

Biomarkers of Exposure to Hexamethylene Diisocyanate

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Skin is a major target for occupational chemical exposure and associated disease. Diisocyanates are powerful skin sensitizers and a leading cause of occupationally induced asthma. We will investigate the relative importance of dermal and inhalation exposure in developing a systemic response to 1,6-hexamethylene diisocyanate (HDI) bound to keratin protein. Samples of epidermis and blood sera from a population of spray painters exposed to HDI will be analyzed for HDI-keratin adducts and antibodies, respectively, using an enzyme-linked immunosorbent assay (ELISA) to be developed in our laboratory. Antibodies specific for dermal and respiratory epithelium keratin adducts will allow investigation of the relative importance of dermal and inhalation exposure. The adducts will provide biomarkers of diisocyanate exposure. Correlation between airborne concentrations of HDI and antibodies to keratin adducts specific for dermal and respiratory epithelium will establish an exposure-dose relationship for HDI exposure. The dermal sampling technique coupled with an enzyme-linked immunosorbent assay (ELISA) represents a non-invasive method for measuring biomarkers. The modified peptide epitopes will be useful as well-characterized reference standards. The assays are intended expressly for use in humans, using biomarkers (modified keratins) that will be readily obtainable.

Implications: It is anticipated that results will yield insights into the correlation of dermal exposure, both with dermal dose and with potential dermal and systemic effects. Furthermore, this approach can be extended to define dermal exposure to any hazardous chemical that reacts with keratin in either occupational or environmental exposure conditions.

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Presentations:

Nylander-French, L.A., Gaines, L., Parron, V., Jayaraj, K., Klapper, D., Ball, L.M., and Gold, A. (2006). Biomarkers of exposure to hexamethylene diisocyanate. Making Sense of Human Biomonitoring Data: An International Workshop on Interpreting Biomonitoring Data, Minneapolis, MN, July 26-27, 2006.

Nylander-French, L.A., Parron, V., Jayaraj, K., Klapper, D., Ball, L.M., and Gold, A. (2007). Biomarkers of exposure to 1,6-hexamethylene diisocyanate. The U.S. Environmental Protection Agency (USEPA) and the International Council of Chemical Associations (ICCA) Public Health Applications of Human Biomonitoring Workshop, Research Triangle Park, NC, September 24-25, 2007.

Fent, K.W., Jayaraj, K., Ball, L., and Nylander-French, L.A. (2008). Quantitative monitoring and statistical modeling of dermal and inhalation exposure to hexamethylene diisocyanate monomer and oligomers in the automotive refinishing industry. American Industrial Hygiene Conference and Exposition, Minneapolis, MN, May 31-June 5, 2008.

Flack, S., Fent, K., Gaines, L., Thomasen, J., Ball, L.M., Whittaker, S., and Nylander-French, L.A. (2008). Quantifying 1,6-hexanediamine in the plasma of workers exposed to 1,6-hexamethylene diisocyanate. American Industrial Hygiene Conference and Exposition, Minneapolis, MN, May 31-June 5, 2008. Received the Best Student Poster Presentation Award in Biological Monitoring Session.

Thomasen, J., Fent, K., and Nylander-French, L.A. (2008). Field comparison of air sampling methods for 1,6-hexamethylene diisocyanate. American Industrial Hygiene Conference and Exposition, Minneapolis, MN, May 31-June 5, 2008. Received the Best of Session, First Place Student Poster Award.

Peer-reviewed publications:

Fent, K.W., Jayaraj, K., Gold, A., Ball, L.M., and Nylander-French, L.A. (2008). Quantitative monitoring of dermal and inhalation exposure to 1,6-hexamethylene diisocyanate monomer and oligomers. *Journal of Environmental Monitoring* 10:500-507.

Fent, K.W., Gaines, L.G., Thomasen, J., Flack, S.L., Herring, A.H., Whittaker, S.G., and Nylander-French, L.A. Quantification and statistical modeling of dermal exposure to monomeric and polymeric 1,6-hexamethylene diisocyanate. *The Annals of Occupational Hygiene*. (Accepted Pending Revisions).

Fent, K.W., Gaines, L.G., Thomasen, J., Flack, S.L., Herring, A.H., Whittaker, S.G., and Nylander-French, L.A. Quantification and statistical modeling of breathing-zone concentrations of monomeric and polymeric 1,6-hexamethylene diisocyanate. *The Annals of Occupational Hygiene*. (Accepted Pending Revisions).

Gaines, L.G.T., Fent, K.W., Flack, S., Thomasen, J., Ball, L.M., Richardson D.B., Whittaker, S., and Nylander-French, L.A. Urine 1,6-hexamethylene diamine (HDA) levels among workers exposed to 1,6-hexamethylene diisocyanate (HDI). *The Annals of Occupational Hygiene*. (In Preparation).

Flack, S., Fent, K.W., Gaines, L.G.T., Thomasen, J., Whittaker, S., Ball, L.M., and Nylander-French, L.A. Quantification and evaluation of a plasma biomarker in workers exposed to 1,6-hexamethylene diisocyanate (HDI). *The Annals of Occupational Hygiene*. (In Preparation).

Other publication(s): None to date.

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