2. MANDATE FROM THE EU COMMISSION SERVICES

Page 9
22 Open questions
23 particularly include the role of e-cigarettes in relation to their use and adverse health effects
24 (i.e.; short- and long-term effects), their role as a gateway to smoking / the initiation of
25 smoking (particularly focusing on young people), their role in harm reduction / cessation of
26 traditional tobacco smoking, as well as risks associated with their chemical composition
27 (e.g.; number and levels of toxicants).

The mandate of the commission includes a comparison of the risks between vape and tobacco, since it requires on the one hand a study of the toxicity of the vape, on the other hand an analysis of its potential as a reduced risk product. In other words, the SCHEER report should include an analysis of the benefit / risk balance. This balance seam useful in order to allow EU commission to take a decision based on science.

The SCHEER report was requested by the EU commission to provide decision-making elements. Defining the strength of the current evidence is in itself necessary but insufficient. The SCHEER report should also quantify the risks, in particular by comparing them with other products known and emitting a similar toxicity: Burned, heated tobacco, snus, NTRs or even a candle (aldehydes), a tomato (heavy metals) or an eggplant (nicotine). When standards or recommendations regarding exposure to toxic components are available, the SCHEER report should cite them and indicate whether existing studies indicate that the toxic emissions from the vape are below or above the standards.

ABSTRACT

Page 2, line 7 to 37

As a general rule, the SCHEER report is limited to saying what is the state of science concerning the various elements, i.e. whether we know enough to make a decision or not.

However, this report does not say what the scientific conclusions are, whether they are strong or weak. Especially when the evidence is considered strong, it means that toxicity should be able to be estimated. For existing studies,

• Are the quantities of toxic emissions higher or lower than the standards? In particular regarding passive vaping, very few studies indicate that the standards can, under extreme conditions, be exceeded.

• Compared to the toxicity of a cigarette, (or any other object emitting the same type of toxicity, such as candles concerning aldehydes) are the quantities of toxic emissions detected in the studies higher, lower or equivalent?

• Is there clinical cases to support the claims of toxicity? Although, as with any new product, we do not yet have 50 years of hindsight but after more than 10 years of existence and on a current estimated panel of several tens of millions of users, the absence or presence of clinical cases is already a clue. For example, studies exist on the weight of new-born or premature births when the mother smokes or vapes. The term being 9 months, a follow-up of 10 years is already sufficient to rule on this subject. The evolution of COPD or the frequency of asthma attacks in smokers passing to vape are also short or medium term indicators that we have.

By not quantifying the degree of emission of toxic compounds, by not giving a scale of magnitude, this report will lead the EU commission to make the wrong decision on the basis of concealing evidence.

To cite just one example per point given, here are some references that might appear in your report in order to quantify toxicity:

«Although the e-cig vapours did not induce sufficient cell mortality to calculate an ED50 (whatever the tested e-cig power or model), ED50 was 45 puffs for HTP aerosol and 2 puffs for 3R4F cigarette smoke.»
https://www.sciencedirect.com/science/article/pii/S0304389420314060

«Concentrations of vaping-related chemicals in our air samples were below occupational exposure limits.»
https://www.cdc.gov/niosh/hhe/reports/pdfs/2015-0107-3279.pdf

«The birthweight of infants born to EC users is similar to that of non-smokers, and significantly greater than cigarette smokers. Dual users of both cigarettes and EC have a birthweight similar to that of smokers»
https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1111/1471-0528.16110

When it comes to talking about the nicotine level, page 66, no worries about comparing vape and tobacco. Without mention, however, that a dose equivalent to a cigarette means interesting efficacy as a substitute product or as a smoking cessation tool. On the other hand, when it comes to toxicity, no comparison is made with cigarettes.

JUUL market share

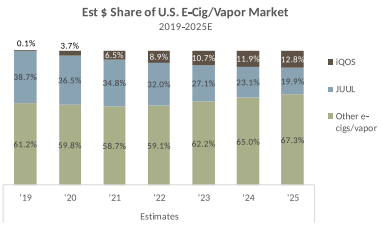
Page 8
13 It is also interesting
14 to note that a modified version of a popular pod device with a 76% US-market share
15 is now on the EU market, with technological adjustments.

These figures are wrong. They come from Nielsen Data, which analysed only the "tobacco channel". This measure is not adequate for the vaping market because specialized shops order either directly from the manufacturer, or via specific vape wholesalers. In the USA, there are an estimated 15,000 companies specializing in vaping. They go under the Nielsen data radar. This shows that independent vaping players are being ignored in an effort to associate vaping with tobacco products and producers. In a more recent publication, Wells Fargo indicates that Juul has a 36.5% market share.

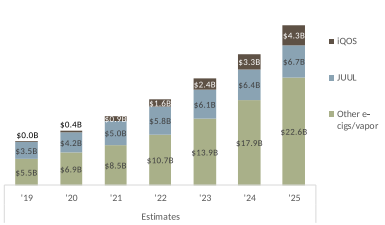
http://www.natocentral.org/uploads/Wall_Street_Update_Slide_Deck_February_2019.pdf
Page 29

We See JUUL & iQOS* As the Strongest Likely Beneficiaries

We Believe JUUL & iQOS Could Represent ≥30% of the U.S. E-Vapor Mkt by 2025



As the Mkt Expands/Matures, Their Mkt Shares May Moderate, But Topline Momentum Should Continue



- JUUL Has Single-Handily Reaccelerated the U.S. E-Vapor Category
- JUUL's Volume Increased +600% in 2018 to Over $450M Refill Kit Pods, Contributing to Over $1B in Net Revenues
- While Not Yet Approved For Sale in the U.S., the Success of iQOS in Several Int'l Markets Bodes Well for its Potential in the U.S.
- iQOS Could be Approved for Commercialization in the U.S. Any Day Now
- We Estimate that iQOS Could Accelerate MO's Revenue and Profit Growth and Drive Significant Incremental Value

Note(*): Assumes FDA approval of iQOS for commercialization. Source for both images: Nielsen; Wells Fargo Securities, LLC estimates
Bonnie Herzog - Wells Fargo Securities, LLC | Tobacco, Beverage & C-Store Sectors

Estimating market share in an unstructured market is difficult, so these figures are very unreliable. In addition, Nielsen Data are intended for investors, so they are probably not interested in Chinese brands like Innokin, Aspire, Joyetech or GeekVape which, although they are dominant in the market, are not open to investors. Surprisingly, SMOORE is publicly traded and does not appear in these analyses, despite its market value being higher than Juul. This is probably due to the fact that the products of the SMOORE group, such as Vaporesso, are not distributed via the "tobacco channel".

Many studies, some of which you use, cite Nielsen data and say that Juul has 76% of the US market. This shows the incompetence of the authors and this is worrying for the quality of the research.

> Page 91
> 37 Walley, S. C., Wilson, K. M., Winickoff, J. P., & Groner, J. (2019). A Public Health Crisis:
> 38 Electronic Cigarettes, Vape, and JUUL. Pediatrics, 143(6). doi:10.1542/peds.2018-2741
>
> Most major e-cigarette brands are owned by big tobacco companies that use similar marketing and advertising strategies to attract youth users as they did with traditional tobacco products. In this review, we provide an overview of e-cigarettes and vape devices with an emphasis on the impact for the pediatric population. We describe the vast array of e-cigarette devices and solutions, concern for nicotine addiction, and the scientific background on the known health harms.

If the authors of this paper have such a misunderstanding of vape that they imagine that "BigT" owns the majority of the brands of vape, how can the rest of their work be credited? Yet this article is quoted in this report. This shows that the SCHEER expert group should have included a fields person.

Gateway

> Page 68
> 35 On the antipode however are a number of studies that indicate that exposure to electronic
> 36 cigarette use may not be directly related to smoking uptake among youth. A time trend
> 37 analyses on national representative data on electronic cigarette and tobacco use in the US
> 38 by Levy et al. (2019) noted a decline in past 30-day smoking prevalence between 2014-
> 39 2017, which coincides with the timeframe of electronic cigarette proliferation in the US,
> 40 however the authors noted that while there has been a decrease in smoking rates during
> 41 the past years in the US, this could also be attributable to the influence of other tobacco
> 42 control interventions.

Whoever does not know history is condemned to relive it.

In 1992, snus was banned from sale throughout Europe, except in Sweden. At that time longitudinal studies were used in the same way to justify the theory of a gateway effect from snus to smoked tobacco. 28 years later Sweden has the lowest smoking rate in Europe, and also the lowest lung cancer rate in Europe, but opponents of snus continue to invoke the gateway effect to justify its ban.

By what mechanism a high prevalence of snus in Sweden coupled with a gateway effect can lead to the lowest smoking rate in Europe, the question seems relevant.

In the USA, France and England, a drop in smoking prevalence has been observed in parallel with the arrival of the vape. We can therefore draw a parallel between the so-called gateway effect of snus and vape. Are the analysis biases the same? Have correlations been unduly considered as evidence of causality? Potential confounding factors, inherent in the comparison of two products that are too close to be able to dissociate the correlation of risk behaviours from true causality, may explain an analytical error.

> The gateway theory is not compatible with either (1) the decrease in smoking prevalence observed in adolescents in countries where vaping increased or (2) an increase in smoking among teenagers after age restrictions were imposed on e-cigarette purchases.
> https://pubmed.ncbi.nlm.nih.gov/28786147/

> ST use has played virtually no role in smoking initiation among White men and boys, the demographic groups among which ST use is most prevalent. There is evidence that, compared with cigarette initiators, ST initiators are significantly less likely to smoke. This suggests that ST may play a protective role.
> https://pubmed.ncbi.nlm.nih.gov/20335282/

> The report also asserted that the common liability theory is a plausible explanation for the association between vaping and smoking (i.e. both are determined by the same risk factors)
> https://www.tandfonline.com/doi/pdf/10.1080/17476348.2018.1453809

> Page 70
> 13 There is also strong evidence that nicotine in
> 14 e-liquids is implicated in the development of addiction.

This part of the report is not supported by the figures stated:

> Page 69
> 19 Previous secondary data set analyses using the 2012, 2014 and 2017 Eurobarometer
> 20 datasets had indicated that ever use of an electronic cigarette in the EU Member states
> 21 increased from 7.2% (95% CI 6.7 - 7.7) in 2012, to 11.6% (95% CI 10.9 - 12.3) in 2014 to
> 22 14.6% (95% CI 13.9–15.3) in 2017. Across the whole of the EU 1.8% of the adult
> 23 population (95% CI 1.5 to 2.1) were current regular electronic cigarette users in 2017,
> 24 compared with 1.5% (1.2–1.8) in 2014 (Filippidis et al., 2018; Laverty et al., 2018

According to the Inpes Youth Health Barometer 2010,

> « chez les jeunes de 20/25 ans ayant fumé leur première cigarette avant 14 ans, 66 % fument quotidiennement et 51 % fument au moins 10 cigarettes par jour. Alors que pour ceux ayant fumé leur première cigarette entre 14 et 17 ans, c'est 52 % qui fument quotidiennement et 30 % qui fument au moins 10 cigarettes par jour »

If vaping was as addictive as tobacco, around half of the people who experimented with vaping in 2014 should be addicted to it in 2017. However, we went from 11.6% of experimentation in 2014 to 1.8% of use in 2017. A majority of them are smokers or ex-smokers for whom the cause of nicotine addiction is tobacco and not vaping. This report therefore claims that vaping is addictive but shows the opposite in the figures.

We know that nicotine is addictive, but also that its addictive potential depends on the mode of absorption. Eggplants and potatoes, which contain nicotine, are not know to be addictive.

Patches are not known to be addictive, nicotine gum is very little. Here again, the SCHEER report mentions evidence without quantifying it and qualities evidences as "strong" even though it is not correlated with demographic data.

> This is to our knowledge the first report of addiction to nicotine gum in never users of tobacco. However, this phenomenon is rare
> https://bmcpublichealth.biomedcentral.com/articles/10.1186/1471-2458-7-159

Due to dissonance between studies, we might be tempted to look into the mechanisms of the gateway effect. Does the gateway effect concern young people who have just experimented vaping or only those who have

become addicted to nicotine? Why will young people who have experimented with vaping choose to smoke or not? Compared to the vape => tobacco gateway effect, what is the tobacco => vape gateway effect?

Are there any qualitative studies on the subject?

> Une porte d'entrée vers le tabagisme ?
> Aucun élément dans les témoignages que nous avons recueillis ne peut laisser penser que la cigarette électronique pourrait être une « porte d'entrée vers le tabac » pour les plus jeunes utilisateurs.
> https://www.cairn.info/revue-sante-publique-2017-6-page-793.htm

Cessation

> Page 8, lines 34 to 46

What this report fails to say, when it cites precisely these data:

> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6317445/
> Younger people were more likely to have reported e-cigarette use for smoking cessation but less likely to have used a cessation service.

We see here that the use of vaping as a smoking cessation tool has increased as vaping has become more common / accessible and that vaping appears to be a more attractive method of quitting, especially for young people, than traditional methods.

Vape as a cessation tool, although it should not prove to be more effective than another method, is interesting since it is more attractive than traditional methods. It is also possible that it affects another segment of smokers. This report indicates that the reasons for using vape among young people are curiosity, the price or the possibility of vaping in places where smoking is prohibited. If it turns out that this can lead young people to quit smoking when they would not have considered another method of quitting, it means that its effectiveness - even relative - become in addition to other methods of smoking cessation.

> Page 71
> 33 There is a lack of robust longitudinal data on the effect of electronic cigarettes on smoking
> 34 cessation.

> Page 70
> 45 To this extent, a Cochrane Review

Your opinion was published just before a Cochrane data update. You should therefore update your review based on the latest information, especially as you indicate that they are necessary and may change your conclusion:

> "More people probably stop smoking for at least six months using nicotine e-cigarettes than using nicotine replacement"
> https://www.cochrane.org/CD010216/TOBACCO_can-electronic-cigarettes-help-people-stop-smoking-and-do-they-have-any-unwanted-effects-when-used

If after including the latest information available you persist in considering that the scientific evidence is not strong enough to determine if vaping is an effective quit smoking aid, you can have another point of view. You will no doubt admit that some people have managed to quit smoking thanks to the vape, so we can say:

In some cases vaping help to quit smoking but in the majority of cases the attempt to quit fails.

With a reported failure rate of 80-97%, the same can be said of all other methods. There's no efficient tool to stop smoking.

The question is therefore not whether vaping is more ineffective or less ineffective than other methods, but to consider that no single method will end the game alone and that it is a set of measures which, combined, represent the best hope. In this context, vaping has a role to play: It has allowed some people to quit smoking and in the countries where vaping is the most common, the smoking prevalence is declining.