How Toxic Is E-liquid? Expert report recommends reclassification of nicotine solutions under CLP (Regulation 1272/2008)

Summary: *European officials have been wrongly labelling e-liquid as extremely toxic. This is the view of ECITA, based on a report by toxicology consultants which has been verified by Professors Riccardo Polosa and Bernd Mayer, and Dr Jacques Le Houezec. The civil servants had been misclassifying e-liquid as either a CLP category 2 product, alongside strychnine, or a category 3 product, alongside formaldehyde. The new report demonstrates that the acute oral and dermal toxic hazards of the strongest consumer e-liquids only merit being classed as category 4 - along with washing-up liquid - while the vast majority of e-liquid (which has nicotine concentrations below 25mg/ml or 2.5%) does not require any type of formal hazard warning. ECITA will still mandate its members to provide clearly labelled e-liquid in child-proof containers.*

There has been a great deal of confusion about how nicotine solutions for use in electronic cigarettes should be classified under CLP. Not only has there been considerable variation between advice given by regulators in different EU member states, but also from other sources.

Our own view differed from much of the advice we had seen, so in order to get a scientifically valid answer, we consulted a specialist toxicological consultancy, bibra http://www.bibra-information.co.uk/company_overview.html.

The full document from bibra is available here, but to summarise, they calculated that, based on the data in the CLP regulation (as amended), the acute oral and dermal toxicity of nicotine solutions of less than 2.5% are not classified under CLP, and that solutions of 2.5 to 5% are classified as category 4 (the lowest).

This came as quite a surprise to us here at ECITA, as while we have long been aware that most of the media and regulatory attention surrounding the risks of nicotine solutions were hyperbole, and exaggerated the risks, we did not anticipate quite this scale of exaggeration.

Bibra undertake in-house peer review in order to ensure their results are of good quality, but given the nature of this result, we felt that we needed to take wider consultation in order to ensure that the classification was appropriate. We approached three people, in three member states, with specific expertise in nicotine, but from different perspectives.

Professor Bernd Mayer, Professor & Chairman of the Department of Pharmacology and Toxicology at Karl-Franzens-University, Graz responded:

"In his report, Peter Watts discusses the LD50 values of nicotine reported for different species. For the calculation of ATE [Acute Toxicity Estimate] he uses the widely accepted oral LD50 for rats (50 mg/kg). Taking the rat LD50 is generally accepted even at courts and every toxicologist will follow this rule. So Peter Watts' calculation is definitively correct."

Professor Riccardo Polosa, Full Professor of Internal Medicine at the University of Catania responded:

"After careful cross-checking of the calculations and verification of the ensuing reclassification, it is clear that the approach, calculations and reclassifications given in the bibra Proposal are correct."

Dr Jacques Le Houezec, an Independent Consultant in Public Health and Tobacco Dependence, and Honorary Lecturer at the UK Centre for Tobacco Control Studies, University of Nottingham responded:

"The bibra report presents the calculations based on different dilutions, including those used for e-liquids. It clearly shows that the current CPL regulation is not following the principles of EC Regulation 1272/2008.

The consequence is that all e-liquids with a concentration of less than 2.5% (25 mg/ml) should not be classified under the EC regulation [for acute oral or dermal toxicity], and that higher nicotine concentrations (up to 5% or 50 mg/ml for dermal classification, and even higher for oral classification) should be considered as CPL category 4".

It seems fairly conclusive, therefore, that the generally assumed CLP (or CPL, for most non-English speaking countries) classification of nicotine is in fact, incorrect.

So, where do we go from here?

As consumer protection is a vital part of ECITA's ethos and purpose, we asked Professor Mayer if 'upgrading' the classifications to a level higher than actually calculated would be a valid way of ensuring consumer protection. He disagreed with this suggestion, stating that:

"My opinion in this matter is both simple and clear. Classification should be according to the CLP regulation. Deviation in either direction would object this regulation and raise confusion. You have commissioned consultancy from a certified expert toxicologist, who correctly classified nicotine containing products according to CLP."

We asked the same question of Mark Gardiner, Joint Lead Officer for Product Safety at the Trading Standards Institute. As an active government enforcement officer, we felt sure that he would be able to

give us specific advice to help us ensure that the level of consumer protection remains sufficiently high – particularly for children – even without the CLP warnings appearing on product labelling. His advice concurred with Prof Mayer. He said:

"It would run the risk of confusing the purpose of the CLP legislation if it is applied to products which shouldn't be classified in that way, which could undermine consumer protection."

And having reflected on their responses, they are clearly correct. The objective of seeking classification guidance from appropriate experts was to reduce confusion, and ignoring their proposed classification can only achieve the opposite.

The problem

Given that nicotine has significant emetic effects, and ingestion – even when non-fatal – is unpleasant and potentially traumatic, clearly the risk of this should be minimised as far as possible. Nicotine also has potential dangers for small children (particularly toddlers) and small animals (and nicotine-free liquid still presents a toxic hazard to cats, which are unable to safely metabolise propylene glycol).

ECITA's advice (the solution?)

In order to maximise the protection of consumers, their children and indeed their pets, we advise the following, regardless of nicotine level, and including for no nicotine products, except for concentrations where CLP *does* apply:

- Child-resistant closures must be used on all e-liquid bottles.
- E-liquid labelling must include, as a minimum:
    - the heading: "**CAUTION:**"
    - the text: "**Store locked up and out of the reach of children and pets**"
    - Nicotine concentration in weight per volume (w/v) percentage and/or milligrams per millilitre (mg/ml) must be marked on the label
    - The text: "**Only for use in electronic cigarettes**"
    - The text: "**Seek medical advice if swallowed**"
    - Contact details must be displayed
    - All of these label elements must be visible, legible and indelible

We asked Mark Gardiner's opinion on this advice, and he agreed:

“This would concur with the GPSR, which requires that the risk of harm should be minimised to a tolerable level. Any potential risk must be minimised in this way in order to comply with GPSR requirements. It’s mandatory.

Whatever regulatory framework you apply, products have still got to be safe, and they’ve still got to minimise the risk of harm. It doesn’t matter if it’s CLP, GPSR, TPD or whatever. It is entirely appropriate for the recognised industry body, ECITA, to recommend appropriate measures to ensure compliance, since they are the experts in this field.”