Optimization of Nonanimal Test Methods for Next-Generation Tobacco Products Requires Scientific Cooperation Among All Stakeholders

Rodger D. Curren and Erin H. Hill

Dear Editor:

THE U.S. FOOD AND DRUG ADMINISTRATION'S (FDA) new regulations for e-cigarettes, cigars, and all other tobacco products offer an opportunity to employ the use of predictive *in vitro* tools to help determine the effects of these products on human health. Although a limited number of *in vitro* methods are currently used by regulatory agencies in the assessment of conventional tobacco products,¹ these new regulations—and the product types being assessed—provide the impetus to utilize these tools to a fuller extent. Many sophisticated models and approaches have been used within

tobacco companies for product stewardship purposes,^{2,3} but their utility in regulatory decision-making has yet to be fully demonstrated. In addition, approaches with *in vitro* methods, as with any new regulatory method, must be standardized and validated to ensure their robustness and uniform use. Although many articles in this Special Edition focus on the use of these new methods and models, the real challenge is the acceptance of these methods by the regulatory agency.

A way forward to achieve harmonization of the performance and regulatory applicability of new *in vitro* methods is collaboration between industry and the regulatory agency. To this end, the Institute for In Vitro Sciences, a nonprofit

TABLE 1. IIVS COLLABORATIVE WORKSHOPS

Name	Date	Publication
Informational Workshop I: In Vitro COPD Models for Tobacco Regulatory Science ^a	December 2014	Workshop report available for download at www.iivs.org Behrsing, et al. Assessment of in vitro COPD models for tobacco regulatory science: workshop proceedings, conclusions, and paths forward for in vitro model use. <i>Altern Lab Anim</i> 2016;44:129–166
Society of Toxicology—Ancillary Meeting: Workshop Report: In Vitro COPD Models for Tobacco Regulatory Science—Highlights and Paths Forward	March 2015	Discussion session only
Technical Workshop I: In Vitro Models for Goblet Cell Hyperplasia, Mucus Production, and Ciliary Beating Assays	June 2015	Pending completion of proof of concept testing
Society of Toxicology—Ancillary Meeting: In Vitro Models for Tobacco Regulatory Science: Collaborative Efforts in Respiratory Toxicology	March 2016	Discussion session only
Informational Workshop II: In Vitro Exposure Systems and Dosimetry Assessment Tools for Inhaled Tobacco Products	April 2016	Workshop report available for download at www.iivs.org

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Institute for In Vitro Sciences, Inc., Gaithersburg, Maryland.

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organization with a history of working in cooperation with both groups, has initiated a series of workshops to draw on the experience of industry and research institutions and to foster communication with the regulatory agency on the potential suitability of *in vitro* methods for regulatory decision-making. Through oral and poster presentations, the Informational Workshops allow the experiences of scientists from many fields to communicate with a broad audience, including government representatives. Follow-on Technical Workshops explore best practices among expert users and provide the information needed to design multilaboratory testing programs to standardize methodology. Dissemination of this information to the broader scientific community is a priority; therefore, proceedings from all workshops are published as both workshop summaries and in peer-reviewed journals (Table 1).

However, financial support for this collaborative program is difficult to obtain. As many academic and research institution representatives have restrictions on attending meetings sponsored by tobacco companies, direct funding from industry is not feasible. Although the FDA has a Small Conference Grants Program—which funded, in part, our first informational workshop—the meeting must be fully planned before the grant will be given. Therefore, an institution must risk holding the meeting on its own if the grant is not awarded. The science explored in the Technical Workshops is highly relevant and applicable; however, it does not reach the high bar of “innovativeness” to qualify for NIH grants. As the outcomes from these collaborative efforts are highly beneficial to both industry and regulators, new funding processes should be developed.

The successes of the first workshops support our view that cooperation from the regulatory agency, industry, and research institutions will lead to the optimization of nonanimal test methods and their eventual use for regulatory decision-making.

Author Disclosure Statement

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References

1. Manuppello JR, Sullivan KM. Toxicity assessment of tobacco products in vitro. *Altern Lab Anim* 2015;43:39–67.
2. Azzopardi D, Patel K, Jaunky T, et al. Electronic cigarette aerosol induces significantly less cytotoxicity than tobacco smoke. *Toxicol Mech Methods* 2016;26:477–491.
3. Zanetti F, Sewer A, Mathis C, et al. Systems toxicology assessment of the biological impact of a candidate modified risk tobacco product on human organotypic oral epithelial cultures. *Chem Res Toxicol* 2016;29:1252–1269.

Address correspondence to:

Erin H. Hill, President
Institute for In Vitro Sciences, Inc.
30 W. Watkins Mill Road, Suite 100
Gaithersburg, MD 20878

E-mail: ehill@iivs.org