ST20: Responsible Practice in E-Vapour Products (EVP) Product Stewardship

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ALL Manufacturers’ Duties

- Care in product design, manufacture and marketing
- Product awareness & understanding
- Respond to new product information
  - Modify
  - Warn
  - Withdraw
- Held to standard of an expert
Responsible Practice
What does this mean for EVPs?

- Compliance with EUTPD II
- Conduct testing
- Adherence to National Standards
- Good Manufacturing Practices
- Information to consumers
- Impact to bystanders
Responsible Practice
Areas covered in this presentation

Responsible practice can be divided into 3 areas:

- Pre-market product stewardship
- Batch release
- Post-market product stewardship

Focus today on pre-market product stewardship
- Emphasis on testing approaches and strategies
“It is important to note that the GRAS provision applies only to food”

“None of the safety assessment programs for flavours, including the GRAS program, evaluate flavour ingredients for use in products other than human food”

“E-cigarette and flavour manufacturers and marketeers should not represent or suggest that the flavour ingredients used in e-cigarettes are safe because they have FEMA GRAS status”

FEMA: Flavour & Extract Manufacturers Association
GRAS: Generally regarded as safe
Risk Assessment of Ingredients Used in E-Liquids (2)

Tiered Approach

- Compositional breakdown of e-liquid
  - YES

- Ingredients are pharmacopeia / food grade
  - YES

- Reject any ingredients with CMR / respiratory sensitizer properties
  - YES

Conduct risk assessment:
- Inhalation data
- Route to route extrapolation
- TTC approaches
- in-silico predictive toxicology
  - YES

Investigate potential toxicity from thermal breakdown products
  - YES

Approve e-liquid for use
  - YES

Reformulate e-liquid
  - NO

CMR: Carcinogenic, Mutagenic or toxic to Reproduction
TTC: Threshold of Toxicological Concern
Device Quality Testing

A number of Guidelines already exist.
Aerosol Chemistry

What should be the focus?

From a regulatory & toxicological perspective the focus should be on nicotine, carbonyls and metals

Most of the other constituents are formation products of combustion *NOT* EVP aerosol

Tayyarah & Long (2014). Comparison of select-analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air
Particles may impact differential toxicity depending on where aerosol is deposited.
A number of assays exist:

- Ames reverse bacterial mutagenicity assay
- In-vitro micronucleus (IVM) assay
- Cytotoxicity – Neutral Red Uptake (NRU) assay
- IL-8 Assay – inflammatory cytokine
Biological Testing (2)
From 2D cell culture to ‘repeat dose’ 3D cell culture

Investigate multiple endpoints after aerosol exposure
Pre-market product stewardship

Summary

Risk assessment of ingredients & materials
- Performed by registered Toxicologist
- Ingredients pharmacopeia / food grade
- No CMRs / respiratory sensitizers

Device Quality Testing
- Stability testing: normal & accelerated
- Extractables & Leachables
- Microbiological testing

Aerosol chemistry & in-vitro toxicology
- Focus on nicotine, carbonyls & metals
- Particle size measurements & characterisation
- In-vitro biological testing
Thank you for your attention!

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