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Regulatory and Market Intelligence for the e-Cigarette Sector

TPD test requirements criticised as vague: what can manufacturers do?

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The wording of the EU's Tobacco Products Directive (TPD) is imprecise and confusing on the question of notifiable toxicology requirements, two UK scientists say.

Richard Young, senior toxicologist at Bibra Toxicology Advice & Consulting, told ECigIntelligence: "The toxicology-related requirements of the TPD are poorly defined and ambiguous, which is disappointing and poses difficulties for notifiers and their support teams. This has inevitably led to a wide range of different approaches to the human-health assessment of companies' products.

"Some will be thorough, health-precautionary and well-documented, others very limited. Unfortunately, those companies taking the latter approach will not be able to ensure the safety of their products, thereby putting consumers at potential – and undefined – health risk. They may also not be fully aware that they bear full responsibility for the safety and quality of their products, as placed on the EU market."

Young and his colleague Pete Watts, Bibra's director of toxicology, see four major challenges for scientists in evaluating e-cigarette safety.

Foremost is the oft-discussed issue that flavours tested for eating are being inhaled. "The first challenge for the sector is that many of the inhalation exposures to flavours exceed the oral exposures traditionally associated with food use. This doesn't mean that they are necessarily unacceptable toxicologically, but the available toxicity studies on flavours were deliberately designed to test only low oral dose levels," said Watts.

"This poses a problem for the risk assessor in that the oral study no-observed-adverse-effect levels (NOAELs) are artificially low, leading to less-than-ideal margins when compared with inhalation exposures. Moreover, chemicals absorbed following inhalation avoid any first-pass metabolism/detoxification, adding to the uncertainty."

Incomplete information

Also of concern is the fact that the exposure protocols of existing inhalation tests on laboratory animals are difficult to extrapolate to vapers.

"The second challenge relates to the potential for respiratory tract irritation. Traditional laboratory animal inhalation toxicity studies – typically exposure with every breath and often nose-only for four to six hours per day – do not mimic the vaping pattern of the e-cig consumer, which involves occasional mouth-only exposure breaths separated by a number of normal, unexposed breaths. There is little real understanding of how this intermittent exposure affects respiratory tract irritation potential."

Lack of toxicity data on ingredients and the uncertain effects of mixing them also pose challenges, Watts said.

"There are frequently incomplete toxicity data sets with the e-liquid ingredients being used. These data gaps increase the uncertainty and hinder the ability of the risk assessor to confidently predict effects on the consumer."

Moreover, Young added, "any synergistic/antagonist/additive effects of complex flavouring mixtures can be difficult to predict, and many companies – particularly SMEs – do not have the expertise or resources to adequately assess such aspects."

Advice for manufacturers

Manufacturers can, however, help address many of these issues, Watts suggested.

They can aid the progress of their products through toxicological evaluation by "designing e-liquids that (a) are of minimal complexity, (b) use the lowest possible inclusion levels of ingredients, (c) use ingredients that are of high-purity, are well understood, and consistent in composition, and (d) use ingredients that have a well-studied and low toxicity potential, if only by the oral route."

To this end, Young "recommends that the toxicity of the ingredients is considered at an early stage in e-liquid product development, and not seen as one of the final steps in the process".

Watts and Young spoke on the role of the toxicologist in e-cigarette health risk assessment at the Regulations for E-Cigarettes conference in Virginia this week.

What This Means: As the Bibra toxicologists point out, the TPD does not demand overall assessments of a product's potential impact on health to be submitted at the point of product notification – which means toxicologists play a crucial role as the gatekeepers for product safety, and anything that can improve the ease and reliability of toxicological evaluation should be welcomed by the industry as well as consumers.

There is also a public relations angle which makes it imperative that the sector can point to diligent toxicology processes when challenged: "Information in the TPD notifications will be made publicly available in time. All notifications will be viewable, and those relating to toxicologically-concerning ingredients and emission profiles will be of most interest to the media and public; all should therefore be of the highest quality.

"The risk is that poor-quality notifications could bolster the current view held by some, that all e-cigarettes are a high-risk alternative to combustible tobacco products, when in reality any health risk will be product-specific."

– ECigIntelligence staff