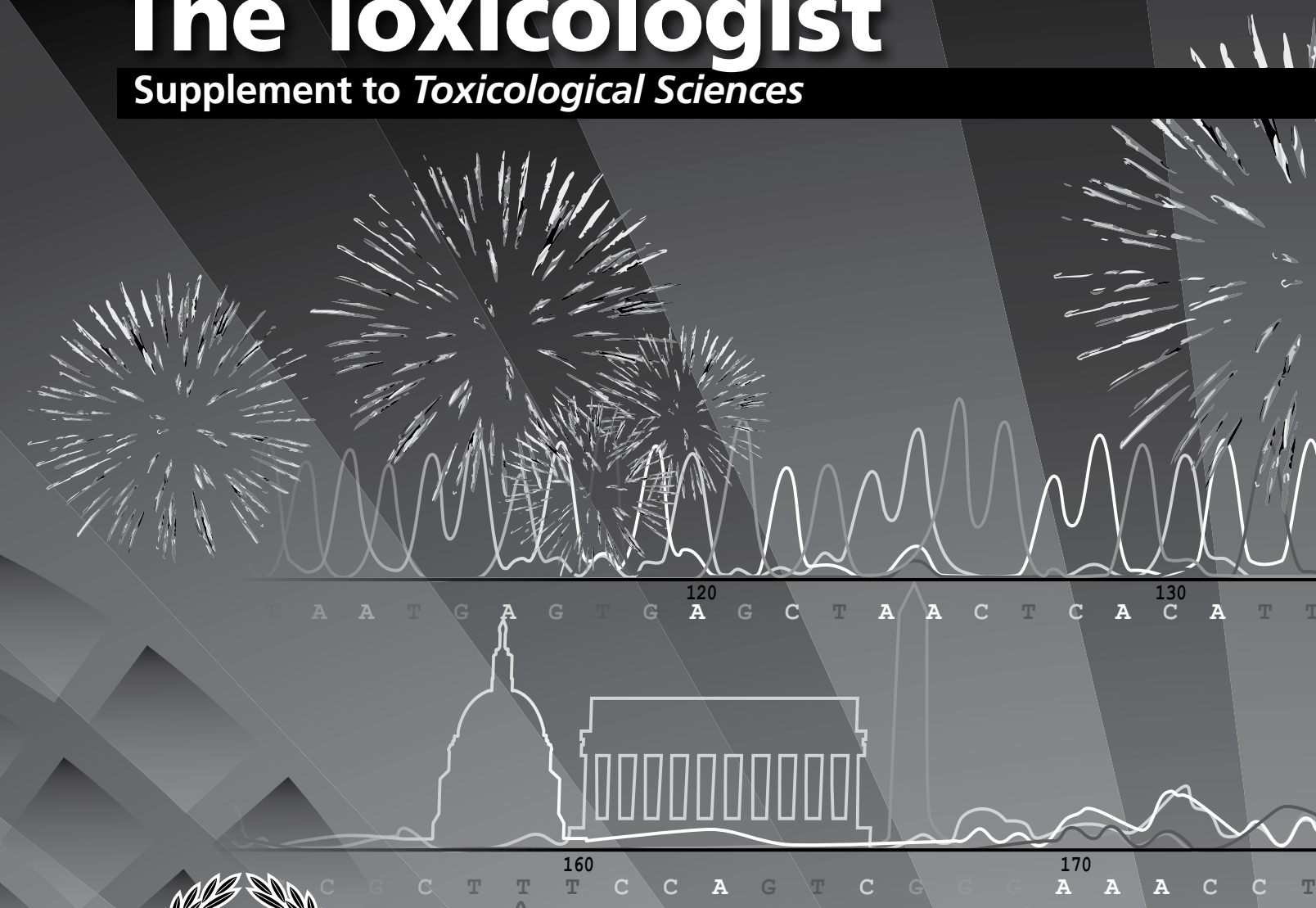

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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