tablishing default assumptions in cases where no data, or very little data, are available for a chemical. The document also describes how data from in-vitro or in-vivo dermal absorption studies may be interpreted in order to derive the "percent dermal absorption" value. Use of this guidance document since 2004 has however indicated further areas where better use of additional data can refine the procedures described in this guidance. Circumstances in which additional data could be incorporated in dermal penetration assessments, while remaining appropriately precautionary, are discussed for the following three areas: - Interpretation of in-vivo and in-vitro studies, considers only penetration of radiolabel, without assessment of the toxicological relevance of the radiolabel; There is limited consideration of the time course of absorption. The degree of dermal penetration is assessed against an "Acceptable Exposure Level" cited as mg/kg bw/day, but the potentially absorbed dose may be the result of multiple days of absorption; and, There is no adequate consideration of relative toxicity by oral and dermal routes. Comparison of oral and dermal LD50s is expressly discouraged, but there is no discussion of the merits of No Effect Levels from comparable oral and dermal toxicity studies. In conclusion, a dermal absorption value should not be derived without consideration of all relevant data, particularly comparable oral and dermal no effect levels (where these are available). This would help avoid unnecessary conservatism based on data which sometimes is less appropriate than toxicity data.

PS 1500 PROTECTING EMERGENCY RESPONSE PERSONNEL FROM CHEMICALS OF HIGH PRIORITY BY DERIVING IMMEDIATELY DANGEROUS TO LIFE OR HEALTH (IDLH) VALUES USING REFINED METHODOLOGY.

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The National Institute for Occupational Safety and Health (NIOSH) has been investigating methods to improve the derivation of Immediately Dangerous to Life or Health (IDLH) values. IDLH values are 30-minute atmospheric concentrations of any toxic, corrosive, or asphyxiant substance that, via inhalation exposure, poses an immediate threat to life or would cause immediate or delayed irreversible adverse health effects or would interfere with an individual's ability to escape from a dangerous atmosphere in the event of a respirator failure. We developed a process to prioritize IDLH development for high priority chemicals of specific interest to emergency response personnel (i.e., chemical terrorism agents or industrial chemicals subject to emergency or uncontrolled releases). The prioritization process included weighted scores to account for metrics of exposure potential, toxicity, and a variety of secondary considerations (such as toxicity data availability and existence of other acute exposure guidance values). We evaluated the impact of a refined weight of evidence approach described in our prior work on methods for developing IDLH values. The refined approach was applied to 20 case study chemicals from the list of agents identified by the prioritization process. The resulting preliminary IDLH values and the rationale for their derivation is presented and contrasted to the IDLH values that would have been developed using a default IDLH calculation approach. Lessons learned from these case studies are used to inform further refinements in the IDLH derivation methods as they apply to chemicals of interest to homeland security applications and emergency preparedness.

PS 1501 DRAFT REVISIONS TO THE GUIDELINES FOR AUTHORS OF DRINKING WATER HEALTH ADVISORIES.

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The EPA's Office of Water is updating the Guidelines for Agency authors for writing Drinking Water Health Advisories (HA). EPA's Office of Water develops HAs to identify non-regulatory concentrations of drinking water contaminants at which adverse health effects would not be anticipated to occur over specific exposure durations in children and adults. EPA develops 1-day and 10-day HAs for a 10 kg child, Longer-term HAs for a 10-kg child and for adults, and a Lifetime HA for adults. The draft updated Guidelines reflect new developments in risk assessment methods, including benchmark dose modeling, updated approaches to uncertainty factors (including chemical-specific adjustment factors), and the 2005 cancer guidelines. In addition, the draft updated Guidelines provide information on data sources and quality, guidance on key decision points, and references to other relevant EPA guidelines. Additional information is provided in the Guidance on consideration of life stages and endpoints relevant to the 1- and 10-day HAs. It is expected that the guidance, when finalized, will result in a more scientifically robust and consistent approach to the development of HAs. [The opinions herein are those of the authors and do not necessarily reflect the opinions of the U.S. Environmental Protection Agency (USEPA)].

PS 1502 EFFECT OF THE IMMUNOSTIMULANT γ-D-GLUTAMYL-L-TRYPTOPHAN ON THE EFFECTOR PHASE OF ASTHMA IN A GUINEA PIG MODEL.

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The dipeptide γ-D-Glu-L-Trp (SCV-07) is being tested as an immunostimulant in clinical and animal studies of cancer and infectious disease. Previous studies suggest that it stimulates Th1 immunity and reduces Th2 immunity. We hypothesized that this pattern of immunomodulation would be of benefit in controlling asthma. Objective: Determine if γ-D-Glu-L-Trp inhibits the effector phase in a guinea pig model of asthma. Animals were sensitized with ovalbumin(OVA) i.p. on day 0. On day 17-21, animals received daily i.p. injections of 1 or 10 μg/kg γ-D-Glu-L-Trp or vehicle phosphate buffered saline (PBS). On day 21 all animals were pre-treated with antihistamine to reduce the acute histamine component of the immediate bronchoconstrictor response that can be fatal. Animals were challenged with 1% OVA or saline (NSS) aerosol for 5 min. During OVA aerosol challenge, animals administered γ-D-Glu-L-Trp experienced significantly reduced cough, labored breathing and distress compared to PBS treated animals given OVA aerosol. γ-D-Glu-L-Trp did not affect the OVA specific IgG1 concentration in serum. Cell infiltration and lung injury were assessed 18 hours after OVA challenge. In animals challenged with NSS aerosol, γ-D-Glu-L-Trp significantly reduced total lung eosinophil peroxidase, suggesting that dipeptide treatment reduced the number of resident eosinophils and modulated eosinophil distribution. The OVA-induced increase in eosinophil infiltration into the lung was not inhibited by γ-D-Glu-L-Trp treatment. OVA challenge significantly increased red blood cell number in the BAL indicating lung injury occurred, and γ-D-Glu-L-Trp treatment markedly reduced this OVA-induced lung injury. Thus, these studies indicate that γ-D-Glu-L-Trp does not prevent eosinophil movement into the allergic lung, but significantly reduces the immediate allergic reaction and subsequent lung damage and may decrease the number of resident eosinophils in the lung. (Research supported by SciClone Pharmaceuticals, Inc.)

PS 1503 ASSESSMENT OF PROTEIN ALLERGENIC POTENTIAL IN MICE : RELATIONSHIPS BETWEEN IMMUNOGENICITY AND ALLERGENICITY.

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Assessment of the potential allergenicity of novel proteins is an important issue, particularly in the context of the safety of genetically modified crop plants. We have shown previously that the measurement of specific IgE production induced by systemic (intraperitoneal; ip) administration of proteins to BALB/c strain mice correlates with allergenic potential. In the current experiments, IgG and IgE antibody responses following ip exposure to a range of proteins have been measured by enzyme-linked immunosorbant assay (ELISA) and homologous passive cutaneous anaphylaxis (PCA) assay, respectively. Intraperitoneal administration of proteins not associated with allergic responses such as potato lectin and purified potato protein stimulated vigorous IgG antibody responses but failed to stimulate IgE antibody production, even at relatively high doses (10%). Exposure of BALB/c strain mice to protein enzymes such as lipolase and termamyl that cause IgE-mediated respiratory allergy induced relatively low titer IgG antibody responses, but comparatively vigorous IgE antibody production. Similarly, ip administration of the major cows' milk allergen β-lactoglobulin and the peanut allergen Ara h 1 stimulated weak IgG antibody responses and detectable specific IgE antibody production. In contrast, exposure to the peanut allergen Ara h 2 failed to provoke detectable IgG or IgE antibody. The relatively poor immunogenicity of both of the peanut proteins may reflect prior exposure to cross-reactive soy proteins in the diet. These data demonstrate the importance of monitoring IgG antibody responses, such that only the failure to observe detectable IgE antibody in the presence of a robust IgG antibody response is interpreted as a secure negative. Furthermore, respiratory sensitizing proteins may also be characterized as a function of induced IgE antibody responses following systemic ip exposure. Experience to date is encouraging that this method may represent a useful approach for the prospective identification of protein allergens.

PS 1504 CIRCUMVENTING THE HYPERSENSITIVITY LIKE REACTION ASSOCIATED WITH REPEAT DOSING OF A HUMANIZED MONOCLONAL ANTIBODY IN TRANSGENIC MICE.

T. Magee, M. M. Flaherty, M. Troutt, C. A. Rogers, T. K. MacLachlan, L. Andrews and R. D. Garman. *Genzyme Corporation, Framingham, MA.*

GMA161, an aglycosyl humanized monoclonal antibody that binds to hCD16A and hCD16B Fc-receptors, has been examined in models for treatment of idiopathic thrombocytopenic purpura. A human double transgenic (Tg) mCD16-/-,

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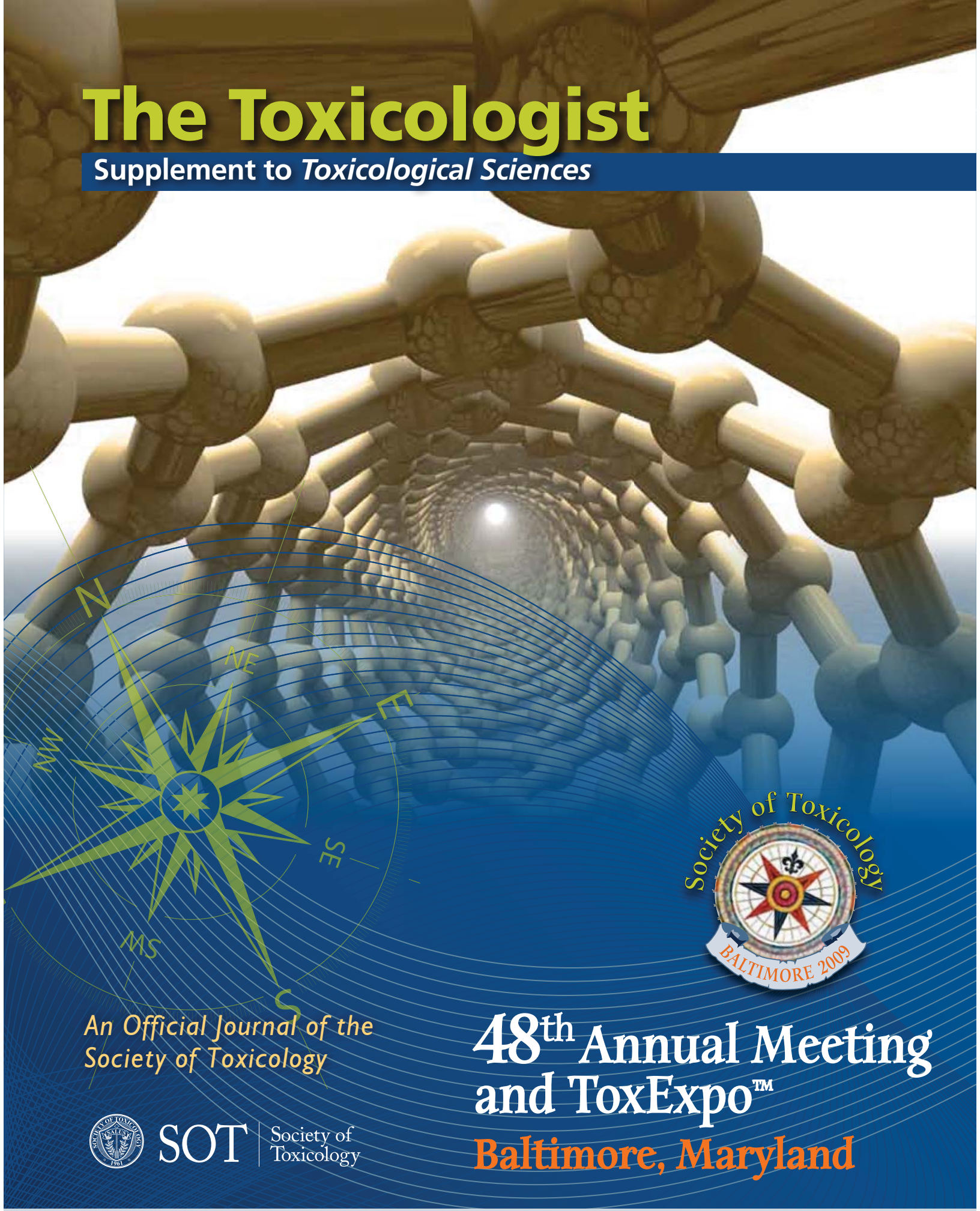

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