QSAR FOR THE FIFTIETH ANNIVERSARY OF THE RD50

Yves Alarie, Ph.D.

Professor Emeritus

Environmental and Occupational Health Department

Graduate School of Public Health

University of Pittsburgh

February 4, 2016

**Description of the seminar**

A wide variety of airborne chemicals can stimulate trigeminal nerve endings (TNE) in the cornea and upper respiratory tract (URT). Sensory irritation (SI) of the eye and URT serves as a basis used by the American Conference of Governmental Industrial Hygienists (ACGIH) to establish guidelines, known as Threshold Limit Values (TLVs), for safe levels of exposure in the workplace. SI is currently the primary basis for at least 33% of the listed TLVs.

A bioassay was published in 1966 relying upon the respiratory reflex reactions due to stimulation of TNE during exposure to airborne chemicals, making it possible to measure the potency (abbreviated as RD50) of any airborne chemical as a sensory irritant.

It was then demonstrated that an excellent correlation existed between RD50 values and TLV values as the number of chemicals evaluated with this bioassay increased to 244 by 1993 and of which 89 of them had an established TLV based on SI.

In 2015, a QSAR was published using a database of RD50s for 145 chemicals, with excellent results.

This lecture will present the longitudinal nature of the research prior to 1966, then the results obtained with the bioassay by numerous investigators, the development of a computerized system for the bioassay thus extending its utility, a complete 2015 update of the RD50 database for volatile organic chemicals (VOCs), a complete 2015 update of VOCs with TLVs based on SI. Finally, the principles followed to obtain reliable estimates of RD50 with QSAR approaches, restricted to VOCs.

These updates, along with principles delineated by the OECD for QSARs development should permit obtaining reliable estimates of TLVs for new chemicals prior to introducing them in the workplace, as well as for storing and transporting them. Also, the computerized system is fully capable of recognizing, classifying and calculating the potency of airborne chemicals acting at any of the three levels of the respiratory tract: URT, conducting airways or alveolar level.