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

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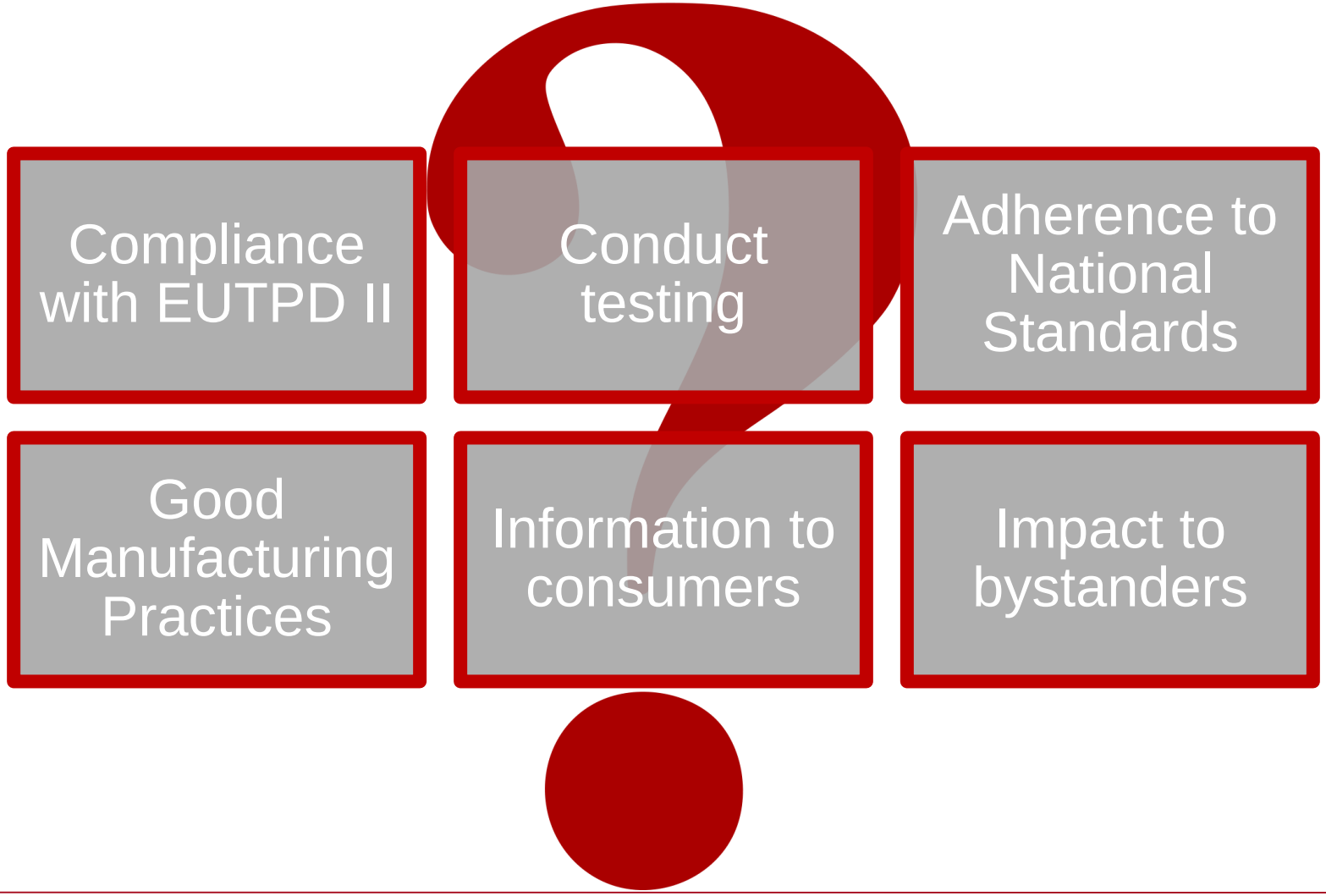
ALL Manufacturers' Duties

- 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?



Responsible Practice

Areas covered in this presentation

Responsible practice can be divided in to 3 areas:

Focus today on pre-market product stewardship

- Emphasis on testing approaches and strategies

Risk Assessment of Ingredients Used in E-Liquids

FEMA 2015 notification on e-Cigarettes

"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"

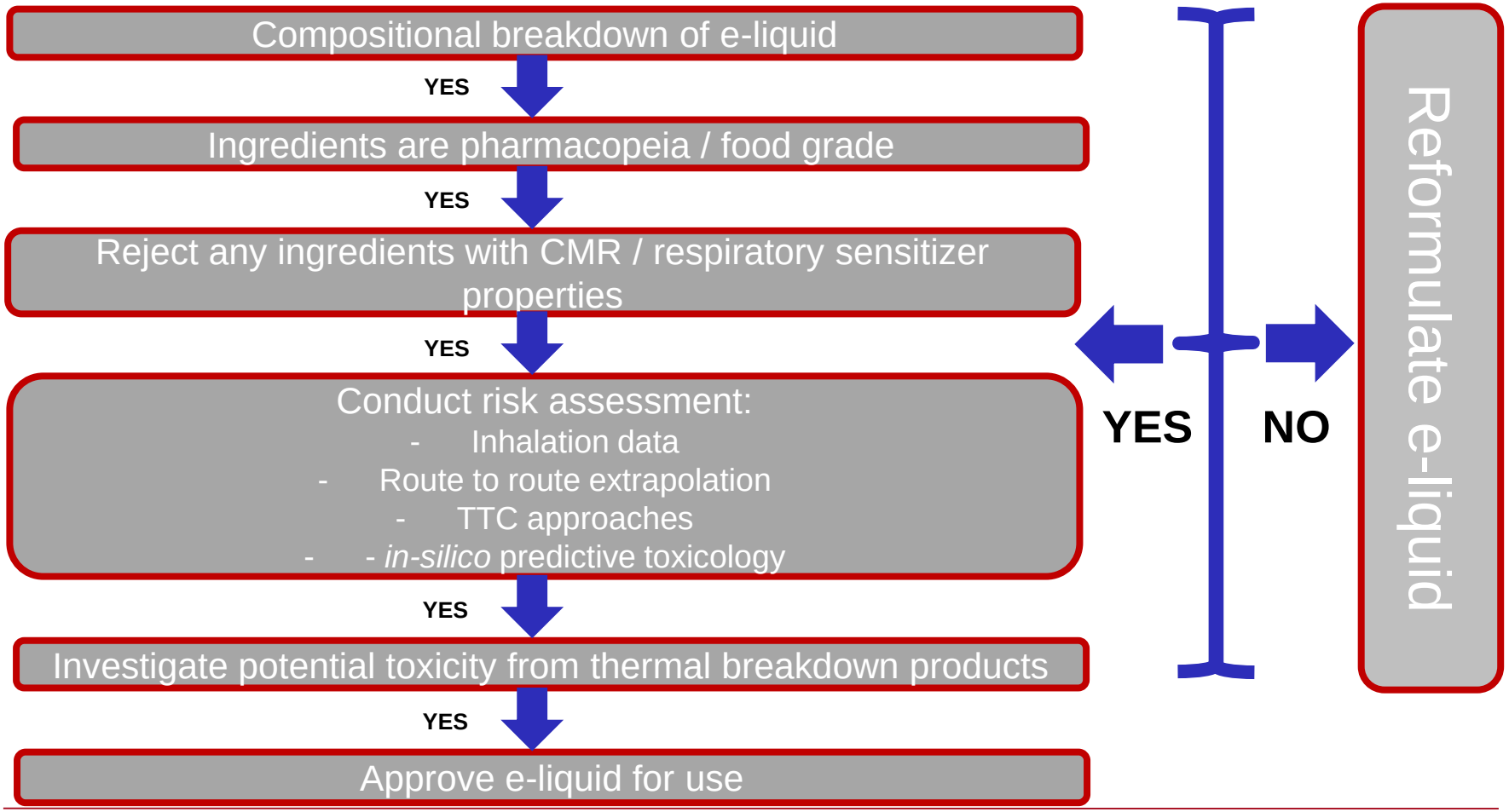
"E-cigarette and flavour manufacturers and marketeers should not represent or suggest that the flavour ingredients used in e-cigarettes are safe because they have FEMA GRAS status"

FEMA: Flavour & Extract Manufacturers Association

GRAS: Generally regarded as safe

Risk Assessment of Ingredients Used in E-Liquids (2)

Tiered Approach



EP/USP: European Pharmacopeia / United States Pharmacopeia

CMR: Carcinogenic, Mutagenic or toxic to Reproduction

TTC: Threshold of Toxicological Concern

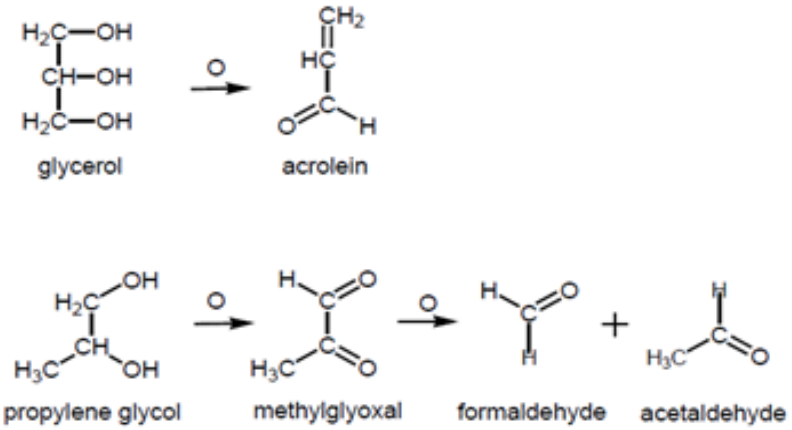
Device Quality Testing

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



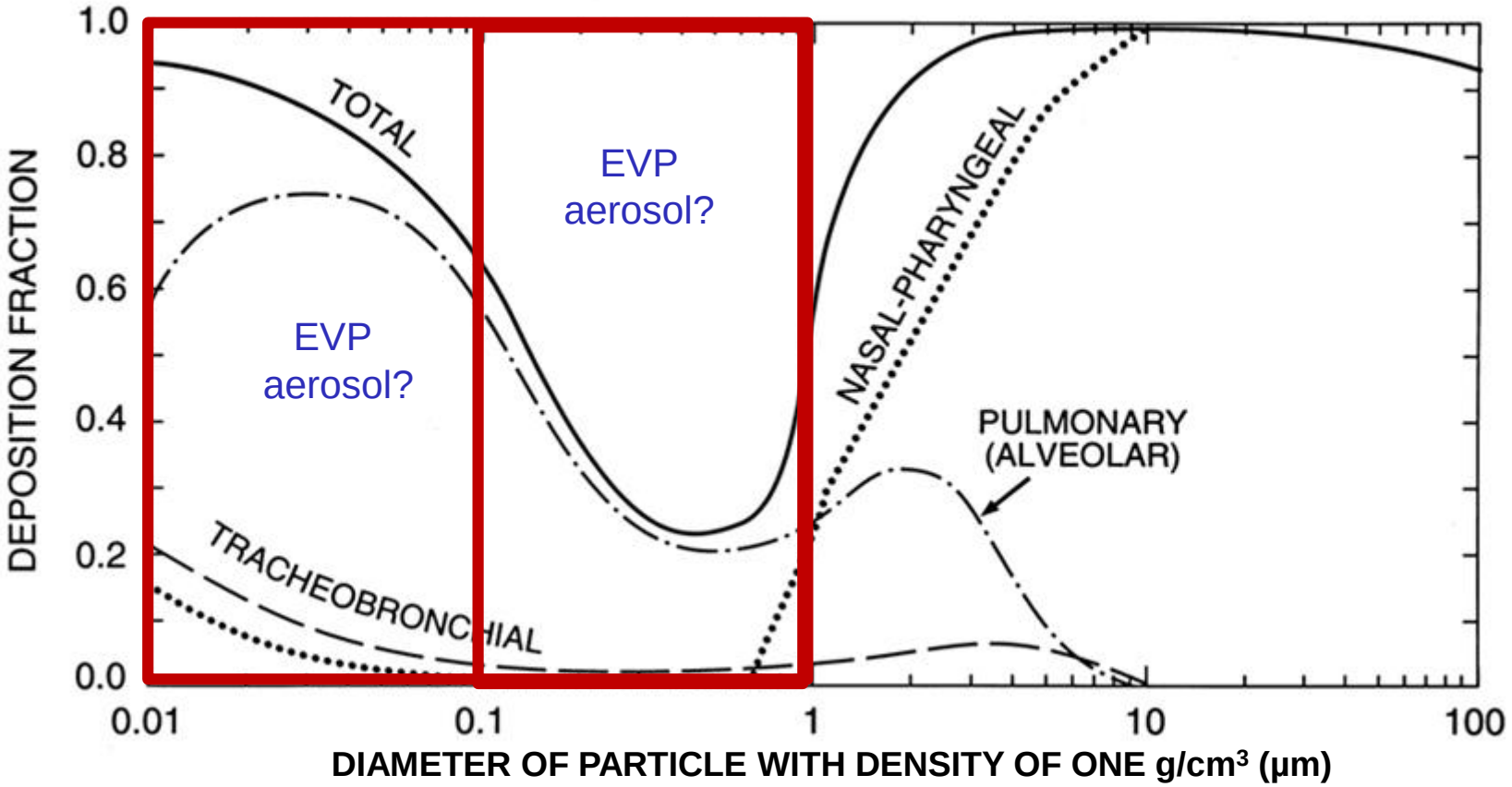
	CO	Carbonyls[a]	Phenolics[b]	Volatiles[c]	Metals[d]	TSNAs[e]	PAA[f]	PAH[g]	Sum
Marlboro Gold Box (mg/cig)	27	1.92	0.204	1.430	<0.00020	0.000550	0.000024	0.00222	<30.6 mg
L&B Original (mg/cig)	22	1.89	0.26	1.02	<0.0002	0.000238	0.000019	0.00219	<25.2
L&B Menthol (mg/cig)	20	1.81	0.17	0.94	<0.0003	0.000185	0.000017	0.00153	<22.9
blu CTD (mg/99 puffs)	<0.1	<0.07	<0.001	<0.001	<0.00004	<0.00002	<0.000004	<0.00016	<0.17
blu MMD (mg/99 puffs)	<0.1	<0.08	<0.001	<0.001	<0.00004	<0.00002	<0.000004	<0.00016	<0.18
blu CCHP (mg/99 puffs)	<0.1	<0.05	<0.003	<0.0004	<0.00004	<0.00002	<0.000004	<0.00014	<0.15
SKYCIG CTB (mg/99 puffs)	<0.1	<0.06	<0.0010	<0.008	<0.00006	<0.000013	<0.000014	<0.00004	<0.17
SKYCIG CMB (mg/99 puffs)	<0.1	<0.09	<0.0014	<0.008	<0.00006	<0.000030	<0.000014	<0.00004	<0.20
Air Blank (blu Set) (mg/99 puffs)	<0.1	<0.06	<0.001	<0.0004	<0.00004	<0.00002	<0.000004	<0.00015	<0.16
Air Blank (SKYCIG Set) (mg/99 puffs)	<0.1	<0.05	<0.0009	<0.008	<0.00006	<0.000013	<0.000014	<0.00006	<0.16

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

Particle Size Measurements & Characterisation

Why is this significant?



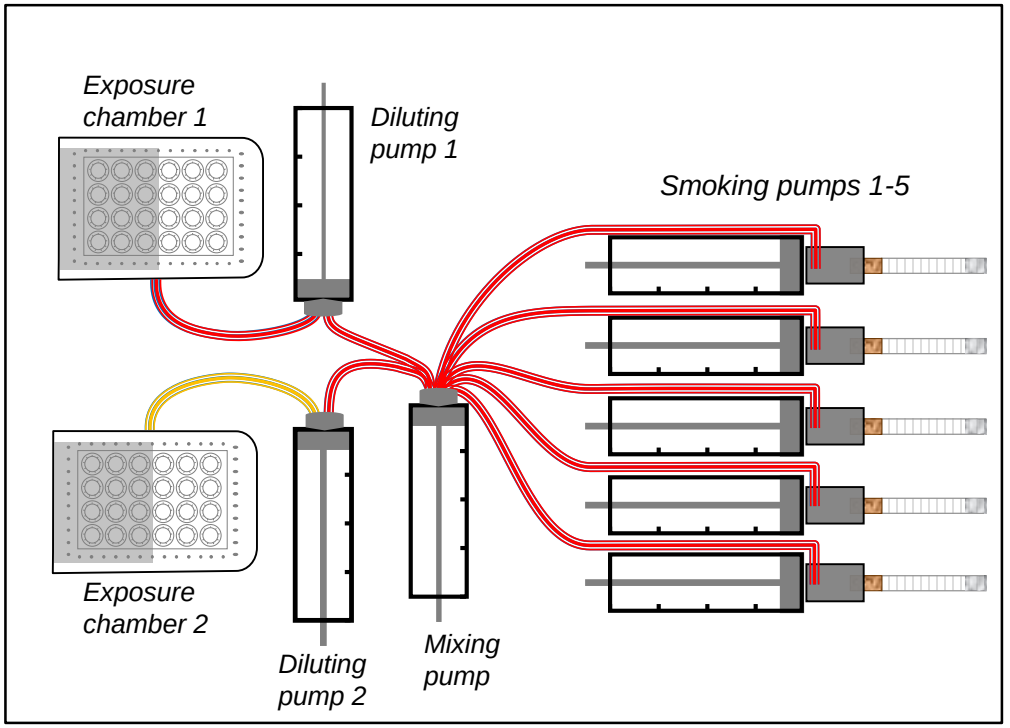
Particles may impact differential toxicity depending on where aerosol is deposited

Biological Testing

In-vitro testing

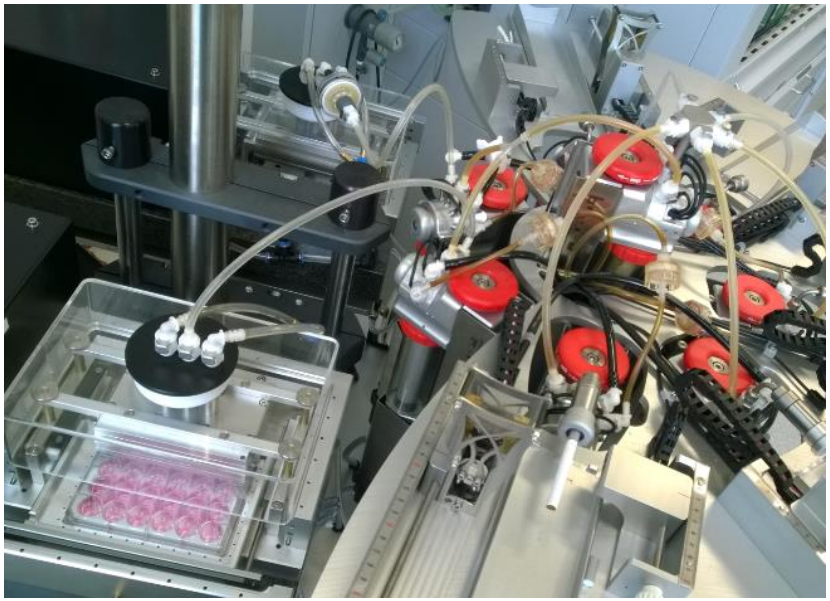
A number of assays exist:

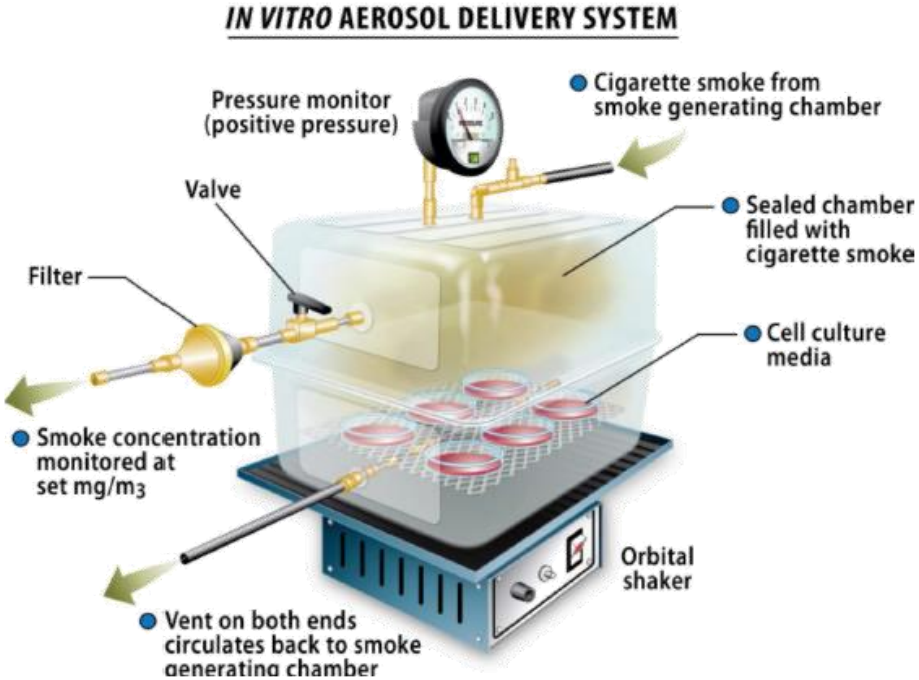
- Ames reverse bacterial mutagenicity assay
- In-vitro micronucleus (IVM) assay
- Cytotoxicity – Neutral Red Uptake (NRU) assay
- IL-8 Assay – inflammatory cytokine



Biological Testing (2)

From 2D cell culture to ‘repeat dose’ 3D cell culture

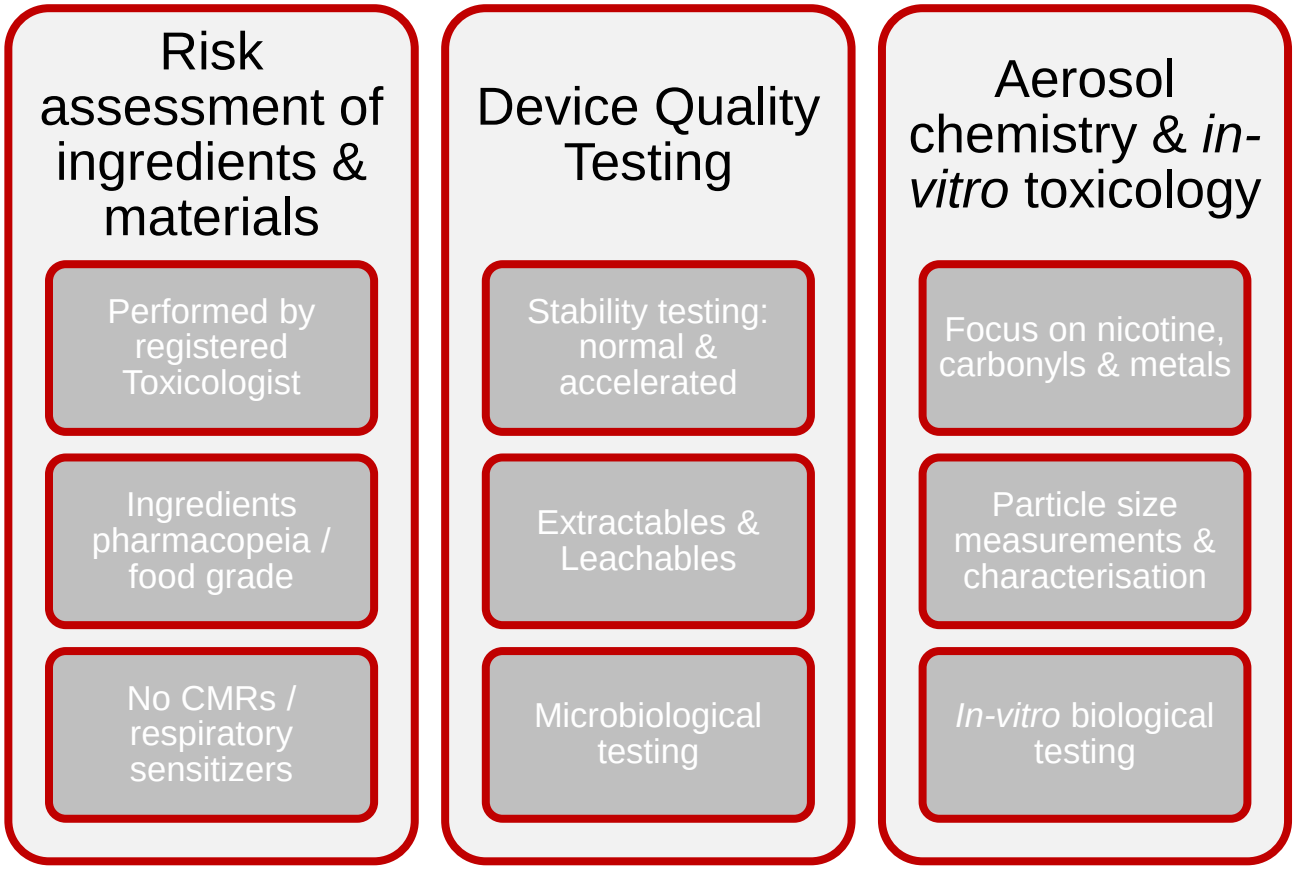




Investigate multiple endpoints after aerosol exposure

Pre-market product stewardship

Summary



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