The Food and Drug Administration Predictive Toxicology Roadmap and its Implementation

Public Hearing Request for Comments

Gary Phillips PhD | Principal Scientist
please note that the views and arguments presented in this paper have been designed to encourage and stimulate debate and do not necessarily reflect fontem ventures’ position

**Limited Guidance**

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**Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems**

**Guidance for Industry**

**Draft Guidance**

1. **Toxicology data from the literature**

   - Analysis of Constituents and other toxicants under both intense and non-intense use conditions as described in section VI.H.1.a;

2. **In vitro Toxicology studies** (e.g., genotoxicity studies, cytotoxicity studies);

3. **In vivo toxicology studies** (to address unique toxicology issues that cannot be addressed by alternative approaches, and;

4. **Computational modelling of the toxicants in the**
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.
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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!
## Solutions

### 2. Research

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<tr>
<th>Guidance required to build a testing framework centred on the use of new and emerging technologies</th>
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<td>Use of reference compounds or product as an example which has been through this process</td>
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<th>Fast track qualification process for New Assessment Methodology (NAMs)</th>
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<td>Use of appropriate standards and positive and negative controls</td>
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<th>Improve and support the qualification process</th>
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<td>Lack of qualified/validated methods for NAMs</td>
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<td>Acceptability of NAMs by FDA e.g. Tox21 partners</td>
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“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.
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

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

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