The Food and Drug Administration Predictive Toxicology Roadmap and its Implementation

Public Hearing Request for Comments

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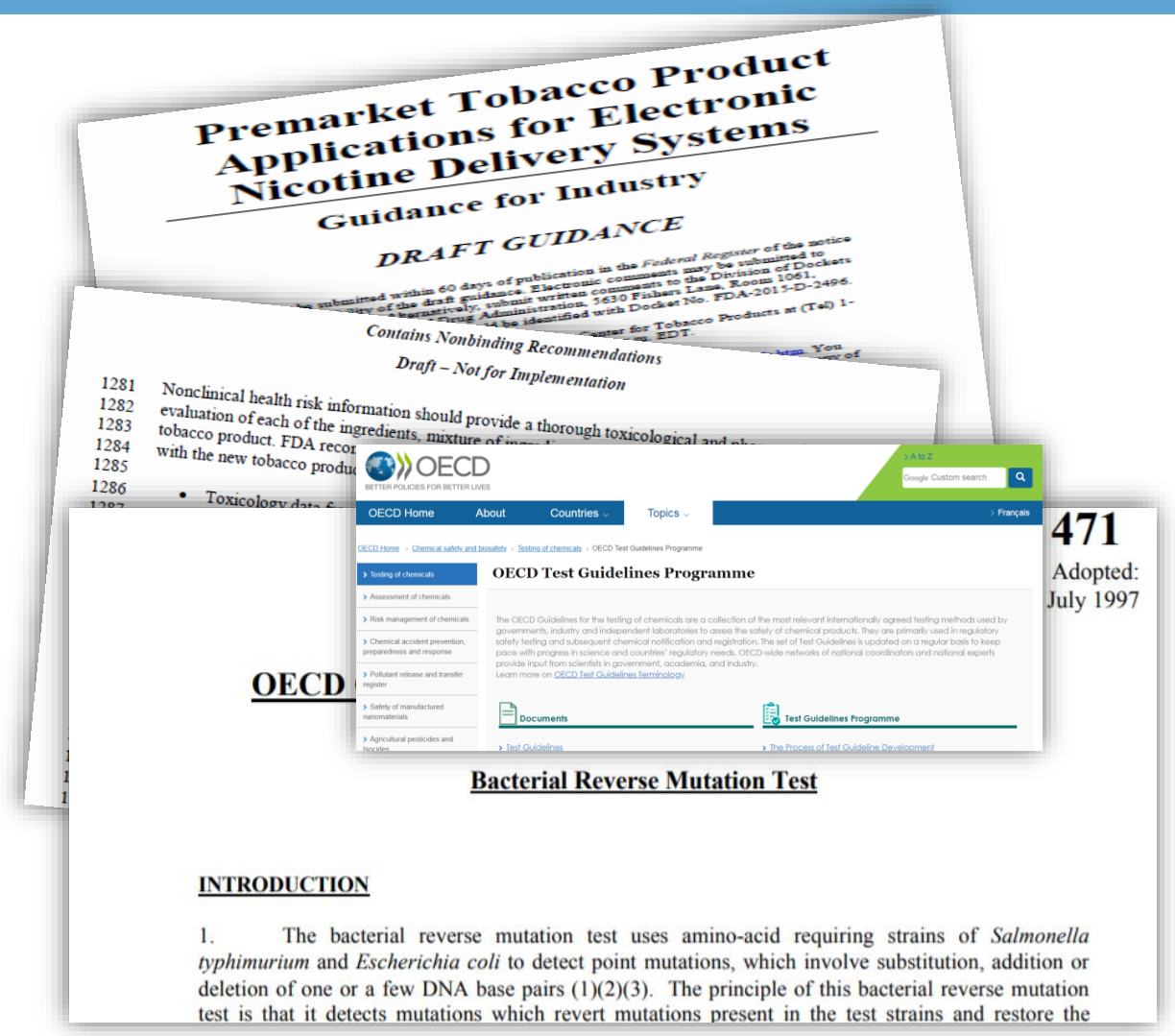
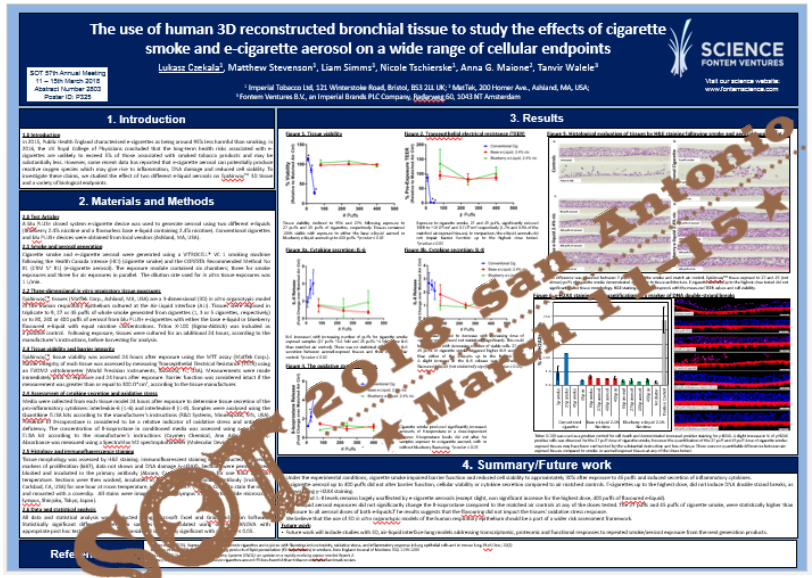
Limited Guidance

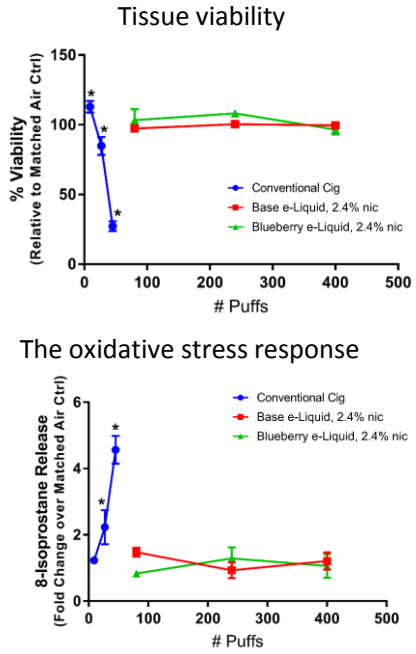


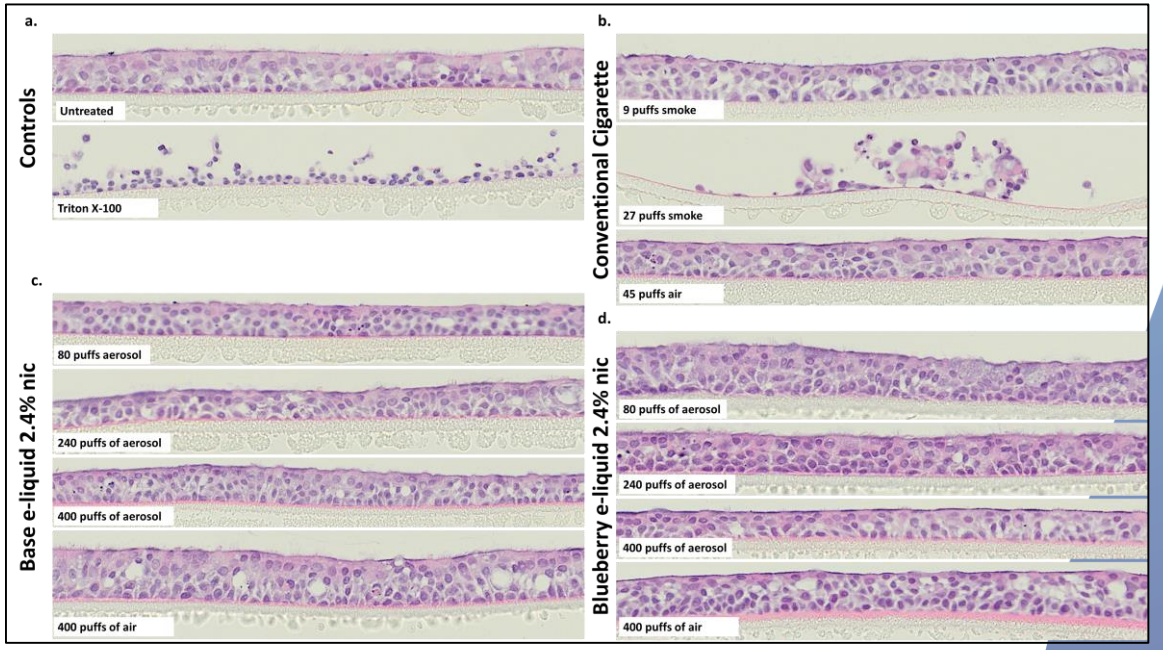
non-intense use conditions as described in section VI.H.1.a;'

- In vitro Toxicology studies (e.g.,genotoxicity studies, cytotoxicity studies);
- In vivo toxicology studies (to address unique toxicology issues that cannot be addressed by alternative approaches, and;
- Computational modelling of the toxicants in the

In vitro Pre-clinical Assessment- Novel Techniques







- This preclinical approach adds weight and mechanistic understanding of specific endpoints.
- Such techniques can also be conducted rapidly and be repeated and reproduced by other qualified laboratories.

In vitro Pre-clinical Assessment

fontem ventures

TT21C

OECD

In vitro regulatory toxicology

Ames

IVM

NRU

Novel human relevant *in vitro* assays

In silico modelling

Clinical samples

CVD endpoints	Cancer endpoints	COPD endpoints	Organ interactions	AOP Development	Pre-clinical and clinical bridging studies
Scratch wound	CTA	3D lung models	2 compartment models	Regional lung deposition	
Monocyte adhesion/ migration	Mechanistic Reporter Assay		Organ-on-a-chip	*In silico* modelling QVIVE	

Systems Toxicology approach

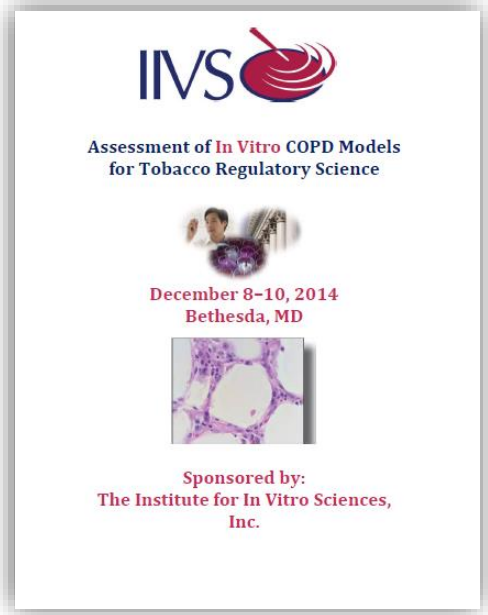
Current Challenges

- Limited Industry-FDA communication and collaboration
- Limited guidance on types and number of assays or tools required to complete an in vitro assessment
  - Inhibits uptake of assays
- No template process map for product assessment

Solutions

1. Collaboration

- Increased FDA and Industry collaborations (e.g. FDA input into the IIVS COPD Ring trial)
- Collaboration with CORESTA and relevant working groups
- Improve regular dialogue with industry. The journey must be taken together!



CORESTA - Cooperation Centre for Scientific Research Relative to Tobacco

Solutions

2. Research

Guidance required to build a testing framework centred on the use of new and emerging technologies

Use of reference compounds or product as an example which has been through this process

Fast track qualification process for New Assessment Methodology (NAMs)

Use of appropriate standards and positive and negative controls

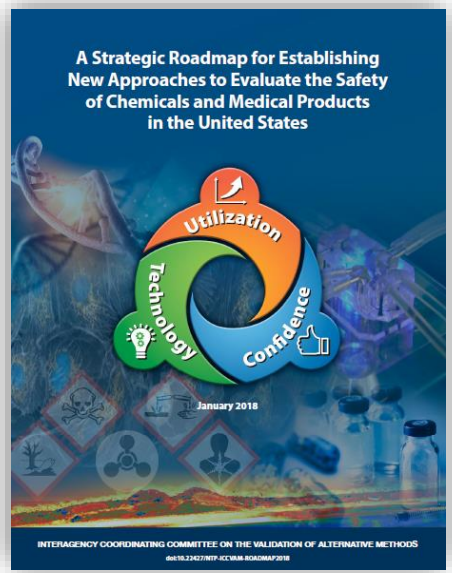
Improve and support the qualification process

Lack of qualified / validated methods for NAMs

Acceptability of NAMs by FDA e.g. Tox21 partners

ICCVAM 2018 Roadmap

“Provide clear language regarding the acceptance of NAMs. Industry stakeholders indicate that lack of clear guidance on the status of regulatory acceptance is a significant factor impeding the use of NAMs. Industries cannot be expected to use new methods if they are uncertain about whether the data will be accepted by regulators. To facilitate use by industry, agencies should provide clear guidance on the use and acceptance of data from NAMs”.



Fontem Ventures supports this statement and welcomes a two way dialogue with the FDA on our Harm reduction approach

ICCVAM :The Interagency Coordinating Committee on the Validation of Alternative Methods

Conclusions

Improve the open, clear and regular dialogue with industry

Expand on collaborations for example IIVS and CORESTA

FDA should release a clear process for the qualification of new assays for Product Assessment

Identify & fast track NAMs likely to be acceptable for next generation product assessment

FDA endorsement of human relevant *in vitro* approaches, supporting a TT21C vision

Animal testing is time consuming & lacks human relevance

Request for clarity on PMTA requirements for Next Generation Products

More Information

For more information on our science, please visit our science websites:

www.ImperialBrandsScience.com

www.FontemScience.com