

# Banned in Nashville: The presentation that would have been too hot for the 62<sup>nd</sup> Tobacco Science Research Conference

John H. Lauterbach, Ph.D., DABT  
Lauterbach & Associates, LLC, Macon, GA 31210-4708 USA

## Abstract

Health experts have called for regulatory limits on several classes of cigarette mainstream smoke toxicants collectively known as the Hoffmann analytes. However, the 40+ analytes selected were those deemed important and measurable in the early 1990s. At the 61<sup>st</sup> Tobacco Science Research Conference (TSRC), we presented a paper (#38) suggesting certain dicarbonyls, cyanohydrins, and free radicals be added to the Hoffmann list before it was used for regulatory purposes (Lauterbach, 2007). In April 2008, Burns *et al.* (Tobacco Control 17:132-41) called for ceilings for certain Hoffmann analytes based on literature data. We had planned to present a critique of Burns *et al.* at the 62<sup>nd</sup> TSRC (Nashville, TN), but our abstract was reportedly rejected for our use of literature data and *in silico* estimates instead of new (and costly) experimental data. Our rationale for additions to the Hoffmann list and their relevance to potential regulation of cigarette designs will be given.

## FDA and cigarettes

Cigarette smoking is likely the most dangerous form of tobacco use. Public health authorities around the world have called for the end of smoking, restrictions on cigarette sale and use, ever increasing taxes on the product, much larger warning labels on the packs, and denormalization of cigarette sales and use. While these measures have been effective at reducing consumption, some experts believe that smoking-related diseases might be reduced if limits were placed on the deliveries of several classes of smoke toxicants (Stellman and Djordjevic, 2009; Burns *et al.*, 2008). Section 915 of the Family Smoking Prevention and Tobacco Control Act calls for the testing of cigarettes and the reporting of smoke constituents (FDA, 2009). However, the question of which constituents to test and how to test them remains to be answered.

In 2007, the Life Sciences Research Office report, "Scientific Methods to Evaluate Potential Reduced-Risk Tobacco Products," stated that lung cancer, chronic obstructive pulmonary disease, and cardiovascular disease were responsible for 90% of the total mortality and morbidity resulting from cigarettes (LSRO, 2007). If we use that statement as a guide, do the lists of cigarette mainstream smoke (MSS) analytes (so-called Hoffmann analytes), which date back to 1986 (Hoffmann and Wynder), make sense for setting limits on the smoke toxicants that need to be controlled in today's products? In many cases the answer is yes. There seems to be agreement on the presence of the tobacco specific nitrosamines (TSNAs) and the polynuclear aromatic hydrocarbons (PAHs) on the lists. The TSNA levels can be controlled to some extent by choices manufacturers make in tobaccos used for their blends and how those tobaccos are processed; however, the viable options for controlling PAH levels appear more remote.

The choice of other MSS analytes to measure [in addition to the obligatory total particulate matter (TPM), nicotine, and water (remember: tar = TPM – nicotine – water)] and smoking machine regimens are much more interesting discussions as is the discussion of the need for *in vitro* toxicological assays of MSS. Earlier version of the legislation that was passed and signed into law contained similar language. So the question of what to test, how to test it, the costs associated with testing have been around for a long time.

## Introduction

The Tobacco Science Research Conference (TSRC) has a long history as the venue for presentation of novel research involving tobacco and tobacco smoke. The Conference was originally known as the Tobacco Chemists' Research Conference, but the name was changed with the 52<sup>nd</sup> Conference in 1998 to reflect the changing nature of the presentations that included the biological and behavioral sciences as well the regulation of tobacco products. Until recently, most of the presentations have come from the tobacco industry and its major suppliers, universities with tobacco research programs, and governmental agencies with interests mainly in the agricultural aspects of tobacco. With consolidations and changes in the domestic tobacco industry, other organizations doing tobacco-related research began to take an increasing share of the program, often presenting a different focus on the chemistry and toxicology of the products. Lauterbach & Associates, LLC, has been one of these companies. We have presented over a dozen papers as an independent company, and many more as a tobacco company researcher. Thus, we were surprised when one of our papers for the 62<sup>nd</sup> TSRC was rejected.

## What to test and how to test it?

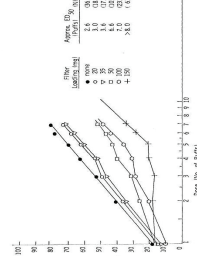
One thought would be to simply adopt the Health Canada regulations (Health Canada, 2004) including use of the Health Canada Intensive (HCI) machine smoking regimen and the Health Canada list of Hoffmann analytes and test methods. The HCI smoking regimen puffs the cigarettes harder and faster than most humans do. The regimen also calls for 100% blocking of any filter ventilation. Thus, under HCI conditions not only are most deliveries increased, the high smoke flow rates through the filter prevent the benefits of selective filtration with activated charcoal from being realized (Laugesen and Fowles, 2006). Data using the Health Canada methods (including use with Massachusetts and ISO puffing regimens) on over forty cigarette brand-styles were reported by Courts *et al.*, 2005.

However, when the Health Canada *in vitro* methods for mutagenicity and cytotoxicity were applied to the MSS from three reference cigarettes (KY2R4F, KY1R5F, CIM-7) generated under ISO and HCI conditions some unexpected effects were seen in the cytotoxicity results and in the hydrogen cyanide (HCN) determinations (Rickert *et al.*, 2007). It was hypothesized that cyanohydrins were being formed in the test system and that these were more toxic than the combined toxicity of the aldehyde and HCN. Also, it has been reported that up to 40% of MSS acetaldehyde and acrolein have been found in the particulate phase (Adam *et al.*, 2006). One possible conclusion from these findings is that the popular test methods for the determinations of MSS carbonyls and HCN need to be reworked to include additional species. It is also likely that MSS cytotoxicity is being caused by alpha-dicarbonyl compounds such as diacetyl, methyl glyoxal, and glyoxal, and these compounds should be added to the list of smoke analytes.

Free radicals in MSS are thought to be associated with smoking-related diseases. These highly reactive species were known to be in MSS at the time the lists of Hoffmann analytes were developed; however, expensive, dedicated instrumentation (ESR spectrometer) has been required to measure them (Valavanidis *et al.*, 2009). More recently, LC and LC-MS/MS methods have been used (Bartalis *et al.*, 2009; Flicker and Green, 2001). Thus, methods and instrumentation for determining free radicals are now similar to those used for the other Hoffmann analytes, and they should be added to the list of analytes.

## Revival time for resin filters?

CHARLOTTE PITCHER FOR RESIN FILTERS



Battista, S.P. New material for reducing catalytic potency of cigarette smoke. *Arthur D. Little report*, 1973

## Conclusions

Regulation of deliveries of cigarette mainstream smoke toxicants can be an important part of a strategy to control smoking-related diseases. However, the choice of toxicants to regulate and the smoking conditions used to determine toxicant deliveries need further study as does the inclusion of *in vitro* toxicological assays for cytotoxicity and mutagenicity.

## Literature cited

Adam T, Mitsche S, Steibel T, Baker RR, Zimmermann R. Quantitative puff-by-puff-resolved characterization of selected toxic compounds in cigarette mainstream smoke. *Environ Health Perspect*. 2007;115(11):1611-1617.  
Bartalis J, Zhao YL, Elora WJ, Payne JB, Wolstein JB. Carbon-centered radicals in cigarette smoke: acyl and alkylammonocarboxyl radicals. *Anal Chem*. 2009;81(2):631-41.  
Battista SP. New material for reducing catalytic potency of cigarette smoke. *Arthur D. Little report*, 1973.  
Burns DM, Dyring E, Gray N, Heat S, Anderson C, Sanner T, O'Connor R, Djordjevic M, Dresler C, Hainaut P, Jarvis M, Oppenhuizen A, Srai K, Mandated by the World Health Organization. *WHO Report on the Tobacco Epidemic*. 2009;12(2):1-14.  
Cigarette and Smoking Research Unit. *WHO Report on the Tobacco Epidemic*. 2009;12(2):1-14.  
Courts WH, Fowles AC, Laugesen S, Wang RA, Hoffmann DV. Smoke composition and preceding relationships for international commercial cigarettes smoked with three machine-smoking conditions. *Regul Toxicol Pharmacol*. 2005;41(3):185-227.  
FDA. Family Smoking Prevention and Tobacco Control Act. U.S. Code, Title 21, Section 851. <http://www.fda.gov/oc/21crr020101.htm>  
Flicker TM, Green SA. Comparison of gas-phase free-radical populations in tobacco smoke and model systems by HPLC. *Environ Health Perspect*. 2001;109(12):1381-90.  
Health Canada. Background on constituents and emissions reported for cigarettes sold in Canada - 2004. [http://www.hc-sc.gc.ca/tobacco/legislation/reginductconstitu\\_e.html](http://www.hc-sc.gc.ca/tobacco/legislation/reginductconstitu_e.html)  
Laugesen S, Fowles AC, Wang RA, Hoffmann DV. Carbon-centered radicals in cigarette smoke. *Anal Chem*. 2009;81(2):631-41.  
Lauterbach JH. What would you regulate if you were the regulator in charge of cigarettes. Program Booklet and Abstracts, 61<sup>st</sup> Tobacco Science Research Conference, Bethesda, MD, 2007.  
Life Sciences Research Office. *Scientific Methods to Evaluate Potential Reduced-Risk Tobacco Products*. 2007.  
Rickert WS, Trivedi AH, Momin RA, Wright WG, Lauterbach JH. Effect of smoking conditions and methods of collection on the mutagenicity and cytotoxicity of cigarette mainstream smoke. *Toxicol Sci*. 2007;99(2):235-53.  
Stellman RD. *WHO Report on the Tobacco Epidemic*. 2009;12(2):1-14.  
Valavanidis A, Vlachogianni T, Fiotakis K. Tobacco smoke: involvement of carcinogenic and synergistic components in respiratory inflammation, damage, carcinogenesis and synergistic carcinogenic effects. *Environ Health Perspect*. 2008;116(4):445-52.