



**Advice
Superior of Health**

**ELECTRONIC CIGARETTE:
EVOLUTION**

**JUNE 2022
CSS N° 9549**



.be

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Federal Public Service for Public Health, Food Chain Safety and the Environment

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OPINION OF THE SUPERIOR HEALTH COUNCIL N° 9549

Electronic cigarette: evolution

In this scientific advisory report on public health policy, the Superior Health Council of Belgium provides an updated for electronic cigarettes (with or without nicotine) for smokers, non-smokers and vapers.

This report aims at providing politicians, public health authorities, healthcare providers, teachers, youngsters, smokers and vapers with specific recommendations on the toxicity and safety of electronic cigarettes (vs. traditional tobacco cigarettes).

Version validated by the College of
June 2022

RESUME

On the basis of new publications and following a series of questions asked by the Federal Public Service (FPS) Public Health, Food Chain Safety and Environment, the Superior Health Council (CSS) has decided to review its opinion CSS 9265 of 2015 concerning "the state of play on the e-cigarette".

This new version of the opinion is divided into 5 main chapters, namely a chapter dedicated to the conclusions and answers to the questions asked, a chapter on regulatory and normative aspects, one on e-liquids and equipment, one on specific groups such as those of people with psychological vulnerability and finally a

on the opportunities and risks associated with the consumption of e-cigarettes. With regard to this last aspect, an inventory of the positions/visions of the various institutions, national and international organizations is included in appendix 1 of this opinion, showing how complex the issue of e-cigarettes is.

The most important key messages are:

- The relative risk of e-cigarettes (with or without nicotine) compared to **not smoking** is clear: e-cigarettes are not without risk, they are potentially dangerous. E-liquids contain many substances for which information on their inhalation toxicity is lacking. Moreover, long-term data on the use of e-cigarettes are still insufficient. The consumption of products containing nicotine is also not recommended for non-smokers due to its addictive effect. **The e-cigarette is therefore not recommended for non-smokers, especially young people.**
- The relative risk of e-cigarettes compared to **smoking** is also clear: e-cigarettes are considered to be significantly less harmful than cigarettes

classics. **It is a better alternative to tobacco for smokers and can be used as a smoking cessation aid.** Smoking being strongly linked to social vulnerability (psychiatric patients, people in prison, people with a low level of education, low-income people, etc.), e-cigarettes can also play a positive role in future smoking cessation policies among these persistent vulnerable groups of heavy smokers. In the current state of knowledge, its exclusive use by (ex)-smokers, provided that they actually stop smoking tobacco, could lead to a reduction significant health risks.

- The e-cigarette must be treated as such by political leaders. The availability and accessibility of conventional cigarettes (tobacco) should be further restricted.

Finally, the **CSS** pleads for this policy to include both the limitation of smoking than vaping and nicotine consumption. It must be ensured that the limitation vaping and nicotine consumption does not compromise the goal of reducing the prevalence of smoking.

TABLE OF CONTENTS

RESUME	1 I INTRODUCTION ET
CONSIDERATIONS PREALABLES	4 1.1.
Introduction.....	4 1.2. Preliminary
considerations.....	5 II CONCLUSIONS AND
RECOMMENDATIONS	7 2.1.
Findings	7 2.2. Responses to requests for
advice	9 2.3. Other Considerations and
Recommendations	24 III
METHODOLOGY	29 IV NORMATIVE AND
LEGISLATIVE ASPECTS	32 4.1. Composition of e-cigarettes and e-
liquids	32 4.2.
Notification.....	38 4.3.
Labeling	39 4.4. Advertising, sale and
consumption in public places	41 V E-LIQUIDS AND
APPLIANCES	44 5.1.
Introduction.....	44 5.2. Nicotine: toxicity and
addictive effects	45 5.3. Other
ingredients.....	52 5.4. Equipment and technical
aspects	56 VI E-CIGARETTES FOR SPECIFIC GROUPS: PEOPLE
WITH PSYCHOLOGICAL VULNERABILITY	62 6.1. Statement
of the problem	62 6.2. Consequences of the increase
in the prevalence of smoking	63 6.3. An urgent
problem	63 6.4. Smoking cessation is more difficult
in this group	64 6.5. The e-cigarette as a possible
device?.....	64 6.6.
Discussion	67 6.7. Critical
reflections	69 6.8. Possible evolution: opinion of
CSS experts	70 VII RISKS AND
OPPORTUNITIES	72 7.1.
Introduction.....	72 7.2. Context: the fight against
tobacco	73 7.3. Emphasis on the risks associated with e-
cigarettes	76 7.4. Focus on the opportunities of the e-
cigarette	78 7.5. Risk reduction: framework and
discussion	80 VIII APPENDIX I - Three major issues arising from the
emphasis on risk and opportunity	85
8.1. Health risk (compared to the absence of use of the e-cigarette and in relation to	
smoking)	85 8.2. Smoking
cessation.....	102 8.3. Young people and non-
smokers	126 IX APPENDIX 2 - Proposals for additional
health warnings and messages on package inserts	143 X
REFERENCES	145 XI COMPOSITION OF
THE WORKING GROUP	174

I INTRODUCTION ET CONSIDERATIONS PREALABLES

1.1. Introduction

In May 2019, the Higher Health Council (CSS) received from the Federal Public Service (FPS) public health, food chain safety and environment and more specifically from the "consumer product inspection service" a request for an opinion relating to cigarettes electronics (e-cigarettes) and e-liquids.

Indeed, since the entry into force of the Royal Decree (RD) of 28 October 2016 relating to the manufacture and marketing of electronic cigarettes, their use is booming in many countries - even if their use in

Belgium remains more limited, the products marketed have evolved and scientific knowledge has increased. The opinion of the CSS 9265 of 2015 concerning "the inventory of fixtures on the electronic cigarette (e-cigarette)" therefore requires a revision following the many new publications, in particular relating to o e-liquids and the health risks,

- o additives and flavors of e-liquids,
- o potential risks and opportunities of e-cigarettes,
- o the use of e-cigarettes as a risk reduction device and smoking cessation,
- o new e-cigarette systems (technical aspects and use of salts of nicotine – topic not covered in our previous opinion).

In addition, certain situations prompted the "consumer product inspection department (tobacco unit)" to extend their request for an opinion from May 2019. These include the following situations:

- the appearance in the United States
 - o in the summer of 2019, severe lung conditions causing numerous deaths linked to the consumption of e-cigarettes (illegal cartridge of γ -9-tetrahydrocannabinol (THC) contaminated with vitamin E acetate) and,
 - o in March 2020 of the "health crisis" declared by certain authorities, linked to the increase in the use of e-cigarettes among young people, including that of the JUUL brand,
- in Belgium, following the death of a young man in November 2019 following lung problems while using an e-cigarette.

Prior to these two requests for an opinion on e-cigarettes and e-liquids, the CSS received a request for an opinion from Minister Maggie De Block on " *heated tobacco products* ". Although the issues related to the consumption of new products based on heated tobacco and e-cigarettes may possibly present approaches similar, the CSS preferred to treat the two files separately. The opinion on new heated tobacco products was validated in April 2020¹ and is available on the CSS *website* .

¹ Opinion of CSS 9538: New tobacco products: heated tobacco products. April 2020

This opinion is therefore limited to e-cigarettes and e-liquids as well as to the various questions identified by the SPF and which are included in the "Conclusions" section of the opinion.

The questions of the two requests for opinion have been collected and grouped by theme, namely regulatory and normative aspects, aspects on e-liquids and devices, specific groups as well as opportunities and risks related to e-cigarettes.

The SPF has left it to the discretion of the CSS to address other issues on e-cigarettes and e-liquids that deserve its attention.

1.2. Preliminary considerations

Since 2015, many new publications on the e-cigarette are available. Faced with this exponential multiplication of publications, the experts decided to focus on reviews and summaries of literature while keeping in mind that not all publications are neutral. Indeed, the selectivity, the methodology, the taking into account of the criticisms or not of the studies, the interpretation of the results in certain scientific publications are sometimes strongly linked to the way in which one wishes to approach the problem; either from a risk point of view (*risk assessment*), or from a point of view of reducing the risk associated with tobacco consumption by using lower-risk products (*harm reduction*). It is for this reason that the two viewing angles (*harm reduction* and *risk assessment*) are taken into account in the opinion.

Experts are aware that

- the literature relating in particular to the e-cigarette was initially dominated by North American publications in which various incidents were described. However, in Europe, all these problems identified (EVALI², "epidemic" of e-cigarette use among young people, etc.) did not occur or at least not in the same way.
- reputable and credible companies as well as public bodies have also produced documents on the risks and opportunities associated with the use of e-cigarettes and on reduction strategies associated with the use of lower risk products such as the e-cigarette.
- positions and policies on e-cigarettes and e-liquids are different from one country to another. Some countries have a more receptive position than Belgium, while others have a more restrictive position.
- The tobacco industry is particularly active in the communication of lower risk products and seems to reappropriate the risk reduction framework for its own benefit.

Although the publications are numerous, they do not address all the themes or the questions raised. This is why, when a summary or a response is supported by scientific data, this will be clearly identified in the opinion. On the other hand, for the points for which data do not exist or too

² EVALI: *e-cigarette or vaping product use associated lung injury*

little, the synthesis or the answer will be the fruit of a reflection of the experts. For some points, recommendations will be made.

The consensus between the experts is sought as much as possible (the recommendations are then formulated under the name of the **CSS**) but given the complexity and the divergences of points of view expressed by **certain experts**, certain aspects will be more nuanced and the arguments of one and the other will then be taken up. It is therefore up to the competent authorities, on the basis of the information and arguments put forward, to take the decisions they deem most timely.

The document is structured as follows:

- a brief introduction,
- a chapter "Conclusions and recommendations" containing the answers to the questions asked, a summary of the new elements and positions of the experts as well as more general recommendations.
- four distinct chapters; each of them detailing the different themes addressed in the conclusions, namely the normative and legislative aspects, the aspects relating to e-liquids and devices, the e-cigarette and specific groups and finally, the risks and opportunities. To understand how the experts have arrived at the conclusions (i.e. on the basis of which publications, discussions and reflections or the arguments put forward, etc.), it is recommended to consult the relevant chapter(s).

Many publications on the e-cigarette appear almost daily. This is a hot topic that is still under development. New publications/studies could cause the CSS to revise its current advice.

II CONCLUSIONS AND RECOMMENDATIONS

2.1. Conclusions

2.2. Answers to questions

2.3. Other Considerations and Recommendations

2.3.1. Distance Selling

2.3.2. Points of sale

2.3.3. Ban e-cigarette displays at points of sale

2.3.4. Communication

2.3.5. Subject e-cigarettes to the measures of the Tobacco Products Directive and the FCTC

2.3.6. Need for further monitoring and research

2.3.7. Need for independent complementary studies

2.1. Conclusions

CSS agrees with the following concepts :

- The relative risk of e-cigarettes compared to not smoking is clear: e-cigarettes are not without risk; it is therefore not recommended for non-smokers, especially young people.
- The relative risk of e-cigarettes compared to smoking is also clear: e-cigarettes are considered less harmful than conventional cigarettes; it is a better alternative to tobacco for smokers and can be used as a smoking cessation aid.
- The e-cigarette must be treated as such by political leaders. The availability and accessibility of conventional cigarettes should be further restricted.

In the current state of knowledge, the exclusive use of e-cigarettes by (ex-) smokers, provided that they actually stop smoking, could lead to a reduction significant health risks.

In the context of public health, current scientific evidence shows that e-cigarettes, when used exclusively, are less harmful than conventional combustible smoking and therefore may have health benefits as an alternative to conventional smoking; however, data on the long-term use of e-cigarettes are still insufficient. It should be emphasized that the e-cigarette is not harmless and therefore not recommended for non-smokers, especially

youth. The e-cigarette should be seen as a temporary way to completely quit smoking and, preferably, to then quit vaping (unless there is a risk of starting to smoke again). The risks of relapsing into smoking among vapers who continue to vape as well as those who practice *dual use* are currently also the subject of studies.

It is also necessary to distinguish between burnt and smoked tobacco and nicotine.

The vast majority of smoking-related risks are not due to nicotine itself but many smokers and ex-smokers mistakenly believe that nicotine is solely responsible for tobacco-related cancers. Nicotine makes smokers addicted to tobacco and the consumption of nicotine itself presents certain risks (point 5.2.). Nevertheless, the health risk associated with nicotine in tobacco smoke is low compared to the risk associated with the many toxic agents (including polycyclic aromatic hydrocarbons) and other carcinogens present in tobacco smoke (PHM, 2020).

From the point of view of the risk of dependence, according to the NASEM report³ there is also "moderate evidence⁴" that the risk and severity of nicotine addiction is lower for e-cigarettes than for tobacco cigarettes⁵.

The **CSS** considers that the use of nicotine e-cigarettes can, under certain conditions, play a role in anti-smoking policy. The **CSS** advocates that this policy encompasses the limitation of smoking as well as that of vaping and nicotine consumption.

However, care must be taken that limiting vaping and nicotine consumption does not compromise the goal of reducing smoking prevalence. Furthermore, from a public health perspective, the **CSS** considers unlimited (continuous) e-cigarette use to be less desirable than "time-limited" vaping, especially in the context of smoking cessation. Care must also be taken that the objective of helping smokers quit smoking does not compromise the protection of non-smokers against the use of e-cigarettes.

For some smokers, smoking cessation therapy is best nicotine replacement therapy (NST) or an e-cigarette containing nicotine, even long-term if necessary, rather than risk relapse into smoking.

For non-smokers (adults and certainly minors), however, it is still advisable not to consume any product containing nicotine. Thus, non-smokers can avoid not only nicotine addiction but also the clearly harmful effects of classic tobacco cigarettes and those (to a lesser extent) of e-cigarettes and e liquids.

The **CSS** recommendations clearly describe both the potential risks of e-cigarettes for minors and non-smokers as well as the potential opportunities of e-cigarettes for smokers (see also the chapter "Risks and opportunities").

In Belgium, regular vaping by non-smokers is quite rare and more frequent among smokers or ex-smokers. E-cigarette policy must continue to focus both on better informing smokers about this alternative less

³ NASEM: *National Academies of Science, Engineering and Medicine*

⁴ **Moderate evidence:** *There are several supportive findings from fair-quality studies with few or no credible opposing findings. A general conclusion can be made, but limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.*

⁵ <https://www.nap.edu/resource/24952/012318ecigaretteConclusionsbyOutcome.pdf>

risky (not without risk) and on the protection of young people against smoking and vaping. For young people (under 18), the focus should be on preventing nicotine use in all its forms.

Smoking is one of the main causes of health inequalities today. Smoking is strongly linked to social vulnerability (psychiatric patients, people in prison, people with a low level of education, etc.) It is necessary to achieve completely smoke-free institutions such as hospitals, psychiatric establishments, prisons, etc According to the **CSS**, e-cigarettes can also play a positive role in future smoking cessation policies among these persistent vulnerable groups of heavy smokers.

The **CSS** would like to stress that, in the context of the e-cigarette debate, deterrence from smoking must play a very important role and that, for policy makers, the absolute risk of smoking must prevail over the relatively lower risk of the e-cigarette. Our country continues to struggle with too many smokers and a decline too slow in smoking prevalence rates.

How can we prevent further discouraging **smoking** in the years to come?

- the application of Article 5.3 of the FCTC: not allowing the tobacco industry to influence in any way the development and implementation of public health policies and regulations. of tobacco.
- higher excise taxes and duties aimed at discouraging smoking,
- a drastic reduction in the many tobacco outlets in our country and a ban on sales via vending machines,
- the prohibition of displays in points of sale⁶
- repeated and tailored campaigns to remaining smokers, encouraging them to make more quit attempts using all effective smoking cessation products available,
- reimbursement of TSN and free admission for the groups of smokers most vulnerable,
- increasing help from smoking cessation professionals for smokers, and in particular for vulnerable groups (for example, those with low levels of education or mental health problems),
- annual monitoring of consumption: both of conventional tobacco products and of new tobacco-free nicotine products.

2.2. Responses to requests for advice

What legislative changes are needed in this area, particularly in terms of what about e-liquids without nicotine? Are the same standards applicable to e-liquids with nicotine should also apply to e-liquids without nicotine?
(Item 4.1.)

⁶ see the positions on the displays for tobacco versus e-cigarettes in point 2.3.3.

The **CSS** is of the opinion that the standards applicable to e-liquids with nicotine are applicable to e-liquids without nicotine and to the ingredients. Apart from nicotine, the ingredients present in these e-liquids are identical. There is therefore no need to regulate them in any other way. As for the aspects of notification, distance selling⁷ labeling, etc. the same regulatory principles are to be applied or harmonized if it concerns nicotine. It is therefore appropriate to adapt the current regulations by incorporating refill bottles (e-liquids) without nicotine.

In order to better apply the current regulations: the CEN/ISO8 standards recently developed in this area reliable? Is it desirable to apply them?

(point 4.2.)

Given the limitation of access to information and the nature of these standards (metrological aspects), the **CSS** considers that the question posed by the administration on this subject of its field of investigation. The **CSS** therefore does not wish to position itself on these standards. However, he insists on the fact that these standards must correspond to the scientific knowledge currently available.

What elements should appear on the leaflets of e-liquids with nicotine and without nicotine?

(point 4.3.; appendix 2)

As with nicotine-containing products, the **CSS** recommends that information present in the obligatory leaflet of the packaging are also included in the products without nicotine.

The **CSS** also calls for additional information via new inserts (small information sheets) on the packaging: inserts with an independent message, determined by the competent authority and therefore not by the producers who have commercial interests. These inserts can deliver smoking cessation messages for smokers, including information about e-cigarettes and the relative risks of smoking and also information for non-smokers. Such inserts are desirable for both conventional cigarette packaging (including rolling tobacco and cigarillos, etc.) and e-cigarette packaging. Unlike health warnings, it is important that these inserts have a positive approach, i.e. they attract and motivate smokers to quit smoking completely and in doing so present the

e-cigarette in a positive light (regarding the comparison between tobacco and e-cigarette use). These inserts can also refer the smoker to further help: ask your pharmacist or doctor or call Tabacstop on 0800 111 00.

The **CSS** also advocates for additional health warnings relating to e-cigarettes. Currently, there is only one warning about the addictive aspect of nicotine. A broader set of warnings formulated in simple terms and easily understood by all users including smokers with little education would be useful (also, for example, warnings about dual use or non-use

⁷ distance selling: this point will be detailed in point 2.2.1.

⁸ CEN/TS 17287 *Requirements and test methods for electronic cigarette devices (2019)* et CEN/TR 17236. - *Electronic cigarettes and e-liquids - Constituents to be measured in the aerosol of vaping products (2018)*.

use of petroleum-containing substances, cf. EVALI⁹ or that of keeping the e-cigarette out of reach of children). If this is not legally possible (cf. the obligation to place the nicotine warning imposed by the Tobacco Products Directive 2014/40/EU), additional warning messages can be included in the inserts but without harming the motivating and positive message on quitting smoking using the e-cigarette and on the lower risk of the latter in comparison with the classic cigarette.

Should the leaflet contain additional information? Side effects, circumstances, illnesses or combinations with medications where e-cigarettes are not recommended or where extra precautions are needed, guidelines for correct use and storage, etc. What do we know about the stability and shelf life of e-liquids? Is it necessary to mention an expiry date ? (item 4.3; item 5.2.4)

The **CSS** recommends that the current regulations (RD 28 October 2016) in terms of instructions be adapted and extended to e-cigarettes without nicotine as well as e-liquids without nicotine.

The **CSS** is in favor of adding an expiry date and a use-by date maximum after opening on e-liquid bottles taking into account the conservation and stability of e-liquids (sensitivity of nicotine to light, for example). The aim is to limit the production of degradation products in e-liquids and to guarantee the indicated nicotine content.

Is plain packaging appropriate? (Item 4.4.)

CSS is not in favor of identical plain packaging with warning pictures as we know it for tobacco products. But the **CSS** is in favor of packaging and labeling of cigarette products which discourage minors and non-smokers. It suggests banning products from the market that appeal to young people in appearance and design, including banning the use of brightly colored packaging, cartoon characters, attractive names such as " *gummy bear* ", the mandatory use of sober tints and color elements in limited areas of the packaging, etc.

The **CSS** is also against any form of advertising, advertising via social networks and the media and supports the regulations in force in Belgium on this subject.

In addition, the **CSS** asks the competent authority for better control so that marketing via influencers and social networks such as Tik-Tok, Instagram, Snapchat, etc. can be better monitored and treated. FPS Public Health inspectors should therefore be authorized to intervene on social networks.

The **CSS** finds it relevant to inform smokers about the lower risk of e-cigarettes (compared to tobacco) and about the potential of e-cigarettes in the context of smoking cessation so as to make them aware of quitting smoking and the fact that the e-cigarette can

⁹ EVALI : *e-cigarette or vaping product use associated lung injury*

possibly allow them to get there. The e-cigarette must, according to the **CSS**, be perceived as a temporary means to completely quit smoking and then also to quit vaping. This targeted information can for example be integrated via inserts in the packs of classic cigarettes and new inserts in e-cigarettes and be communicated/discussed by tobacco specialists, general practitioners, dentists, pharmacists, etc.

Should a minimum price be set?

The opinions of experts on this subject are **divided**.

A few recent empirical studies (Pesko et al., 2020; Kenkel et al., 2020) have been conducted on the effect of excise duties on the sales and consumption of e-cigarettes. US states that have taxed these products have observed a decrease in the use of e-cigarettes but, at the same time, an increase in the consumption of conventional cigarettes (Abouk et al., 2021). Both products (e-cigarette and conventional cigarette) seem to act as economical substitutes. In this context, measures that push down (or up) the use of one product increase (or decrease) the use of the other product.

However, if the imposition of excise duties on e-cigarettes were to be considered in order to discourage their use among non-smokers and young people, these excise duties should be low enough so as not to divert smokers from e-cigarettes, but high enough to discourage young people. Expert evaluation to find the right balance is paramount. There must be a significant difference with excise duty on conventional cigarettes. The excise duties on e-cigarettes must also evolve at the same time as the excise duties on tobacco.

The competent authority could encourage "independent" producers of e-cigarettes to achieve (also) medical standards for their products so that doctors can prescribe them. **CSS focuses** on e-cigarette manufacturers "independent" because doctors and the competent authority have many difficulties in intervening on the ethical level for the e-cigarettes of a tobacco manufacturer. If the selling price of e-cigarettes respecting a medical standard were to be high, as is the case for the TSN for example, this product would become less accessible to smokers from less privileged socio-economic classes.

Some experts point out that the use of e-cigarettes as a (financially) accessible consumer product (the current situation) should not be compromised because the chances of reaching smokers are higher if the e-cigarette remains a (financially) accessible consumer product. According to them, the two paths can coexist. They believe that the objective is not to "medicalize" the e-cigarette again. According to them, the e-cigarette should not be recognized as a smoking cessation drug or as a nicotine product presenting a lower risk than tobacco.

Other experts point out that the potential of the e-cigarette, considered as a smoking cessation device, will not be fully exploited until an e-cigarette

meeting a medical standard will not be marketed. Indeed, the “medicalization” of the e-cigarette has many advantages. To only cite a few :

- Physicians or tobacco specialists can then approach smokers more proactively by presenting them with the advantages of e-cigarettes if it is demonstrated that the disadvantages/risks are controlled thanks to higher safety standards.
- The e-cigarette is most effective as a smoking cessation tool when used in conjunction with behavioral counseling (short or long term) in order to tackle not only physical addiction but also the habits or psychological dependence.
- Likelihood of dual use or long-term/lifetime substitution life is reduced.

The **CSS** emphasizes that it is preferable to ensure the sustainability of the supply circuit as a consumer product rather than to close it, but that all maximum protective measures must be taken to keep non-smoking young people and young adults away from e-cigarettes. As soon as an e-cigarette meeting a medical standard is marketed, the competent authority could do everything possible to ensure that this product remains affordable, possibly by contributing to the purchase cost.

The **CSS** recommends that the gradual abandonment of the sale of tobacco and the gradual introduction of the sale of e-cigarettes, including as medicine, be accompanied by a long-term strategic plan so that the points of sale (supermarkets, bookstores, *vapeshops*) know what we are moving towards.

Are there ingredients in the composition of e-liquids that should be introduced or regulated with regard to addictive or toxic effects? Are there any combinations of ingredients that could pose a risk? Are there any flavorings and allergens that should be banned in e-liquid? (Item 4.1; point 5.3.)

The composition of e-liquids and e-cigarettes with nicotine is regulated in article 4 of the Royal Decree of 28/10/2016 with regard to toxic, stimulating and attractive effects (prohibition of vitamins including vitamin E acetate, caffeine, taurine, and other stimulant additives, additives with carcinogenic, mutagenic and reprotoxic properties, etc.). This is described in point 4.1.1. The **CSS** is of the opinion that the standards applicable to e-liquids with nicotine are application to e-liquids without nicotine.

The most common category of additives is flavorings. Most flavors used are synthetic flavourings, also used in foodstuffs. These flavors are considered safe based on data provided by the companies involved. Information on the inhalation toxicity of flavorings (or their vaporization) are lacking. Flavor toxicity research is limited to only some of the flavors available. There is currently little information available on the toxicity of e-liquid itself. So far, mainly studies focused on *in vitro* cytotoxicity and mutagenicity are available in which e-liquid is tested as a complete blend of different flavors in combination with propylene glycol and glycerol. To guarantee the safety of flavors in e-liquids, it is necessary, on the one

on the one hand, to obtain more toxicological data (for example, carcinogenicity, endocrine disruption, toxicity by inhalation, presence of allergens by inhalation) and, on the other hand, to determine the concentration which may give rise to toxic exposure when it is used as an additive in e-cigarettes. Such a risk assessment of flavorings is necessary to better regulate them and restrict their use, if

necessary.

With regard to the regulation of ingredients, the current law places the responsibility on the manufacturers, which means that at present more than 1,800 substances have been notified and are de facto authorised. However, the **CSS** considers that work should be done to create a positive (limited) list of the only ingredients whose safety of use, including by inhalation, has been reasonably demonstrated and whose presence may be authorized as an additive in e-cigarettes.

The **CSS** is of the opinion that the existing list of authorized substances should be “frozen” so that no new substances can be added. Furthermore, it is important that the list is limited as soon as possible to substances which, on the basis of international *peer-reviewed literature*, can reasonably be considered as not hazardous to health. In particular, it is important that substances which may have endocrine disrupting, genotoxic, carcinogenic or cancer promoting properties are removed from the list. This approach, based on current literature, will already provide clear protection but it cannot be perfect as many data are lacking, especially regarding the inhalation and heating toxicity of chemicals when used in e- cigarette.

Starting from the observation that a limited positive list based on the current literature does not guarantee safety when using the e-cigarette and therefore during inhalation, that a list based on the current literature leaves room for procedures complex legal issues between the competent authority and the manufacturers and that the list should also leave enough space

to offer an acceptable palette of flavors (a flavor does not consist of a single component but of a series of components which together determine the taste), a second proposal has been formulated. A “scalable and adaptable” positive list, as described in section 4.1, can then be used. This involves setting a list of additives and no longer authorizing others unconditionally once the list has been published (additives whose notification file has already been validated will be included on this list). This list would be defined and adapted by ministerial order and requires an amendment to Royal Decree 28/10/16. The ingredients on this list can then be analyzed in detail and those that will be identified

as problematic/dangerous would then be removed from the list and banned from the market. This will thus gradually make it possible to guarantee a supply of safer e-cigarettes in our country and also in accordance with European Union regulations.

(EU). This pragmatic solution is however less effective from a public health point of view because it will take many years before the 1,800 substances on the current list are sufficiently studied.

The attention of the competent authorities should be drawn to the fact that the creation of such a list is above all a pragmatic solution which has certain advantages but which could give consumers the impression that the health authorities certify that the various additives on the market are risk-free and that therefore the e-cigarette is too.

This is obviously not the case. The **CSS** would like to point out that, from a toxicological point of view, the presence of many ingredients in e-liquids (more than 1,800 on the market) whose non-toxicity cannot be guaranteed is difficult to accept.

The **CSS** proposes to support independent manufacturers of e-cigarettes who wish to embark on the path of a medically acceptable smoking cessation aid.

Finally, in the specific case of the “*do it yourself*” (DIY)¹⁰ practice, some consumers sometimes buy products not initially intended for consumption by inhalation. However, it is difficult to control this type of practice and the resulting mixtures. Good and regular communication is recommended to

warn of the potential dangers of DIY practice (with ingredients that are not suitable for not vaping) for which the risks cannot be fully controlled (e.g. vitamin E acetate, etc.).

What is the impact of the use of nicotine salts, particularly with regard to consumer perception, smoking cessation and product toxicity?

(point 5.2.)

In some cases, particularly in pods¹¹, nicotine salts are used instead of free base nicotine. The most common nicotine salts are nicotine lactate, benzoate, levulinate, salicylate, maleate, and tartrate (Harvanko et al., 2020). Recent studies have shown that the protonated form of nicotine, the form in the presence of salts, is responsible for the rapid and higher absorption of nicotine compared to the nicotine base in e-liquids (Gholap et al., 2020). These nicotine salts are used because they are more pleasant to inhale because they mask the aversive effects of nicotine like throat irritation (Barrington-Trimis & Leventhal, 2018). This is also the reason why vaping liquids with a high concentration of nicotine (60 mg/ml) are available in the United States. The user thus experiences little or no roughness typical of a high concentration free nicotine base (Duell et al., 2019). Such high nicotine concentrations (not permitted in the EU) can lead to addiction more quickly in non-smokers and adolescents/young adults

(Mallock et al., 2020) but can, on the other hand, provide smokers with sufficient nicotine through relatively limited consumption of e-liquids.

There is little evidence of a difference in the effect on smoking cessation efficacy of free base nicotine compared to protonated nicotine (Russell et al., 2019).

No studies are available on the safety of nicotine salts by inhalation.

What are the striking characteristics of new generations of e-cigarettes compared to older products? (Item 5.4.)

Explosive batteries in e-cigarettes have been reported several times in the past. There are no figures for the number of cases in Belgium but, at the level international, several cases of burns due to explosive batteries during the use of

¹⁰ DIY: i.e. preparing your own e-liquid

¹¹ Pods: replaceable cartridges for e-liquids and nicotine salts

the e-cigarette have been reported. Many e-cigarettes use lithium batteries. However, the inherent characteristics of lithium batteries can create a risk of fire and explosion. Poor design, use of poor quality materials, manufacturing defects and malfunctions as well as

improper handling can contribute to "thermal runaway", i.e. the internal temperature of the battery can increase to the point of causing a fire or even an explosion.

Manufacturers have provided other safety measures in e-cigarettes to prevent battery overheating and explosion, such as protection circuits against overload, thermal circuit breakers and internal protection mechanisms against surprises (NASEM, 2018).

Compared to the previous opinion, certain technical aspects of e-cigarettes have clearly evolved, such as battery life and batteries with adjustable power allowing the heating temperature to be modulated. A detailed description of these developments is given in point 5.4.

Are there certain types of e-cigarettes with a higher risk of incidents or misuse? For example, rechargeable or non-rechargeable systems refillable, temperature-adjustable e-cigarettes, etc. (Item 5.4.)

As described above, e-cigarette designs have evolved and are still evolving with design improvements. Therefore, models that do not have these new features may have a potentially higher risk of incidents and abuse such as:

- Models that are not equipped with a temperature control (" *dry hit protection* ") useful to avoid overheating of the resistance when the wick is no longer sufficiently soaked in e-liquid or when the resistance is too powerful and vaporizes the e-liquid from the wick too quickly, there is a risk of a " *dry hit* ". This phenomenon can produce toxic fumes (such as formaldehyde).
- Opaque reservoirs without a " *dry hit protection* " system which do not allow to control the filling nor to ensure that the atomizer is well supplied with e liquid.
- The mechanical TUB MODS12 which do not have an electronic circuit making it possible to regulate the voltage of the accumulator. There is therefore no system of protection against overheating or against thermal runaway. 13 The **CSS**
recommends the prohibition of these systems.

If the consumer is misinformed, refillable systems can lead to handling errors such as incorrect nicotine concentrations, inadequate flavor concentrations, ingredients not originally intended for consumption by inhalation, etc.

There is also a difference between rechargeable and non-rechargeable systems; the risk of (skin) nicotine poisoning is higher in e-cigarette devices with refillable systems where you have to fill the e-tank yourself

¹² MODs : modified e-cigarettes

¹³ <http://vapereviewblog.blogspot.com/2015/01/thermal-runaway-what-it-is-and-how-do-i.html>

liquid than in non-refillable systems such as cartridges and pods (Maina et al., 2016 ; Maina et al., 2017).

However, **most experts** recommend not banning these rechargeable devices which are popular with users and contribute, among other things, to smoking cessation aid through their accessibility and flexibility of use, as well as having an impact less environmental (compared to disposable products).

According to the **CSS**, disposable e-cigarettes (integral single-use device) should be banned.

Which technical aspects can influence toxicity or addictive properties?

For example, battery capacity, etc. (Item 5.4.)

Several studies have been conducted on the impact of the technical aspects of the e-cigarette and the exposure to toxic metals and carbonyls linked to the health risks of the user. The **CSS** draws attention to the fact that metals have, in many cases, properties that are harmful to health. This is even the case for essential metals such as copper, iron, manganese, zinc or magnesium, which have harmful effects on health in the event of supra-physiological internal exposure.

Regarding exposure to metals, it is most likely due to contact with the heating element of the e-cigarette as a study has shown higher concentrations of metals in the aerosol and the e-liquid in the tank. of the e-cigarette compared to the e-liquid in its packaging. Different types of metals and metal concentrations have been found for the different types of coils used in the heating element. The reported metal concentrations vary from study to study, so it is impossible to draw conclusions that some materials pose a higher risk than others (Williams et al., 2017).

A lot of research has been done on the different e-cigarette systems and their possible link to increased exposure to toxic carbonyls. _____
However, it is very difficult to compare studies or draw firm conclusions. on the different devices because, in addition to the technical aspects of a device, the topography of vaping behavior (how draws are made) also has a influence on the formation of toxic carbonyls (Beauval et al., 2019).

The formation of thermal degradation products such as toxic carbonyls is the result of higher temperatures in the device. As described in V.5.4.2, degradation determinants include wicking (transfer) efficiency and heat transfer. A lack of wick (transfer) efficiency can result in a dry coil and overheating of the e-liquid (dry draw). If there is not enough time to cool between draws, the efficiency of the wick is hampered, which promotes thermal degradation of the e-liquid components. Other factors are high e-liquid viscosity (less capillary transfer to the wick) and expired or substandard coils (Jensen et al., 2017).

A study was conducted by Gillman (2016) to compare the concentration of toxic carbonyls between different devices (low and high power). The higher the efficiency of the production of the aerosol (lower resistances) via the increase in the power delivered by the coil, the higher the concentration of toxic carbonyls in the emissions is low. This effect is pronounced in e-liquids without nicotine because the pH is higher in e-liquids containing nicotine and the formation of toxic carbonyls is catalyzed in an acidic environment (Cirillo et al., 2019).

Besides the power, the material of the coil can also have an influence on the release of toxic carbonyls. Some are more marked than others but we cannot unequivocally prove that material X is superior to material Y because other factors also influence the production of the toxic carbonyls. However, the same study also showed that used coils release higher values of toxic carbonyls compared to new, unused coils. It is therefore recommended to change coils regularly to reduce exposure to carbonyls

(Saliba et al., 2018).

Early studies show that pod systems (PODS) have lower toxic carbonyl values in emissions compared to others e-cigarette devices. This would be related to the material of the wick rather than the power of the device. The wick is made of a stretchy material so it can feed the coil in e-liquid faster and more stably (Mallock et al., 2020).

The autonomy of the battery plays a role in the duration of the consumption of the e cigarette. The potential risk of a battery with a high autonomy is the diffuse or even continuous consumption throughout the day (compared to the consumption of cigarettes classic whose consumption punctuates the day with a clearly identified beginning and end). However, this risk seems rather theoretical since users regulate their consumption by self-titration of nicotine. In addition, models that are equipped with sensors indicating the number and duration of inhalations make it possible to control consumption.

[Regarding the protection of young people: How to reduce the appeal of e-cigarettes?](#)

[Should certain \(categories of\) flavorings be prohibited](#) (see above)?

[Is plain packaging appropriate](#) (see above)? [Should a minimum price be set](#)

(see above) ? (point 4.1.; point 4.4.; point 5.3.; point 8.3.)

The **CSS**, like many institutions, draws attention to the need to protect properly minors and young adults. There is a link between youth vaping and smoking, but the likelihood that vaping facilitates the transition to smoking is certainly possible, but insufficiently demonstrated. The relationship between the two is complex and divides many institutions. The same goes for **CSS experts**.

However, **all agree** on a common objective, which is to discourage the use of nicotine among youth and young adults for three reasons:

- The action of nicotine on brain development (demonstrated on animals laboratory).
- The nicotine dependence effect: the use of e-cigarettes can lead to nicotine dependence and increased consumption of e-cigarettes and can

also go hand in hand with simultaneous or subsequent use of tobacco. The objective is to prevent young experimenters from becoming regular users (nicotine, tobacco).

- Young people who smoke today are more likely to have grown up in a home where they smoke or to be in contact with friends who smoke. Young people from these households, like more privileged young people growing up in more protective environments, are entitled to a nicotine-free start at an early age.

To reduce the appeal of e-cigarettes to young people, the **CSS** recommends acting at different levels: on legislation, information, communication, research and prevention.

From a legislative point of view, e-cigarettes with or without nicotine are treated as tobacco products with regard to rules on advertising, sale and consumption in public places. This implies that

- Advertising and sponsorship for e-cigarettes is prohibited.
- it is forbidden to sell e-cigarettes to young people under the age of 18.
- It is forbidden to consume e-cigarettes in closed public places and in a covered vehicle where a person who has not reached the age of 18 is present.
- the packaging is sober
- distance selling is prohibited (see also point 2.2.1.)

The **CSS** is of the opinion that the standards applicable to e-liquids with nicotine are for nicotine-free e-liquids and ingredients.

The composition of e-cigarettes and e-liquids with nicotine is also regulated and certain ingredients are prohibited. The ingredients currently present in e-liquids (and on the market) have not all been studied with regard to their toxicity and/or attractiveness. As indicated above, the composition of e-cigarette liquid must, in the near future,

be limited to a positive list of products whose harmlessness is reasonably established (this is the pragmatic solution, in particular the "upgradable and adaptable positive list" described in point 4.1).

With regard to prevention, information and communication, the **CSS**

- pleads for additional information via the inserts on the packaging of e-cigarettes (see above).
- also advocates for additional health warnings in the conventional cigarette packs and e-cigarettes (see above).
- to continue information sessions on the prevention of vaping and on the nicotine in schools (the distinction between tobacco and nicotine).
- to include information on vaping and on nicotine in the current campaigns aimed at young people (the campaigns are already adapted to young people who smoke and vape more).

[Updates relating to the gateway hypothesis to conventional cigarettes](#) (point 7.3.; point 7.4. ; point 8.3.2.)

There is a link between youth vaping and smoking but it has no proof causation to date. The relationship between the two is complex. **Most experts** are of the opinion that the gateway hypothesis cannot be sufficiently substantiated scientifically.

This factor plays a major role in the e-cigarette debate. Caution is however when it comes to young people and nicotine consumption. The use of e-cigarettes by young people must be appropriately monitored and strict regulations on sales, distribution, marketing and distribution must continue to be applied.

advertising to young people.

Relative risk: distinction between (smoked) tobacco and nicotine

What emerges from the different positions is that the limited relative risk of vaping (compared to smoking) is accentuated and accepted by many institutions and authorities. The distinction between (smoked) tobacco and nicotine is essential. The "risk continuum" that exists within available tobacco and nicotine products – from low-risk products like e-cigarettes to high-risk products like tobacco

smoked - is very widely accepted around the world.

At the same time, these institutions highlighting the opportunities also point out that vaping is not without risk and a recurring question concerns, among other things, its long-term effects. Most of these organizations also emphasize that the e-cigarette is not intended for non-smokers and young people.

The policy relating to the e-cigarette must aim at the same time, to better inform smokers about this less risky (but not without risk) alternative and to protect youth and young adults from nicotine and smoking.

Critical monitoring by the competent authority of the recovery of the concept of risk reduction is however necessary because the tobacco industry is taking up this philosophy as part of its own market development strategies. In the years to come, the sector will probably focus even more on a world called "smokeless" and "smokeless products". Indeed, the tobacco industry targets smokers who switch to nicotine (not smoked) and non-smokers who quit smoking tobacco and nicotine use. With its discourse on a world without smoked tobacco, the tobacco industry also wants to take on another role, in particular its role as an actor and partner in health policy. Today, the tobacco industry is very present on the e-cigarette market, but the majority of the e-cigarette market could remain in the hands of independent companies (2019 figures¹⁴).

Belgium has signed the framework convention of the World Health Organization (WHO) for tobacco control for a long time (WHO, 2005). Belgium is therefore committed to following Article 5.3 15 of this convention which, moreover, enjoins in particular the Member States members to protect their Health Promotion policies against the influences and

¹⁴ See the University of Bath's Tobacco Tactics website: <https://tobacotactics.org/wiki/e-cigarettes/> (page last updated on 15/3/21). Based on Euromonitor figures from 2019, this page states: "Overall independent e-cigarette companies maintained the larger share of the global market, although this fell from over 80% in 2014 to just over 56.2% in 2019."

¹⁵ In defining and applying their public health policies on tobacco control, Parties shall ensure that such policies are not influenced by the commercial and other interests of the tobacco industry, in accordance with national law.

interests of the tobacco industry. Tobacco companies certainly bear a heavy responsibility for the high incidence of lung cancer and a number of chronic diseases. It is very likely that the tobacco industry wants to exploit nicotine addiction to sell its e-cigarettes and other nicotine-based products. unsmoked nicotine. It is obvious that society must remain very vigilant regarding the intentions and strategy of tobacco manufacturers. However, this should not hide the fact that the e-cigarette, thanks to the combination of nicotine and the action of putting the e-cigarette in the mouth, which resembles that of smoking, can indeed play a role in the smoking cessation.

Update on the effectiveness of e-cigarettes in the tobacco control process. (point 7.2.; point 7.5.; point 8.2.)

The positions of the various institutions and countries on the place of the e-cigarette in the tobacco control processes are **shared**, as they are, moreover, within the **CSS working group experts**. The “risks” and “opportunities” perspectives confront each other and feed the debate on this subject.

In the evaluation of the e-cigarette as a smoking cessation device, there are once again tensions. Institutions (WHO, etc.) that currently remain faithful to recognized smoking cessation medications and behavioral support attribute also a role for the e-cigarette with nicotine (some smokers can benefit from it). They often insist on the medical status of the e-cigarette if it is used as an aid to smoking cessation. Other institutions (e.g. PHE¹⁶) that recommend e-cigarettes, regardless of recognition as a medical status, advocate faster implementation of vaping as a means of smoking cessation among smokers and therefore faster positive communication regarding e-cigarette.

Still other institutions (e.g. ERS¹⁷) point out that the current scientific evidence for the use of e-cigarettes as a smoking cessation agent is insufficient (McAlinden et al. 2021).

Are there any guidelines on the best way to use the e-cigarette like smoking cessation agent”? What framework is needed? For example, additional information and advice from tobacco specialists? (point 7.2. ; point 7.5.)

The e-cigarette is an alternative source of nicotine and can have its place in the fight smoking and, with clear guidelines, it can be combined with the best aid to smoking cessation (tobacco specialist, smoking cessation drugs).

In our country, the e-cigarette could have a role to play as part of the traditional smoking cessation service (it can be combined with a TSN, with a behavioral support by a tobacco specialist) in consultation with the smoker. Also in outside the smoking cessation supervision framework (among the general population who does not use smoking cessation aids), there is potential but also many

¹⁶ PHE: *Public Health England*

¹⁷ ERS: *European Respiratory Society*

warnings (point 7.5). According to the **CSS**, the e-cigarette may also play a role positive in quitting smoking for specific target groups, such as people with mental (psychic) health problems, people in social vulnerability, etc.

The available evidence is still conflicting to definitively answer the question. question of knowing to what extent and for which more or less smokers, e-cigarettes are effective for smoking cessation and can facilitate long-term abstinence. The smoking cessation studies known to date with the e-cigarette have a maximum follow-up of one year.

However, the results suggest that, pending further large-scale studies, the use of e-cigarettes for the purpose of quitting smoking may increase abstinence rates in combination or not with behavioral therapy (Myers Smith et al., 2021).

The results seem to indicate that e-cigarettes can also be used for smoking cessation in specific contexts (eg psychiatry) and in consultation with the smoker.

In clinical practice, one also encounters smokers who have quit traditional cigarettes by using the e-cigarette and who now wish to quit vaping and for this we must also formulate practical guidelines to help stop vaping.

In the United Kingdom, a pharmacovigilance system for e-cigarettes has been set up, even if e-cigarettes are not recognized as medicines. With drugs, pharmacovigilance is automatically put in place. This aspect ("spontaneous reporting of suspected side effects") should also be taken into account for the e-cigarette as a consumer product, in particular when the e-cigarette is more widely recommended.

Are there profiles of users who benefit/do not benefit from the e-cigarette as a smoking cessation agent? (point 6; point 7.2.)

People with lower socio-economic status (SES) and people with reduced situation of social vulnerability smoke more and therefore experience more morbidity and tobacco-related mortality. Smoking is therefore one of the main causes of health inequalities in our society. These groups should be targeted more via measures based on the level of the population and an offer of adapted smoking programs, including e-cigarettes.

The e-cigarette can play a role in smoking cessation in specific target groups such as people with mental (psychic) health problems. However, young non-smokers should be kept away from these products.

Regarding the place of e-cigarettes in pregnant women, in the UK the *Smoking in Pregnancy Challenge Group*, a coalition of organizations seeking to reduce smoking during pregnancy, has developed guidelines on the use e-cigarettes for health professionals involved in pregnancy and

infographics for pregnant women themselves. 18 The *Royal College of Midwives* (2019) also does not disapprove of the use of e-cigarettes by pregnant women who want to quit smoking.¹⁹ For pregnant women elsewhere in the world, TSN is only recommended for those who want to quit smoking. Indeed, the consumption of nicotine, in any form whatsoever, is strongly discouraged for pregnant women, except in the context of smoking cessation. Nicotine is teratogenic; it has adverse effects on reproduction and the fetus. However, nicotine replacement therapy can be used to encourage pregnant women to quit smoking because continuing to smoke is even more harmful to the fetus. Currently, in our country, e-cigarettes are not used by pregnant women to quit smoking but classic TSNs (recognized drugs for smoking cessation) are.

The prison population is also a group that is particularly exposed to smoking-related risks. Some health promotion associations, working in prison, speak of more than 80% of smokers within this population. Currently, the use of e-cigarettes is not authorized there (Al Kurdi, 2021; Moliner-Dubost, 2012; Picot-Ngo et al., 2020).

Smoking among people with mental (psychological) health problems is an acute and urgent problem: its prevalence is very high and a large proportion of health problems and deaths in this group are due to smoking.

Traditional smoking cessation methods do not seem to work or work less well in this group. For this reason, several researchers put forward the e-cigarette as an alternative. **Some** CSS experts also point to the past and current lack of interest in smoking cessation counseling within mental health services.

According to some studies (see chapter 6), the e-cigarette is accepted within this target group and “vaping” is less harmful than smoking tobacco at least in the short term, which argues in favor of the recommendation of e-cigarettes as a temporary aid to smoking cessation among this target group.

Psychiatrists should also be better informed about e-cigarettes so that a shared decision can be made with the patient on whether or not to use e-cigarettes. in the context of smoking cessation. The first priority remains the reduction of tobacco consumption.

Based on informed choice and shared decision-making, it is possible to select the best way to quit smoking for the smoker in this target group specific. Of course, the traditional methods for smoking cessation via tobacco specialists remain of great importance. Tobacconologists wishing to offer smoking cessation assistance to vulnerable groups should be trained to advise these groups and familiarize themselves with the use of the e-cigarette as a smoking cessation device in the event that, after an informed choice, the e-cigarette is the chosen method.

The combination of a TSN and an e-cigarette is also an option. At the same time, it is important that good scientific research is carried out on the effectiveness of the e-cigarette as a smoking cessation tool within the target group

¹⁸ <https://smokefreeaction.org.uk/smokefree-nhs/smoking-in-pregnancy-challenge-group/smoking-in-pregnancy-challenge-group-resources/e-cigarettes-in-pregnancy/>

¹⁹ <https://www.rcm.org.uk/media/3394/support-to-quit-smoking-in-pregnancy.pdf>

specific to smokers with a mental (psychological) health problem and on the long-term effects of using e-cigarettes. This should take into account the specific behavior and characteristics of people with mental disorders as well as the relationship between nicotine addiction and other addictions (such as alcohol or drugs) and the best way to deal with combined addictions.

2.3. Other Considerations and Recommendations

2.3.1. Distance Selling

With regard to distance selling, the position of the experts is **divided**. A **majority** of them is in favor of the ban on distance selling while a **minority** pleads for regulated distance selling under certain exceptional conditions. Some consumers today fall back on the newsagent; point of sale more accessible. However, these newsagents mainly offer a limited supply of e-cigarettes from the tobacco industry (there are also products from independent producers). Vendors at newsstands offer minimal advice on e-cigarette use (because these vendors get their information mainly from tobacco companies and are not e-cigarette specialists, while the sellers of the *vapeshop* shops have much more knowledge about the product). It should be noted that advice is totally absent during distance selling.

Moreover, the **majority of experts** put forward arguments in favor of banning distance selling, in particular,

- the role of sellers in the context of smoking cessation is essential for provide advice/explanations, which cannot be done over the *Internet*. However, this role should be taken more seriously and supported.
- Checking age over the *Internet* is almost impossible.
- The quality of the products sold by *Internet* is sometimes lower compared to the products sold through stores.

2.3.2. Points of sale

The e-cigarette should not be treated more strictly than conventional cigarettes in terms of accessibility and packaging/labelling. Conventional cigarettes should be more difficult to access than e-cigarettes.

The **CSS** recommends that the sale of e-cigarettes remain sufficiently accessible in (non) specialized points of sale and this to give adult smokers the chance to have access to lower-risk products. Currently, e-cigarettes are available in specialized *vapeshops*, newsagents, gas stations, night shops or supermarkets.

Pending the theoretical day when a medicinal e-cigarette will be available in pharmacies, the **CSS** recommends the sale of a limited range of quality e-cigarettes, considered attractive by smokers - as a consumer product (therefore not only in

as a drug) - in pharmacies in addition to sales made elsewhere.

The advantages are:

- o The pharmacist is reliable and easily accessible, he can credibly encourage smokers to use this smoking cessation product.
- o The pharmacist can help the smoker to quit smoking and give him advice (for example on the combination of e-cigarettes and NRTs) and can refer to the professional offer of help with smoking cessation (Tabacstop or tobacco specialists).
- o Conditions and criteria:
 - training of the pharmacist
 - ethical criterion: can only be offered in pharmacies
 - vaping products from independent producers (= not related to the tobacco industry).
 - wholesalers must be able to offer quality vaping products.
- the prevention sector provides pharmacists with tools to steer sales in the right direction and correctly inform purchasers, for example brochures to distribute or training courses organized for them. Budgets should be provided for this purpose.

2.3.3. Ban e-cigarette displays at points of sale

Some experts suggest banning e-cigarette displays in retail outlets.

sale with the exception of specialized points of sale (such as *vapeshops*) where the e-cigarette may still be visible. Specialty stores mainly attract an audience looking for nicotine products. Night shops, newsagents, neighborhood grocery stores, gas stations, etc. are frequented by all,

understood by young people who stop there to buy school supplies or sweets. The ban on displays in these latter points of sale aims to counter impulsive purchases by young people but also by ex-smokers or *ex-vapers*. The ban on displays will contribute to better protection of minors against the use of e-cigarettes according to the supporters of this ban. After all, displaying products in a highly visible manner is a form of inducement and influences the likelihood that the product will be purchased by young people especially now that the big tobacco companies are stepping up their promotion to young people through social media or at festivals. In addition, a display ban makes it more difficult to violate advertising bans, facilitates enforcement of advertising laws, and reduces the risk of lengthy and costly litigation.

Other experts disagree with the display ban because it discourages adult smokers from coming into contact with the e-cigarette (the visual stimulus is absent) and using it as a smoking cessation tool. This ban also confirms and reinforces the negative perception of the e-cigarette. The presentation of lower-risk products is a form of incentive: it can steer adult smokers towards a less dangerous choice. Many *vapeshops* have disappeared in recent years, leaving

many smokers turn to other outlets to gain exposure to e-cigarettes.

The prohibition of displays in low "level" points of sale (such as kiosks

to newspapers) but not in *vapeshops* also lacks logic. Plain packaging for e-cigarettes (as this review recommends) is a better measure to discourage use by minors (such packaging is however not a useful measure if it has to be hidden afterwards) . A distinction must also be made between display bans and displays. The former is a form of advertising and is currently prohibited by law. Enforcement of this ban is important, but it

is separate from the discussion of banning displays. What is necessary and urgent, on the other hand, is to put in place a ban on tobacco displays. This system has still not been introduced in our country although it has been in place for years in many European countries.

CSS supports banning tobacco displays .

The **CSS** recommends that the gradual abandonment of the sale of tobacco and the introduction of e-cigarettes, including those sold as medicines, be accompanied by a long-term strategic plan so that the current points of sale (supermarkets, newspapers, *vapeshops*) know what we are tending towards.

2.3.4. Communication

The **CSS** is of the opinion that smokers should be informed about the relative risks of the e-cigarette compared to smoking and compared to not smoking and about the potential of the e-cigarette as a smoking cessation device.

Sixty-four percent of smokers think e-cigarettes are as harmful (55%) or more harmful (9%) than smoking tobacco products (STK Tobacco Survey, 2021).

In order to correct the many misconceptions concerning the harmfulness of e-cigarettes, it is suggested that the following parties and authorities provide information to smokers:

o The **competent authority**

• through inserts and mandatory health warnings,

• by specialized points of sale (*vapeshops*): examine what roles they can play in disseminating standardized information on the relative risks of vaping in relation to smoking or not.

o **Smoking cessation aid organizations and those in contact with health**

professionals: these organizations are aimed at smokers (directly or indirectly via tobacco specialists, Tabacstop and other health professionals) ; they develop methodologies, offer smoking cessation aids, stay in contact with various health professionals in certain sectors, organize or participate in campaigns, etc.

o **Health professionals** and other professionals (in companies, municipalities, hospitals, etc.) who are in contact with smokers.

In fact, correct communication with smokers should be sought:

- point out that e-cigarettes also present health risks, but to a much lesser extent than smoked tobacco;

- help smokers understand that vaping is less dangerous than smoking;
- emphasize that e-cigarettes can play a positive role in helping smokers quit.

2.3.5. Subject e-cigarettes to the measures of the Directive on tobacco products and the FCTC

The general rule is that the e-cigarette must fall under tobacco law (i.e. Belgian law, EU Tobacco Products Directive and FCTC 20).

Within these frameworks, specific adaptations can then be made to the e-cigarette, taking into account the recommendations of this opinion. Removing e-cigarettes from existing tobacco regulations is bad for public health protection. Within this general framework, the reduction of risks by using the e-cigarette is a strategy to be implemented within the framework of the WHO FCTC.

2.3.6. Need for further monitoring and research

In our country, there is a lack of regular monitoring and figures, as well as research on many of the subtopics that help shape the e-cigarette debate.

It is essential to better monitor the use of e-cigarettes (and other lower-risk products) by young people and adults: today, we only have the Sciensano survey on health (all 4 years), the Tobacco Survey on Smoking of the Foundation Against Cancer (FCC), the Eurobarometer and very limited regional youth use figures and data

(VAD²¹).

- **Qualitative research with smokers is very useful:** what are the needs/wants/barriers/difficulties of smokers: What do they do/think/want, what are their experiences with quitting, why do they make so few quit attempts, how do smokers who say they will quit without help quit, what can the recognized smoking cessation offer learn from it (how to better adapt this offer to the current behavior of the smoker) , how is the e-cigarette used as a smoking cessation tool, how can it play a role in reducing smoking and tobacco-related health inequalities?
- **Research on marketing to young people online:** how are young Belgians approached online by tobacco and e-cigarette manufacturers?
How does social media work as an advertising channel for young Belgians? What (other) forms of marketing do young Belgians face today? How can the competent supervisory authority react precisely to possible new marketing strategies?

²⁰ FCTC : Framework Convention on Tobacco Control

²¹ VAD: *Vlaams expertisecentrum voor Alcohol en andere Drugs*- Flemish association for problems with alcohol and other drugs

- **Market analysis:** Currently, it is difficult to find independent information on our market (and its evolutions). It would be interesting to get a good overview of the products on our market today and where they come from. The **CSS** recommends clarifying the division of the market between tobacco companies and independent producers and suggests integrating this point

in the European notification system (EU-CEG).

2.3.7. Need for independent complementary studies

The **CSS** is of the opinion that it is desirable that the list of authorized chemical substances in e-cigarettes be limited as soon as possible to substances which can reasonably be assumed to have no properties harmful to health. If the Belgian authorities wish to implement this restricted list in the short term, a working group composed of independent toxicologists and prevention experts should be set up to propose, on the basis of the scientific literature, to remove from the list substances with potentially toxic properties. A substance for which data indicate a carcinogenic, genotoxic, endocrine disrupting or reprotoxic effect is then withdrawn without waiting for formal proof that the toxic effect actually occurs (or may occur) in humans.

If, in particular (see point 4.1.2.) for legal reasons, stemming for example from European regulations, the Belgian authorities decide to follow a slower procedure which is more in line with the European approach, the advice from the aforementioned working group for the reduction of the list and for the extension of the list of authorized substances, to await additional research which may include *in silico*, *in vitro*, *in vivo*, molecular epidemiological and epidemiological studies. This study can therefore address the specific risk linked to exposure by inhalation and the possible toxicity due to the heating of the components. This procedure may also lead to the setting of maximum permissible levels of flavourings.

In order to guarantee the quality of products on the market, it is necessary to:

- strengthen controls on ingredients and their content, as well as on the presence of impurities and toxic volatile organic compounds (VOCs),
- promote studies on the **long-term** effects of the consumption of e cigarette,
- promote studies on the effects of inhaling **nicotine** alone (outside the context of tobacco),
- promote studies on the effect of inhaling **nicotine salts** and their impact in the context of smoking cessation (versus *freebase* nicotine).

These types of studies or working groups should be organized at EU level. If each Member State were to do this independently, the cost would be enormous when so many other needs in the field of consumer protection against toxic substances, prevention of smoking and smoking cessation remain unmet due to the lack of public funding.

3 METHODOLOGY

After analyzing the request, the College and the chairman of the working group identified the expertise needed. On this basis, an *ad hoc* working group was set up within including expertise in tobacco, toxicology, oncology, physiology, carcinogenesis, psychology of dependence/addiction, chemistry of contaminants and additives, pulmonology, tobacco prevention, behavioral change, health inequality were represented. The experts in this group completed a general and *ad hoc* declaration of interests and the Ethics Committee assessed the potential risk of conflicts of interest.

Representatives of associations in the field and of the various administrations concerned by this issue were also heard as part of the work of the working group.

The opinion is based on a review of the scientific literature, published both in scientific journals and reports of national and international organizations competent in the field (*peer-reviewed*), as well as on the opinion of experts.

After approval of the opinion by the working group, the College validated the opinion as a last resort.

Keywords and MeSH descriptor terms²²

MeSH terms*	Keywords	Keywords Mots clés	keywords
Electronic Nicotine Delivery Systems	Electronic cigarette	Electronic Cigarette Cigarette electronic	Cigarette electronic
Tobacco	Tobacco	Plate Tobacco	Plate
Behavior, addictive	Addiction	addiction Addiction	Seeks
Smoke	Smoke	To smoke To smoke	Smoking
Nicotine	Nicotine	Nicotine Nicotine	Nicotine
Cessation, smokeless tobacco	Smoking cessation	Quit smoking Tobacco withdrawal Stop smoking	smoking cessation
Cigarettes	Cigarette	Cigarette Cigarette	Cigarette
	Vaping	Dampen Vaping	vaping

MeSH (Medical Subject Headings) is the NLM (National Library of Medicine) controlled vocabulary thesaurus used for indexing articles for PubMed <http://www.ncbi.nlm.nih.gov/mesh>.

²² The Board would like to point out that the terms MeSH and keywords are used for referencing purposes and easy definition of the scope of the notice. For more information, see the "Methodology" chapter.

List of abbreviations used

DNA	Deoxyribonucleic acid
WITH	Royal decree
ASH	<i>Action on Smoking and health</i>
AVP	<i>Advanced Personal Vaporizers</i>
ONE	<i>British American Tobacco</i>
COPD	Chronic obstructive pulmonary disease
CBD	Cannabidiol
CCLAT	Framework Convention for Tobacco Control
CDC	<i>Centers for Disease Control</i>
CEN	<i>European Committee for Standardization - European Committee for Standardization</i>
CIRC	International Agency for Research on Cancer - IARC: <i>International Agency for Research on Cancer</i>
CLP	<i>Classification, labelling, packaging</i>
CMR	<i>Carcinogenic, mutagenic or toxic for reproduction</i>
CSS	Superior Health Council
CO	Carbon monoxide
COV	Volatile organic compounds
DIY	<i>Do it yourself</i>
DL 50	Median lethal dose
ECHA	<i>European Chemicals Agency</i>
e-cigarette e-liquid	Electronic cigarette Liquid contained in the cartridges
EFSA	<i>European Food Safety Authority</i>
ENDS	<i>Electronic Nicotine Delivery Systems</i>
EN&NNDS	<i>Electronic nicotine and non-nicotine delivery systems</i>
ERS	<i>European Respiratory Society</i>
ESG	General secondary education
ESP	Vocational secondary education
IS	Technical secondary education
EU-CEG	<i>EU Common Entry Gate</i>
EVALI	<i>e-cigarette or vaping product use associated lung injury</i>
FCC	cancer foundation
FDA	<i>Food and Drug Administration</i>
FEDITO	Brussels Federation of Institutions for Drug Addicts
FEMA	<i>Federal Emergency Management Agency</i>
FRONT	<i>Gamma-aminobutyric acid</i>
HDL	<i>High-density lipoprotein</i>
HPA	<i>Hypothalamic- pituitary-adrenal - hypothalamic-pituitary-adrenal</i>
HPHC	<i>Hazardous & Potentially Hazardous Compounds – harmful and potentially harmful components</i>
IQOS	<i>I-Quit-Ordinary-Smoking</i>
ISO	<i>International Organization for Standardization - Organisation international standardization</i>

EVE	<i>Independent European Vaping Alliance</i>
YEARS	tobacco control
LDL	<i>Low-density lipoprotein</i>
ALONE	<i>National Academies of Science, Engineering and Medicine</i>
NICE	<i>National Institute for Health and Care Excellence</i>
OMS	World Health Organization – WHO: World Health Organization
PG/GV	Propylene glycol / vegetable glycerin
PHE	<i>Public Health England</i>
PMI	<i>Philip Morris International</i>
RCP	<i>Royal College of Physicians</i>
RCT	<i>Randomized controlled trial</i>
REACH	<i>Registration, Evaluation, Authorization and restriction of CHemicals</i>
RIVM	<i>National Institute for Public Health and the Environment - Pays-Bas</i>
SGH	Globally Harmonized System
SKT	Foundation against Cancer
SNC	<i>Central nervous system</i>
SPD	<i>Serious psychological distress - severe psychological distress</i>
SPF	Federal public service
SSE	Socio-economic status
SSM	Mental health care
SVHC	<i>Substance of very high concern</i>
TC	<i>Tobacco control</i>
THC	ÿ-9-tetrahydrocannabinol
THR	<i>Tobacco Harm Reduction</i>
TSN	Nicotine replacement therapies
UE	European Union
WHAT	<i>Flemish expertise center for Alcohol and other Drugs Association</i> Flemish for alcohol and other drug problems
VLDL	<i>Very-low-density lipoprotein</i>
YPLL	<i>Years of potential life lost</i>

IV NORMATIVE AND LEGISLATIVE ASPECTS

4.1. Composition of e-cigarettes and e-liquids

4.1.1. Current situation

4.1.2. Evolution possible

4.2. Notification

4.2.1. Current situation

4.2.2. Desired development

4.3. Labeling

4.3.1. Current situation

4.3.2. Desired development

4.4. Advertising, sale and consumption in public places

4.4.1. Current situation

4.4.2. Desired development

4.1. Composition of e-cigarettes and e-liquids

4.1.1. Current situation

The composition of e-cigarettes and e-liquids with nicotine is specifically regulated in article 4 of the Royal Decree of 28/10/2016 relating to the manufacture and marketing of electronic cigarettes which transposes the article 20 of Directive 2014/40/EU.

It emerges in particular that:

Nicotine-containing liquid does not contain nicotine above 20 milligrams per milliliter.

The liquid containing nicotine does not contain the following additives:

- vitamins or other additives creating the impression that the e-cigarette has beneficial health effects or that the health risks it presents have been reduced. It follows from the interpretation of this provision that the presence of cannabidiol (CBD) and vitamin E acetate is, for example, prohibited (only

in liquids with nicotine);

- caffeine or taurine or other additives and stimulants associated with energy and vitality;
- additives which give coloring properties to emissions;
- additives which, without combustion, have CMR23 properties .

Only are used in the liquid containing nicotine, with the exception of nicotine, ingredients which, heated or not, do not present risks to human health.

Only high purity ingredients are used for the manufacture of the nicotine containing liquid.

²³ CMR: carcinogenic, mutagenic and reprotoxic

Finally, liquids containing nicotine are only placed on the market in specific refill bottles with a maximum volume of 10 millilitres, in disposable e-cigarettes or single-use cartridges. These bottles are child resistant and tamper evident.

4.1.2. Evolution possible

Several options were considered and discussed in the working group:

- No modification of the current regulations. This proposal was not considered acceptable by the experts.
- Total or drastic ban on flavorings in e-liquids. Some parliamentarians introduced bills calling for a total ban on flavorings or a drastic reduction in their number. This total or drastic ban is not the solution, according to experts. This option may not be compatible with the needs of users and could therefore create frustration among them with the risk of abandoning the e-cigarette. It should not be forgotten that there is a substantial market of flavors (in particular flavors authorized for food) which can be purchased and added to e-liquids. Obviously, ingredients with known toxic properties should be prohibited. The e-liquids present on the market must be the most "safe" possible for users and therefore be regulated to limit the risk, but a total ban on flavorings can compromise the potential of the e-cigarette as a smoking cessation aid.
- Prohibition of characterizing flavors as proposed for tobacco products in the directive. However, it is difficult to apply this concept to e-cigarettes: how to define if a product contains a characterizing aroma, which product is to be authorized or prohibited? Some countries (in Hungary, Finland and envisaged by the Netherlands) try but encounter various problems. This option is therefore not retained in part because it does not allow control of the market and in practice leaves the choice of ingredients to producers in countries that have applied this option.
- Creation of a negative list of prohibited additives because they present an unacceptable risk from a toxicological point of view versus creation of a positive list of authorized additives because they present an acceptable risk from a toxicological point of view. As specified in chapter V on aromas, research on their toxicity is currently limited to certain flavors. Studies on the interactions between different aromas and the formation of toxic heating products are rare.

A negative list would therefore be limited to products for which data are available but would provide no guarantee as to the acceptable risk of e-cigarette mixtures present on the market.

Experts believe that a restricted (positive) list of harmless substances should be drawn up, the presence of which as additives may be authorized in e-cigarettes, to replace the more than 1,800 substances currently authorized. The

toxicological properties of the vast majority of these substances are not sufficiently known. These are essentially flavors or fragrances. Only additives for which it is reasonably established that they are harmless to health may be authorized. Firstly, toxicological evaluation criteria such as genotoxic, endocrine disruptor or carcinogenic effect can be taken into account. However, the experts would like to point out that a correct positive list can only be established on the basis of a comprehensive risk assessment on a scientific basis. Several necessary data are not available here, such as exposure data (intensity of vaping, content of additives, etc.) and toxicological reference values. In addition, in order to assess the level of toxicological risk

acceptable, allowable doses/concentrations and possible ingredient interactions must be determined.

A **first proposal** for a positive shortlist concerns its development by a working group made up of toxicologists and prevention experts, on the basis of the available scientific literature. The CSS refers here to its opinion 9404 on physico-chemical hygiene and the importance of early exposure (CSS 9404, 2019). The intention is then to include in the positive list only those substances for which no data has been found in the literature indicating a possible genotoxic, endocrine disrupting or carcinogenic effect. It should also be noted that for many flavorings there is information on oral absorption but inhalation may sometimes be associated with specific toxic effects.

The e-cigarette is destined to seduce several hundred thousand people in Belgium and not only smokers or former smokers. It is very likely that it is much less harmful than tobacco smoke, but it is also certain that it too involves exposure to substances harmful to health. The extent of the adverse health effects of e-cigarettes (cancer, cardiovascular disease, diabetes, obesity, infertility, impaired development and cognition, immune system diseases) will only be determined with some precision in a few decades. at least because of the long latency period of cancer (Nadler & Zurbenko, 2014) and some other diseases of civilization. Moreover, epidemiological studies only rarely identify a risk factor causing cancer with a relative risk of less than a factor of 1.5 (Ehrenberg, 1996). Furthermore, even after decades, it will be extremely difficult to determine which ingredients in e-cigarettes are responsible for any proven health damage. At present, more than 1,800 substances can be added to the liquid of the e-cigarette. The acquisition of sufficient toxicological knowledge of these 1,800

substances will take far too long, a period during which the Belgian population will continue to be exposed to the effects of toxic substances among these 1,800 additives. It is likely that a high percentage of reactive substances (and probably about 10% of non-polymers) have genotoxic and carcinogenic properties (see Alberts et al., 1994, p. 243; Huff, 1993; Huff & Hoel, 1992). With regard to endocrine disruption, in September 2017, 1,409 chemicals were already listed as possible endocrine disruptors based on data published in *peer-reviewed* literature (TEDX, 2017).

To give an idea of the magnitude of this problem of identifying and regulating toxic substances, here is an excerpt from an article (Bourguignon et al.,

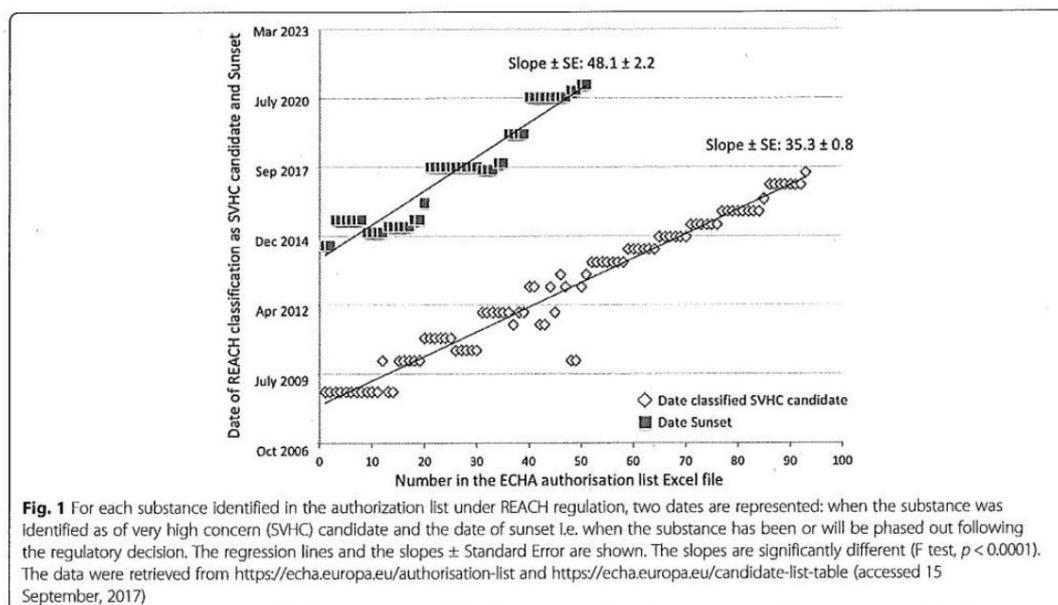
2018) published by a working group of CSS 9404, 2019 in *Environmental Health*, a reputable periodical:

“The REACH24 regulation, which applies since 2008, allows action under its authorization regime: a hazardous substance can be included in the candidate list, i.e. identified as of very high concern (SVHC) and subsequently included in the so-called “authorization” list, i.e. banned as of a sunset date (European Parliamentary Research Service). The data on these two regulatory actions (European Chemical Agency, 2017 candidate list; 2017 authorisation list) indicate that there is on average a 7-year time span between the moment a substance has been identified as a SVHC and the moment it is being phased out. This time span however appears to increase with time (Fig. 1) as indicated by the slopes of the regression lines which are significantly different (F test, $p < 0.0001$).

The time span is longer (F test, $p < 0.001$) for substances identified as SVHCs in the period 2011-2013 (7.67 ± 1.41 yrs, mean \pm SD) than 2008-2010 (6.46 ± 0.69 yrs).

Between October 2008 and June 2013, 52 substances have been regulated as SVHC accounting for 10 chemicals regulated each year. The regulatory decision about those 52 chemicals refers most frequently to carcinogenicity ($n = 28$) and toxicity for reproduction ($n = 14$), not excluding associated endocrine disrupting properties such as observed with phthalates (Gore et al., 2015). Also shown in Figure 1, there are 42 substances that have been identified as SVHCs between December 2013 and July 2017 (European Chemical Agency, 2017 candidate list) but no decision to phase them out has been taken so far (European Chemical Agency, 2017 authorisation list).

Figure 1. Substances as very high concern



We must not forget that there are more than 100,000 chemical substances on the market and that approximately 140,000 substances are listed under the European REACH program (Backhaus et al., 2010). Prior to 2008, the European Union (the European Chemicals Agency (ECHA)) had pre-registered 145,297 chemical substances (last updated August 11, 2017). There are therefore other priorities than concentrating the resources available on toxicological testing of the 1,800 ingredients in a stimulant.

²⁴ REACH : *Registration, Evaluation, Authorization and restriction of CHemicals*

But even this positive list does not offer absolute protection. Indeed, many data are lacking, particularly with regard to toxicity by inhalation. Indeed, the above approach would rely primarily on genotoxic or carcinogenic properties, endocrine disrupting activity and oral toxicology data.

In principle, according to current regulations, producers must demonstrate that their product is free of these properties, but practice shows that the information provided by producers is sometimes incomplete or insufficiently objective.

Starting from the observation that a limited positive list based on the current literature does not guarantee not safety when using the e-cigarette and therefore inhaling, that a list based on the current literature leaves room for complex legal procedures between the competent authority and the manufacturers and that the list must also leave enough room to offer an acceptable palette of aromas (an aroma is not made up of a single

component but of a series of components which together determine the taste), a second proposal has been formulated.

This **second proposal** is an evolving positive list based on the existing market.

The e-cigarette market has developed very rapidly and continues to be very active. It appears that the number of new liquids put on the market intended for consumption in e-cigarettes is significant and that new additives continue to arrive on the market constantly.

The idea developed here is the creation of a positive list of additives authorized in liquids for e-cigarettes. It would be made up initially of all the additives present legally, on a certain date, on the market. This means additives used in liquids whose notification file has been validated and which are included in the positive list

communicated by the FPS Public Health. Any new additives would be prohibited once the list is published.

To give an order of magnitude, the joint action on tobacco control carried out data analysis at EU level. It shows that 1,473 unique ingredients were present in the EU-CEG25 database for Belgium at the beginning of 2020 .

legislative, this list will be defined in a ministerial decree, under the responsibility of the Minister of public health.

This starting list can then be analyzed in detail, without new additives being able to constantly be added to the market. Additives or combinations additives identified as problematic would then be removed from this list and therefore banned from the market.

Given that the list would be defined by ministerial decree, its creation would be up to the Minister of Public Health. Reducing the number of additives on this list would therefore be a theoretically political choice. On such a subject, a strong scientific basis is however necessary to guide the Minister's choice. The criteria (indicative list) that could justify the deletion of certain additives from the list could initially be:

²⁵ EU-CEG: *EU Common Entry Gate*

- The legal criteria currently already in place, defined in article 4 § 3 and § 5 of the Royal Decree of October 28, 2016 relating to the manufacture and placing on the market e-cigarettes which transposes article 20 of directive 2014/40/EU as specified in point 1.2.1.
- Some of these criteria are easy to apply because data exists. These are, for example, the CMR properties of certain unburnt additives. others criteria require in-depth analysis and therefore significant work carried out by a team with specialized skills. This is the obligation to use only additives which, heated or not, do not present a risk to human health. For many of them, the data, especially when they are heated are missing.
- The criteria relating to increasing the attractiveness of e-liquids for non-smokers, while taking into account the need to offer sufficiently satisfactory products to smokers wishing to quit tobacco consumption.

Such detailed analysis work, in particular with regard to the criteria defined by article 4 § 3 and § 5 of the Royal Decree of October 28, 2016, requires recognized expertise as well only appropriate means.

This positive list solution based on the market situation at a specific time is a pragmatic solution that has many advantages:

- Just like a classic positive list, it prevents manufacturers from constantly marketing new additives of which nothing is known.
- Contrary to a classic positive list, it however returns the responsibility for the presence of an additive on the list to the producers who placed the additive on the market. There is no certification from the authorities that these additives present in the market are safe. • Just like a negative list, this system makes it possible to prohibit additives problematic.
- Unlike a negative list, it freezes the situation and gives the authorities time to analyze the additives on the market without being constantly overwhelmed by new additives appearing on the market.
- This system allows smokers who wish to quit smoking to find sufficient diversity in the products already on the market to help them achieve this goal. For example, this would no longer be the case if all flavorings were prohibited. • The list will be defined by ministerial decree, which allows a reaction capacity quick in case of emergency to ban an additive.

The constitution of such a list, just like a classic positive or negative list, could however give consumers the impression that the health authorities certify that the various additives on the market are risk-free and that the consumption of e-cigarettes is risk-free. too. This would obviously not be the case and it would therefore be necessary to be particularly attentive to the communication of the competent authority at this level.

Special case of "do it yourself" e-liquids

The " *do it yourself*" (*DIY*) consists of preparing the e-liquid yourself. One of the systems/cases more common is the mixture of a non-nicotine PG/GV²⁶ base, a nicotine booster (e-liquid containing 20 mg of nicotine) and aroma(s) (in liquid form). These ingredients are available in *vapeshops*. All of these (flavors, nicotine, PG/GV, etc.) must be of high purity. The quality standards and the rules for their use must be identical to the standards that apply to the ingredients present in ready-to-use e-liquids.

Based on the information provided by certain sellers during inspections, it seems that all people who adopt DIY do not necessarily use products intended for the manufacture of e-liquid. However, there are no studies or figures that quantify this behavior. They sometimes mix food flavorings in liquid form with the PG/GV which may not be pharmaceutical grade. It is difficult to predict the consequences of such a practice on health, but it could be potentially harmful for the consumer²⁷.

All e-liquids consumed by means of an e-cigarette, whether ready-to-use e-liquid or liquid based on self-mixed ingredients (*DIY*), must meet the same standards (quality and safety) in terms of composition.

It is necessary to prevent consumers from buying products not initially intended for consumption by inhalation, even if it is difficult to control this type of practice and the resulting mixtures. Good communication to warn and raise awareness of the potential dangers of such a problematic practice is essential.

4.2. Notification

4.2.1. Current situation

The Royal Decree of 28 October 2016 requires manufacturers/importers marketing e-cigarettes and e-liquids with nicotine to provide the FPS Public Health, 6 months before the planned date of marketing, with the following information: the contact details of the manufacturer and importer, a qualitative and quantitative list of all the ingredients, the toxicological data relating to the ingredients and emissions of the product, information on the dosage and inhalation of nicotine, a description of the components of the product, a description of the production process and a statement that the manufacturer and importer assume full responsibility for the quality and safety of the product when it is placed on the market and under normal or reasonably foreseeable conditions of use.

Certain data must also be provided annually: sales volumes, information on the preferences of different consumer groups, the way products are sold and summaries of any market research carried out in respect of the above.

²⁶ PG/GV: propylene glycol / vegetable glycerin

²⁷ US case EVALI – serious lung effects that can lead to death

Once the files have been verified and validated, the products are included in a positive list of products. Only products appearing on this list can be placed on the market. This list is published on the FPS Public Health *website*²⁸.

CEN/ISO Standard

The opinion of the CSS was also requested regarding the CEN/ISO standards, namely the CEN/TS 17287 *Requirements and test methods for electronic cigarette devices* and CEN/TR 17236 - *Electronic cigarettes and e-liquids - Constituents to be measured in the aerosol of vaping products*.

These standards are developed by the European sector with the aim of harmonizing certain processes or measures (eg the method for quantifying the rate of certain ingredients in the aerosol). This harmonization allows analysis and comparison between the products of different manufacturers. These standards are chargeable and their access is therefore limited.

Given the limitation of access to information and the nature of these standards (metrological aspects), the CSS considers that the question asked by the administration on this subject falls outside its field of investigation. The CSS therefore does not wish to position itself on these standards.

However, he insists on the fact that these standards must correspond to the scientific knowledge currently available.

4.2.2. Desired development

The current regulations (RD 28 October 2016) in terms of notification must be adapted and extended to e-cigarettes and e-liquids without nicotine.

The CSS insists on encouraging manufacturers to communicate their sales data both devices as types of e-liquids for nicotine-free products. It is indeed essential to have this data in order to follow market trends and to in relation to the type of consumer and the type of product.

4.3. Labeling

4.3.1. Current situation

Specific rules applicable to the labeling of e-cigarettes and e-liquids with nicotine are set in the Royal Decree of 28/10/2016. It emerges in particular that:

The packaging of e-cigarettes and refill bottles bear the following warning on the two largest surfaces: "*The nicotine contained in this product creates a strong dependence. Its use by non-smokers is not recommended*".

The following elements must also appear on the label:

- all the ingredients contained in the product in descending order of their weight,
- an indication of the nicotine content of the product and the quantity delivered per dose,
- the batch number,
- a recommendation that the product should be kept out of the reach of children.

A leaflet (a notice) must be inserted in the packaging and contain:

²⁸ <https://www.health.belgium.be/fr/notification> -des-des -de-la-e-cigarette

- instructions for use and storage,
- contraindications,
- side effects,
- the effects of dependence and toxicity,
- the details of the manufacturer or importer.

Finally, certain attractive elements cannot appear on the packaging:

- the suggestion that a given e-cigarette or refill bottle is less harmful than others or aims to reduce the effect of certain harmful components of the smoke or has vitalizing, energizing, healing, rejuvenating properties, natural, organic or has beneficial effects on health or lifestyle;
- the resemblance to a food or cosmetic product;
- the suggestion that a given e-cigarette or refill bottle is more easily biodegradable or has other environmental benefits.

In addition to these specific rules, a series of cross-cutting legislation also apply in terms of labelling: - The CLP²⁹ regulation applies to e-liquids with or without nicotine. Indeed, all mixtures containing dangerous substances must be classified

in one or more hazard categories (for example: "acute toxicity" or "sensitization"). The dangers of an e-liquid must be indicated on the label, by means of official pictograms, danger phrases, precautionary measures and a danger triangle detectable by touch.

- The electrical and electronic components of the e-cigarette are waste which are not part of residual waste and must therefore bear a specific pictogram.
- The provisions regarding electromagnetic compatibility apply to e-cigarettes (RD of 1 December 2016 relating to electromagnetic compatibility).

4.3.2. Desired development

A. Labeling

The current regulations (RD 28 October 2016) on labeling must be adapted and extended to e-cigarettes and nicotine-free e-liquids. The health warning must be adapted to e-cigarettes without nicotine.

As specified in chapter 5.2.4., the experts are in favor of adding a date of expiry date on e-liquids.

B. Leaflet

As with products containing nicotine, experts recommend that the information in the mandatory leaflet on the packaging should also be included in products without nicotine.

The message that should appear is the following: the use of this product results in significantly lower exposure to "harmful and potentially harmful components"

²⁹ CLP : classification, labelling, packaging

(HPHC30) than tobacco (cigarette) smoking, and is therefore likely to reduce the risk of serious health problems. Only by switching completely from smoking to vaping will this exposure to HPHCs be reduced to such an extent that the risk of serious health problems will potentially be reduced. A lower exposure to HPHC does not mean that there is no health risk. The consumption of the e-cigarette is not without risk and must be part of smoking cessation.

In the instructions, after the mention of the elements listed in point 4.3.1., different simple health warnings understandable to all should appear on this leaflet. Various institutions have proposed warnings along these lines, which can be found in appendix 1 to this opinion.

C. New inserts

Messages, aimed at countering misperceptions about e-cigarettes, have a better place in inserts (both in traditional tobacco products than in e-cigarettes). These inserts must have a positive approach, i.e. motivate smokers to quit (the e-cigarette can be used as an aid smoking cessation) and provide information on the relative risks of e-cigarettes by relation to smoking.

4.4. Advertising, sale and consumption in public places

4.4.1. Current situation

With regard to the rules on advertising, sale and consumption in public places, e-cigarettes with or without nicotine are assimilated to products with tobacco base.

This implies that all the provisions applicable to tobacco products in the law of 24 January 1977 on the protection of consumer health with regard to foodstuffs and other products apply to e-cigarettes. In practice, this means in particular that:

- Advertising and sponsorship for e-cigarettes is prohibited.
- it is forbidden to sell e-cigarettes to young people under the age of 18.

The law of December 22, 2009 establishing general regulations relating to the prohibition of smoking in closed places accessible to the public and to the protection of the population against tobacco smoke also applies to e-cigarettes. It is therefore prohibited to use e-cigarettes in enclosed public places and in a covered vehicle in the presence of minors.

Finally, the RD of 28/10/2016 prohibits the distance selling of e-cigarettes and e-liquids with nicotine.

30HPHC : *Hazardous & Potentially Hazardous Compounds*

4.4.2. Desired development

The provisions on advertising, sale and consumption in public places are already relatively restrictive for e-cigarettes in Belgium, compared to what is made among other EU countries.

The question that arises in terms of legislation is how to adequately inform smokers about a less dangerous (but not without risk) alternative such as the e-cigarette and, at the same time, protect young people from nicotine and smoking.

CSS does not support identical plain packaging with picture warnings as we know it for tobacco products. But the **CSS** is in favor of packaging and labeling of cigarette products that discourage minors and non-smokers. It suggests banning products from the market that appeal to young people in appearance and design, including banning the use of brightly colored packaging, cartoon characters, attractive names such as " *gummy bear* ", the mandatory use of sober tints and color elements in limited areas of the packaging, etc.

The **CSS** is also against any form of advertising, advertising via social networks and the media and the **CSS** supports the regulations in force in Belgium on this subject.

In addition, the **CSS** asks the competent authority for better control so that marketing via influencers and social networks such as Tik-Tok, Instagram, Snapchat, etc. can be better monitored and treated. FPS Public Health inspectors should therefore be authorized to intervene on social networks.

The **CSS** finds it relevant to inform smokers about the lower risk of e-cigarettes (compared to tobacco) and about the potential of e-cigarettes in the context of smoking cessation in way to make them aware of quitting smoking and the fact that the e-cigarette can allow them to do so. The e-cigarette should be seen as a temporary way to completely quit smoking and, preferably, also to quit vaping. This targeted information can, for example, be integrated via inserts in conventional cigarette packs and new inserts in e-cigarettes and be communicated/discussed by tobacco specialists, general practitioners, dentists, pharmacists, etc. It is important that this information comes from the public competent authority and not from producers who have as their first priority commercial interests and not public health. He is

also suggested that the law state positively what will be permitted rather than what is prohibited.

With regard to distance selling, the position of the experts is divided. A majority of them are in favor of banning distance selling while others plead for regulated distance selling under certain conditions. Distance selling to smokers is supported, by these experts, in particular by the limited number of points of sale

(*vapeshops*). Some consumers then fall back on the newsagent; more accessible point of sale. However, these newsagents offer an offer

limited number of e-cigarettes and offer minimal guidance/explanation on the use of the e-cigarette (because these newsboys get their information

mainly tobacco manufacturers and are not e-cigarette specialists, while *vapeshop* sellers may have much more knowledge about the product).

Furthermore, the majority of experts put forward arguments in favor of banning distance selling, in particular,

- the role of sellers in the context of smoking cessation is essential to provide advice/explanations, which cannot be done via the *Internet*.
- Checking age over the *Internet* is almost impossible.
- The quality of the products sold by *Internet* is sometimes lower compared to the products sold through stores.

V E-LIQUIDS AND DEVICES

5.1. Introduction

5.2. Nicotine: toxicity and addictive effects

- 5.2.1. Toxicity and health risks
 - 5.2.1.1. Lethal toxicity
 - 5.2.1.2. Morbid toxicity
- 5.2.2. Addictive effects of nicotine
 - 5.2.2.1. Effects of nicotine on the nervous system
 - 5.2.2.2. Neuroadaptation and tolerance
 - 5.2.2.3. Clinico-neurological aspects of nicotine addiction and psychoactive effects of nicotine
 - 5.2.2.4. Addiction Vulnerability
- 5.2.3. Nicotine salts
- 5.2.4. Stability and shelf life of e-liquids

5.3. Other ingredients

- 5.3.1. Aromas and their toxicity
 - 5.3.1.1. Genotoxicity/carcinogenicity
 - 5.3.1.2. Inhalation toxicity
 - 5.3.1.3. Inhalation allergens
- 5.3.2. Other additives

5.4. Equipment and technical aspects

- 5.4.1. Types of e-cigarettes
- 5.4.2. Elements of the e-cigarette

5.1. Introduction

An e-cigarette has three basic elements:

- a tank containing liquid (e-liquid),
- a vaporizer intended to vaporize the liquid (with a heating element),
- a battery for the vaporizer.

The composition of e-liquids varies according to brands and ranges. The base of the e liquid is PG/GV³¹ or sometimes the less popular 1,3-Propanediol, which produces a visible smoke during evaporation. The e-liquid also contains water, flavorings and, possibly, nicotine. The variety of flavors is immense.

This section will address the most relevant elements, namely nicotine, the ingredients as well as certain specificities related to the different types of equipment.

Various aspects must be taken into account during the risk assessment, in particular the toxic properties of the ingredients, their dose/concentration, their exposure, the

³¹ PG/GV: Propylene glycol / vegetable glycerin

formation of new products, etc. It is also important to take into account the type of user, the user's overall consumption (frequency, number of puffs, duration of puffs, etc.) and the inherent absorption properties of the ingredients via lung epithelium, mucous membranes of the mouth and throat as well as the resulting blood level. These latter aspects will not be developed in this chapter.

5.2. Nicotine: toxicity and addictive effects

5.2.1. Toxicity and health risks

Although nicotine is the most addictive ingredient in tobacco (see below), these are often other components of tobacco smoke that cause cancers and other smoking-related morbidities. In other words, people smoke for the nicotine but instead die from the tar, carbon monoxide, and other harmful substances inhaled along with the nicotine. Of course, nicotine also has proven toxic health effects that can lead to morbidity and mortality. These effects are proven and important for all forms of nicotine delivery, including vaping.

5.2.1.1. Lethal toxicity

It should be recognized in the interpretation of toxicity figures in laboratory animals that the route of administration is an important determinant of toxicity. The lethal dose varies greatly depending on the route of administration. Rapid intravenous injections result in the highest blood and brain concentrations and cause toxicity at the lowest doses. Unlike intravenous injection, the oral route requires higher doses to cause toxicity.

This is partly due to the pre-systemic (" *first pass* ") metabolism of nicotine, whereby nicotine is metabolized by the liver after its assimilation in the portal venous circulation and before reaching the systemic venous circulation. The lethal dose of nicotine after oral ingestion is difficult to extrapolate from studies in laboratory animals due to the wide variability in nicotine toxicity and its

complex metabolism in different species of laboratory animals. For humans, different LD50 (median lethal dose) have been reported for nicotine, among which 1 mg per kg of body weight has long been considered the norm.

However, due to the large individual differences in the extent to which nicotine is absorbed, metabolized and eliminated, ECHA³² decided that the LD50 of nicotine per oral administration is between 3.34 and 24 mg/kg body weight. In some cases, symptoms of poisoning may appear from 0.3 mg/kg in adults (especially in those who have not developed dependence) and from 0.2 mg/kg in children (Lazukta et al., 1969; RAC, 2015). However, there is now also quite a bit of literature data indicating that it takes well over 60 mg of oral nicotine to have a lethal effect in adults, namely, over 500 mg (Mayer, 2014). No conclusive data on inhalation toxicity are available. A number of poisonings and deaths from nicotine ingestion, mainly related to the use of nicotine-containing pesticides, have been reported in humans. poisoning with

³² ECHA: *European Chemicals Agency*

nicotine causes nausea, vomiting, abdominal pain, diarrhoea, headaches, sweating and paleness. In the most severe cases, it causes dizziness, weakness and confusion, which progresses to convulsions, hypotension and coma. Death will usually be due to paralysis of the respiratory muscles and/or central respiratory failure. Exposure of the skin to nicotine can also lead to poisoning. Such exposures have been reported

following spills or the application to the skin or clothing of insecticides containing nicotine and following contact with tobacco leaves in the context of an occupational activity. Acute poisoning can quickly occur in children

after the consumption of tobacco products. A case report mentions that four children who each smoked two cigarettes developed salivation, vomiting, diarrhea, tachypnea, tachycardia and hypertension within 30 minutes followed by slowed breathing and cardiac arrhythmia within 30 minutes. 40 minutes and convulsions within 60 minutes. All have recovered

without experiencing any complications. Although tobacco use is common, deaths directly related to this are extremely rare, due to premature vomiting and first-pass metabolism of absorbed nicotine. However, nicotine remains a particularly dangerous chemical substance (Benowitz, 2009;

Fagerstrom, 2014; Karaconji, 2005, Le Houezec, 2003; Mishra et al., 2015).

5.2.1.2. Morbid toxicity

Nicotine may contribute to tobacco-related diseases like lung disease and cancer but the direct cause is unclear as nicotine is commonly consumed together with a large number of other potentially harmful substances present, among others, in tobacco smoke. Today, it is possible to consume nicotine in the form of chewing gum or via other delivery systems such as the e-cigarette and the potential health consequences of chronic exposure to nicotine therefore deserve careful thought.

Smoking is the main cause of chronic obstructive pulmonary disease (COPD) and inhaled nicotine plays an obvious role. This is mainly due to inhalation tobacco smoke. There is still insufficient research to show that inhaling nicotine through vaping can actually cause COPD. It takes years for COPD to appear and e-cigarettes haven't been around that long. A short-term study found that mice exposed to nicotine-containing e-cigarette aerosol showed more COPD-associated symptoms than those without (Garcia-Arcos et al., 2016) but other studies did not could not confirm this correlation. Readily absorbed through the lungs and distributed to tissues including bone marrow, nicotine increases elastase gene expression, leading to increased elastase protein concentration per cell, suggesting a pathophysiological mechanism emphysema. In healthy subjects, inhaled nicotine causes concentration-dependent coughing and airway obstruction probably through stimulation of afferent nerve endings in the bronchial mucosa and via parasympathetic cholinergic pathways.

Nicotine is a substance that increases heart rate and contractility, constricts blood vessels in the skin and coronary arteries, and temporarily increases blood pressure. Nicotine also reduces insulin sensitivity and can aggravate or accelerate diabetes and also contribute to endothelial dysfunction. The modification of physiology

blood vessels can also lead to erectile dysfunction.

Nicotine certainly has direct neurological and cardiovascular effects, but cigarette smoke also contains many other cardiovascular toxins. Smoking appears to cause acute heart problems through three mechanisms, the most important of which is the production of a state of hypercoagulability that promotes thrombosis. Nicotine can

cause atherosclerotic disease by its effects on lipid metabolism and coagulation, by hemodynamic effects and/or by endothelial damage. Compared to non-smokers, cigarette smokers show an increase in low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) as well as a decrease in high-density lipoproteins (HDL), a profile associated with a risk increased atherosclerosis. The products of lipid peroxidation can cause irreversible damage to the membrane structure of cells. Some studies show that

administration of nicotine to laboratory animals results in abnormalities of endothelial cells and reduces the synthesis of prostacyclin (an inhibitor of platelet aggregation). Nicotine increases heart rate by activating the sympathetic nervous system. Research on nicotine replacement therapy indicates that the risks of consuming nicotine without tobacco combustion products (cigarette smoke)

are less compared to smoking but remain a concern in people with cardiovascular disease. E-cigarettes that deliver nicotine without

Tobacco combustion appears to pose a lower cardiovascular risk in healthy users, at least for short-term use (Benowitz & Burbank, 2016).

Normally, the gastrointestinal mucosa is protected from injury by a layer of mucus and by secretion of bicarbonate by gastric and duodenal epithelial cells to neutralize gastric acid. If these protective mechanisms are weakened or there is talk of increased levels of harmful factors, ulceration may occur. Nicotine and other components of cigarettes increase reflux of duodenal contents to the stomach and mouth, decrease pancreatic bicarbonate secretion, reduce the production of gastric mucus and cytoprotective prostaglandins, and promote the production of free radicals and the release of vasopressin, a potent vasoconstrictor (Wu & Cho, 2004).

Nicotine may not be a direct carcinogen, but it is feared that it is a tumor promoter. Animal studies show that nicotine can inhibit apoptosis, resulting in better cancer cell survival. Nicotine also promotes angiogenesis in animals, an effect that could lead to greater tumor invasion and metastasis. At present, there is no unequivocal answer to the question of whether nicotine directly induces or promotes cancer in humans. In studies involving chemical/physical carcinogens or transgenic models, evidence for an association between nicotine exposure and the presence or absence of a modulating (stimulating) effect on carcinogenesis appears to be insufficient. This is mainly due to the large number of conflicting studies. In

However, a majority of studies provide sufficient evidence of an association between exposure to nicotine and acceleration of carcinogenesis of cancer cells inoculated into mice. This modulating effect was particularly marked in mice with weakened immune systems. Nicotine has no obvious carcinogenic genotoxic properties but it does have tumor promoting properties. This has been demonstrated in laboratory animals and, in general, anything that is carcinogenic or tumor-promoting in laboratory animals is also in humans. Even in humans, there are indications of tumor-promoting effects of nicotine (Tyagi et al., 2021).

Nicotine is teratogenic; it has adverse effects on reproduction and the fetus. The consumption of nicotine in any form is strongly discouraged for pregnant women unless they cannot quit smoking without taking nicotine. In animal studies to investigate neurotoxic effects on the fetus, nicotine has been found to target neurotransmitter receptors in the fetal brain, leading to decreased cell proliferation and therefore altered synaptic activity. It has also been observed that prenatal exposure to nicotine causes structural changes in the lungs of the fetus. Nicotine can have a direct toxic effect on the cardiovascular system of the fetus, resulting in reduced blood flow. Harmful effects of nicotine have also been observed

during breastfeeding. Maternal nicotine use during pregnancy is an important risk factor for sudden infant death syndrome. Fetal hypoxemia is also thought to be a contributing cause of behavioral abnormalities, such as hyperactivity, impaired attention, poor spelling and reading test scores; or abnormalities more frequently observed in children whose mothers smoked during pregnancy and lactation.

Nicotine is a powerful skin vasoconstrictor and can interfere with wound healing. However, clinical studies of the use of nicotine replacement therapy to help surgical patients quit smoking indicate that it is clearly preferable to quit smoking with nicotine treatment, rather than continuing to smoke.

The effects of nicotine on the central and peripheral nervous systems have been most clearly documented; see below.

5.2.2. Addictive effects of nicotine

5.2.2.1. Effects of nicotine on the nervous system

After inhaling cigarette smoke or vapor containing nicotine while vaping, the nicotine is rapidly absorbed into the pulmonary bloodstream. It then travels rapidly from the lungs to the rest of the body and the brain to attach to cholinergic and nicotinic receptors on neurons. This binding of nicotine then results in the release of neurotransmitters. One of these neurotransmitters, dopamine, creates an experience of pleasure and reward in the corticolimbic system of the brain, and plays a crucial role in the addictive effects of nicotine.

Nicotine also increases the production of glutamate, which facilitates the release of dopamine, and the production of gamma-aminobutyric acid (GABA), which inhibits the reuptake of dopamine. With prolonged exposure to nicotine, some receptors cholinergics become insensitive. As a result, GABA-mediated inhibitory tone decreases while glutamate-mediated arousal persists, increasing excitation of dopaminergic neurons and further enhancing the response to nicotine. (Benowitz, 2008).

5.2.2.2. Neuroadaptation and tolerance

Repeated exposure to nicotine leads to neuroadaptation (tolerance) to some of the effects of nicotine. Desensitization of neuronal receptors occurs; it makes the receptors less inclined to bind and more insensitive. This is a homeostatic reaction of the body to an apparently too high concentration of dopamine (negative feedback effect).

As this neuro-adaptation continues, the number of binding sites on nicotinic cholinergic receptors in the brain changes, likely in response to nicotine-induced receptor desensitization. Desensitization plays an important role in addiction: *craving* symptoms appear in smokers as receptor desensitization progresses.

Too weak a bond can cause stress and even anxiety. take nicotine always more and repeatedly increases the nicotine load on these receptors, to relieve this feeling of stress, but also increase the desire to smoke. Smoking cigarettes in amounts typical of a "chronic" smoker therefore maintains almost complete saturation of the nicotinic cholinergic receptors. Also, smokers and vapers try to avoid withdrawal symptoms by maintaining a sufficient concentration of nicotine in the plasma. The rewarding effects of conditioned behaviors associated with smoking, such as taste, inhalation sensation, and experience environmental, also play a role in this dependency.

5.2.2.3. Clinico-neurological aspects of nicotine addiction and psychoactive effects of nicotine

Nicotine reduces stress and anxiety. Smokers consume it to regulate their well-being and control their mood. Quitting smoking leads to the appearance of symptoms of withdrawal: irritability, depressed mood, agitation and anxiety. Stopping consumption of nicotine can also be accompanied by anhedonia.

When a person addicted to nicotine stops using, the urge to resume is there and persists long after the withdrawal symptoms have disappeared. A person who smokes regularly associates specific moods, situations, or environmental factors—signals related to smoking—with the rewarding effects of nicotine. It is these signals that usually cause the relapse. The link between these cues and the expected effects of nicotine, and the resulting urge to use nicotine, is a form of conditioning. Experimental studies on

Animals Show Nicotine Exposure Causes Changes in Brain Cell Protein Expression and Synaptic Connections – a process called neural plasticity – which underlies conditioning. Nicotine

also reinforces behavioral responses to conditioned stimuli, which can contribute to compulsive smoking. In addition, studies in nicotine-dependent laboratory animals show that conditioned stimuli associated with nicotine withdrawal increase the extent of withdrawal by raising the threshold of brain reward. Thus, the signs associated with nicotine withdrawal may reduce the function of brain reward systems. The urge to smoke is partially maintained by this conditioning. Smokers usually take a cigarette after a meal, with a cup of coffee or an alcoholic drink, or in the company of friends who smoke. Other aspects – the handling of smoking products, or the taste, smell or feel of smoke in the throat – are also associated with the pleasurable effects of smoking. Even unpleasant moods can become conditioned invitations to smoke: a smoker can "learn" that not having a cigarette causes him to become irritable, and that smoking relieves him. After repeated experiences of this kind, this smoker may experience irritability, whatever the source, as a cue to smoke.

Physiologically, smoking is ultimately a very efficient form of consuming dope. Inhaled nicotine quickly enters the bloodstream via the lungs and reaches the brain in seconds. The rapid absorption and penetration into the brain causes a powerful "rush". Besides this rapid release of nicotine in the brain, additives are added to cigarettes to increase their addictive effect.

Unlike cigarettes, some nicotine replacement products release nicotine slowly and the risk of relapse to "real smoking" is high.

The basis of nicotine addiction is a combination of positive reinforcements, such as as improving mood and mental or physical functioning and avoiding withdrawal symptoms. Smokers tend to take the same amount of nicotine day to day to achieve the desired effects. They adapt their behavior and frequency of use to compensate for changes in nicotine availability (eg, smoking more when switching to lower nicotine products).

Light smokers (5 cigarettes per day) and occasional smokers smoke primarily due to the positive reinforcing effects of nicotine and experience minimal withdrawal symptoms. They smoke mainly in combination with certain activities (after a meal or while drinking alcohol) and are less likely to smoke as a reaction to a negative effect. Despite generally less severe withdrawal symptoms. Importantly, many light and occasional smokers also find it difficult to quit. Some of them show a high degree of dependence but with different pharmacodynamics than heavy smokers.

5.2.2.4. Addiction Vulnerability

Smoking usually begins in adolescence; 80% of smokers start smoking before the age of 18. Risk factors for childhood smoking or adolescence include the influence of peers and parents, behavioral problems (or poor academic performance), certain personality traits (rebelliousness, risk taking, depression and anxiety) and genetic influences. The risk of

Nicotine dependence increases if (chronic) nicotine use begins at a younger age. Studies of brain development in animals laboratory suggest that nicotine can cause lasting changes that can lead to addiction. Changes in the brains of laboratory animals teenagers exposed to nicotine are greater than those of adult exposed laboratory animals. Adolescent laboratory animals exposed to nicotine exhibit higher rates of nicotine self-administration than adult laboratory animals, which is consistent with the idea that early exposure to nicotine increases the severity of the smoking phenomenon. addiction.

Besides young people, women are often more susceptible to nicotine addiction. They metabolize nicotine faster than men on average, which may contribute to this increased sensitivity and higher tobacco consumption. Nicotine is primarily metabolized to cotinine by the CYP2A6 liver enzyme. People with a genetic basis for slower nicotine metabolism (those whose CYP2A6 gene variant is associated with reduced enzyme activity) smoke fewer cigarettes per day than those with faster metabolisms. Rapid nicotine metabolism is associated with more severe withdrawal symptoms and a lower chance of successfully quitting smoking.

5.2.3. Nicotine salts

In some cases, especially in pods, nicotine salts are used instead of free base nicotine. The most common nicotine salts are nicotine lactate, benzoate, levulinate, salicylate, maleate, and tartrate (Harvanko et al., 2020). Recent studies have shown that the protonated form of nicotine, the form in the presence of the salts, is responsible for the rapid and higher absorption of nicotine compared to the nicotine base in e-liquids (Gholap et al., 2020). Furthermore, these nicotine salts are used because they are more pleasant to inhale since they mask the aversive effects of nicotine as throat irritation (Barrington-Trimis & Leventhal, 2018). This is also the reason why vaping liquids with a high concentration of nicotine (60 mg/ml) are available in the United States. The user experiences little to no roughness typical of a high concentration free nicotine base (Duell et al., 2019). Such high nicotine concentrations may lead to addiction more quickly in non-smokers and adolescents/young adults (Mallock et al., 2020) but, on the other hand, may provide smokers with enough nicotine through relatively limited consumption. of e-liquid. There is little evidence of a differential effect on smoking cessation efficacy of free base nicotine versus protonated nicotine (Russell et al., 2019).

No studies are available on the safety of nicotine salts by inhalation. Nicotine salts are present as solid particles in the aerosol and so we may need to consider potential local effects in lung tissue. However, we do not yet have scientific proof of such effects (Shao & Friedman,

2020). However, nicotine salicylate is toxic by inhalation and skin absorption (EACHA-REACH, 2020). On the other hand, toxicity studies have been carried out on vaping liquids and e-cigarette aerosols containing nicotine salts. These are *in vitro* studies that indicate the cytotoxicity of these fluids and aerosols (Duell et al., 2019; Ghosh et al., 2020; Pinkston et al., 2020). However, we cannot distinguish whether it is an effect specific to the nicotine salt or the flavors used.

5.2.4. Stability and shelf life of e-liquids

There is little data on the long term stability of nicotine in e-liquids.

Nicotine strength studies have repeatedly shown that nicotine strength does not always match the stated strength.

However, no association has been made between the lower concentrations found and the stability of nicotine because the production date is not always mentioned on the packaging.

Stability studies have been described using nicotine alkaloids used as indicator (Barhdadi et al., 2021; Flora et al., 2016; Liu et al., 2017). These studies showed nicotine oxidation with significant nicotine N-oxide formation, more pronounced at higher temperatures and relative humidity (Liu et al., 2017). Flora et al. have described a slight increase in nicotine alkaloids, namely nicotine N-oxide, myosmine and nor nicotine, but the Barhdadi stability study showed a more pronounced increase with values for Nicotine N oxide exceeding the limit of impurities in nicotine for medical use. The difference between the two studies was in the packaging of the e-liquids. In the study by Flora et al, the e-liquid was packaged in a blister which protects against humidity, while in the study by Barhdadi et al, the e-liquids were stored in a transparent packaging.

Currently, no studies have been conducted on the potential role of other ingredients (flavors, etc.) on the stability of nicotine in e-liquids. The stability study by Barhdadi et al. showed that 1,3-propanediol as a carrier liquid reduces the stability of nicotine and accelerates the formation of nicotine alkaloids compared to GV/PG.

An expiry date and a maximum use-by date after opening are recommended in order to limit nicotine impurities in the products used so that the

Nicotine used always meets quality and purity requirements.

5.3. Other ingredients

5.3.1. Aromas and their toxicity

The flavors used in e-cigarettes can be subdivided into artificial flavors and flavors of natural origin (eg essential oils, plant extracts). The flavors used in e-cigarettes are mostly synthetic flavors authorized in food. Generally speaking, there is not yet a lot of research on the clinical effects of vaporizing aroma inhalation. For most food flavourings, assessments are available from EFSA³³ in the EU or FEMA³⁴ in the US. However, these do not take into account the inhalation toxicity of flavourings. Additionally, for these food flavorings, it is unknown what potential end products may be formed due to heat and/or interactions with other ingredients. The effects of these potentially generated products are also unknown. However, the assessments provided by these official bodies provide the necessary information on the potential carcinogenic, mutagenic or toxic for reproduction (CMR) properties of the components because they are independent of the route of exposure. The complete composition of the aromas must therefore be

³³ EFSA : *European Food Safety Authority*

³⁴ FEMA : *Federal Emergency Management Agency*

known. This is not as obvious for plant and herbal extracts, as it depends on the plant of origin, the extraction methods applied as well as natural variation.

In addition to the toxicity of the aromas used, it is also important to know exposure to flavorings to enable risk assessment. Therefore, in addition to the full composition of each aroma, information on the amount of each aroma in the e-liquid and in the aerosols of the e-cigarette are necessary. Greater cytotoxic effects were observed at higher concentrations of flavorings (Hua et al., 2019; Omaiye et al., 2020). Furthermore, it has been found that the aromas particularly sweet flavors contain more flavor components than tobacco and menthol flavors (Czoli et al., 2019). One possible option to reduce the risk of potential toxic effects of flavors is to reduce the number and amount of flavor components.

Regarding toxicity, the previous CSS opinion (CSS 9265, 2015) concluded that too little is known about the effects of flavorings in e-cigarettes. In the meantime, Further research has been conducted on the toxicity of flavorings used in e-cigarettes.

The studies published in the literature can be divided into two categories:

- toxicity studies on e-liquids/aerosols of e-cigarettes and analysis of the content, and
- studies for the selection of e-liquids/aerosols for e-cigarettes for flavors that would be toxic (by inhalation) according to the literature.

In toxicity studies, the main focus is on *in vitro* toxicity testing with cellular toxicity as an endpoint (Hua et al., 2019; Omaiye et al., 2020; Sassano et al., 2018). These studies focus on the toxicity of the whole e-liquid, as a mixture of different flavors in combination with PG/GV solvents.

There are very few studies that focus on aroma heating products. In a study of flavored e-cigarette heaters, Khlystov and Samburova found a correlation between the formation of toxic aldehydes and the amount of flavors in e-liquids (Khlystov & Samburova, 2016). The results of these experiments have not been confirmed since then. A study by Klager et al could not confirm this correlation (Klager et al., 2017). Studies of this type should be carried out more often in order to better understand what type of aroma they apply to. The heating of the sucrose and liquids containing glucose would also lead to the formation of toxic furans : 5-hydroxymethylfurfural and furfural (Soussy et al., 2016). In addition to heating products, Interaction products are also possible due to the reaction of different flavors in a mixture. Erythropel et al. described the formation of aldehyde propylene glycol acetal adducts formed in the e-liquid matrix with flavoring agents such as benzaldehyde, cinnamaldehyde, citral, ethyl vanillin and vanillin. The toxicological properties of these new products should also be evaluated (Erythropel et al., 2019).

Flavors must be assessed against the various endpoints of toxicity.

5.3.1.1. Genotoxicity/carcinogenicity

Substances with CMR properties are prohibited in e-liquids whether or not they are present in aerosols (see point 4.1.2).

Several evaluations of the genotoxicity and carcinogenicity of the different flavors are already available, in particular the opinions of the EFSA. They should also serve as a basis to the evaluation of flavors in e-cigarettes. A study shows that e-liquids can contain genotoxic components such as: safrole, estragole, furylmethylketone, dimethylhydroxyfuranone and pulegone (Barhdadi et al., 2021; Jabba & Jordt, 2019). For some flavourings, indications would suggest that the substance is

likely to have CMR properties or there are insufficient data to exclude their genotoxicity. These should be assessed a priori (Barhdadi et al., 2021; Kang & Valerio, 2020). This list includes the following components: diacetyl, acetylpropionyl, γ -phellandrene, isodene, acetophenone, maltol, ethylmaltol, ionone, damascenone.

Some of these substances have been found in e-liquids because they are used in the composition of plant extracts. It should be noted that there are different classifications to know when a chemical product can be considered as CMR. There is CLP labeling (*classification, labeling and packaging*), IARC35 classification, individual experimental results, etc.

The literature on the genotoxic properties of e-cigarettes is rather limited. Tobacco industry-sponsored studies found no mutagenic effects on cells

in vitro or on bacteria (Misra et al., 2014; Thorne et al., 2016; Thorne et al., 2018; Thorne et al., 2019; Takahashi et al., 2018). The academic study by Tommassi et al. (2017) also found no significant increase in the number of mutations in mouse or human cells *in vitro*. With regard to the genotoxicity of the e-cigarette, academic research reveals worrying observations.

The increased expression of enzymes that activate pro-carcinogens to carcinogens has been observed in human keratinocytes *in vitro* by Sun et al. (2019) and *in vivo* in rats by Canistro et al. (2017). The formation of DNA adducts was predicted by *in silico* studies by Kang et al. (2020) Genotoxic activity was predicted by *in silico* studies by Barhdadi et al. (2021). Oxidative stress has been observed in mice (Platel et al. 2022) and is reported in human head, neck and mouth cells in a systematic review by Wilson et al. (2022). Induction of DNA repair enzymes has been observed in mice *in vivo* and in human cells *in vitro* (Lee et al., 2018). DNA breaks or other forms of DNA damage have been observed in mammalian cells (Lee et al., 2018) and *human cells in vitro* (Lee et al., 2018; Holliday et al., 2016) and *in vivo* in animals by Canistro et al.

(2017), Platel et al. (2022) and Espinoza-Derout et al. (2019) and in human buccal cells by Cheng et al. (2022). Mutations have been observed in mice *in vivo* by Espinoza-Derout et al. (2019), and Platel et al. (2022) and *in vivo* in rats by Canistro et al. (2017). An increase in the number of micronuclei was observed in rats *in vivo* by Canistro et al. (2017). Pop et al (2021) found an increase in the number of micronuclei in mouth cells in e-cigarette users. The average number of micronuclei per 1000 cells was 3.6 ± 1.08 for smokers,

³⁵ IARC: International Agency for Research on Cancer

3.21 ± 1.12 for e-cigarette users and 1.95 ± 1.05 for non-smokers. This is an important finding because the number of micronuclei, measured at least in peripheral blood lymphocytes, is a predictive biomarker of cancer risk in a population of healthy individuals (Bonassi et al., 2007). However, one of the limitations of the Pop et al. (2021) lies in the fact that people who had already used conventional tobacco products “at least three months before” were not excluded from the study. In summary, it can be said that it is clear that e-cigarettes can have genotoxic effects but it is unknown if and to what extent this can occur in e-cigarette users.

5.3.1.2. Inhalation toxicity

Particular attention must be paid to the toxicity of aromas by inhalation and in particular to their toxicity for the pulmonary epithelium. The inhalation toxicity of chemicals has not been studied as thoroughly as oral or dermal toxicity. The known examples come mainly from retrospective studies on the illnesses of workers after exposure to chemical substances during their working hours. It should be noted that they cannot be compared directly to chemical inhalation through e-cigarette use because the exposure pattern

is different (Hubbs et al., 2015). The best-known examples of flavorings that are safe for oral use but cause inhalation toxicity are diketones:

diacetyl and acetylpropionyl. A study showed that in 2018, 37% of sweet tasting e-liquids on the Belgian market contained one or two diketones (Barhdadi et al., 2021).

Another much-discussed flavoring is cinnamaldehyde. This aroma has been reported as cytotoxic in several *in vitro experiments*. In addition, it would suppress the ciliary motility of bronchial epithelial cells and thus increase the risk of respiratory infections (Clapp et al., 2017; Clapp et al., 2018; Clapp et al., 2019).

Other examples described in the literature are benzyl alcohol, benzylaldehyde, vanillin, banana oil, 3-hexene-1-ol acetate, 4-methyl-2-phenyl-1,3-dioxolane, 5-heptyldihydro-2(3H)-furanone, 2-propenyl-hexanoic acid and benzaldehyde propylene glycol acetal (Czoli et al., 2019; Girvalaki et al., 2018). These flavors were also found in e-liquids and contained an indication that inhaling these flavors would be toxic. Inhalation toxicity was best indicated by a Globally Harmonized System (GHS) classification or, in doubtful cases, by a self-classified GHS classification.

5.3.1.3. Inhalation allergens

Respiratory *sensitizers* represent a toxicological parameter that is not currently taken into account much in research on e-cigarettes. This is despite reported cases of allergic reactions after e-cigarette use (Azevedo et al., 2019). It is believed that skin sensitization, also known as delayed hypersensitivity, cell-mediated hypersensitivity or hypersensitivity of

type IV, also plays a role in exposure to e-cigarette aromas. There are already a series of fragrance substances used in cosmetics which are known for their allergenic properties. It is currently being investigated whether these substances can also

induce a process of sensitization by inhalation. A study by RIVM³⁶ showed that **isoeugenol** can have negative effects on the respiratory immune system by inhalation (Ter Burg et al., 2014). However, it is uncertain whether this applies to all allergenic fragrances (Basketter & Kimber, 2015). In addition to allergenic fragrances, e-liquids contain other chemicals **classified under the GHS** as inhalation allergens (H334), such as **methylcyclopentalone** and **γ-ionone**.

(Girvalaki et al., 2018).

5.3.2. Other additives

The composition of e-cigarettes and e-liquids with nicotine is specifically _____ regulated by the Royal Decree of 28/10/2016 relating to the manufacture and marketing of e-cigarettes which transposes article 20 of Directive 2014/40/EU.

The liquid containing nicotine does not contain the following additives:

- vitamins or other additives creating the impression that the e-cigarette has beneficial health effects or that the health risks it presents have been reduced. It follows from the interpretation of this provision that the presence of CBD and vitamin E acetate is, for example, prohibited (only in liquids with nicotine)
- caffeine or taurine or other additives and stimulants associated with energy and vitality;
- additives which give coloring properties to emissions;
- additives which, without combustion, have CMR properties.

Only high purity ingredients are used for the manufacture of the nicotine containing liquid.

In the fall of 2019, several young people died in the United States from lung disease linked to the use of e-cigarettes. The vast majority of people diagnosed with EVALI³⁷ had used THC in their e-liquids. Following research, the *US Centers for Disease Control* (CDC) identified vitamin E acetate as a most likely suspicious ingredient that may be related to EVALI (Blount et al., 2020). Vitamin E acetate is a thickener used in THC oils. Vitamin E acetate has been shown to disrupt the phospholipid bilayer and it is hypothesized that this disruption reduces the effectiveness of the lung surface active ingredient.

5.4. Equipment and technical aspects

5.4.1. Types of e-cigarettes

There are different kinds of e-cigarettes. These different families of objects have different sizes, weights and dimensions and therefore induce a different gesture/method of inhalation, more or less distant from that of smoking tobacco and more or less ostentatious. They each have different qualities in terms of battery life and e-liquid reservoir capacity. They also allow more or less fine adjustments and offer various qualities in terms of steam volume and temperature, " *throat hit* " (sensation of contraction or brief tingling in the pharynx during

³⁶ RIVM: *National Institute for Public Health and the Environment*

³⁷ EVALI : *e-cigarette, or vaping, product use associated lung injury*

passage of steam), " *air-flow* " (more or less airy or tight draw) and the rendering of flavors and aromas of the e-liquid. For example, first-generation devices produce weak aerosols with a low concentration of nicotine, while more recent devices deliver a quantity of nicotine equivalent to that of tobacco cigarettes.

(Wagener et al., 2017). Moreover, these design variations may also lead to differences in potential health risks, including the presence of (potentially) harmful components in the aerosol emission (Farsalinos et al., 2017).

The 1st generation e-cigarette or the *cig-a-like* is an e-cigarette that looks like a tobacco cigarette. These are discreet models, which mimic the size and maintain the gesture of the classic cigarette. This type of device was first disposable once the battery was empty. For environmental reasons, batteries have also been introduced. It is a closed system. While the battery is separated from the other compartments, the liquid and heating compartments are united in a cartomizer, which is a combination of the cartridge and the atomizer (= heating compartment). A cartridge is a liquid-soaked polyurethane foam (polyester fiber spongy material) that serves as a container for e-liquid. The heating element, consisting of a metal coil, is integrated in this compartment for the liquid. When the e-cigarette is activated, the resistance wire coil heats up and the liquid around it vaporizes. The pre-filled cartomizer is discarded when empty and all liquid has

evaporated. The user realizes this when the vapor starts to taste burnt due to heating an insufficient amount of liquid and a dry coil. There are also rechargeable cartomizers. The e-liquid cartridges are of low capacity and the batteries have little autonomy.

Second generation e-cigarettes or "Tube MODS38 " are characterized by their larger size and cylindrical shape. These devices are also called "tank" systems because of the reservoir which can hold larger quantities of e liquid than the first generation cartridge models. This tank or *clearomizer*

is the reservoir for the liquid. The tank is refillable. The atomizer is the part that contains the resistance and a wick part that saturates with e-liquid and transfers the e-liquid to the resistance. This is an open model (LRSH, 2016).

Third generation e-cigarette devices or "Box MODS" include a diverse range of products (cylindrical or box-shaped), all characterized by a large capacity lithium battery that allows the user to adjust the voltage and /or the power delivered to the atomizer. These batteries can be combined with second generation atomizers or with adjustable atomizers where the user can adjust the type of resistance and wick himself. This is why the devices of this third generation are called **MODS** (a term that refers to modifications) or **Advanced Personal Vaporizers** (AVP). These new devices also produce a larger aerosol than previous generations and therefore have an even greater impact on the amount of chemical (e.g. nicotine) delivered to the user.

³⁸ MOD: "modified electronic cigarette"

So-called **fourth generation** e-cigarettes are actually third generation e-cigarettes with an **additional temperature setting**, which means the user can set a temperature limit. The vaporization temperature therefore remains stable during longer and more frequent draws, which reduces the risk of dry and burnt draws (Farsalinos et al., 2017).

Finally, there are **mechanical models** in which there is no electronic circuit to regulate the voltage of the accumulator. The power adjustment is done by acting on the value of the resistance. They have no protection system protecting against overheating.

The pods are more compact and shaped like a USB key. They are composed of a cartridge (including the tank and the resistance) and a battery.

There are changeable resistance pods, rechargeable cartridge pods and sealed cartridge pods. In the first two cases, the cartridges can be filled several times and for the changeable resistance pods, the resistance can also be changed.

In the case of pods, e-liquids are consumed at low power and therefore the pods do not need large capacities (battery and resistance) to be effective.

They are generally intended for a small consumption of liquid and often with high nicotine concentrations (often protonated nicotine, " *nicotine salts* " see point 5.2.3.).

The popularity of pods continues to grow due to their modern, user-friendly design that only requires a flavor pod (nicotine cartridge) to be inserted into the device for use compared to older refillable e-cigarette models. The pods use nicotine salts (see point 5.2.3.). Nicotine-normalized formaldehyde and total aldehyde levels in pod devices are lower than in other e-cigarettes and tobacco cigarettes previously studied (Reilly et al., 2019).

The size of most pods and their resemblance to a USB stick make them easy to hide and use discreetly in places where smoking is prohibited, also known as "stealth vaping". Given the new user experience, attractive flavors and product design, the pods may be more appealing to young people than previous e-cigarette products. In a recent report, 80% of 15-24 year olds who had ever tried JUUL also said they had used it in the past 30 days (Willett et al., 2019), suggesting that young people who try JUUL are very likely to continue using it.

5.4.2. Elements of the e-cigarette

The e-cigarette is made up of different elements: the tank, the wick, the resistor/"coil" and the battery.

E-liquid is usually contained in a refillable cartridge or reservoir.

The **reservoirs** (or tank) are of variable capacity which influences the autonomy and size of the object. The material of the tank can be in:

- Pyrex: resistant to heat and temperature variations.

- Stainless steel: very resistant from a physical point of view but its capacity thermal insulation is low.
- Resin: low physical resistance and lower performance in terms of insulation
- Glass or PEI (polyetherimide)
- Plastic: more sensitive to traces of taste left by aromas than glass tanks (LRSH, 2016).

Before the production of the aerosol, the e-liquid must be transferred from the tank/container to the heating element. The heating element heats the liquid contained in a wick. This **wick** is made of heat-resistant absorbent materials. The most commonly used materials are cotton, silica, and oxidized stainless steel wire mesh.

Bamboo and hemp are less common. The main function of this wick is to retain the e-liquid so that it can be transferred to the resistance wrapped around the wick. In theory, these materials are heat resistant although wick contaminations in aerosol emissions are not uncommon. The wick also controls the delivery of e-liquid to the heating element thanks to its capillary properties. If the amount of e-liquid transferred through the wick is insufficient, the heating element will reach an extremely high temperature. The wick material, which is wrapped around the heating element, then burns off, giving an unpleasant aerosol burnt smell and taste (so-called "*dry puff*") (Fearon et al., 2018). The liquid saturation level of the wick material is important to avoid "dry draws". Depending on where the heating element is located in a liquid reservoir, bottom or top, the liquid flow rates are variable making them less or more prone to dry draws. Top coil tanks, which have the heating element above the liquid tank, require longer wicks. They are therefore more likely to have dry wicks, which also means that the maximum power that can be applied to the heating element is limited. Bottom coil tanks, with the heating element at the bottom of the e-liquid reservoir, require very short wicks because the transfer of e-liquid to the wick is also gravity dependent. These devices are best suited for high battery power devices as they are less

prone to dry printing (Chen et al., 2018). Finally, there is a small group of users who manually add or drip e-liquid directly onto the wick and coil.

This method of e-cigarette use is very prone to dry draws and is discouraged.

The actual formation of the aerosol is done by heating the e-liquid by contact with **the heating element**. Heating e-liquid requires voltage supplied to a resistance wire metallic. The heating process of e-cigarettes is based on the Joule effect. The heating element is the most important part of the e-cigarette because it converts electrical energy into heat. This heating element is a heat-resistant metal filament, called a coil. The most commonly used materials are Nichrome and Kanthal, as their resistance remains relatively constant with changes in temperature. Most heating elements use 80/20 nichrome wire (80% nickel, 20% chromium) which is an ideal material as it has a relatively high resistance. Also, when first heated, it forms a layer of chromium oxide, which

prevents the wire from breaking or burning because the material under the chromium oxide layer does not oxidize. Thanks to this high corrosion resistance, nichrome can withstand temperatures of up to 1150°C. Kanthal is an alloy of iron,

chrome and aluminum which has high strength and good resistance to high temperature corrosion.

The resistance of the heating element and the voltage across it determine the temperature of the heating element. The coil heating temperature is an important parameter that affects aerosol properties, such as the amount and composition of aerosol emitted by e-cigarettes. The standard resistance values of the first e-cigarette devices are between 1.8 and 2.8 Ohms. However, the resistance of the coil does not only depend on the material of the filament. A wide variety of coil configurations can also contribute to the wide variability in performance between different devices, even within the same brand. This shows the importance of characterizing the design of the devices.

The frequency of renewal of the coil depends on the frequency of use but also on the composition of the liquid used which can foul the resistance more or less quickly. The more viscous the liquid (vegetable glycerin content > 30%), the faster the resistance clogs.

In addition to the heating element, the **power** supplied to the heating element also determines the production of the aerosol. The **power** of an e-cigarette, expressed in Watts (depending on the model, sometimes the voltage is displayed, sometimes the wattage) will influence the heating temperature of the e-liquid and therefore the quantity of aerosol produced and the intensity of the *hit*. Batteries of different capacities are available. First generation e-cigarette batteries delivered low voltages, down to 3.7V. Later generation devices allow users to adjust the power applied to the heating element to deliver voltages between 3 and 8 V. The combination of a low resistance heating element and high power allows users to produce large amounts of aerosol. However, if the power applied to the coil is too high, it can lead to overheating.

The problem with overheating, as already mentioned, is *dry draw*, which is associated with the release of toxic carbonyl compounds (formaldehyde, acetaldehyde, acrolein) due to the thermal decomposition of the e-liquid. The latest generation of e-cigarettes has a built-in feature that prevents the coil from overheating. So-called temperature control allows the user to set a temperature limit for the coil (between 100°C and 315°C) (Dibaji et al., 2018). The power sent to the coil is then automatically adjusted to maintain the coil at the chosen temperature. The concept of temperature control is based on the principle that the resistance of certain metals (nickel, titanium, stainless steel) similarly changes when the temperature changes (Ehrenreich, 1967). As these changes in wire resistance are predictable, the battery output power is adjusted to

maintain the temperature set by the user.

High wattage systems produce a lot of vapor, they have a large volume, are used most often with a low concentration of nicotine, and the temperature is regulated. In the case of a low nicotine concentration system, users tend to absorb a larger volume of aerosol. There is a negative linear relationship between the nicotine concentration and the volume of aerosol absorbed: the more the

nicotine concentration/ml is low, the greater the volume of vapor consumed (and absorbed). The consumption of a larger volume of e-liquid implies a greater absorption of nicotine but also a greater exposure to HPHC39 . This aspect is rarely taken up in the literature. In addition, for some users, the gradual reduction in nicotine may be illusory if they vape larger volumes.

Low wattage systems have high nicotine concentrations but smaller puff volumes (eg JUUL). The pharmacokinetics of high-concentration nicotine appears to approximate that of nicotine in conventional cigarettes

(Goldenson et al., 2020; Hajek et al., 2020).

³⁹ HPHC *Hazardous & Potentially Hazardous Compounds*

VI E-CIGARETTES FOR SPECIFIC GROUPS: PEOPLE WITH PSYCHOLOGICAL VULNERABILITY

- 6.1. Statement of the problem
- 6.2. Consequences of increasing smoking prevalence
- 6.3. An urgent problem
- 6.4. Smoking cessation is more difficult in this group
- 6.5. The e-cigarette as a possible device?
- 6.6. Discussion
- 6.7. Critical Reflections
- 6.8. Evolution possible : opinion des experts du CSS

6.1. Statement of the problem

Scientific research shows that there is a high prevalence of smoking among people with mental (psychological) health problems. For example, Sharma et al. point to the high prevalence of smoking among patients with severe mental disorders in Australia, despite the fact that the percentage of smokers in this country has decreased considerably in recent years (Sharma et al., 2017). For example, in patients with schizophrenia, the percentage of smokers is 70% and in patients with bipolar disorder it is 61%, compared to 16% in people without mental disorders (Sharma et al., 2017). A similar fact is reported for the United Kingdom by Ratschen, who refers to the fact that in the group of patients suffering from severe mental disorders, more people smoke than in the average population, so much so that 40% of cigarettes smoked in the United Kingdom are by this group. In addition, there are also more heavy smokers in this group (Ratschen, 2014).

About half of the cigarettes marketed in our Western society are sold to people who suffer from mental (psychological) illnesses, and more clearly still to people who suffer from addiction or psychotic disorders, a population in which around 80% of patients are declared dependent tobacco (Dom, 2015).

These data are confirmed by a recent study by Weinberger et al. who, based on the *National Health Interview Survey* in the United States, found a 39.5% prevalence of smoking among people with "severe psychological distress" (SPD) (compared to 13.4% in people without SPD). This prevalence also remained unchanged over the period 2014-2017, while the prevalence in the group of people without SPD decreased over this period (Weinberger et al., 2020). Similarly, the study of 380 respondents who suffered from psychiatric disorders shows

a prevalence of 39.5% of smokers, of which 52.3% were nicotine dependent, measured using the Fagerström test for nicotine dependence (Asharani et al., 2020; Shahwan et al., 2019).

People with an indication of a mental health problem were more dependent on tobacco (Brose et al., 2020).

6.2. Consequences of increasing smoking prevalence

The higher prevalence of smoking and greater dependence lead to the fact that in the group of patients with severe mental disorders, there is also more tobacco-related morbidity and mortality (Ratschen, 2014) .

For example, there is an increased risk of heart disease due to metabolic side effects of atypical antipsychotics (Gartner et al., 2015).

Dom refers to research showing that approximately 20 years of life expectancy are lost when battling a severe psychiatric disorder and that much of this loss can be attributed to the effects of smoking (Dom, 2015) .

Scientific research shows that the life expectancy of people with severe mental disorders is thirteen to twenty years shorter than that of the general population. Sixty percent of the higher morbidity and mortality can be attributed to physical disorders associated with an unhealthy lifestyle, including long-term smoking (De Hert M et al., 2011; Jespers et al., 2021) .

But nicotine also speeds up a number of psychopharmaceuticals (such as antidepressants and antipsychotics). Therefore, patients must take much higher doses to reach a therapeutic level and the risk of (often dangerous) side effects increases.

6.3. An urgent problem

Considering the above, we can say that there is a serious problem because people die prematurely primarily due to their unhealthy lifestyle, including smoking behavior, and not necessarily due to their psychiatric disorder (Dom, 2015). In this sense, Mendelsohn mentions that smoking cessation should be an integral part of the management of patients with severe mental (psychological) disorders, precisely because this group is more likely to die from a tobacco-related disease than from their primary psychiatric disorder (Mendelsohn, 2021).

The growing trend of mental health services to adopt a smoke-free environment can be seen as an opportunity. In its report ' *Smoking and mental health* ', the *Royal College of Physicians* mentions that all healthcare facilities used by people with mental disorders be completely smoke-free (RCP, 2013). In the Trimbos report, the development of a universal smoke-free policy for the mental health sector is also given as a first recommendation (Blankers et al., 2015). From 2022, the *Vlaams Instituut Gezond Leven*

will start working on an anti-smoking policy in psychiatric hospitals Flemish, but it is not yet clear whether the organization will succeed in making Flemish psychiatric hospitals completely smoke-free. As part of a new policy for tobacco-free hospitals in Belgium (which aims to make hospitals completely smoke-free in the long term), the aim will also be to make psychiatric hospitals completely smoke-free in the near future.

6.4. Smoking cessation is more difficult in this group

Despite the seriousness of tobacco-related problems, Brose et al. point out that people with mental health problems are definitely motivated to quit smoking, smoke less, use nicotine replacement therapy or use e-cigarettes and have tried to quit in the past year (Brose et al., 2020).

However, for several reasons, effective smoking cessation in the group of people with severe mental disorders is more difficult (Sharma et al., 2017).

Conventional smoking cessation methods seem to be less successful in this group (Sharma et al., 2017; Ratschen, 2014). Schluger also notes that in the group of patients with severe mental disorders, there are few methods effective in smoking cessation or tobacco harm reduction (Schluger, 2014).

Although there is a desire to quit smoking, for some patients with, for example, schizophrenia, quitting smoking will be even more difficult due to socioeconomic status, cognitive impairment or lack of social support. from family or peers (Gartner et al., 2015).

6.5. The e-cigarette as a possible device?

First of all, there is a need for smoke-free policy in the area of addiction care and health care in general. Conventional methods for quitting smoking are not as effective with the group of psychiatric patients. Therefore, one can study if and how e-cigarettes can be an alternative in this group of people with mental disorders, certainly when more safety guarantees can be provided.

Brose et al. mention that this group, among others, appears to be motivated to use e-cigarettes and that their use has been found to be strongly associated with the likelihood of successful smoking cessation, both in individuals with and without additional psychiatric diagnosis (Brose et al., 2020).

According to Sharma et al, long-term use of e-cigarettes offers a potential alternative to traditional smoking cessation methods that don't seem to work. They refer to the much lower health risk of vaping compared to smoking, which allows for risk reduction, such as the supply of methadone for heroin users. They also see benefits in dual-use, which often results in the complete cessation of conventional cigarette smoking. The authors also expect a higher compliance rate because it is an acceptable product

for this target group (Sharma et al., 2017). It should be noted, however, that unlike methadone, the e-cigarette is not a drug; which also poses an ethical problem with the e-cigarettes offered by tobacco manufacturers.

Mendelsohn also advocates tobacco risk reduction, which encourages smokers to switch from high-risk cigarettes in which the tobacco is burned to lower-risk alternative nicotine intake, such as vaping. Here, the main objective is to avoid the risks associated with smoking but not necessarily to eliminate the risk of continuous nicotine consumption, because, at low doses, the harmfulness of nicotine is limited.

(Mendelsohn, 2021).

Ratschen also sees a place for e-cigarettes as a method of withdrawal or reduction in smoking in the group of people with mental disorders. "If these patients are prohibited from smoking in the institution against their will, all sorts of unpleasant negative effects can occur, such as not wanting to return to the institution if smoking is prohibited there. or an escalation of the measures and in particular the application of strict measures, for example, the search in order to search for the attributes of the smoker,...

(Ratschen, 2014)". At this level, she refers to a study carried out on patients with schizophrenia which gave good results. Even if this of course does not solve all the problems, it pleads in favor of the integration of e-cigarettes in the anti-smoking strategy within institutions (Ratschen, 2014)".

A more recent study has

revealed that smoking even a single cigarette in an enclosed space with natural ventilation and low ventilation rate leads to passive bystanders potentially being exposed to a concentration of ultrafine particles significantly higher than that associated with 20 minutes of vaping and that, regardless of the liquid used in the e-cigarette. Since the inhalation of high concentrations of nanoparticles could be a high risk factor for passive vapers due to the high penetrating capacity in the deepest regions of the lungs, the authors

point out that particle size should be considered as an important factor when assessing the risk of passive exposure in enclosed spaces from both e-cigarettes and tobacco cigarettes (Palmisani et al., 2019) which contrasts with the 2018 NASEM report

In their study, Bianco et al. conclude that the high rate of spontaneous e-cigarette use by participants (42.1%) suggests that e-cigarettes are an attractive strategy to use nicotine during a smoking cessation intervention. This strategy could be used as a smoking cessation tool or to limit smoking (Bianco et al., 2019).

According to O'Brien et al., whose study aimed to determine the extent to which e-cigarettes may have an effect on smoking cessation in people with mental disorders and while more or less beneficial than traditional nicotine replacement therapy (NRT), people who used e-cigarettes had higher percentage reductions in smoking. smoking, treatment compliance and acceptability. This leads the authors to conclude that the use of e-cigarettes in smoking cessation appears to be as effective and acceptable for people with mental disorders as for people without mental disorders (e-cigarettes have previously been shown to have a similar or better effect than NRT on smoking cessation).

In people with mental disorders, e-cigarettes may be as effective as patches, but more acceptable and lead to a greater reduction in smoking (O'Brien et al., 2015). Hartmann-Boyce et al. found in a Cochrane systematic review that there is evidence with a limited degree of certainty that the rate of occurrence of adverse effects when using NRT and e-cigarettes as a smoking cessation aid was similar, although with a fairly high degree of imprecision. Severe adverse effects were rare and there is no evidence that their frequency differs between nicotine e-cigarettes and NRT, although again the degree of imprecision is substantial. These authors consider that there is evidence, with a degree of *'moderate-certainty'*, that e-cigarettes with nicotine increase the

smoking cessation percentages compared to nicotine-free e-cigarettes and compared to NRT (Hartmann-Boyce et al., 2021).

Research on the use and impact of e-cigarettes on people with mental disorders has been conducted (Pratt et al, 2016; Valentine et al., 2018). However, the study by Valentine et al. focused on a very specific target group (US Army veterans with psychiatric comorbidity) and the studies of both Pratt and of Valentine only involved a very small number of participants.

Ms. Pratt and her colleagues examined the extent to which people with severe mental (psychic) disorders are drawn to the use of e-cigarettes. Twenty-one smokers with severe mental disorders, who tried to quit without success and did not participate in smoking cessation treatment, were included in the study. Researchers provided e-cigarettes and instructions on how to use them, and participants were assessed weekly for four weeks. However, the small number of participants included in this study is a limitation.

Nineteen participants were fully assessed. Between the start of the study and the time of the final assessment, self-reported cigarette consumption decreased from 192 to 68 cigarettes per week, which was confirmed by a reduction in carbon monoxide (CO) in the air expired. E-cigarette use did not increase over the four weeks. Temporary and mild side effects, such as dry throat, sore throat, nausea, dizziness and cough, were reported by 58% of participants. To the end of the study, measures of consumption, satisfaction with regular cigarettes and willingness to buy e-cigarettes were high. In conclusion, people suffering from severe mental disorders could find in e-cigarettes an interesting alternative to conventional cigarettes. No indication of increased nicotine addiction was found (Pratt et al., 2016).

Valentine et al. conducted research in a specific group of 43 US Army veterans with psychiatric comorbidity, with the aim of evaluating the impact of e-cigarettes on consumption of conventional cigarettes, willingness to quit smoking, and changes in nicotine addiction. Participants were given an e-cigarette device that they could use at will, along with other tobacco products. They were encouraged to undergo a weekly laboratory visit and a follow-up visit after one month. The outcome variables were the number of cigarettes smoked per day, the frequency of e-cigarette use, the amount spent on tobacco cigarettes, the level of CO in expired air and the levels of urinary cotinine.

They found significant reductions in CO in exhaled air and in the number of cigarettes smoked per day. No severe negative effects have been reported. Smoking cessation, supported by biochemical data, was observed in three participants. After one month of follow-up, motivation to quit smoking remained significantly higher and nicotine dependence was significantly lower, compared to baseline.

The authors conclude that e-cigarettes are acceptable for smokers with psychiatric comorbidity, which was underscored by frequent and sustained use of e-cigarettes by 90% of participants, which may promote the reduction and/or smoking cessation. E-cigarettes appear to be a viable harm reduction modality for smokers with psychiatric morbidity (Valentine et al., 2018). However, the small number of participants and the specific characteristics of the participants included do not allow the results to be generalised.

The literature review conducted by Hefner and colleagues on the use of e-cigarettes by adults with psychiatric disorders and substance abuse problems and how this can lead to potential positive and negative consequences, showed that e-cigarettes -cigarettes are considered a viable alternative to conventional cigarettes by adult smokers suffering from

mental disorders. E-cigarette use among this group also did not appear to lead to an increase in nicotine addiction or psychiatric symptoms (Hefner et al., 2017).

6.6. Discussion

Although the population of people with mental disorders often wishes to quit smoking, it seems that traditional methods of smoking cessation generally do not work well. The suggestion to use the e-cigarette as a smoking cessation device in this group is therefore regularly made. This is all the more so since the e-cigarette seems to be a very acceptable alternative in this population. However, this situation also raises a number of concerns.

Parrot's commentary addresses the psychobiological issues of long-term nicotine addiction among e-cigarette users. These include, according to the authors, daily mood swings, increased stress, increased depression, deterioration of memory and indications of other deficits.

neurocognitive. In summary, Parrot claims that nicotine is a powerful central nervous system stimulant with a wide range of side effects (see point 5.2.). Parrot further states that its addictive potential is widely recognized but its effects

harmful psychobiological and health effects on heart rate, mood, alertness, neurocognitive abilities, sleep, the *hypothalamic-pituitary-adrenal* (HPA) axis, cortisol and stress are much less known. These psychobiological problems are likely to be found in regular users of e-cigarettes, even those who use them alone (i.e. without smoking tobacco cigarettes simultaneously).

However, he advocates studying this empirically in e-cigarette users (Parrott, 2015). Parrot's suggestion to set up studies

Empirical studies on this subject with e-cigarette users does not exclude that other results/contrary may emerge.

Sharma et al, advocate advising the group of people with severe mental disorders first and foremost to quit smoking using traditional methods, such as NRT, varenicline or bupropion, in combination with *counseling* behavior and support. For those who are unwilling or unable to quit conventional methods, they however feel that there should be proper advice and information on the pros and cons of e-cigarettes and that they should be supported in their efforts. to switch to e-cigarettes (Sharma et al., 2017).

Mendelsohn views the use of e-cigarettes as a way to reduce or quit smoking as a form of tobacco harm reduction. He considers vaping as a good/better form of nicotine replacement therapy, especially for the group of people with severe mental disorders. He also mentions that the British authorities encourage vaping in establishments for people with mental health problems. According to him, psychiatrists should be trained in vaping so that they can answer questions from patients,

providing appropriate counselling, prescribing nicotine and helping smokers switch to a safer alternative (Mendelsohn, 2021). In the Belgian context, this can certainly also be a task for tobacco specialists as long as they are or have become experts in the field.

Schluger takes a nuanced view. He does not want to exclude e-cigarettes a priori as a means of reduction or smoking cessation for people with mental disorders and thinks that it is not because the manufacturers of e-cigarettes are mainly interested in selling addiction to nicotine that this would mean that careful use of their product could not benefit smokers. On the other hand, he questions the advisability of using e-cigarettes as a smoking cessation tool in this population. Nicotine is a highly addictive product and there is no evidence of its long-term safety, whether the e-cigarette containing nicotine is used "alone" or in the context of dual use (Schluger, 2014). It should be noted here that if the e-cigarette is used as a smoking cessation product, long-term safety plays a less important role, because its use is for a relatively short period during which without its use smokers would otherwise smoke. This can be a problem when it comes to permanent/continuous use of nicotine, such as the permanent *switch* from tobacco to vaping.

Seliya et al. conclude in their study that dual use of tobacco and vaping (JUUL) decreases over time, while at the same time exclusive vaping increases. According to them, this suggests that for most smokers, dual-use is only about a transition period leading to a shift to exclusive vaping (Selya et al, 2021). It is important to note that the tobacco harm reduction consultancy of two of the authors is solely for the opinion of *Juul Labs Inc.* and that the other two authors are or have been employed by Juul Labs Inc.

As there is an urgent need to find strategies to reduce smoking and the harm caused by tobacco smoke in patients with mental disorders, Schluger proposes to conduct well-designed clinical trials, in particular to assess the effectiveness of e-cigarettes as a smoking cessation tool in the group of smokers with mental disorders (Schluger, 2014). Despite Schluger's proposal, since its publication, we are not aware of any clinical trials examining the effectiveness of e-cigarettes as a smoking cessation tool in the group of mentally ill smokers. The large EAGLES trial resulted in several publications on the effectiveness of smoking cessation in smokers with mental health problems, but these publications did not include e-cigarettes (Anthenelli et al., 2016; Ayers et al., 2019; Curtis et al., 2018; Evins et al., 2021; Heffner et al., 2019).

Although in their study, Pratt et al. are quite positive about the use of e-cigarettes as a smoking cessation tool for smokers with mental disorders, they also believe that further research is still needed, both on the attractiveness of e-cigarettes for this group and on toxicity (Pratt et al., 2016). Hefner et al.

also warn that the long-term effects of e-cigarette use on conventional cigarette smoking and other health indicators are still largely unknown. In order to determine whether there are any particular areas of concern

As part of developing strategies and health messages regarding the prevention of smoking in adults with mental disorders, they say there is a need to know more about the risks and benefits of using the e-cigarette in this vulnerable group. This point is particularly important because, as with conventional cigarettes, people with mental disorders could

develop specific habits of e-cigarette use that differ from those of the general population, including a habit of more frequent and intense use (Hefner et al., 2017).

6.7. Critical Reflections

An important question in research on smoking and smoking cessation in people with mental disorders is the question of causation: what is cause and what is effect? In the opinion piece by Vermeulen & van den Brink, reference is made to a recent meta-analysis by Firth et al. which shows that the evidence that smoking is a risk factor for the development and worsening of psychiatric disorders and can no longer be denied (Firth et al., 2020). Therefore, the

smoking is neither an effective coping strategy nor an effective form of medication or self-medication for cognitive impairment or negative symptoms in patients with schizophrenia (Vermeulen & van den Brink, 2020). The question is whether mental disorders lead to (more) smoking, whether smoking leads to mental disorders or whether it is a combination of both. Despite all the research carried out on the subject, the question of causality has so far remained unanswered and above all confined to philosophical reflections, in which it is also not known exactly what the contribution of nicotine is on the one hand and other constituents of tobacco smoke on the other hand.

Furthermore, the harmfulness of (long-term) use of e-cigarettes is far from clear. It is important that scientific research based on this subject continues. Risk reduction is often mentioned when it is proposed to introduce e-cigarettes to people with mental disorders to get them to reduce or stop smoking.

However, the comparison that is sometimes made with the administration of methadone as a substitute for heroin is incorrect. The safety standards for methadone are clear, those for e-cigarettes are not (yet). On the one hand, the precautionary principle would lead us to recommend and only offer substitute products that meet the required safety standards. On the other hand, safety standards are

rarely or never absolute, but one can strive to use them as safely as possible. It is important to find a balance between, on the one hand, the safety of the product

(e-cigarette) and, on the other hand, the prevention of more or less extensive use.

Discouraging e-cigarettes because they are not 100% safe may lead smokers with a mental health condition to continue smoking when the health risk is likely much higher. Finding that balance is likely to be a longer process. While, on the one hand, efforts must be made to make the e-cigarette as safe as possible, this does not exclude, on the other hand, the simultaneous implementation of a solid and widely supported anti-tobacco policy in the addiction and mental health care, with the possible use of e-cigarettes as an additional smoking cessation tool for the target group of people with mental disorders. If intervention by the competent authority were to be considered, it is important that the products are independent and remain independent of the

tobacco.

The **CSS** would like to point out that there are also health gains to be made in our country by making nicotine substitutes more financially accessible. NRTs are currently available over-the-counter in pharmacies without a doctor's prescription. As it is cost-effective smoking cessation aids, the purchase price of which constitutes an obstacle for certain smokers who have, for example, replacement income, the CSS recommends that the competent authority provide for adequate intervention for NRTs.

The terms “ *harm reduction* ” should also be used with caution. Indeed, it seems very likely that this term - in itself neutral - has been used for some time by the big tobacco companies for a tactical adaptation

opportunistic to a change in marketing- and sales policy rather than as a genuine commitment to risk reduction (Peeters & Gilmore, 2015).

However, this should not be contradicted by the fact that the result (weaning smoking, more use of low-risk products), especially for the target group specific to smokers with a mental health problem, is also extremely important.

6.8. Evolution possible : opinion des experts du CSS

Mental health services, such as psychiatric hospitals, psychiatric departments in general hospitals, and mental health centers, should focus more on smoking cessation policies and cessation

smoking as part of this anti-smoking policy. Smoking should no longer be approached as a free choice or a way of life, but as an addiction requiring

treatment. Every patient should be offered behavior counseling smoking, integrated into his psychiatric treatment.

There is an urgent need to push for e-cigarettes to be as safe as possible.

Ideally, as a recognized drug for smoking cessation and, until this is the case, as a consumer product with as many guarantees of safety as possible.

The sale of tobacco and nicotine products through vending machines on the premises of psychiatric hospitals should be prohibited. The distribution of nicotine substitutes should become a more formal part of the assistance given to smokers. The **CSS** is already pleading for intervention in the purchase price of TSN. The price of an e-cigarette must also remain at an accessible level.

VII RISKS AND OPPORTUNITIES

7.1. Introduction

7.2. Background: Tobacco Control

7.3. Focus on the risks associated with the e-cigarette

7.4. Focus on e-cigarette opportunities

7.5. Risk reduction: framework and discussion

7.1. Introduction

The debate on the e-cigarette essentially focuses on these three questions:

- What are the health risks (compared to smoking tobacco or related to not smoking)?
- How can e-cigarettes represent a risk for young people?
- What possibilities does it offer adult smokers to quit smoking?

E-cigarette policies vary widely from country to country. Just compare the policies and regulations of New Zealand with those of Australia or those of the United Kingdom with those of Finland. The same goes for reviews from reputable institutions around the world. Within the working group that drew up this opinion, there are also various points of attention. Nevertheless, there is also broad consensus on certain issues around the world and the debate cannot (always) be described in terms of black and white, but more often in terms of clearly different emphases.

How to explain the polarized discussion on the e-cigarette? Two different perspectives shape the current global debate: risks and opportunities. In their article entitled “ *The e-cigarette debate: what counts as evidence?*” Fairchild et al.⁴⁰ (2019) describe how two major and fairly recent evaluations of e-cigarettes – one in the United States by the *National Academies of Science, Engineering and Medicine* (NASEM) and the other by *Public Health England* (PHE) - come to very different conclusions when answering the question of what evidence can a policy rely on, who has to make decisions on e-cigarettes. These differences are due to the fact that the two reports focus on different priorities. They help determine what counts as evidence in the debate over the impact of e-cigarettes on smokers, non-smoking relatives and minors. This includes the question of who presents the risk that should take center stage. “*Fundamentally, the 2 reports differed on whose risk was to be given priority. For PHE, the central public health concern was how to protect the health of current smokers. For the United States, the pivotal issue was the protection of*

40 <https://ajph.aphapublications.org/doi/10.2105/AJPH.2019.305107>

children and nonsmokers—innocent bystanders. The formulation of the questions and inclusion and exclusion criteria is always a value-based process ».

« For NASEM, the core question was how to protect nonsmokers from the potential risks of exposure to nicotine and other contaminants or from the risk of smoking combustible cigarettes through renormalization. A precautionary standard was imperative, making evidence that could speak most conclusively to the question of causality paramount. For PHE, the priority was how to reduce the burdens now borne by current smokers, burdens reflected in measurable patterns of morbidity and mortality. With a focus on immediate harms, PHE turned to evidence that was “relevant and meaningful ».

The two reports do indeed also have methodological differences as their backdrop. Fairchild et al. (2019) report that PHE “*did weigh randomized controlled trials, it did not hold them to be the gold standard for its evidentiary review*” because *« the demands of randomized controlled trials were “discordant with what happens in real life” and therefore were not generalizable at the policy level ».* Le rapport de la NASEM (2018) met un accent différent: *« Considering their strength in determining causality, randomized controlled trials and prospective longitudinal studies provided the most robust evidence ».*

Based on these methodological differences, the article by Fairchild et al. (2019) schematically presents what the opposing perspectives – PHE on the one hand and NASEM and the major US agencies (CDC and Surgeon General) on the other – mean in terms of risk estimates for smokers, those exposed and minors (see table 1 of article 41).

7.2. Background: Tobacco Control

The debate on the e-cigarette is inevitably linked to that on smoking. Tobacco control organizations and professionals share the following concerns.

Smoking causes enormous damage to health (mortality, morbidity) and remains the main preventable cause of premature death (YPLL - *years of potential life lost/years of potential lives lost*). If no one smoked, we could avoid one in three cancers in our country (FCC, 2018). In Belgium, one in seven deaths is still due to a tobacco-related disease. Each year, around 14,000 Belgians die prematurely from tobacco use. In addition to human suffering, smoking also has a huge social cost due to the negative impact on the household budget (more poverty), on the economy and productivity, on health care, on the environment, and especially also on the emergence of health inequalities between population groups in society⁴². Smoking is one of the main causes of the latter because, today, it is strongly linked to socio-economic status (SES): people with lower SES and who are in a situation of social vulnerability smoke any further. And because smoking has such a significant impact on health, they are significantly more affected by

⁴¹ In the rest of the text, the views of PHE and the Surgeon General reappear, but in their most recent. For the NASEM report, see <https://www.nap.edu/catalog/24952/public-health-consequences-of-e-cigarettes>

⁴² <https://www.gezondleven.be/gezondheidsongelijkheid>

illness and death (ASH, 2019)⁴³. Inequalities in tobacco consumption contribute strongly to socio-economic differences in quality and length of life.

In the past, smoking played a major role in creating and increasing health inequalities between different socio-economic groups in society, and it still does so today. In the UK, smoking is thought to be the main health inequity factor (ASH, 2019)⁴⁴.

that it Data from Sciensano (Health Survey; Gisle et al., 2019)⁴⁵ demonstrate There are pronounced social inequalities in terms of smoking: “ *The most educated people (higher education diploma) obtain the best results for all the indicators studied. This also applies to young people aged 15 to 24 who belong to households with the highest level of education* ”

⁴⁶. The percentage of smokers in households in the lowest income quintile has changed little in a few decades compared to the very marked downward trend in the general population.

In 1997, there were 32% of smokers in the lowest income quintile group, in 2018 - the last moment of measurement - 29%. In the general population, on the other hand, a remarkable evolution has taken place: the proportion of smokers was 30% in 1997 and 19% in 2018. The Tobacco Survey conducted by the Foundation against Cancer (FCC, 2021) shows that most current smokers come from the lowest socio-economic classes⁴⁷. Among young people, the level of education is also strongly associated with smoking. The student survey of the Flemish Center of Expertise on Alcohol and Other Drugs (VAD)⁴⁸ shows that the differences between the different forms of education in Flanders remain significant: in vocational secondary education (ESP), there are more smokers than in technical secondary education (EST), in EST more than in general secondary education (ESG). There are also significantly more regular and daily smokers in ESPs and young people start smoking earlier.

Differences in tobacco use between low-skilled and high-skilled people have also increased in recent decades as a relatively higher proportion of high-skilled people have quit smoking. Research also shows that health inequities in terms of

tobacco use and its harmful effects, begin before birth and continue throughout the life cycle: during childhood, when people start smoking, when they stop, and when they deal with the health problems caused by smoking. These inequalities also accumulate throughout life. They stack up and reinforce each other (WHO, 2014)

⁴⁹

⁴³ https://ash.org.uk/wp-content/uploads/2019/09/ASH-Briefing_Health-Inequalities.pdf

⁴⁴ <https://ash.org.uk/category/information-and-resources/health-inequalities/> and https://ash.org.uk/wp-content/uploads/2019/09/ASH-Briefing_Health-Inequalities.pdf

⁴⁵ https://www.sciensano.be/sites/default/files/ta_rapport2_his2018_nl_v3.pdf

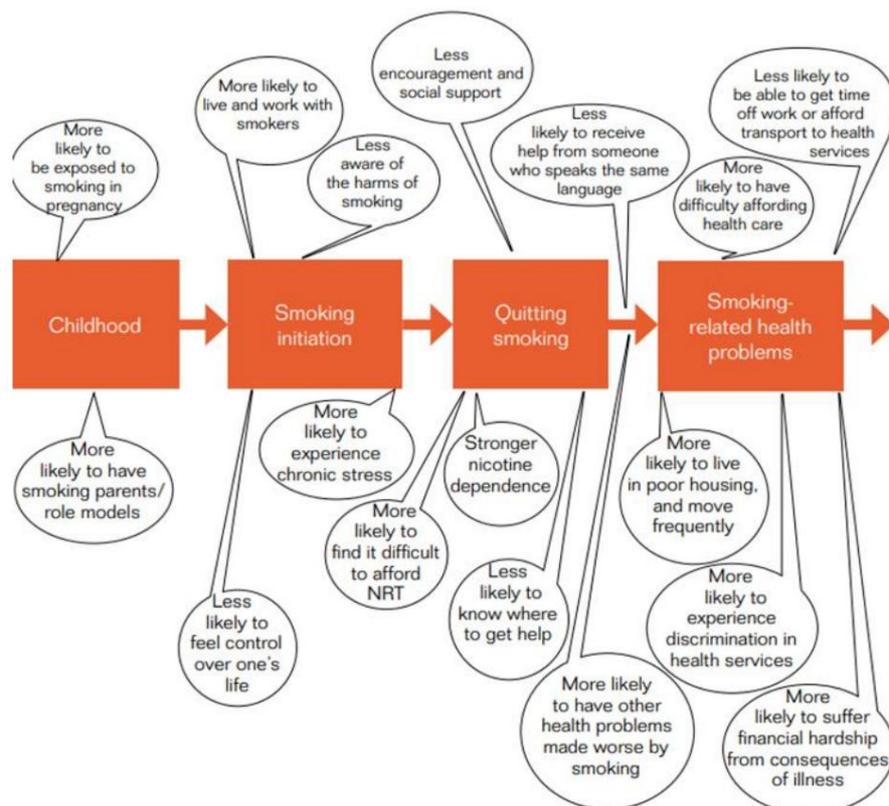
⁴⁶ https://www.sciensano.be/sites/default/files/ta_rapport2_his2018_nl_v3.pdf, p. 6

⁴⁷ https://www.kanker.be/sites/default/files/def_ipsos_rapport_rookenquete_2021_nl_pg_99.pdf

⁴⁸ <https://www.vad.be/onderzoek/vad-leerlingenbevraging>

⁴⁹ https://www.euro.who.int/_data/assets/pdf_file/0005/247640/tobacco-090514.pdf?ua=1

Figure 2 : How smoking inequities compound over the life course (repris du rapport de WHO, 2014)



Why is smoking more prevalent among less educated people and those in socially vulnerable situations? Three factors play a role.

First, the social determinants of health (defined by the WHO as “*the conditions in which people are born, grow, live, work and age*”). The better a person’s socio-economic living conditions, the more likely they are to live a long and healthy life. The distribution of these social determinants within the population is

unequal and the impact of the social determinants of health is also uneven⁵⁰. People in socially vulnerable situations are more likely to live, work and live in conditions that threaten their health rather than protect it, leading to health inequalities. When looking at the most vulnerable groups, smoking and continuing to smoke is a behavior where other factors also play a major role: stress, poverty, debt, loneliness, financial problems, etc. When people are trying to survive, it’s hard to quit.

Second, smoking behavior (apart from genetic predisposition) is also strongly determined by environmental factors, primarily by the socio-cultural environment. Smoking is often passed down from generation to generation

⁵⁰ For example, for people in a situation of social vulnerability, the impact of a humid environment on health will be greater than for people who are not in a situation of social vulnerability. Indeed, this humid environment is combined with other health-determining factors, such as a higher risk of (passive) smoking, exposure to chronic stress, less healthy diet, etc.

as part of a "tobacco culture". Values and norms about smoking are transmitted through a process of socialization within the family. For young people, greater exposure to tobacco increases the risk of starting to smoke and, once addicted, of having problems quitting (ASH, 2019)⁵¹. It is more difficult for adult smokers to quit smoking in a smoking environment.

Third, smoking is also highly addictive and even more so for smokers who continue to smoke today. Vulnerable and less skilled smokers have more difficulty quitting and make fewer quit attempts. They also started smoking earlier and are more addicted to tobacco (Tabaknee, 2019)⁵².

The remaining groups of smokers should be targeted more by population-level measures (excise duties, legislation, broad and repeated campaigns tailored to the remaining groups of smokers and encouraging them to make more quit attempts, etc.), by measures at the level of the environment and the target group (anti-smoking policy in municipalities, health care, etc.) and by a tailor-made smoking cessation offer (for example, by integrating the offer of tobacco specialists into health and of well-being).

7.3. Focus on the risks associated with the e-cigarette

Those emphasizing this point describe the central themes and concerns as follows:

- Lack of knowledge about the negative impact of vaping on health and lack of data on the long-term effects of e-cigarette use.
- The use of the e-cigarette should not only be compared to smoking, but also to non-use by the non-smoker: for a non-smoker, it is healthier and safer not to vape than to vaping.
- There is a correlation between vaping and (later) smoking in young people and possibly also a gateway effect: a causal relationship between starting to vape and then becoming a regular smoker, whereas these young people would not have become regular smokers without starting to use e-cigarettes.
- For various reasons, the e-cigarette can only play a limited role in stopping smoking permanently. The e-cigarette is not a drug recognized for smoking cessation, but a consumer product (not marketed as a smoking cessation drug). Therefore, established smoking cessation medications that have been shown to be effective remain the first choice for smoking cessation unless the smoker has used them before or does not want to use them.

As part of a smoking cessation program focused on behavior change (tobacco specialist), the e-cigarette can only be used after having used recognized smoking cessation products with proven efficacy (unless the smoker himself indicates a preference for the e-cigarette). When informing smokers about smoking cessation aids, a distinction should be made between first-choice aids (recognized smoking cessation drugs and behavioral support) and second-choice aids (e-cigarettes). A

⁵¹ https://ash.org.uk/wp-content/uploads/2019/09/ASH-Briefing_Health-Inequalities.pdf

⁵² <https://www.tabaknee.nl/dossiers/laagopgeleiden-en-roken>

Once the e-cigarette is a recognized medicine for smoking cessation (with more safety standards), it can really play a role as a medicine for smoking cessation. • If the e-cigarette plays a role today as a smoking cessation tool for some smokers, it is only for the individual smoker. The e-cigarette plays no role in answering the question of how to reach the still large group of remaining smokers in our country in the future. The e-cigarette has no global impact on the population.

- Large tobacco companies are increasingly active in the tobacco market. e-cigarette and on the market for (relatively) new nicotine-based products such as the e-cigarette. They want to keep smokers addicted to nicotine and create new nicotine addicts (young people) through these products. Harm reduction is primarily a strategy of the tobacco industry. It is thus trying to ensure its future interests while tobacco consumption (at least in the Western world) is declining. • The distinction between tobacco and nicotine and its importance for the smoker should be

be recognized, but with a specific focus. The “ *tobacco endgame* ” is not just about ending smoking, but also about discouraging the use of alternative nicotine products. They are less harmful to health, but they are

still. This is why, in the future, the “ *tobacco endgame* ” must also include the fight against nicotine consumption and its harmful effects both among minors

que chez les fumeurs adultes. Les dernières phrases du huitième « *WHO report on the global tobacco epidemic* » (2021)⁵³ l'indiquent clairement: « *We must all recommit to strengthening implementation of the WHO FCTC, strive to adopt MPOWER measures at the highest level of achievement, and ensure that all the people of the world are protected from the harms of tobacco and nicotine* ».

- *Dual use* among smokers switching to e-cigarettes is a (persistent) problem. In the words of the WHO: “*Most ENDS users do not quit smoking combustible cigarettes but rather use both ENDS and combustible cigarettes, which, at the least, maintains the substantial health risks associated with cigarette smoking and may increase their health risks*”. (WHO, 2021)⁵⁴
- Many smokers who replace tobacco cigarettes with e-cigarettes do not stop vaping. Long-term e-cigarette use may be cause for concern. A smoker who quits smoking tobacco and switches to the exclusive use of the e-cigarette is not a smoker who quits smoking. Comme l'indique l'OMS : « *The scientific evidence on e-cigarettes as cessation aids is inconclusive and there is a lack of clarity as to whether these products have any role to play in smoking cessation. Switching from conventional tobacco products to e cigarettes is not quitting* »⁵⁵
- EVALI (the abbreviation found by the *Centers for Disease Control and Prevention* (CDC) for *E-cigarette or Vaping product use-Associated Lung Injury*) has resulted in 68 deaths and thousands of hospitalizations in the United States. EVALI had specific causes (to dilute the viscous cannabis oil used in e-cigarettes, vitamin E acetate was added, a practice related to patterns

⁵³ <https://www.who.int/publications/i/item/9789240032095>

⁵⁴ <https://www.who.int/publications/i/item/9789240022720>

⁵⁵ <https://www.who.int/news-room/commentaries/detail/quit-tobacco-to-be-a-winner>

economic criminals). But it is not excluded that the use of the e-cigarette as intended is also at the origin of the EVALI.

- Policy measures that emphasize the risks of e-cigarettes for young people and non-smokers should be preferred to those that preserve potential opportunities for adult smokers. If a balance is sought between the two, the main emphasis should be on the former. There is a risk that this balance will not be found and that the measures taken will not (in the future) sufficiently protect the general population - in particular young people and non-smokers - from the risks of vaping.

Within the focus on risks and opportunities, there are of course gradations in the designs (same for the focus on opportunities). Not everyone who emphasizes risk agrees with all of the emphases listed above.

The emphasis placed on the risks is today mainly expressed by the WHO, but also by several American medical organizations (*American Heart Association, American Cancer Society, American Lung Association, American CDC, etc.*). WHO recognizes the potential opportunities of e-cigarettes for some adult smokers but these are secondary to the focus on potential risks, evidence-based smoking cessation provision (behavioral support and pharmacological products), tobacco industry strategies and the policy framework of the Framework Convention on Tobacco Control (FCTC)⁵⁶.

7.4. Focus on e-cigarette opportunities

Those emphasizing this point describe the central themes and concerns as follows:

- The impact of vaping on health must be weighed against the consequences of smoking. When it comes to major smokers, the distinction between smoked tobacco and nicotine is essential. Many smokers and ex-smokers mistakenly believe that nicotine is responsible for tobacco-related cancers and cardiovascular pathologies. Nicotine makes smokers addicted to tobacco and itself presents some risks, but the health damage caused by nicotine is minimal compared to the thousands of other chemicals present in tobacco smoke, which cause almost all the damage.
- Compared to smoked tobacco, the e-cigarette is a lower risk product. The "risk continuum" - the distinction between high-risk nicotine products (smoked tobacco) and low-risk nicotine products (such as e-cigarettes) - is widely recognized in the scientific community and should constitute the basis of the policy relating to these products. Policy measures must be proportionate to the risk associated with the use of the product (risk proportionality policy). This means that the measures needed to discourage smoking must be stricter than those needed to regulate the use of e-cigarettes.

⁵⁶ <https://fctc.who.int/>

- There is “ *moderate evidence* ” that the severity of nicotine addiction is lower for e-cigarettes than for tobacco cigarettes (NASEM, 2018)⁵⁷ .
- Until today, the gateway hypothesis cannot be scientifically substantiated. Explanations for the link between vaping and youth smoking go in another direction. • The e-cigarette with nicotine plays a positive role in smoking cessation, both for individual smokers and at the population level. At a population level, e-cigarettes may contribute to more quitting, according to data and research from the UK and France. The e-cigarette is now also the smoking cessation product most used by smokers

in our country (Health Survey, 2018⁵⁸), it could (eventually) affect more smokers than smoking cessation drugs and the tobacco specialist. • The e-cigarette is above all a consumer product. However, it is used by smokers as a smoking cessation aid (or as a way to reduce tobacco consumption). The e-cigarette is not a recognized drug for smoking cessation, but it could become one in the future. This path of medicalization of the e-cigarette is useful, but it does not replace the e-cigarette as an affordable consumer product, accessible to all smokers who wish to use it, outside of a medical context. • If the smoker who wants to quit smoking chooses the e-cigarette with nicotine, he must

encourage him. The e-cigarette must also be included in the analysis of smoking cessation aid: what are the developments in terms of vaping?

how is the smoker informed about this (correct information, encouraging, discouraging)? The smoker must be better informed and heard and he must be autonomous and free in his choice of smoking cessation aid. There are six methods and tools that can benefit the smoker who wants to quit smoking: the tobacco specialist, Tabacstop, smoking cessation medication, the general practitioner and the pharmacist, the e-cigarette with nicotine and Allen Carr.

- In countries that emphasize risk reduction, smoking prevalence rates are falling: in Sweden, there are still 7% of smokers (snus replaces tobacco there); in the United Kingdom, there are still 12% of smokers (CE, 2020⁵⁹; PHE, 2021⁶⁰). The United Kingdom shows that a focus on harm reduction strengthens tobacco control policies (the United Kingdom has since

for a long time at the top of the countries with the best tobacco control policy in Europe⁶¹). Dual use is decreasing in countries that commit to it and that ensure a positive framework for e-cigarettes. • *Randomized controlled trials* (RCT's) are not the only evidence on which to base a policy concerning the e-cigarette as a means of smoking cessation. There are other studies (observational studies, population data), but testimonials from smokers and former smokers (worldwide) are also an important source of information.

⁵⁷ <https://www.nap.edu/resource/24952/012318ecigaretteConclusionsbyEvidence.pdf>

⁵⁸ https://his.wiv-isp.be/nl/Gedeelde%20%20documenten/TA_NL_2018.pdf

⁵⁹ Figures from the recent Eurobarometer: <https://europa.eu/eurobarometer/surveys/detail/2240>

⁶⁰ Public Health England mentions in the Evidence Update 2021 other tobacco prevalence rates, namely 14% or 16%, selon la source, <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-february-2021/vaping-in-england-2021-evidence-update-summary>

⁶¹ <https://www.tobaccocontrolscale.org/>

- Risk reduction is a valuable strategy in itself. The FCTC and the WHO must make room for risk reduction. • The “ *end game* ” in tobacco control concerns the end of smoking, not the end of nicotine consumption. By opposing the two, we weaken the fight against smoking, which must be intensified in the years to come. • A smoker who quits smoking tobacco and switches to the exclusive use of e-cigarettes is a smoker who quits smoking. This is also the view of the English *National Institute for Health and Care Excellence* (NICE) and UK policy.⁶²
- EVALI is a misleading name because what happened cannot be linked to normal vaping of nicotine and normal e-cigarette use. EVALI was a local problem (in the United States) not present in Europe and was linked to the use of oils containing cannabis in e-cigarettes and to criminal practices (black market). Vitamin E acetate cannot be added to nicotine e-liquids. But EVALI raised a lot of fears and fueled the negative perception of e-cigarettes until today.
- Policy measures to protect adolescents and young adults (non-smokers) from nicotine use should not compromise the opportunities that e-cigarettes represent for adult smokers. A balance must be sought, but the accent must be placed on this last point. This is possible due to the fact that at present the e-cigarette does not seem to pose a major threat to minors in our country (and elsewhere in Europe). Low-risk products must be and remain accessible to smokers. When introducing a measure, it is important to consider the potential impact in this regard: will access for smokers become more difficult? Does the measure have a negative impact on the (already negative) image of the product? Etc. When adopting additional measures to protect young people, it is also necessary to take into account the existing legislation (how strict is the legal framework already and are young people already well protected?) and the use actual use of e-cigarettes by minors rather than just experimental use.
- Smokers have the right to correct information on the relative harms of e-cigarettes and on e-cigarettes as a tool for smoking cessation. The current perception of the e-cigarette is rather negative among many of them. The research shows that people of lower socio-economic status and those in a situation of social vulnerability - who belong to the groups that smoke the most today - are the least well informed about these aspects of the e-cigarette. These smokers, who on average have less health skills, should therefore be better proactively informed through simple messages and various channels.

7.5. Risk reduction: framework and discussion

The *harm reduction* factor plays a major role in evaluating the e-cigarette debate.

⁶² <https://www.nice.org.uk/guidance/ng209>

Some countries, such as the United Kingdom and New Zealand, and some organizations active in the field of tobacco control draw their approach and policy proposals from an emphasis on harm reduction. For example, in the UK, the focus is on the relative risk of e-cigarettes and the assessment of nicotine consumption as " *minimum risk of harm to health* "

63

The US Food and Drug Administration (FDA) authorizes certain tobacco products to be presented as ' *modified risk tobacco products* ', in particular certain snus (FDA, 2019)⁶⁴ and IQOS, "heated tobacco", from tobacco company Philip Morris (FDA, 2020)⁶⁵ . Now that the registration of *Premarket Tobacco Product Applicants for Electronic Nicotine Delivery Systems* (ENDS) is ⁶⁶ underway, there will also be a recognized and regulated market for ENDS in the United States (FDA, 2020). The first products have already been approved (FDA, 2020)⁶⁷ .

The FCTC (WHO) framework allows for a focus on risk reduction. The Framework Convention contains this definition of tobacco control: " *Tobacco control*" means a range of supply, demand and harm reduction strategies that aim to improve the health of a population by eliminating or reducing their consumption of tobacco products and exposure to tobacco smoke (see article 1, Use of Terms, p. 4) . Recently, several academics have called on the WHO to effectively engage in risk reduction within the framework of the FCTC⁶⁸. The most recent call from 100 experts in nicotine science and policy is from October 2021⁶⁹ .

In the Lancet, the article " *Nicotine without smoke: fighting the tobacco epidemic with harm reduction*" appeared in 2019, with among the authors some former WHO ⁷⁰ « *The tobacco harm minimisation strategy complements other tobacco control strategies but has been underappreciated because for many in tobacco control the emphasis has been on achieving abstinence of all tobacco and nicotine use. However, abrupt cessation of nicotine has had low population success rates—for example, 4–5 % in the USA. Regrettably, many smokers find it hard to quit and go on to die prematurely—around 8 million a year. The latest WHO report on the global tobacco epidemic stresses the importance of best-practice tobacco cessation services based on a medical treatment model. Unfortunately, this approach has had limited population-level impacts because of low uptake, and is in contrast to the much more promising consumer-led approach to cessation based on safer*

⁶³ <https://publichealthmatters.blog.gov.uk/2020/03/05/8-things-to-know-about-e-cigarettes/>

⁶⁴ <https://www.fda.gov/tobacco-products/advertising-and-promotion/fda-authorizes-modified-risk-tobacco-products>

⁶⁵ <https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-iqos-tobacco-heating-system-reduced-exposure-information>

⁶⁶ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-tobacco-product-applications-electronic-nicotine-delivery-systems-ends>

⁶⁷ <https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-e-cigarette-products-marking-first-authorization-its-kind-agency>

⁶⁸ See the 2014 letter sent to the WHO by 56 public health and nicotine specialists. This letter denounces the fact that the emphasis on risk reduction is underused and marginalized, whereas according to these authors, it is a "part of the solution, not part of the problem is": <https://nicotinepolicy.net/documents/letters/MargaretChan.pdf>. A response to the letter and another comment followed: <https://tobacco.ucsf.edu/129-public-health-and-medical-authorities-31-countries-write-who-dg-chan-urging-evidence-based-approach-ecigs> and <https://nicotinepolicy.net/documents/letters/response-to-glantz-et-al-letter-to-who.pdf>. See also the more recent open letter titled: 'Innovation in tobacco control: developing the FCTC to embrace tobacco harm reduction', <https://clivebates.com/documents/WHOCOP8LetterOctober2018.pdf> . And further, the response to the "First Report of the WHO Independent High-level Commission on Non-Communicable Diseases": <https://www.clivebates.com/documents/NCDCCommissionMay2018.pdf>

⁶⁹ <https://clivebates.com/one-hundred-specialists-call-for-who-to-change-stance-on-tobacco-harm-reduction/>

⁷⁰ <https://www.clivebates.com/lancet-commentary-nicotine-without-smoke-fighting-the-tobacco-epidemic-with-harm-reduction/> , [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)31884-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31884-7/fulltext)

alternatives to smoked tobacco. The potential of vaping is that it combines high efficacy with widespread uptake ».

Le site Web de la « *New Nicotine Alliance* » décrit la *Tobacco Harm Reduction* (THR) comme « *a term used by the Department of Health, Public Health England and the National Institute of Health and Care Excellence amongst others to describe ways of reducing harm from cigarette smoking without necessarily giving up the use of nicotine* »⁷¹

C. Bates, avocat de la THR, la décrit comme suit: « *Tobacco harm reduction is a public health strategy that makes use of regulation, fiscal measures, communications and support services to reduce the harms associated with tobacco or nicotine use, including the secondary harms induced by tobacco or nicotine policy. In practice, this primarily means encouraging smokers or would-be smokers to adopt non-combustible nicotine products such as e-cigarettes rather than combustible, smoking products such as cigarettes. Harm reduction is widely practised in public health, for example in illicit drugs and sexual health, because 'abstinence-only' approaches are ineffective. Harm reduction is acknowledged as within the definition of tobacco control in the Framework Convention on Tobacco Control* »

72

« *Tobacco Tactics* », le site web de l'université de Bath qui suit d'un œil critique l'industrie du tabac, décrit la THR comme suit : « *Tobacco harm reduction is a pragmatic approach to reducing the harm of smoking related diseases. People smoke because they are addicted to nicotine and seek a 'hit', but it is the other toxins in tobacco smoke that cause most of the harm. Nicotine can be obtained from a range of products, which vary in their level of harm and addictiveness, from smoked tobacco (i.e. cigarettes) at the top end of the harm/addiction*

spectrum, to medicinal nicotine (i.e. nicotine replacement therapy products) at the bottom end. A harm reduction approach to tobacco control encourages those smokers that cannot, or are unwilling to, stop smoking, to switch to using nicotine in a less harmful form, and ideally would result in them ultimately quitting nicotine use altogether ».

The *harm reduction* discussion is important to understanding the e-cigarette debate. Contrary to the approach taken in a country like the UK, an organization like the *European Respiratory Society* (ERS) rejects THR altogether: "*The tobacco harm reduction strategy is based on well-meaning but incorrect or undocumented claims or assumptions. 40 countries have already banned e cigarettes and/or nicotine e-liquid. The human lungs are created to breathe clean air, not "reduced levels of toxins and carcinogens", and the human body is not meant to be dependent on addictive drugs. ERS cannot recommend any product that is damaging to the lungs and human health. Therefore, ERS strongly supports implementation of World Health Organization's Framework Convention on Tobacco Control, which also provides regulation to novel products, and cannot recommend tobacco harm reduction as a population-based strategy*" (Pisinger, 2019)⁷³. ERS sparked a reaction in the UK, including from various healthcare professionals (heart, lung, etc.) associated with universities and the smoking cessation organization ASH-UK: "*In our view, the recent ERS Tobacco Control Committee statement on tobacco harm reduction,*

⁷¹ <https://nnalliance.org/nna-uk/about-us>

⁷² <https://www.clivebates.com/vaping-tobacco-harm-reduction-nicotine-science-and-policy-qa/> . Other organizations working on tobacco harm reduction are IEVA (<https://www.eurovape.eu/>) and the *New Nicotine Alliance* (<https://nnalliance.org/>).

⁷³ See the article in which the ERS presents seven arguments, <https://erj.ersjournals.com/content/54/6/1902009>

though well-intentioned, appears to be based on a number of false premises and draws its conclusions from a partial account of available data. It also presents a false dichotomy between the provision of “conventional” tobacco control and harm reduction approaches. We therefore respond, in turn, to the seven arguments presented against the adoption of harm reduction in the Committee’s statement » (Britton et al., 2020)⁷⁴. Cet avis a de nouveau fait l'objet d'une réponse de l'ERS (Pisinger & Vestbo, 2021)⁷⁵

The tobacco industry is now also adopting the harm reduction approach related to tobacco, presumably as a strategy to secure its own future interests. A critical follow-up is therefore necessary. *“Science has been at the center of attempts by major industries, including tobacco, chemical, and pharmaceutical, to delay progress in tackling threats to human and planetary health by, inter alia, obscuring industry harms, and opposing regulation.”* ⁷⁶ Un récent éditorial publié dans la revue *Tobacco Control* traite de the use of risk reduction strategy by tobacco manufacturers.

« Multinational tobacco companies, such as British American Tobacco (BAT) and Philip Morris International (PMI), have adopted harm reduction in their public relations initiatives and marketing communication, which provides them an opportunity to showcase their engagement in new product development of self-styled ‘next-generation products (...) The underlying goal, however, for the tobacco industry is the maximisation of sales, profit and return to shareholders, which places them at odds with serving a mandate of harm reduction » (Dewhirst, 2020)⁷⁷.

Une étude de l'université de Bath, basée entre autres sur des documents internes de l'industrie, avance la conclusion suivante : *« Transnational tobacco companies’ harm reduction discourse should be seen as opportunistic tactical adaptation to policy change rather than a genuine commitment to harm reduction. Care should be taken that this does not undermine gains hitherto secured in efforts to reduce the ability of the tobacco industry to inappropriately influence policy » (Peeters & Gillmore, 2015)⁷⁸* Le site *Tobacco Tactics*, also linked to the University of Bath, also has a dossier on harm reduction, including a focus on current low-risk products from big tobacco companies and research that promotes harm reduction but is funded by industry .

However, “harm reduction” is more than just a big tobacco company marketing strategy. It is also a science-based framework that cannot be tied to the tobacco industry's marketing strategies or the research on safer products that tobacco companies conduct or fund themselves. This is an older framework, which has become more relevant to the topic of tobacco since the appearance on the market of lower-risk products that are used by many smokers. The Belgian smoking cessation organizations also recognize this approach, to a greater or lesser extent, and ask for certain measures

⁷⁴ <https://erj.ersjournals.com/content/erj/early/2020/02/20/13993003.00166-2020.full.pdf>

⁷⁵ <https://erj.ersjournals.com/content/55/5/2000355>

⁷⁶ Zie 'The science for profit model',

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0253272#:~:text=The%20model%20shows%20that%20the,aspects%20of%20industry%20unfavourable%20science>

⁷⁷ <https://tobaccocontrol.bmj.com/content/early/2020/08/11/tobaccocontrol-2020-056059>

⁷⁸ <https://tobaccocontrol.bmj.com/content/24/2/182>

⁷⁹ <https://tobaccotactics.org/wiki/harm-reduction/#:~:text=A%20harm%20reduction%20approach%20to,ultimately%20quitting%20nicotine%20use%20altogether.>

policies that fall within this framework (such as lower taxes for e-cigarettes than for tobacco). Today, the tobacco policies of countries such as the UK and New Zealand fall within the framework of the WHO FCTC but

also in risk reduction. The "*Harm Reduction Journal*"⁸⁰, a specialized medical journal that has existed since 2004, regularly publishes articles on tobacco⁸¹.

Within the working group that prepared this opinion, a vision of the e-cigarette as a risk reduction tool was provided by FEDITO BXL (*Brussels Federation of Institutions for Drug Addicts*, 2020). FEDITO argues that risk reduction

applied to tobacco and within the framework of a public health policy also means that the social costs of tobacco consumption will be drastically reduced.

At *Tobacco Control* too, some reputable voices are calling for a rebalancing because they believe that the risks of e-cigarettes dominate debate, perception and politics too much. In the article published in "*The American Journal of Public Health*" (Balfour et al., 2021)⁸², "*Balancing consideration of the risks and benefits of e-cigarettes*" (2021), 15 former presidents of the Society for Research on Nicotine and Tobacco (SRNT)⁸³ plead for the rehabilitation of the image of the e-cigarette with legislators, the public and the media. According to these authors, the potential of the e-cigarette for adult smokers is overshadowed by the one-sided attention paid to the risks for minors, which could harm public health. The authors propose a "*sensitive mix of policies*".

⁸⁰ <https://harmreductionjournal.biomedcentral.com/>

⁸¹ See, among others, the thematic series "Global and local perspectives on tobacco harm reduction", <https://www.biomedcentral.com/collections/tobaccoperspectives>.

⁸² <https://ajph.aphapublications.org/doi/10.2105/AJPH.2021.306416>

⁸³ <https://www.srnt.org/>

VIII ANNEX I: Three major questions arising from the emphasis on risks and opportunities

The appendices are provided for information purposes and their content does not in any way engage the responsibility of the CSS.

The positions of the various institutions and countries with regard to the risks, opportunities and place of the e-cigarette in the smoking cessation process are very shared. They are also within the experts of this working group. **The opinions expressed in this appendix are not supported as a whole by all the experts.** This

The purpose of the appendix is therefore to resume the "risks and opportunities" perspectives of different recognized institutions.

Three major challenges that are debated worldwide are discussed: the assessment of health risks in comparison with smoking, the e-cigarette as a smoking cessation device and its use by minors.

8.1. Health risk (compared to no e-cigarette use and compared to smoking)

8.2. Smoking cessation

8.2.1. Preamble

8.2.2. Scientific basis

8.2.3. Potential of the e-cigarette for our country?

8.3. Young people and non-smokers

8.3.1. Use of e-cigarettes

8.3.2. Relationship between vaping and smoking in young people

8.3.3. Flavors

8.1. Health risk (compared to not using e-cigarettes and compared to smoking)

Vaping is less harmful to health than tobacco: there is now a broad scientific consensus on this subject. A number of reputable scientific institutes and organizations active in the field of tobacco and public health have recognized the significant risk reduction of vaping. But in a nuanced way, ie the relative safety (the link with smoking) is underlined as well as the lack of knowledge on the impact of long-term use.

The **NASEM** report (2018) has 47 conclusions on the main aspects of the e-cigarette according to the level of evidence. Conclusions are also presented based on the results, namely conclusions on ingredients, health effects, initiation (starting with vaping), e-cigarette as a smoking cessation product and conclusions on risk reduction⁸⁴.

⁸⁴ <https://www.nap.edu/resource/24952/012318ecigaretteConclusionsbyOutcome.pdf>

Lorsqu'il s'agit de comparer les risques de la e-cigarette et du tabac pour les fumeurs, le rapport est le plus proche de l'approche de **Public Health England** (PHE). On peut en effet y lire que « *there is conclusive evidence that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes.* » Il y a aussi « *substantial evidence that completely switching from regular use of combustible tobacco cigarettes to e-cigarettes results in reduced short-term adverse health outcomes in several organ systems.* » Il y a aussi « *substantial evidence that except for nicotine, under typical conditions of use, exposure to potentially toxic substances from e-cigarettes is significantly lower compared with combustible tobacco cigarettes* ».

Concernant la réduction des risques du tabac en général, le rapport conclut: « *Completely substituting e-cigarettes for combustible tobacco cigarettes conclusively reduces a person's exposure to many toxicants and carcinogens present in combustible tobacco cigarettes and may result in reduced adverse health outcomes in several organ systems. Across a range of studies and outcomes, e-cigarettes appear to pose less risk to an individual than combustible tobacco cigarettes* ».

But the report also highlights potential health risks. The conclusions on the ingredients of e-cigarettes are as follows:

- *“Conclusion 5-1. There is conclusive evidence that in addition to nicotine, most e cigarette products contain and emit numerous potentially toxic substances. • Conclusion 5-2. There is conclusive evidence that, other than nicotine, the number, quantity, and characteristics of potentially toxic substances emitted from e-cigarettes are highly variable and depend on product characteristics (including device and e liquid characteristics) and how the device is operated. • Conclusion 5-4. There is substantial evidence that e-cigarette aerosol contains metals. The origin of the metals could be the metallic coil used to heat the e-liquid, other parts of the e-cigarette device, or e-liquids. Product characteristics and use*

patterns may contribute to differences in the actual metals and metal concentrations measured in e-cigarette aerosol.”

This report outlines the possible risks of passive (unintentional) vaping:

- *“Conclusion 3-1. There is conclusive evidence that e-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments compared with background levels.*
- *Conclusion 3-2. There is limited evidence that e-cigarette use increases levels of nicotine and other e-cigarette constituents on a variety of indoor surfaces compared with background levels.”*

When it comes to ingredients, the overall conclusion of the report is as follows:

« *Overall, e-cigarette aerosol contains fewer numbers and lower levels of toxicants than smoke from combustible tobacco cigarettes. Nicotine exposure can mimic that found with use of combustible tobacco cigarettes, but it is highly variable. The exposure to nicotine and toxicants from the aerosolization of flavorings and humectants depends on device characteristics and how the device is used.* »

The conclusions regarding the health effects of e-cigarettes are as follows:

- *“Conclusion 7-1. There is substantial evidence that e-cigarette aerosols can induce acute endothelial cell dysfunction, although the long-term consequences and outcomes on these parameters with long-term exposure to e-cigarette aerosol are uncertain.*
- *Conclusion 7-2. There is substantial evidence that components of e-cigarette aerosols can promote formation of reactive oxygen species/oxidative stress. Although this supports the biological plausibility of tissue injury and disease from longterm exposure to e-cigarette aerosols, generation of reactive oxygen species and oxidative stress induction is generally lower from e-cigarettes than from combustible tobacco cigarette smoke.* • *Conclusion 9-1. There is no available evidence whether or not e-cigarette use is associated with clinical cardiovascular outcomes (coronary heart disease, stroke, and peripheral artery disease) and subclinical atherosclerosis (carotid intima media thickness and coronary artery calcification).*
- *Conclusion 9-2. There is substantial evidence that heart rate increases shortly after nicotine intake from e-cigarettes.* •
- *Conclusion 9-3. There is moderate evidence that diastolic blood pressure increases shortly after nicotine intake from e-cigarettes.*
- *Conclusion 9-4. There is limited evidence that e-cigarette use is associated with a short-term increase in systolic blood pressure, changes in biomarkers of oxidative stress, increased endothelial dysfunction and arterial stiffness, and autonomic control.*
- *Conclusion 9-5. There is insufficient evidence that e-cigarette use is associated with long-term changes in heart rate, blood pressure, and cardiac geometry and function.*
- *Conclusion 10-1. There is no available evidence whether or not e-cigarette use is associated with intermediate cancer endpoints in humans. This holds true for e cigarette use compared with use of combustible tobacco cigarettes and e cigarette use compared with no use of tobacco products.*
- *Conclusion 10-2. There is limited evidence from in vivo animal studies using intermediate biomarkers of cancer to support the hypothesis that long-term e cigarette use could increase the risk of cancer; there is no available evidence from adequate long-term animal bioassays of e-cigarette aerosol exposures to inform cancer risk.*
- *Conclusion 10-3. There is limited evidence that e-cigarette aerosol can be mutagenic or cause DNA damage in humans, animal models, and human cells in culture.*
- *Conclusion 10-4. There is substantial evidence that some chemicals present in e cigarette aerosols (e.g., formaldehyde, acrolein) are capable of causing DNA damage and mutagenesis. This supports the biological plausibility that long-term exposure to e-cigarette aerosols could increase risk of cancer and adverse reproductive outcomes. Whether or not the levels of exposure are high enough to contribute to human carcinogenesis remains to be determined.*
- *Conclusion 11-1. There is no available evidence whether or not e-cigarettes cause respiratory diseases in humans.*

- *Conclusion 11-4. There is moderate evidence for increased cough and wheeze in adolescents who use e-cigarettes and an association with e-cigarette use and an increase in asthma exacerbations.*
- *Conclusion 11-5. There is limited evidence of adverse effects of e-cigarette exposure on the respiratory system from animal and in vitro studies.* • *Conclusion 12-1. There is limited evidence suggesting that switching to e-cigarettes will improve periodontal disease in smokers.*
- *Conclusion 12-2. There is limited evidence suggesting that nicotine- and non nicotine-containing e-cigarette aerosol can adversely affect cell viability and cause cell damage of oral tissue in non-smokers.*
- *Conclusion 13-1. There is no available evidence whether or not e-cigarettes affect pregnancy outcomes.*
- *Conclusion 13-2. There is insufficient evidence whether or not maternal e-cigarette use affects fetal development.* •
- Conclusion 14-1. There is conclusive evidence that e-cigarette devices can explode and cause burns and projectile injuries. Such risk is significantly increased when batteries are of poor quality, stored improperly, or modified by users.*
- *Conclusion 14-2. There is conclusive evidence that intentional or accidental exposure to e-liquids (from drinking, eye contact, or dermal contact) can result in adverse health effects including but not limited to seizures, anoxic brain injury, vomiting, and lactic acidosis.*
- *Conclusion 14-3. There is conclusive evidence that intentionally or unintentionally drinking or injecting e-liquids can be fatal.*

The last three conclusions refer more to consumer issues, namely the safety and safe handling of products and liquids.

En ce qui concerne les effets sur la santé en général, ce rapport conclut : « Overall, the evidence reviewed by the committee suggests that e-cigarettes are not without biological effects in humans. For instance, use of e-cigarettes results in dependence on the devices, though with apparently less risk and severity than that of combustible tobacco cigarettes. Yet the implications for long-term effects on morbidity and mortality are not yet clear ».

Dans les « messages clés » d'un récent briefing (2020), l'**OMS⁸⁵** déclare que « EN&NNDS (electronic nicotine and non-nicotine delivery systems) are not harmless. Although the consequences for long-term effects on morbidity and mortality have not yet been studied sufficiently, EN&NNDS are not safe for young people, pregnant women and adults who have never smoked. While it is expected that use of EN&NNDS in these groups might increase their health risks, non-pregnant adult smokers who completely and promptly switch from combustible tobacco cigarettes to use of unadulterated and appropriately regulated EN&NNDS alone might reduce their health risks. This potential has been recognized by WHO, NASEM and the CDC.» (...) «Scientists are still learning about the long-term health effects of EN&NNDS. Currently, there is insufficient research to determine with certainty

⁸⁵ <https://www.euro.who.int/en/health-topics/disease-prevention/tobacco/publications/2020/electronic-nicotine-and-non-nicotine-delivery-systems-a-brief-2020>

whether unadulterated and appropriately regulated EN&NNDS use is associated with cardiovascular, lung or cancer diseases ».

L'OMS reconnaît qu'il existe des preuves concluantes que « *completely substituting EN&NNDS for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes* ». Il existe également, selon l'OMS, des « *preuves substantielles* » que « *EN&NNDS aerosol can cause some human cells to malfunction – it is not clear what this means in terms of the long-term consequences of chronic use of EN&NNDS, but it is possible that it could increase the risk of some diseases, such as cardiovascular disease, cancer and adverse reproductive outcomes, although the risk is probably lower than from combustible tobacco cigarette smoke* » et il y a des preuves substantielles que « *completely switching from regular use of combustible tobacco cigarettes to EN&NNDS results in reduced short-term adverse health outcomes in several organ systems* ».

Au sujet de l'aérosol, l'OMS déclare: « *The aerosol users breathe from EN&NNDS contains numerous potentially toxic substances, in addition to nicotine when included in the e-liquid.*

The number, quantity and characteristics of potentially toxic substances in the aerosol emitted by EN&NNDS are highly variable and depend on product characteristics (including device and e-liquid features) and how the device is operated by the user. Under typical conditions of use, however, the number and concentrations of potentially toxic substances emitted from unadulterated EN&NNDS are lower than in tobacco smoke, except for some metals. The main substances in the aerosol that raise health concern are metals, such as chromium, nickel, and lead, and carbonyls, such as formaldehyde, acetaldehyde, acrolein and glyoxal ». Il note également les types et les concentrations de métaux en fonction de l'utilisation de la e-cigarette : « *The types and concentrations of metals depend on the product features and inhaling patterns of use. Exposure to certain levels of some metals may cause serious health effects, such as diseases of the nervous, cardiovascular and respiratory systems. The number of metals in the aerosol could be greater than in combustible tobacco cigarettes, and in some cases is found at higher concentrations than in cigarette smoke. It is suspected that metals come mostly from the metallic coil used to heat the e-liquid and soldered joints of the device. Metal emissions can largely be prevented through appropriate engineering of devices* ».

En ce qui concerne les composés carbonylés, **l'OMS** déclare : « *Carbonyl compounds are potentially hazardous to users. Formaldehyde is a human carcinogen, acetaldehyde is possibly carcinogenic to humans, acrolein is a strong irritant of the respiratory system and glyoxal shows mutagenicity. Most carbonyls come from the thermal decomposition of humectants, propylene glycol and glycerol. The number and levels of carbonyls detected in the aerosol are lower than in smoke from combustible tobacco, but even these levels raise health concerns* ». Il est également fait référence à d'autres substances potentiellement dangereuses pour la santé : « *Other substances in the aerosol of possible health concern are particulate matter and some flavourings. The particle count and size in EN&NNDS aerosols do not differ greatly from those found in mainstream combustible tobacco smoke. The composition of the particles nevertheless is dissimilar and likely to have a different health*

impact. Aerosol particulates from EN&NNDS consist mostly of a mix of aqueous and humectant droplets, whereas particles in combustible tobacco smoke are mostly complex organic constituents that contain known or suspected carcinogens. Although of health

concern, particles from EN&NNDS are therefore expected to have smaller health risks than particles in tobacco smoke. Certain flavourings, such as diacetyl, cinnamaldehyde and benzaldehyde, have been cited as a source of health concerns when heated and inhaled ».

En ce qui concerne l'exposition passive aux vapeurs du vapotage, l'OMS déclare: « *Second hand exposure to nicotine and particulates is lower from EN&NNDS aerosol compared with combustible tobacco cigarettes but are higher than the smoke-free level recommended by the WHO Framework Convention on Tobacco Control (WHO FCTC). No available studies have evaluated the health effects of second-hand EN&NNDS exposure, so the risks to health of exposure to exhaled aerosol remain unknown. It is expected, however, to present some health risks for bystanders, although at lower levels than from exposure to second hand tobacco smoke* ».

The WHO also makes recommendations in this briefing on how to regulate these products: "As indicated by WHO, the key to any policy on EN&NNDS is to "appropriately regulate these products, so as to minimize consequences that may contribute as well as to the tobacco epidemic and to optimize the potential benefits to public health » "avoiding nicotine initiation among non-smokers and particularly youth while maximizing potential benefits for smokers ». Pour les recommandations, voir le document proprement dit.

A **WHO** report was published in 2021 and is mentioned on the site as follows: " *New WHO report sheds light on the dark impact of e-cigarettes and heated tobacco products* » ⁸⁶
« *One of the main recommendations in the new report is that policy-makers should maintain focus on evidence-based measures to reduce tobacco use, as outlined in the WHO Framework Convention on Tobacco Control (WHO FCTC). This includes novel and emerging tobacco products, which are being pushed by the tobacco industry* ». Une recommandation notable faite dans ce rapport est « *to prohibit the sale of electronic nicotine delivery systems and electronic non-nicotine delivery systems in which the user can control device features and liquid ingredients (that is, open systems)* » ⁸⁷. This new report comprehensively examines the risks of e-cigarettes, the unanswered questions around them, and how to regulate e-cigarettes. How to check the risk posed by e-cigarettes? "ENDS and ENNDS are highly variable categories of products, although they share many features. The variation in e-liquids and devices makes it impossible to assess the health risks of this group of products. Risks should therefore be assessed for each individual device, liquid and use. Alternatively, indicators of risk could be highlighted, such as specific ingredients or specific settings of a device, that could be applied to many products". Recommendations are made for risk assessment⁸⁸.

⁸⁶ <https://www.euro.who.int/en/health-topics/disease-prevention/tobacco/news/news/2021/9/new-who-report-sheds-light-on-the-dark-impact-of-e-cigarettes-and-heated-tobacco-products>

⁸⁷ In our country, these "open-system ENDS" are the most popular electronic cigarettes, see the report "Use of electronic cigarette - Health survey: " According to the data of the health survey, the most popular devices currently are those with a self-filling liquid tank (47.0% of vapers) and those that are fully modular and personalized (30.8%). This means that, taken as a whole (as in the following analyses), 77.7% of vapers fill their e-liquids themselves. (p.17) . See also the Eurobarometer:

<https://europa.eu/eurobarometer/surveys/detail/2240>. « More than two thirds of current and former ecigarettes users (72%) say they use(d) a refillable device which contains a tank that is refilled with an e-liquid from a separate container » (Summary, p. 18).

⁸⁸ See report p. 198-199.

The report does not make a strict distinction between smoking (*tobacco use*) and nicotine consumption (nicotine use). However, a distinction is made between ENDS (e-cigarettes) and heated *tobacco products*. It is only with regard to the latter that it is recommended “to apply the most restrictive tobacco control regulations”.

In the United States, medical (professional) organizations such as **the American Heart Association⁸⁹, the American Cancer Society⁹⁰, the American Lung Association⁹¹ and the American Thoracic Society⁹²** strongly emphasize the risks of e-cigarettes:

« *E-cigarettes have been linked to thousands of cases of serious lung injury, some resulting in death. While the exact cause is still not confirmed, the CDC recommends that people not use e-cigarettes.*”⁹³ (...) “*The long-term health effects of e-cigarettes are not well understood yet. But the science clearly indicates vaping is not a safe or healthy alternative to smoking.*” 94

“*E-cigarettes pose a threat to the health of users and the harms are becoming increasingly apparent. In the past few years, the use of these products has increased at an alarming rate among young people in significant part because the newest, re-engineered generation of e cigarettes more effectively delivers large amounts of nicotine to the brain. Many e-cigarettes sold in the U.S. contain far more nicotine than e-cigarettes sold elsewhere, which increases the risk of addiction and harm to the developing brains of youth and young adults. Marketing tactics targeting young people have contributed to the rapid increase in use. The long-term*

risks of exclusive use of e-cigarettes are not fully known but evidence is accumulating that e cigarette use has negative effects on the cardiovascular system and lungs. Without immediate measures to stop epidemic use of these products, the long-term adverse health effects will increase.”⁹⁵ “*The mid-to-long-term consequences of e-cigarettes are not yet known, as it’s a new product and has been sold for less than a decade in the U.S. While much remains to be determined about these lasting health consequences of these products, we are very troubled by what we see so far. The inhalation of harmful chemicals can cause*

irreversible lung damage and lung diseases ».

⁹⁶

For the European Union and at the request of the European Commission, the **SCHEER** - *Scientific Committee on Health, Environmental and Emerging Risks* - a récemment passé en reviews scientific and technical studies on e-cigarettes (04/29/2021). The final report⁹⁷ states the following:

« . “*For users of electronic cigarettes : 1. The overall weight of evidence is moderate for risks of local irritative damage to the respiratory tract of users of electronic cigarette due to the cumulative exposure to polyols, aldehydes and nicotine. However, the overall reported incidence is low.*

2. The overall weight of evidence for risks of long-term systemic effects on the cardiovascular system is moderate.

⁸⁹ <https://www.heart.org/en/healthy-living/healthy-lifestyle/quit-smoking-tobacco/is-vaping-safer-than-smoking>

⁹⁰ <https://www.cancer.org/healthy/stay-away-from-tobacco/e-cigarettes-vaping/e-cigarette-position-statement.html>

⁹¹ <https://www.lung.org/quit-smoking/e-cigarettes-vaping/lung-health>

⁹² <https://www.thoracic.org/professionals/clinical-resources/disease-related-resources/vaping-the-threat-to-public-health-and-the-ats-response.php>

⁹³ <https://www.heart.org/en/healthy-living/healthy-lifestyle/quit-smoking-tobacco/is-vaping-safer-than-smoking>

⁹⁴ The same

⁹⁵ <https://www.cancer.org/healthy/stay-away-from-tobacco/e-cigarettes-vaping/e-cigarette-position-statement.html>

⁹⁶ <https://www.lung.org/quit-smoking/e-cigarettes-vaping/lung-health>

⁹⁷ https://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scheer_consultation_10_en

3. The overall weight of evidence for risks of carcinogenicity of the respiratory tract due to long-term, cumulative exposure to nitrosamines and due to exposure to acetaldehyde and formaldehyde is weak to moderate. The weight of evidence for risks of adverse effects, specifically carcinogenicity, due to metals in aerosols is weak.

4. The overall weight of evidence for risks of other long-term adverse health effects, such as pulmonary disease CNS and reprotoxic effects based on the hazard identification and human evidence, is weak, and further consistent data are needed.

5. To date, there is no specific data that specific flavourings used in the EU pose health risks for electronic cigarette users following repeated exposure.

6. The overall weight of evidence for risks of poisoning and injuries due to burns and explosion, is strong. However, the incidence is low.

For second-hand exposed persons:

1. The overall weight of evidence is moderate for risks of local irritative damage to the respiratory tract mainly due to exposure to glycols.

2. The overall weight of evidence for risks of systemic cardiovascular effects in second-hand exposed persons due to exposure to nicotine is weak to moderate.

3. The overall weight of evidence for carcinogenic risk due to cumulative exposure to nitrosamines is weak to moderate ».

Enfin, le rapport **SCHEER** souligne: « *Electronic cigarettes are relatively new in terms of exposure to humans. More research is needed, in particular on long-term health effects* ».

Regarding the safety of flavorings, the aforementioned **WHO** report states:

« *Another concern is that chemicals in flavours may contribute to the toxicity of these products" (...) "Additionally, emerging evidence suggests that flavours may contribute to the toxicity of newer products such as ENDS in unique ways" (...) "This report on flavours in nicotine and tobacco products calls for adoption of common terminology for flavours in nicotine and tobacco products and consideration of policy for reducing the availability of flavoured nicotine and tobacco products on the market to those for which there is clear evidence of benefit in assisting smokers in quitting use of traditional smoked tobacco*

products ». The report lists study questions that still need to be answered, priorities and policy recommendations for flavourings⁹⁸ .

In Belgium, **Sciensano**⁹⁹ has recently (2021) carried out an analysis of flavors that could pose a health risk. Sciensano analyzed 129 e-cigarette liquids available in Belgium for their genotoxicity. If a substance is found to be genotoxic, it means that there is a potential health risk. The results make

appear that among the liquids analysed, 5 chemical substances are possibly genotoxic: these are estragole, safrole, 2-acetylfuran, furanone and trans-stilbene. One flavouring substance, safrole, is a chemical found in Sassafras oil that is

⁹⁸ <https://www.euro.who.int/en/health-topics/disease-prevention/tobacco/news/news/2021/9/new-who-report-sheds-light-on-the-dark-impact-of-e-cigarettes-and-heated-tobacco-products>

See chapter 9, from p. 207

⁹⁹ <https://www.sciensano.be/fr/coin-presse/certains-aromes-contenus-dans-les-cigarettes-electroniques-potentiellement-dangerous-for-your-health>

Following the study, Sciensano analyzed 24 liquids: four of them proved positive for two of the five genotoxic substances mentioned above.

Le rapport **NASEM** indique sur les arômes: « *Most of the flavorings used in e-cigarettes are generally regarded as safe by the FDA, although these designations relate to oral consumption (flavorings used in food), and most have not been studied for safety when inhaled with an e-cigarette. The primary humectants are propylene glycol and glycerol (also known as vegetable glycerin). Similar to flavorings, they are generally regarded as safe for ingestion, but less is known about their health effects when inhaled* »

100

In Australia, the **Australian Government - Department of Health** responds to the question of whether e-cigarettes are safe as follows: “ *No. Even though scientists are still learning about e-cigarettes, they do not consider them safe. Hazardous substances have been found in e-cigarette liquids and in the aerosol produced by e-cigarettes, including these known cancer-causing agents: formaldehyde, acetaldehyde, acrolein. Some chemicals in e cigarette aerosols can also cause DNA damage. E-cigarettes do not produce the tar produced by conventional cigarettes which is the main cause of lung cancer. However, many scientists are concerned that using e-cigarettes could increase risk of lung disease, heart disease and cancer.* » En Australie, la réglementation est stricte. Les personnes qui souhaitent utiliser une e-cigarette ne peuvent le faire que sur prescription médicale.

The **French High Council of Health** recently published an opinion on the e-cigarette. In this document, the question of whether SEDENs ("electronic nicotine delivery systems") constitute a form of risk reduction in relation to tobacco finds an answer formulated in the form of hypotheses: " *It can be hypothesized that the overall risk of completely stopping smoking with exclusive use of SEDEN (residual risk + risk related to SEDEN) is lower than the risk of continuing to smoke. (...) "We can hypothesize that the reduction in cigarette consumption associated with the use of SEDEN, dual use or "vaping", does not modify the smoker's risk profile: it 101 At the s' is the risk due to smoking plus the risk inherent in the use of SEDEN.* »

end of the text, the conclusions develop the issue of risk reduction. A number of elements are highlighted. “ *In view of these elements, SEDEN cannot currently be presented as tools for reducing the risks associated with tobacco. A*

exception could be given: that of people who have a low acceptance of reference treatments (in particular TSN102) and who conversely adhere to SEDEN.

This seems to be the case for certain vulnerable populations (see question 2). This may also be the case in the general population by individual preference. Thus, one can think that for a person who, in the absence of SEDEN, would not take any other treatment in the context of smoking cessation, the use of SEDEN could represent an opportunity versus the absence of treatment. As recalled above, this remains hypothetical and subject to the conditions listed”.

There are many positions that emphasize the relative health risk of e-cigarettes, as this list shows with a brief overview of around a hundred organizations in the sectors

¹⁰⁰ <https://www.nap.edu/resource/24952/012318ecigaretteHighlights.pdf>

¹⁰¹ <https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=1138>

¹⁰² TSN = Thérapie de Substitution Nicotinique (the medically recognized nicotine replacements).

authorities and public health: <https://docs.google.com/document/d/1Ty7pgRBxv11nuJzHWxclzNlu569Hozn6/edit>.

Following the popularity of the JUUL e-cigarette in the United States, the US **Food and Drug Administration** (FDA) a déclaré en 2018 : « *Make no mistake. We see the possibility for ENDS products like e-cigarettes and other novel forms of nicotine-delivery to provide a potentially less harmful alternative for currently addicted individual adult smokers who still want to get access to satisfying levels of nicotine without many of the harmful effects that* 103 *come with the combustion of tobacco. But we've got to step in to protect our kids* ». within the FDA as a regulatory agency, the potential recognition of a lower risk of a product if it benefits the health of the population is well established¹⁰⁴ . The first approvals for ENDS (" *electronic nicotine delivery systems* ") have meanwhile been issued¹⁰⁵ . The FDA is also actively working to correct misperceptions about nicotine: "*Nicotine Myths: Most people know that cigarettes and other tobacco products are addictive, but many people do not understand the role of nicotine*

in tobacco addiction, disease, and death. Nicotine is what addicts and keeps people using tobacco products, but it is not what makes tobacco use so deadly. Tobacco and tobacco smoke contain thousands of chemicals. It is this mix of chemicals—not nicotine—that causes serious disease and death in tobacco users, including fatal lung diseases, like chronic obstructive pulmonary disease (COPD) and cancer FDA, 2021) » ¹⁰⁶

L'American Association of Public Health Physicians se base sur l'hypothèse d'une sécurité relative des e-cigarettes et établit un lien explicite avec la réduction des risques sur son site internet: "*Harm Reduction: Smokers who have tried, but failed to quit using medical guidance and pharmaceutical products, and smokers unable or uninterested in quitting should consider switching to a less hazardous smoke-free tobacco/nicotine product for as long as they feel the need for such a product. Such products include pharmaceutical Nicotine Replacement Therapy (NRT) products used, off-label, on a long term basis;*

electronic cigarettes, dissolvables (sticks, strips and orbs), snus, other forms of moist snuff, and chewing tobacco". (...) « *Harm reduction should be considered as an addition to current tobacco control policies and programming and should be done in a way that will minimize initiation of tobacco/nicotine use, maximize quit rates and assure that dual use does not increase potential harm to the user* » (AAPHP, 2019) ¹⁰⁷

In the United Kingdom, the e-cigarette is part of the policy to reduce smoking and tobacco-related health risks. On the NHS (**National Health Service**) **website**, questions about the safety of e-cigarettes and the risks of nicotine are answered as follows: "*How safe are e-cigarettes?" In the UK, e-cigarettes are tightly regulated for safety and quality. They're not completely risk free, but they carry a small fraction of the risk of cigarettes. E-cigarettes do not produce tar or carbon monoxide, two of the most harmful elements in tobacco smoke. The liquid and vapor contain some potentially harmful chemicals also found in cigarette smoke, but at much lower levels. What about risks from*

¹⁰³ <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-enforcement-actions-and-youth-tobacco-prevention>

¹⁰⁴ <https://www.fda.gov/tobacco-products/advertising-and-promotion/modified-risk-tobacco-products>

¹⁰⁵ <https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-e-cigarette-products-marking-first-authorization-its-kind-agency>

¹⁰⁶ <https://www.fda.gov/tobacco-products/health-information/nicotine-addictive-chemical-tobacco-products>

¹⁰⁷ <https://www.aaphp.org/Tobacco>

nicotine? While nicotine is the addictive substance in cigarettes, it's relatively harmless.

Almost all of the harm from smoking comes from the thousands of other chemicals in tobacco smoke, many of which are toxic. Nicotine replacement therapy has been widely used for many years to help people stop smoking and is a safe treatment. »

¹⁰⁸ Every year, the English authorities publish their own independent report (evidence update), commissioned by **PHE**. The aim is to summarize the existing evidence on vaping products to inform policy makers and regulators. The edition of

2020¹⁰⁹ reiterated an important conclusion from the previous one: vaping regulated nicotine products carries only a small fraction of the risks of smoking, but that does not mean they are risk free. In the accompanying comments

l'Evidence Update de 2021, le professeur J. Newton, Directeur *Health Improvement* au PHE, le répète : « *PHE's advice remains that smokers should switch to vaping products to help them quit smoking, but non-smokers should not take up vaping. Vaping products contain significantly less harmful chemicals than cigarettes but are not without some risks* »

¹¹⁰

This is repeated on the PHE¹¹¹ blog. In addition to the discussion points covered in the following chapters of this text (young people, smoking cessation), this blog addresses various questions on e-cigarettes and health:

- Heart disease: particular reference is made to the study by Prof. Glantz, which was published in the "*Journal of the American Heart Association*" and which aroused worldwide attention, but which was withdrawn by the newspaper after criticism scientific showing that the study did not take into account the fact that almost all of the vapers concerned were smokers or former smokers and that most of the heart problems dated from the period before the start of the use of e- cigarette.
- Lack of knowledge of the relative safety of e-cigarettes among smokers: " *Only one in three adults in England knows that vaping is far less harmful than smoking.* »
- La nocivité relative de la nicotine (et encore une fois le manque de connaissances à ce sujet) : « *Four out of 10 smokers and ex-smokers wrongly think nicotine causes most of the smoking-related cancers, when evidence shows nicotine actually carries minimal risk of harm to health. Although nicotine is the reason people become addicted to smoking, it is the thousands of other chemicals contained in cigarette smoke that cause almost all of the harm.* »
- Vapotage passif : « *E-cigarette liquid is typically composed of nicotine, propylene glycol and/or glycerine, and flavourings. Unlike cigarettes, there is no side-stream vapour emitted by an e-cigarette into the atmosphere, just the exhaled aerosol. Our 2018 report found there have been no identified health risks of passive vaping to bystanders and our 2022 report will review the evidence again. People with asthma and other respiratory conditions can be sensitive to a range of environmental irritants, and PHE advises organisations to take this into account and make adjustments to policies where appropriate* ».

¹⁰⁸ <https://www.nhs.uk/live-well/quit-smoking/using-e-cigarettes-to-stop-smoking/>

¹⁰⁹ <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-march-2020>

¹¹⁰ <https://www.gov.uk/government/news/vaping-better-than-nicotine-replacement-therapy-for-stopping-smoking-evidence-suggests>

¹¹¹ <https://ukhsa.blog.gov.uk/2020/03/05/8-things-to-know-about-e-cigarettes/>

L'EVALI est aussi abordé et PHE souligne ne pas avoir modifié sa position sur la e-cigarette en réponse à l'EVALI (aux États-Unis) : « *PHE has not changed its advice on nicotine containing e-cigarettes: Smokers should consider switching completely and vapers should stop smoking. We are as certain as ever that e-cigarettes are far less harmful than smoking, which kills almost 220 people in England every day. The evidence still shows that vaping carries a small fraction of the risk of smoking. Using a nicotine-containing e-cigarette makes it much more likely someone will quit successfully than relying on willpower alone. But it's important to use regulated e-liquids and never risk vaping home-made or illicit e-liquids or adding substances* » (PHE, 2019)¹¹² .

In the Evidence update of 2021¹¹³ le point de départ est répété: « *Smoking remains the largest single risk factor for death and years of life lived in ill-health and is a leading cause of health inequalities in England and in other parts of the world. Alternative nicotine delivery devices, such as nicotine vaping products, could play a crucial role in reducing the enormous health burden caused by cigarette smoking.* » L'intitulé « développements récents » de ce rapport mentionne également : « *A safety review by the [Committee on Toxicity of Chemicals](#)*

in Food, Consumer Products and the Environment (COT) concluded that the risk of adverse health effects from vaping products is expected to be much lower than from cigarettes. The review found that exposure to particulate matter and nicotine could be associated with adverse health effects and that the effects of inhaling flavouring ingredients is uncertain.

The COT also suggested people who had not smoked tobacco but vaped would likely experience some adverse health effects ».

The Evidence Update 2021 also demonstrates again that the perception of the harmfulness of vaping compared to smoking is not accurate. "38% of smokers in 2020 believed that vaping is as harmful as smoking – 15% believed that vaping is more harmful" (...)

"What is concerning is that smokers, particularly those from disadvantaged groups, incorrectly and increasingly believe that vaping is as harmful as smoking. This is not true and means fewer smokers try vaping." (Prof Ann McNeill, King's College London) ¹¹⁵

Other British authorities also comment on the relative safety of the e-cigarette.

The **National Institute for Health and Care Excellence (NICE)** published in 2021, in collaboration with PHE, a guideline on combating the adverse health effects of smoking. In particular, it invites health professionals to provide clear and up-to-date information on e-cigarettes to people wishing to use them as a smoking cessation tool and to inform the public that " *e-cigarettes are substantially less harmful than smoking, but that the long-term health effects of e-cigarettes are still uncertain*".

(...) "The draft recommendations state that people should be advised on where to find information on nicotine-containing e-cigarettes, that e-cigarettes are substantially less harmful than smoking, but that the long-term health effects of e-cigarettes are still uncertain.

¹¹² <https://publichealthmatters.blog.gov.uk/2019/10/29/vaping-and-lung-disease-in-the-us-phes-advice/>

¹¹³ <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-february-2021/vaping-in-england-2021-evidence-update-summary> . The evidence update 2021 is the 7th in a series of independent reports commissioned by Public Health England (PHE). It notably includes the latest data on the prevalence and patterns of vaping in England by young people and adults, with a particular focus on new data available since the penultimate update (from 2020). The report also includes updated evidence on the impact of vaping products on smoking cessation, which was last reviewed in detail in the 2018 e-cigarettes and heated tobacco evidence report.

¹¹⁴ <https://www.gov.uk/government/news/vaping-better-than-nicotine-replacement-therapy-for-stopping-smoking-evidence-suggests>

¹¹⁵ <https://www.gov.uk/government/news/vaping-better-than-nicotine-replacement-therapy-for-stopping-smoking-evidence-suggests>

People should also be advised on how to use e-cigarettes correctly and be informed that they should stop smoking completely if they decide to start using nicotine-containing e cigarettes » 116. Dans ses récentes recommandations (novembre 2021) sur le sevrage tabagique, NICE déclare que « most smoking-related health problems are caused by other components in tobacco smoke, not by the nicotine »

117

Le **Royal College of Physicians** (RCP) a déclaré en réponse à l'« EVALI »: « *The RCP's 2016 report 'Nicotine without smoke: tobacco harm reduction' underlined that people smoke because they are addicted to nicotine, but are harmed by the other constituents of tobacco smoke, and that provision of the nicotine without the other harmful components can prevent most of the harm from smoking. The report noted that the hazard to health arising from long term vapour inhalation was unlikely to exceed 5 % of the harm from smoking tobacco. The report also noted that health risks were likely to arise from contaminants and components generated by the vapourisation process, which could be reduced as better technology and purer products became available, but these risks were still likely to be substantially lower than those of smoking. It recommended that regulation of ecigarettes should aim to minimise potential exposure to harmful vapour constituents* » .” Le RCP (2019) décide entre autres ceci quant à la sécurité (des e-cigarettes après EVALI): *Our advice on ecigarettes remains unchanged — vaping isn't completely risk-free but is far less harmful than smoking tobacco*” 118

Cancer Research UK fournit sur son site web des informations sur la e-cigarette sous forme de questions-réponses¹¹⁹. Le vapotage est-il nocif? « *Research so far shows that e cigarettes are far less harmful than smoking. For people who smoke, e-cigarettes are an option to help them stop. E-cigarettes are not risk-free. We don't yet know their long-term effects, so people who have never smoked shouldn't use them.*” L'institut précise plus en détail que : “*Lots of people want to know if e-cigarettes are safe and it's too soon to say for sure. But studies so far show that e-cigarettes are far less harmful than smoking. Most of the toxic chemicals in cigarettes are not present in e-cigarettes. Some potentially dangerous chemicals have been found in e-cigarettes. But levels are usually low and generally far lower than in tobacco cigarettes. Exposure may be the same as people who use nicotine replacement therapy (NRT) such as patches or gum. There is no good evidence that vaping*

causes cancer. But e-cigarettes are not risk-free. They have only become popular recently, so we don't know what effects they might have in the long term. They should only be used to help you stop smoking, or to stop you going back to tobacco. If you have never smoked, you shouldn't use e-cigarettes. You may have heard about vaping causing an outbreak of lung illness in 2019 in the United States. An investigation found the cases were linked to contaminated illegal products. It was not linked to vaping regularly or in the long term. There was no similar outbreak in the UK, and the chemicals of concern are banned in e-cigarettes here. There is no good evidence that e-cigarettes bought from legal places cause lung disease ».

¹¹⁶ <https://www.nice.org.uk/news/article/nice-and-phe-publish-comprehensive-draft-guideline-to-tackle-the-health-burden-of-smoking>

¹¹⁷ <https://www.nice.org.uk/guidance/ng209/resources/tobacco-preventing-uptake-promoting-quitting-and-treating-dependence-pdf-66143723132869>

¹¹⁸ <https://www.rcplondon.ac.uk/projects/outputs/rcp-advice-vaping-following-reported-cases-deaths-and-lung-disease-us>. See for the report 'Nicotine without smoke': <https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction>

¹¹⁹ <https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/smoking-and-cancer/is-vaping-harmful>

À la question de savoir si la nicotine est nocive, Cancer Research UK répond : « *Nicotine is the chemical that makes cigarettes addictive. But it is not responsible for the harmful effects of smoking. Nicotine does not cause cancer, and people have used nicotine replacement therapy safely for many years. Nicotine replacement therapy (NRT) is safe enough to be prescribed by doctors.* » Concernant le vapotage passif, l'institut déclare : « *There is no good evidence that second-hand vapour from e-cigarettes is harmful. As vapes are still relatively new, we can't be sure there aren't any long-term effects to people who breathe in someone else's vapour. But this is unlikely to be harmful. Passive vaping is not the same as passive smoking. This is because e-cigarettes do not contain tobacco.* M. Mitchell, Directeur général de Cancer Research UK, déclare en réponse à la nouvelle Evidence Update (2021) de PHE : « *E-cigarettes are a still relatively new product – they aren't risk-free as we don't yet know their long-term impact. We strongly discourage people who haven't smoked from using them, particularly young people. But research so far shows that vaping is less harmful than smoking tobacco and, as this report emphasises, can help people to stop smoking. The long-term effects of e-cigarettes are unknown but the long-term harms of tobacco are*

indisputable » ¹²⁰.

The **British Medical Association (BMA)** says there is little information on the long-term impact of vaping, that the standards for e-cigarettes as consumer products are not as rigorous as those applicable to authorized medicinal products, that some of the toxic substances present in tobacco smoke have also been detected in e-cigarette vapour, but at much lower levels, and that there is also a growing consensus that e-cigarettes are much safer than smoking tobacco. BMA makes the report ' *E cigarettes: balancing risks and opportunities*' available on its website.¹²¹

Le Royal College of General Practitioners,¹²² , the *British Lung Foundation*¹²³, the *Stroke and Association UK* ¹²⁴ the *Royal Society for Public Health*¹²⁵ have also already commented on the relative safety of e-cigarettes (but there are no very recent declarations on the e-cigarette on their sites). The *British Heart Foundation* makes a statement on the relative safety of e-cigarettes on the site¹²⁶ .

The **ASH-UK Smokers' Help Center** also assumes the relative risk caused by e and ASH Scotland share ¹²⁷ ASH Wales ¹²⁸ this view. ASH Scotland cigarettes.

associe cet objectif à l'aide aux fumeurs et au pragmatisme : « *ASH Scotland does not take a simplistic view either "for" or "against" electronic cigarettes. Our interest is in helping people improve their health by reducing the enormous harm caused by tobacco use. Our approach to electronic cigarettes will be guided by that principle.* » ¹²⁹

The organization refers to the National Health Service (NHS) Health Scotland with which they have drawn up, along with around 20 other organizations such as universities, medical professional organisations, health organizations etc. a position in which one

¹²⁰ The same

¹²¹ <https://www.bma.org.uk/what-we-do/population-health/drivers-of-ill-health/e-cigarettes-balancing-risks-and-opportunities>

¹²² <https://www.rcgp.org.uk/clinical-and-research/about/clinical-news/2018/september/ecigarettes-is-vaping-safe.aspx>

¹²³ <https://www.blf.org.uk/your-stories/e-cigarettes> ;

https://cdn.shopify.com/s/files/1/0221/4446/files/BK10_Smoking_v4.1_2019_PDFdownload.pdf

¹²⁴ https://www.stroke.org.uk/sites/default/files/new_pdfs_2019/our_policy_position/psp_-_e-cigarettes.pdf

¹²⁵ <https://www.rsph.org.uk/about-us/news/new-phe-review-strengthens-consensus-on-harm-reduction-role-of-e-cigarettes.html>

¹²⁶ <https://www.bhf.org.uk/informationsupport/risk-factors/smoking>

¹²⁷ https://ash.org.uk/wp-content/uploads/2019/04/E-Cigarettes-Briefing_PDF_v1.pdf

¹²⁸ <https://ash.wales/campaign/electronic-cigarettes/>

¹²⁹ <https://www.ashscotland.org.uk/what-we-do/campaign/e-cigarettes/>

peut lire entre autres : in *E-cigarettes have been available for purchase for just over a decade Scotland. They have become increasingly popular. Based on current evidence, vaping e cigarettes is definitely less harmful than smoking tobacco. There is still a lot we do not know about e-cigarettes. Although they contain nicotine, which is addictive, vaping carries less risk than smoking tobacco. It would therefore be a good thing if smokers used e-cigarettes instead of tobacco cigarettes, only as a potential route towards stopping smoking. Further research is required to understand the risks of e-cigarettes.*"¹³⁰ ¹³¹

In a dossier on nicotine, the smoking cessation organization **ASH-UK** points out:

« *Almost all of the harm from smoking comes from the inhalation of tobacco smoke rather than nicotine. There are some risks to health from nicotine but overall they are relatively minor. Nicotine increases heart rate and blood pressure and can also increase gastric acid secretion leading to peptic ulcers. Smoking during pregnancy is associated with a number of disorders and nicotine is believed to be a factor in adversely affecting fetal brain and lung development* »

¹³²

Following "EVALI" the French " *National Academy of Medicine*" made a statement :

"It is established that the vaporette is less dangerous than the cigarette: As indicated the National Academy of Medicine in 2015, so it is better for a smoker to vape »

¹³³

The French National Cancer Institute also clearly states on its website that there is a difference between smoking and vaping: " *While knowledge is progressing rapidly on this product, there are still uncertainties regarding its effects on health. However, the irritating and/or toxic effects of the components of SEDEN appear to be lower than those of tobacco. It could therefore be assumed that the risks of cancer will be reduced in tobacco smokers who switch to the use of electronic nicotine delivery systems (SEDEN). However, it is not known whether there may be other health effects in return for prolonged use of this device; this is why **health experts currently advise against it for non-smokers**. Even if the World Health Organization (WHO) calls for vigilance on electronic cigarettes, it is necessary to assess the risk-benefit balance between this device and cigarettes, which are the cause of 75,000 deaths each year in France. Studies are underway to assess the harmfulness of electronic cigarettes. In France, the National Agency for Food, Environmental and Occupational Health and Safety (Anses) is currently working on the assessment of the risks associated with the use of vaping products. (...)*

"There are still uncertainties about the risks of using SEDENs (electronic cigarettes) and their potential role in initiating smoking. These products are consumer products, they can thus be used by the population outside (or in addition to) support for smoking cessation, within the framework of the healthcare system. The lack of evidence-based knowledge does not exclude the possibility that the benefit/ risk ratio of these products used outside the healthcare system may represent assistance for certain consumers and thus contribute to improving their health. »

134

¹³⁰ <http://www.healthscotland.scot/health-topics/smoking/e-cigarettes>

¹³¹ http://www.healthscotland.scot/media/1576/e-cigarettes-consensus-statement_sep-2017.pdf

¹³² <https://ash.org.uk/wp-content/uploads/2019/10/NicotineAndAddiction.pdf>

¹³³ <http://www.academie-medecine.fr/lacademie-nationale-de-medecine-rappelle-les-avantages-prouves-et-les-inconvenients-unduly-alleged-of-the-electronic-cigarette-vaporette/>

¹³⁴ <https://www.e-cancer.fr/Comprendre-prevenir-depister/Reduire-les-risques-de-cancer/Tabac/La-cigarette-electronique>

Sur le site internet du **ministère néo-zélandais de la Santé**, on peut lire : *between smoking and vaping* The difference is that smoking delivers nicotine by burning tobacco, which can cause smoking-related illnesses, and vaping can deliver nicotine by heating a liquid in a much less harmful way.

Smoking is bad for your health as the toxins produced by burning tobacco cause smoking related illnesses. The majority of health benefits are seen when you stop smoking completely. Some people find cutting down as a helpful step to quitting, but stopping

*smoking completely should be the end goal. Vaping is not harmless, but it is much less harmful than smoking. **The healthiest option is not to vape or smoke. Don't vape if you don't smoke. Only vape to quit smoking***

¹³⁵ . This principle is endorsed by many organizations and professional groups in New Zealand¹³⁶ .

La **Cancer Society New Zealand** a aussi déclaré dans une prise de position que « *e-cigarettes may help reduce smoking prevalence – and achieve the Smokefree goal – if they act as an effective aid to quitting smoking, completely particularly as they have a high degree of acceptability as a quit tool amongst smokers. E-cigarettes may also help reduce smoking prevalence by acting as a substitute for smokers who cannot or do not want to quit and who switch completely to their use, as they are likely to be very much less harmful than tobacco smoking, although not harmless* »

137

In May 2021, what was described earlier in the different emphases by NASEM and PHE (cf. 1.1) seemed to be repeated, but this time between the reports of the **European Commission** (EC, 2021)¹³⁸ and the Royal College of Physicians (RCP)¹³⁹ ,

140

The " *Report from the Commission to the European Parliament, the Council, the Economic Committee and Social Affairs and to the Committee of the Regions on the application of Directive 2014/40/EU*

on the manufacture, presentation and sale of tobacco products and tobacco products provides an overview of the successes and 141 related » challenges of the tobacco products directive

tabac. En ce qui concerne les e-cigarettes, ce rapport fait référence au rapport SCHEER : « *Views on the actual health effects of e-cigarettes are divided, ranging from harmful to harmreducing for the individual, compared to conventional tobacco products for smoking. As scientific consensus has yet to be reached, the precautionary principle prevails and the TPD takes a careful approach in regulating these products* » (...) "E-cigarettes contain nicotine, a toxic substance. The Commission will base its risk management decisions on e-cigarettes on the SCHEER scientific opinion. The SCHEER opinion underlined their health consequences

and the important role they play in smoking initiation. This opinion supports the careful and precautionary approach taken so far. However, it should be explored whether some provisions could be further developed or clarified, such as tank size or labelling requirements; use of flavours; use of nicotine-free liquids; and advertising provisions. Insofar as e-cigarettes are smoking cessation aids, their regulation should follow the pharmaceutical legislation ».

¹³⁵ <https://vapingfacts.health.nz/vaping-vs-smoking/>

¹³⁶ Cf. <https://docs.google.com/document/d/1Ty7pgRBxv11nuJzHWxclzNlu569Hozn6/edit>

¹³⁷ <https://www.cancer.org.nz/cancer/our-advocacy-work/position-statements/e-cigarettes/>

¹³⁸ <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52021DC0249&from=EN>

¹³⁹ <https://www.rcplondon.ac.uk/projects/outputs/smoking-and-health-2021-coming-age-tobacco-control>

¹⁴⁰ A good representation of the various statements on the Physicians for a smokefree Canada website: <https://smoke-free-canada.blogspot.com/2021/05/europes-diverging-tobacco-control.html>.

¹⁴¹ <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52021DC0249&from=EN>

In the UK, as a result of Brexit, people will no longer be required to follow EU tobacco control guidelines in the future. The “plans to identify where we can sensibly deregulate without harming public health or where EU regulations limit our ability to deal with tobacco” strategy

¹⁴² government was already written in 2017 in “Towards a Smokefree Generation. A Tobacco Control Plan for England”. This plan positively addressed harm reduction and lower-risk tobacco alternatives.

To contribute to the UK approach, the **Royal College of Physicians** (RCP) has now presented a new report. This report entitled “Smoking and health 2021 - a coming of age for tobacco control?” was published 60 years after the publication of the first RCP report on tobacco. It takes stock of the decline in smoking prevalence in the UK and makes a series of policy proposals. The report assumes that with unchanged policy, the proportion of smokers below 5% will only be reached after 2050, while the United Kingdom aims to become smoke-free by 2030 ¹⁴³. The recommendations of the report focus on assessment, health promotion and communication, tobacco prevention, tobacco-free environments, treatment of tobacco dependence, and regulation of tobacco and nicotine products. About the latter, the report mentions: “Nicotine product regulation should be used more proactively to reduce harm from smoked tobacco and promote substitution with alternative nicotine products. Hence, measures such as prohibiting cigarette filter vents, minimizing filter porosity and imposing lower maximum standard tar, nicotine, and carbon monoxide yields, may be helpful in making cigarettes less desirable, and might encourage smoking cessation or substitution with less-hazardous nicotine delivery systems. Reporting requirements on the content and emissions of non-tobacco consumer nicotine products such

as electronic cigarettes should be standardised and made easily available to the public.

Substitution with non-tobacco nicotine products should be encouraged by allowing the use of comparative health claims in promotional materials ».

The report contrasts the health risks of tobacco with the lower-risk nicotine products available. Some specific recommendations in the other chapters also reflect this distinction: “UK tobacco tax structures need to be reformed with the aim of making smoked tobacco substantially less affordable and reduced harm nicotine alternatives much more affordable”, “mass media campaigns support the use of electronic cigarettes as a quitting aid or substitute for smoking, and rectify false perceptions about the safety of e-cigarettes compared with cigarettes”, “health warnings on e-cigarette packs include a statement that e-cigarette vapor is likely to be substantially less

harmful than tobacco smoke”. We also ask to include e-cigarettes in all smoking cessation programs, the government is invited to review the current restrictions on advertising for e-cigarettes, the same for the limits of nicotine in e liquids “and to assess the extent to which the regulations support switching from smoking”.

The differences with the SCHEER report are striking, no precautionary measure concerning e-cigarettes is underlined.

Another interesting comment is that of Fairchild (see also 7.1.) on the interpretation of research following some of these recent review studies and the changed context for the e-cigarette between 2018 and 2020 (“EVALI”, panic of young people in the USA):

¹⁴²https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/630217/Towards_a_Smoke_free_Generation_-_A_Tobacco_Control_Plan_for_England_2017-2022_2_.pdf

¹⁴³ <https://smokefreeaction.org.uk/Smokefree2030/>

« For those primarily concerned about potential unintended consequences of vaping to those who do not currently use e-cigarettes, precaution warrants setting the evidentiary bar low.

For those primarily concerned about reducing the immediate harms to smokers while minimizing unintended consequences, moderate evidence is good enough. For some, then, this most recent analysis will not meet even a low evidentiary bar. For others, it will exceed that bar. Still others will call the evidence from the updated 2020 Cochrane review into question. In other words, debates about quality of the evidence should not mask competing values about the risks of inadvertent harms of e-cigarettes, whether to smokers themselves or to nonsmoking or nonvaping bystanders. Evidence and value judgments about which harms are most concerning and what represents an acceptable trade continue to intersect.

The key question from a policy perspective is not only “Do e-cigarettes contribute to smoking cessation?” but also “What level of evidence is good enough to accept e-cigarette harm reduction? »

¹⁴⁴ . (the Cochrane on e-cigarettes as a means of smoking cessation referred to is discussed in the next chapter).

8.2. Smoking cessation

8.2.1. Preamble

Are e-cigarettes an effective smoking cessation device? (How) can smokers use it to quit smoking? For the smoker himself, these are relevant questions. The Health Survey¹⁴⁵ indicates that the main reasons for using e-cigarettes are to quit smoking (35%) and to reduce smoking (29%). The Cancer Foundation's smoking survey also shows that e-cigarettes are used to smoke less (32% of current users and 28% of former users) or quit smoking (27% of current users and 38% former users).¹⁴⁶ The recent Eurobarometer shows similar motivations among smokers.¹⁴⁷

The difference in emphasis between risks and opportunities again plays a role in answering questions about the effectiveness of e-cigarettes as a smoking cessation tool and what this means for policy makers.

In terms of risks, it is emphasized that the evidence for the effectiveness of the e-cigarette as a smoking cessation device is not clear, that in comparison with recognized smoking cessation drugs, the available scientific evidence is (yet) insufficient or too contradictory to definitively answer questions about efficacy and likelihood of long-term quitting smoking. It is also emphasized that e-cigarettes are not recognized smoking cessation medications and should remain the smoker's first choice. It is generally undeniable that e-cigarettes can play a role in terms of smoking cessation for some smokers. If used, it is recommended to do so in a clinical setting or in the context of recognized smoking cessation provision, for example with frequent counselling. Medical recognition of the e-cigarette as a smoking cessation device is considered by some authorities to be the only possible way in the longer term.

¹⁴⁴ <https://ajph.aphapublications.org/doi/10.2105/AJPH.2020.306078>

¹⁴⁵ https://www.sciensano.be/sites/default/files/ta_rapport2_his2018_nl_v3.pdf

¹⁴⁶ https://www.kanker.be/sites/default/files/def_ipsos_rapport_rookenquete_2021_nl_-_pg_99.pdf

¹⁴⁷ <https://europa.eu/eurobarometer/surveys/detail/2240>

Those who highlight the opportunities support the effectiveness of the e-cigarette as a smoking cessation tool by various studies (RCT, Cochrane, population studies), but also by the numerous testimonies of former smokers. They consider the e-cigarette as a smoking cessation product in its own right that can be combined with traditional smoking cessation aids (behavioral support and/or medication), but which can also be used independently of this smoking cessation offer by smokers.

who wish. Likewise, for smokers who cannot or do not want to do without of nicotine, the e-cigarette can be a longer-term alternative to smoked tobacco.

Those who question the effectiveness of the e-cigarette as a smoking cessation device therefore point out that to date, there has been no recognition as a medical smoking cessation device following an initiative by a pharmaceutical company or other originator. In the European Tobacco Products Directive (TPD) of 2014, this path was foreseen, but without concrete implementation so far. There are no e-cigarettes on the market as a recognized drug for smoking cessation.

An exception is an initiative of the tobacco industry itself: *British American Tobacco* (BAT) succeeded in 2016 in having an e-cigarette recognized in the United Kingdom as a medical smoking cessation product, but this product was not marketed¹⁴⁸. In the UK, however, work is now actively being done on the track. The *Medicines and Healthcare products Regulatory Agency* (MHRA) has launched an initiative in this direction¹⁴⁹.

“ *The MHRA seeks to encourage the licensing of electronic cigarettes (e-cigarettes) and other inhaled NCPs as and aims to support companies to submit medicines marketing authorization applications for these products* ”. ASH-UK, an organization specializing in smoking cessation, recently said that it would be interesting to explore further the way of e-cigarettes as a recognized smoking cessation agent/medicine¹⁵⁰. This would mean that this e-cigarette could then be unreservedly recommended as a smoking cessation device, could be dispensed on prescription and could be a route to products that could contain more than 20 mg/ml of nicotine. According to ASH-UK, the UK Medicines Authority welcomes this lead and such an e-cigarette could be available in the UK within the next couple of years.

ASH-UK and tobacco harm reduction organizations also state that such an e-cigarette does not replace e-cigarettes as an accessible consumer product. However, the first track (smoking cessation medication) can go hand in hand with the second and have advantages. Moreover, the second is a reality, the first has yet to be realized. And it is not known if this will happen and how, if and how e-cigarettes will be able to meet the recognition criteria imposed (since the e-cigarette has never been marketed as a medicine and works in a different way from the substitutes recognized medicinal nicotine), and how much time and financial resources this process will take.

8.2.2. Scientific basis

Here is what the conclusions of the **NASEM** report (2018) say ¹⁵¹ about the e-cigarette as a smoking cessation tool:

¹⁴⁸ <https://www.theguardian.com/society/2016/jan/04/british-american-tobacco-e-cigarette-wins-uk-medicine-licence>

¹⁴⁹ <https://www.gov.uk/guidance/licensing-procedure-for-electronic-cigarettes-as-medicines>

¹⁵⁰Cf. <https://vimeo.com/557518712>

¹⁵¹ <https://www.nap.edu/resource/24952/012318ecigaretteConclusionsbyOutcome.pdf>

- *Conclusion 17-1. Overall, there is limited evidence that e-cigarettes may be effective aids to promote smoking cessation.*
- *Conclusion 17-2. There is moderate evidence from randomized controlled trials that e-cigarettes with nicotine are more effective than e-cigarettes without nicotine for smoking cessation.*
- *Conclusion 17-3. There is insufficient evidence from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared with no treatment or to Food and Drug Administration–approved smoking cessation treatments.*
- *Conclusion 17-4. While the overall evidence from observational trials is mixed, there is moderate evidence from observational studies that more frequent use of e cigarettes is associated with an increased likelihood of cessation.”*

Le rapport **SCHEER** de la Commission européenne conclut sur le rôle des e-cigarettes dans le sevrage tabagique « *that there is weak evidence for the support of electronic cigarettes' effectiveness in helping smokers to quit while the evidence on smoking reduction is assessed as weak to moderate.*”¹⁵² (...) *“There is a lack of robust longitudinal data on the effect of electronic cigarettes on smoking cessation. Until such research is available, electronic cigarettes should only be considered to support smoking cessation for a limited time and under supervision. Furthermore, it should also be noted that the conclusions of some of the RCTs and reviews are only based on quitting at six months and do not take into account what proportion of smokers may relapse into smoking or dual use of e-cigarettes*

and cigarettes after the initial six months. However, as the majority of RCT assessed within the literature possibly referred to devices of earlier design, further research is needed to assess the impact of newer e-cigarette products on population based smoking cessation, using large population-based cohort data, with sufficient follow up time to assess potential relapse ».

The SCHEER report also states this about existing research: *“We must note however that these studies may have included earlier forms of e-cigarettes and may not have represented the nicotine delivery capable of electronic cigarettes now on the market in the EU”* . *Public Health England's* recent annual evidence update (2021), which includes new research on e-cigarettes as a smoking cessation tool (see below), is not included in this SCHEER report.

The WHO recognizes the potential of the e-cigarette as a smoking cessation tool only partially and not systematically. On the occasion of May 31 - World No Tobacco Day - 2021, the organization announced that e-cigarettes " *are not proven cessation aids*

». La e-cigarette semble être considérée comme un outil stratégique de l'industrie du tabac et l'approche de la réduction des risques est rejetée : « *Over the last decade, the tobacco industry has promoted e-cigarettes as cessation aids under the guises of contributing to global tobacco control. Meanwhile, they have employed strategic marketing tactics to hook children on this same portfolio of products, making them available in over 15,000 attractive flavours.*” (...) *The scientific evidence on e-cigarettes as cessation aids is inconclusive and there is a lack of clarity as to whether these products have any role to play in smoking cessation. Switching from conventional tobacco products to e-cigarettes is not quitting »*

153

¹⁵² https://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scheer_consultation_10_en

¹⁵³ <https://www.who.int/news-room/commentaries/detail/quit-tobacco-to-be-a-winner>

In a recent briefing on e-cigarettes (2020), **the WHO** referred to the NASEM study of 2018¹⁵⁴:
“ *The NASEM review concluded that there is insufficient evidence from randomized controlled trials about the effectiveness of ENDS as cessation aids compared with no treatment or approved smoking-cessation treatments, although it did not include a recent trial whose results depart from this conclusion. Moderate evidence, however, shows that some smokers may successfully quit tobacco by using some types of ENDS frequently or intensively, while others experience no difference or are even prevented from quitting*”.

Dans les messages clés et les conclusions de ce document, l'organisation résume la situation:
« *Some types of ENDS help some smokers quit under certain circumstances, but the evidence is insufficient to issue a blanket recommendation to use any type of EN&NNDS as a cessation aid for all smokers* »

The *unmentioned* RCT referred to by the WHO is that of Hajek et al (2019) . *nicotine-replacement therapy, when both products were accompanied by behavioral support*”. The RCT has been criticized, notably by the *European Respiratory Society* (ERS), for the fact that e-cigarette users continued to use nicotine in the study:

« *However, 80 % of former smokers continued to use e-cigarettes after quitting conventional cigarettes and thus remained nicotine dependent* » (Pisinger et al., 2019)¹⁵⁶ .

In an article in response to the ERS position on harm reduction, Britton et al. (2020)¹⁵⁷ point to evidence of e-cigarettes as a smoking cessation agent. They do également référence à certains RCT récents, dont celui de Hajek : « *When smokers use a nicotine replacement product to substitute for cigarettes, even in the absence of intention to quit, they are approximately twice as likely to proceed to quit smoking completely* ¹⁵⁸. *It would be astonishing if nicotine delivered via e-cigarettes was uniquely ineffective in helping people to quit smoking. In fact, in a definitive head-to-head randomised controlled clinical trial, e cigarettes proved to be twice as effective as combination nicotine replacement therapy (NRT) when delivered as part of an evidence-based smoking cessation intervention*¹⁵⁹, *and in a recently published smaller New Zealand trial, four times more effective than nicotine patches alone*¹⁶⁰ . *Whether e-cigarettes are “highly effective” is a question of definition, but it is not an “undocumented assertion” to observe that they are certainly at least as effective as medicinal NRT*¹⁶¹ ».

The **Surgeon General** also talks about e-cigarettes as a means of withdrawal smoking in the recent report “ *Smoking cessation* ” (2020). “*e-cigarettes, a continually changing and heterogeneous group of products, are used in a variety of ways. Consequently, it is difficult to make generalizations about efficacy for cessation based on clinical trials involving a particular e-cigarette, and there is presently inadequate evidence to*

¹⁵⁴ <https://www.euro.who.int/en/health-topics/disease-prevention/tobacco/publications/2020/electronic-nicotine-and-non-nicotine-delivery-systems-a-brief-2020>

¹⁵⁵ <https://www.nejm.org/doi/full/10.1056/nejmoa1808779>

¹⁵⁶ <https://erj.ersjournals.com/content/54/6/1902009>, cf. argument 2

¹⁵⁷ <https://erj.ersjournals.com/content/55/5/2000166>, cf. argument 2

¹⁵⁸ <https://www.nice.org.uk/guidance/ph45>

¹⁵⁹ <https://www.nejm.org/doi/10.1056/NEJMoa1808779>

¹⁶⁰ [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(19\)30269-3/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(19)30269-3/fulltext)

¹⁶¹ See the two previous RCTs mentioned in this quote

conclude that e-cigarettes, in general, increase smoking cessation. » (...) "The evidence is inadequate to infer that e-cigarettes, in general, increase smoking cessation. However, the evidence is suggestive but not sufficient to infer that the use of e-cigarettes containing nicotine is associated with increased smoking cessation compared with the use of e-cigarettes not containing nicotine, and the evidence is suggestive but not sufficient to infer that more frequent use of e-cigarettes is associated with increased smoking cessation compared with less frequent use of e-cigarettes »

162

À la fin, il y a un commentaire important et une liste des recherches qui doivent être poursuivies : « *It is particularly important to emphasize the current diversity of e-cigarette products: they do not comprise a homogenous product category, and they have changed rapidly in design and characteristics since first entering the U.S. marketplace in 2007.*

Consequently, much of the existing scientific literature on cessation relates to past generations of e-cigarette products. Therefore, further research is needed on the effects that e-cigarettes have on smoking cessation, including research on differential effects based on the type of e-cigarette product (e.g., newer vs. older devices); Comparison groups (e.g., e-cigarettes that do not contain nicotine, NRT, no cessation aid); Components in e-cigarette devices and the settings at which they are used (e.g., temperature of the heating coils); Frequency of use (e.g., daily vs. less frequent use); Informational context (e.g., forms of marketing and promotion, communication about risk and harm, behavioral support for use as a cessation aid); Potential variations in effects across geographies, and real-world use of e-cigarettes in different regulatory contexts. Such research will shed light on whether and how it may be possible to leverage e-cigarettes (or certain types of e-cigarette products) to maximize positive smoking cessation outcomes while minimizing adverse consequences related to youth initiation and use»

163

In **Australia, the Department of Health** responds on its website to the question of whether e-cigarettes can help smokers quit smoking as follows: " *Currently, there is insufficient evidence to promote the use of e-cigarettes for smoking cessation. If you need additional support to quit, the most successful approach is behavioral support combined with medicines (such as TGA-approved nicotine patches, gums and lozenges) and follow-up.*

E-cigarettes containing nicotine are not first-line treatments for smoking cessation. If you have tried to quit smoking using TGA approved medicines and been unsuccessful, speak to your doctor about whether or not e-cigarettes containing nicotine are a suitable option. In Australia, you must have a prescription to obtain e-cigarettes that contain nicotine »

164

In **France, an opinion of the High Council of Health** on the e-cigarette was recently published (2022)

¹⁶⁵ . Regarding the e-cigarette as a smoking cessation device, a distinction is made between its use within the framework of medical care and outside it. He is Smoking cessation counselors working in the medical field are advised not to use e-cigarettes. Outside the health care system, the Haut Conseil de la Santé advocates a pragmatic approach because, according to them, the e-cigarette can play a useful role when it comes to vulnerable groups. " *The hypothesis is strong that SEDEN could become first-line nicotine replacement therapy, but the*

¹⁶² <https://www.hhs.gov/sites/default/files/2020-cessation-sgr-executive-summary.pdf>

¹⁶³ <https://www.hhs.gov/sites/default/files/2020-cessation-sgr-full-report.pdf>, p. 532

¹⁶⁴ <https://www.health.gov.au/health-topics/smoking-and-tobacco/about-smoking-and-tobacco/about-e-cigarettes>

¹⁶⁵ <https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=1138>

number of trials is low and their methodological quality is lower than that recommended for such therapeutic trials (...)

He expresses the opinion: “ None of the studies reported here implements a rigorous methodology like that required for clinical trials. in other therapeutic areas or for the registration of health products in a therapeutic indication. This methodological inadequacy results in uncertainty as to the benefit/ risk ratio of SEDEN. It is for this reason that international recommendations do not recommend SEDEN with or without nicotine as therapeutic tools in the management of smoking cessation by health professionals ”. When it comes to groups of vulnerable smokers, the conclusion is as follows: “ In conclusion, a pragmatic approach must take into account the fact that some smokers will prefer to use a SEDEN rather than resorting to the health system”.

This leads to the following recommendations:

- “ Recommendation No. 1: Health professionals who accompany a smoker in a process of smoking cessation must use medicinal or non-medicinal treatments that have proven their effectiveness. Evidence-based knowledge is insufficient to propose SEDEN as smoking cessation aids in the management of smokers by health professionals. • Recommendation No. 2: These products are consumer products, they can therefore be used by the population outside (or in addition to) treatment within the framework of the healthcare system. The absence of evidence-based knowledge does not exclude the possibility that the benefit/ risk ratio of these products used outside the health system may represent a help for certain consumers and thus contribute to improving their health ”.

An appendix to the opinion shows, based on a survey by the **Société francophone de tabacologie** (SFT), that while 95% of French tobacco specialists consider the e-cigarette to be a smoking cessation tool, many of them say not have enough information to determine the role of e-cigarettes compared to drugs with proven efficacy such as TSN, varenicline and bupropion¹⁶⁶ .

The opinion of the French Haut Conseil de la Santé has been criticized by the medical professionals concerned and the dependency care sector¹⁶⁷ .

In Ireland, the Department of Health has recently (2022) published smoking cessation recommendations¹⁶⁸ . These "national clinical guidelines" emphasize behavioral support (by various means), alone or in combination with pharmacological support (including varenicline and the combination of medically approved nicotine substitutes). Regarding the e-cigarette, the guideline states that “Some people may choose to use an e-cigarette to support them in their quit attempt or may

¹⁶⁶ See appendix 8, p. 92.

¹⁶⁷ See, among others, the comments of Pr. Dautzenberg (pneumologist-tobacologist) and Pr. William Lowenstein (addiction specialist) in the French media. According to professors Benjamin Rolland (addiction) and Sébastien Couraud in an article in Le Monde (co-signed by other professors), the French High Council for Health adopts an “antivape” position based on “antivax” arguments: https://www.lemonde.fr/idees/article/2022/03/04/on-the-electronic-cigarette-the-high-council-of-public-health-has-a-position-antivape-with-arguments-antivax_6116192_3232.html ; see also the position of the Addiction Federation: <https://www.federationaddiction.fr/avis-du-hcsp-sur-la-vape-de-timides-advanced-mais-des-experts-tres-en-retard-sur-the-progress-of-society-and-patients-in-the-fight-against-smoking/#:~:text=The%20HSCP%20consid%20%C3%A8re%20only,of%20substitution%20nicotinic%20%E2%80%93%20TSN%20ou>

¹⁶⁸ <https://www.gov.ie/en/publication/4828b-stop-smoking/>

consider switching from smoking to using an e-cigarette. The following points can be used in discussion of this choice :

- E-cigarettes are consumer products. There is some regulation in place to protect consumers of e-cigarettes but not the same quality and safety system as would be in place for a licensed drug or medical device.
- People who do not smoke or use e-cigarettes should not start using them.
- For people who smoke and want to quit, advise them that there are a range of recommended and accessible support options with well-established effectiveness and safety profiles.
- Smoking tobacco is extremely dangerous and, compared to this, e-cigarettes are likely to be less harmful. They are not harm-free and there is some uncertainty at the moment regarding their health impact.
- Evidence regarding the effectiveness and safety profile of e-cigarettes as a stop smoking support is evolving.
- To reduce the harm from smoking, dual use of tobacco and e-cigarettes should be avoided.
- Health Service Executive stop smoking services can provide support to those who wish to use an e-cigarette to make an attempt to quit smoking.”¹⁶⁹

There is a **Cochrane** review of e-cigarettes as a smoking cessation aid, which reviewed studies comparing e-cigarettes to other smoking cessation aids (Hartmann-Boyce et al., 2021). It is now a “ *living systematic review* ” (regularly updated)¹⁷⁰. The *Cochrane Reviews* are accepted by many as the gold standard for research on existing evidence for health care interventions. The authors summarize the key messages as follows: *Nicotine e-cigarettes probably do help people to stop smoking for at least six months. They probably work better than nicotine replacement therapy and nicotine-free e-cigarettes. They may work better than no support, or behavioral support alone, and they may not be associated with serious unwanted effects. However, we need more evidence to be confident about the effects of e-cigarettes, particularly the effects of newer types of e-cigarettes that have better nicotine delivery than older types of e-cigarettes.* In the conclusions they speak of ‘*moderate certainty-evidence*’: “*There is moderate-certainty evidence that ECs with nicotine increase quit rates compared to NRT and compared to ECs without nicotine.*

Evidence comparing nicotine EC with usual care/no treatment also suggests benefit, but is less certain. More studies are needed to confirm the effect size. Confidence intervals were

for the most part wide for data on AEs, SAEs and other safety markers, with no difference in AEs between nicotine and non-nicotine ECs. Overall incidence of SAEs was low across all study arms. We did not detect evidence of harm from nicotine EC, but longest follow-up was two years and the number of studies was small. The main limitation of the evidence base remains imprecision due to the small number of RCTs, often with low event rates, but further RCTs are underway”.

¹⁶⁹ See *National clinical guideline*, summary, p. 4

¹⁷⁰ https://www.cochrane.org/CD010216/TOBACCO_can-electronic-cigarettes-help-people-stop-smoking-and-do-they-have-any-unwanted-effects-when-used, cf. also the “Let’s talk e-cigarettes” podcasts: <http://podcasts.ox.ac.uk/series/lets-talk-e-cigarettes>. See also the conference “The evidence of e-cigarettes for smoking cessation – when is enough enough?” by lead author J. Hartmann-Boyce at the 2021 E-cigarette summit USA: <https://vimeo.com/showcase/9170785>

The tobacco control association **ASH-UK** made a brief presentation of this Cochrane study¹⁷¹. When asked what this Cochrane review means for the pratique, l'organisation a répondu ceci : « *This authoritative review builds our confidence and certainty in the knowledge that e-cigarettes can be effective smoking cessation aids which current evidence shows are more effective and no more harmful than routinely offered NRT like patches and gum. With an increasing proportion of smokers holding false beliefs about the relative safety of e-cigarettes, it's vital that healthcare professionals and stop smoking services and advisors proactively offer e-cigarettes to smokers attempting to quit and communicate their relative safety and effectiveness for quitting smoking. Failing to reverse negative perceptions of e-cigarette safety would result in many people continuing to smoke, becoming ill and dying prematurely where they might have otherwise quit using an e cigarette* ».

The WHO indicates in its eighth " WHO report on the global tobacco epidemic " ¹⁷² (2021) que « *to date, evidence on the use of ENDS as a cessation aid is inconclusive* ». Elle fait référence à l'étude Cochrane mais aussi au rapport de SCHEER et au rapport du Surgeon General. Au sujet de l'étude Cochrane, le rapport indique : « *A recent Cochrane Review suggests that e-cigarettes can help smokers quit. This review compared ENDS to behavioural support and other nicotine replacement therapy (NRT) and pooling the results of four studies found a small but significant increase in quitting rates among ENDS users. The results suggested that out of 100 people using NRTs, six of them are likely to quit successfully, while 10 out of 100 people using e-cigarettes to quit are likely to be successful.*

There are a number of caveats to this conclusion. Firstly, the authors note that the certainty of these findings is low (for the comparison to behavioural support) to moderate (for the comparison to NRTs). Secondly, the studies included used a single product type in a therapeutic environment, and this is not considered comparable to the current real-world context of e-cigarette use. Thirdly, and perhaps most significantly, there is the question of defining cessation. Cessation may be seen to be the quitting of smoked tobacco products,

the quitting of any tobacco product or the quitting of any nicotine product. In the Cochrane Review, cessation was considered successful if people quit smoking any tobacco product. In other words, a person could move from conventional cigarettes to ongoing use of ENDS and be considered to have successfully "quit". This leaves open the question about the duration for which a person would be expected to continue using ENDS as a cessation device, especially since longer-term use may entail increased exposure to the potential health risks associated with ENDS. NRTs are designed such that nicotine content is progressively reduced throughout the treatment so as to reduce dependence on nicotine ».

In the UK and as part of the focus on harm reduction, it is more often pointed out that RCTs are not the only source of evidence for e-cigarettes as a smoking cessation tool. There is also evidence from observational studies, population data, trends and testimonials from (ex)-

smokers.

A recent **observational study by Jackson** et al. (2019) with 19,000 participants montre que ¹⁷³ "use of e-cigarettes and varenicline are associated with higher

¹⁷¹ <https://ash.org.uk/wp-content/uploads/2020/10/ASH-Cochrane-Review-of-e-cigarettes-explained-Oct2020.pdf>

¹⁷² <https://www.who.int/publications/i/item/9789240032095>, cf. p. 39

¹⁷³ <https://pubmed.ncbi.nlm.nih.gov/31117151/>

abstinence rates following a quit attempt in England." A longitudinal cohort study of adult American smokers showed that "daily but not non-daily e-cigarette use was associated with higher odds of prolonged cigarette smoking abstinence over 2 years, compared to no e-cigarette use. Daily use of e-cigarettes may help some smokers to stop smoking combustible cigarettes." (Kalkhoran et al., 2020)¹⁷⁴ E-cigarette use is also associated with increased smoking cessation at the population level.

Une étude de Zhu et al ¹⁷⁵ (2017) montre que *the substantial increase in e-cigarette use among US adult smokers was associated with a statistically significant increase in the smoking cessation rate at the population level.*" Une étude de l'University College London ¹⁷⁶

(Beard et al, 2019) suggests that increased use of e-cigarettes by smokers in the UK may be positively linked to an increase in the success rate of quit attempts and the overall rate of smoking cessation. On the

Based on this study, it was estimated that in 2017 between 50,000 and 70,000 smokers quit smoking which would not have happened otherwise, i.e. without e-cigarettes¹⁷⁷ (There are also older studies in the UK which already show a positive link between e-cigarette use and smoking cessation¹⁷⁸). The *Barometer of Public Health France* reports a large number of cases of smoking cessation: "The number of ex-daily smokers who have quit smoking for more than six months and who think that vaping has helped them to quit smoking is estimated at around 700,000 people since the arrival of the e-cigarette on the market in France" ¹⁷⁹

These observational cohort and population studies provide a good indication of the "real" effectiveness of e-cigarettes in terms of smoking cessation. The limitations of these studies are that the observed association does not necessarily imply a causal relationship between e-cigarette use and smoking cessation and that they are often based on self-report. Other equally interesting studies are listed below¹⁸⁰.

In addition, there are also thousands of positive testimonials from vapers who have struggled with smoking cessation and/or other cessation methods.¹⁸¹

The recent **Eurobarometer** " *Attitudes of Europeans towards tobacco and electronics*¹⁸² shows that 57% of e-cigarette users declared having *cigarettes* "

started vaping to quit or reduce their tobacco use. More than a third (37%) started smoking because they thought vaping was less harmful than

¹⁷⁴ <https://pubmed.ncbi.nlm.nih.gov/31298296/>

¹⁷⁵ <https://www.bmj.com/content/358/bmj.j3262>

¹⁷⁶ <https://onlinelibrary.wiley.com/doi/full/10.1111/add.14851>

¹⁷⁷ <https://www.ucl.ac.uk/news/2019/oct/e-cigarettes-may-help-over-50000-smokers-quit-england-each-year>

¹⁷⁸ See also mentioned in this document: [https://ash.org.uk/wp-content/uploads/2019/04/E-Cigarettes Briefing_PDF_v1.pdf](https://ash.org.uk/wp-content/uploads/2019/04/E-Cigarettes-Briefing_PDF_v1.pdf)

¹⁷⁹ <https://www.santepubliquefrance.fr/determinants-de-sante/tabac/documents/enquetes-etudes/barometre-de-sante-publique-france-2017.-usage-de-la-cigarette-electronique-tabagisme-et-opinions-of-18-75-year-olds>

¹⁸⁰ See Beard et al., 2016; Berry et al., 2019; Farsalinos & Niaura, 2020; Farsalinos & Barbouni, 2021; Gagne et al., 2021; Johnson et al., 2019; Kalkhoran et al., 2018; Kalkhoran et al., 2020; Levy et al., 2018; Zhuang et al., 2016

¹⁸¹ In the fight against smoking, these testimonials seem to receive little attention, at least as evidence that the e-cigarette has a role to play as a smoking cessation agent. They can be found on the sites of consumer associations such as CASAA which defend "reduced harm alternatives to smoking": <http://www.casaa.org/testimonials/>

¹⁸² <https://europa.eu/eurobarometer/surveys/detail/2240> Published in 2021, this Eurobarometer is a survey that examines the relationship that European citizens have with tobacco and related products such as electronic cigarettes. Over 28,000 respondents are affected in 27 EU countries and the UK. A separate fact sheet is available for each country.

le tabac. En outre, les e-cigarettes ont effectivement aidé un nombre croissant de fumeurs à arrêter de fumer : « *Three in ten smokers and former smokers who use, or have used, e cigarettes and/or heated tobacco products say that these products helped them to stop smoking tobacco completely. A further 17 % say that they stopped smoking tobacco for a while but then they started again, and more than one quarter (27 %) that they reduced their tobacco consumption but did not stop. Finally, one quarter of these respondents answer that these products did not help them to reduce smoking, with 22 % saying they did not reduce their tobacco consumption at all and 3% affirming that they actually increased their tobacco consumption. In 2017, a majority of former or current e-cigarette users (52 %) said that these devices did not help them to reduce their tobacco consumption at all, while this proportion stands at 22 % in the present survey. In addition, while 30 % of former or current e cigarettes and/or heated tobacco product users now say that these products helped them to stop smoking tobacco completely, this proportion stood at only 14 % among former or current e-cigarette users in 2017 and 2014*».

In **New Zealand**, there is an attempt to balance risk and opportunity in regulation and policy: protecting young people from e-cigarettes while actively encouraging smokers to switch¹⁸³ . Under the wing of the Ministry of Health, New Zealand smokers are invited to "vape to quit smoking:

<https://vapingfacts.health.nz/vaping-to-quit-smoking/> Le site web mentionne également en gras : « *The healthiest option is not to vape or smoke. Don't vape if you don't smoke. Only vape to quit smoking* ».

In the UK, the e-cigarette is actively used by adult smokers as a smoking cessation tool. There is a fairly broad consensus on this in the public health sector. For example, the e-cigarette will have a place in the treatment of smoking cessation within the framework of the NHS¹⁸⁴ .

« *Will an e-cigarette help me stop smoking? Many thousands of people in the UK have already stopped smoking with the help of an e-cigarette. There's growing evidence that they can be effective. Using an e-cigarette can help you manage your nicotine cravings. To get the best out of it, make sure you're using it as much as you need to and with the right strength of nicotine in your e-liquid. A major UK clinical trial published in 2019 found that, when combined with expert face-to-face support, people who used e-cigarettes to quit smoking were twice as likely to succeed as people who used other nicotine replacement products, such as patches or gum. You will not get the full benefit from vaping unless you stop smoking cigarettes completely. You can get advice from a specialist vape shop or your local stop smoking service. Getting expert help from your local stop smoking service gives you the best chance of quitting smoking for good* ».

Public Health England states on GOV.UK that evidence suggests that vaping works better than nicotine replacement therapy for smoking cessation¹⁸⁵ . A detailed draft guidance published (2021) by the *National Institute for Health and Care Excellence (NICE)* and *Public Health England (PHE)* states that “ *The evidence shows that nicotine-containing e-cigarettes can help people to stop smoking and are similarly effective to other cessation options such as a combination of short- and long-acting*

¹⁸³ <https://www.health.govt.nz/our-work/regulation-health-and-disability-system/regulation-vaping-and-smokeless-tobacco-products>

¹⁸⁴ <https://www.nhs.uk/live-well/quit-smoking/using-e-cigarettes-to-stop-smoking/>

¹⁸⁵ <https://www.gov.uk/government/news/vaping-better-than-nicotine-replacement-therapy-for-stopping-smoking-evidence-suggests>

nicotine replacement therapy (NRT). The expert committee agreed that people should be able to use e-cigarettes as one of several options to support smoking cessation, if they so choose. The draft recommendations advise that, combined with behavioural support, the option of either a combination of short- and long-acting NRT or nicotine-containing e cigarettes are more likely to result in people successfully stopping smoking »

A recent update (November 2021) of the NICE smoking cessation guidelines¹⁸⁷ states the following about e-cigarettes (distributed in the guidelines): In the definition of smoking cessation, " moving on to NRT or nicotine-containing e cigarettes" is also considered to be quitting smoking. " Stopping the use of tobacco, smoked or smokeless. This includes stopping use of tobacco and moving on to pharmacotherapies (including nicotine replacement therapy) or nicotine-containing e cigarettes ".

The list of " stop-smoking interventions " (see 1.12) includes e-cigarettes as one of three key elements:

Stop-smoking interventions

- Tell people who smoke that a range of interventions is available to help them stop smoking. Explain how to access them and refer people to stop-smoking support if appropriate.

- Ensure the following are accessible to adults who smoke:
 - behavioural interventions:
 - o behavioural support (individual and group)
 - o very brief advice
 - medicinally licensed products:
 - o bupropion (see BNF information on bupropion hydrochloride)
 - o nicotine replacement therapy– short and long acting
 - o varenicline (see NICE's technology appraisal guidance on varenicline for smoking cessation and the BNF information on varenicline)
 - nicotine-containing e-cigarettes.

The current opinion on e-cigarettes with nicotine is as follows:

Advice on nicotine-containing e-cigarettes

These recommendations are for people providing stop-smoking support or advice to adults.

- Give clear, consistent and up-to-date information about nicotine-containing e-cigarettes to adults who are interested in using them to stop smoking (for example, see the [NCSCT e-cigarette guide](#) and [Public Health England's information on e-cigarettes and vaping](#))

- Advise adults how to use nicotine-containing e-cigarettes. This includes explaining that:
 - e-cigarettes are not licensed medicines but are regulated by the [Tobacco and Related Products Regulations \(2016\)](#)

¹⁸⁶ <https://www.nice.org.uk/news/article/nice-and-phe-publish-comprehensive-draft-guideline-to-tackle-the-health-burden-of-smoking>

¹⁸⁷ <https://www.nice.org.uk/guidance/ng209>

- *there is not enough evidence to know whether there are long-term harms from e-cigarette use*
- *use of e-cigarettes is likely to be substantially less harmful than smoking*
- *any smoking is harmful, so people using e-cigarettes should stop smoking tobacco completely.*

o Discuss:

- *how long the person intends to use nicotine-containing e-cigarettes for*
- *using them for long enough to prevent a return to smoking **and***
- *how to stop using them when they are ready to do so.*

- *Ask adults using nicotine-containing e-cigarettes about any side effects or safety concerns that they may experience. Report these to the MHRA Yellow Card scheme, and let people know they can report side effects directly.*

- *Explain to adults who choose to use nicotine-containing e-cigarettes the importance of getting enough nicotine to overcome withdrawal symptoms, and explain how to get enough nicotine.*

Il y a également dans l'avis un chapitre intitulé « *Why the committee made the recommendations* » 188: « *Evidence showed that nicotine-containing e-cigarettes can help people to stop smoking and are of similar effectiveness to other cessation options such as varenicline or long-acting and short-acting NRT* ». Il aborde les avantages et les inconvénients des e-cigarettes: « *The extensive harms of smoking are well known, and the committee agreed it is unlikely that e-cigarettes could cause similar levels of harm. But they also agreed that for people who do not smoke, it is unlikely that inhaling vapour from an e cigarette is as low risk as not doing so, although the extent of that risk is not yet known. They discussed the potential benefits and risks of using nicotine-containing e-cigarettes to stop smoking. There was a small amount of evidence about short-term adverse events of e cigarettes that did not show that they caused any more adverse events than NRT, e cigarettes without nicotine or no treatment. The committee had low confidence in this evidence because studies were usually designed to investigate effectiveness and not adverse events, meaning they may not have been large enough to show an effect. There*

were only 2 studies about the long-term harms of using nicotine-containing e-cigarettes, and the committee discussed the uncertainty of the evidence and their concerns with these studies. A call for evidence did not produce any additional evidence in this area. The committee agreed that there is insufficient evidence to tell whether e-cigarettes cause long term effects. E-cigarettes are relatively new devices, and it is important to understand whether they cause any health harms or benefits aside from their potential to reduce smoking-related harm (see the research recommendation on health effects of e-cigarettes).

The committee recognised the need for evidence about what factors may influence use of e cigarettes. So they made research recommendations relating to any possible impacts of the amount of nicotine and frequency of use, and flavourings ».

La justification fait également référence à **EVALI** : « *The committee discussed the outbreak of serious lung disease in the US in 2019, which US authorities identified was largely caused by vaping cannabis products containing vitamin E acetate. They also noted there has been a*

188 <https://www.nice.org.uk/guidance/ng209/chapter/Recommendations-on-treating-tobacco-dependence#stop-smoking-interventions>

Medicines and Healthcare products Regulatory Agency (MHRA) Drug Safety Update highlighting serious lung injury with e-cigarettes issued in January 2020 (E- cigarette use or vaping: reporting suspected adverse reactions, including lung injury). The committee discussed that the UK has well-established regulations for e-cigarettes that restrict what they can contain ».

Le suivi des éventuels effets nocifs des e-cigarettes est abordé : « Experts from the MHRA described to the committee the monitoring process for both short- and long-term harms of using e-cigarettes. Monitoring is ongoing and the evidence may change in the future, but the committee was not aware of any major concerns being identified. Accurate information relies on adverse events being reported, so the committee recommended that people providing stop-smoking support or advice should actively report any suspected adverse events and encourage people to report any that they experience ».

Et enfin, l'évaluation du risque, l'information du public et la nécessité d'un apport adéquat en nicotine : « The committee used their knowledge and experience to supplement the very limited and uncertain evidence about harms. They agreed that because many of the harmful components of cigarettes are not present in e-cigarettes, switching to nicotine-containing e cigarettes was likely to be significantly less harmful than continuing smoking. So, the committee agreed that people should be able to access them as part of the range of interventions they can choose to use (see the section on stop-smoking interventions). They also agreed that people should be given up-to-date information on what is known about e cigarettes to help them make an informed decision about whether to use them. The committee agreed that with the limited data on effects of longer-term use, people should only use e-cigarettes for as long as they help prevent them going back to smoking. They also agreed that people should be discouraged from continuing to smoke when using e cigarettes, even if they are smoking less, because there is no information on whether this will

reduce their harm from smoking. The committee discussed that it is more likely that people will not get enough nicotine to help them stop smoking, than get too much. They agreed that not getting enough nicotine is likely to increase the risk that the person will return to smoking, so they recommended that people should be encouraged to use as much as they need and told how to use the products effectively. How the recommendations might affect practice: extra time may be needed to discuss e-cigarettes with people who are interested in using them. If these recommendations lead to more successful quit attempts, this may mean fewer appointments per person and substantial savings in downstream costs associated with smoking ».

The recent report from the **Royal College of Physicians** (RCP) assumes that the e-cigarette is an effective smoking cessation device. One of his recommendations is the suivante : « *E-cigarettes are included in standard protocols to treat tobacco dependency* »¹⁸⁹. Cancer Research UK considère les e-cigarettes comme « *an option to help smokers stop* ».¹⁹⁰ « *Vaping is far less harmful than smoking. So, your health could benefit from switching. But you need to stop using tobacco completely to get the benefits. E-cigarettes can help people stop smoking and are a popular stop smoking tool. They can give people who smoke the nicotine hit they need to help beat their cravings. Vaping can also feel similar*

¹⁸⁹ <https://www.rcplondon.ac.uk/projects/outputs/smoking-and-health-2021-coming-age-tobacco-control>

¹⁹⁰ <https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/smoking-and-cancer/is-vaping-harmful>

to smoking, like holding a cigarette and breathing in. For the best chance of stopping smoking for good, get advice from your local stop smoking service, GP or pharmacist » ¹⁹¹

The **National Center for Smoking Cessation and Training** (NCSCCT, 2016) provides "Advice for services on making e-cigarettes": "Incorporating e-cigarettes into your Stop Smoking Service: Making the case and addressing concerns. Produced in consultation with the Office for Health Improvement and Disparities this document aims to support English stop smoking services to make e-cigarettes (vapes) available to their clients. It outlines the evidence for providing e-cigarettes as an option for clients alongside licensed stop smoking medications such as nicotine replacement therapy (NRT). The document also addresses common cited misconceptions and concerns about vaping, and offers a checklist for issues to consider when deciding how your service will provide customers with access to vaping products". A mass media campaign such as Stoptober presents the e-cigarette as a smoking cessation tool in an encouraging way.¹⁹² There is ongoing research in the UK into how smoking cessation professionals deal with e-cigarettes and the role that it can play in reducing tobacco-related health inequalities (Hiscock et al., 201).

The e-cigarette is also recommended for smoking cessation in target groups that are difficult to reach, such as pregnant women and people with mental health problems. The **Smoking in Pregnancy Challenge Group**, a coalition of organizations seeking to reduce smoking during pregnancy, has developed guidelines on the use of e-cigarettes for healthcare professionals involved in pregnancy and infographics for women themselves.¹⁹³ The guidelines state in particular: "While licensed Nicotine Replacement Therapy (NRT) products such as nicotine patches, gum and inhalers are the recommended option, if a pregnant woman chooses to use an e-cigarette and if that helps her to quit smoking and stay smokefree, she should be supported to do so." The **Royal College of Midwives** (2019) also does not disapprove of the use of e-cigarettes by pregnant women who want to

stop smoking. Elsewhere in the world, only TSN is currently recommended for pregnant women who want to quit smoking. The **French High Council of Health**

advises against its use in pregnant women in its recent opinion on e-cigarettes: "Recommendation No. 3: The HCSP advises against the use of SEDEN and SEDESN in pregnant women who smoke in the absence of data on efficacy, and as a precautionary principle in the absence of risk data. There is an alternative

effective and having proven its innocuousness with the TSN within the framework of an assumption of responsibility by a health professional". ¹⁹⁵

¹⁹¹ https://www.ncsct.co.uk/publication_Service_advice_e-cigarettes.php

¹⁹² <https://www.nhs.uk/better-health/quit-smoking/>. Sous la rubrique « Read up on stop smoking aids », les cigarettes électroniques sont mentionnées aux côtés de la TSN, de la varencline et du bupropion : « An e-cigarette is an electronic device that delivers nicotine in a vapour. This allows you to inhale nicotine without most of the harmful effects of smoking, as the vapour contains no tar or carbon monoxide. Research has found that e-cigarettes can help you give up smoking, so you may want to try them rather than the medications listed above. As with other approaches, they're most effective if used with support from an NHS stop smoking service. There are no e-cigarettes currently available on prescription. For now, if you want to use an e-cigarette to help you quit, you'll have to buy one. Costs of e-cigarettes can vary, but generally they're much cheaper than cigarettes »

¹⁹³ <https://smokefreeaction.org.uk/smokefree-nhs/smoking-in-pregnancy-challenge-group/smoking-in-pregnancy-challenge-group-resources/e-cigarettes-in-pregnancy/>

¹⁹⁴ <https://www.rcm.org.uk/media/3394/support-to-quit-smoking-in-pregnancy.pdf>

¹⁹⁵ <https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=1138>

ASH-UK 's recent factsheet ' *Smoking and Mental Health* ' (2019)¹⁹⁶

puts the finger on the wound: the higher smoking rate among people with mental health problems is the main cause of their shorter life expectancy. The link between smoking and mental health problems grows stronger as the problem worsens, with the highest smoking rates recorded among patients in psychiatric centres. Smoking also increases the poverty of many adults with mental disorders. People with mental health conditions suffer greatly from tobacco use and face specific issues and challenges when it comes to smoking cessation. In the UK, the possibility of using e-cigarettes to help them quit smoking is being studied.¹⁹⁷

Que dit la récente *evidence update de PHE* (2021)¹⁹⁸ à propos de la e-cigarette comme outil de sevrage tabagique ? Le rapport fournit d'abord quelques informations sur le contexte de l'utilisation de la e-cigarette dans le cadre du sevrage tabagique au Royaume-Uni : « *Similar to findings in our 2018 report, in England, according to STS data, vaping products remain the most common aid used in a quit attempt and are positively associated with successfully quitting. Other tobacco control measures, such as extending the licence of NRT to aid tobacco harm reduction and the use of varenicline when used as part of a quit attempt are also positively associated with smoking cessation, underscoring the importance of ensuring people who want to give up smoking have a choice of cessation aids available to them.*

However, as vaping is more popular than licensed medication, the impact of vaping products at a population level may be greater than that of licensed aids. » In 2020, 27% of people used a vaping product to quit smoking, 15.5% a NRT (one-time purchase or prescription) and 4.4% varenicline. Vaping is positively associated with quitting success: in 2017, more than 50,000 smokers quit using a vaping product, smokers who would otherwise have continued to smoke, according to the report.

How are vaping products used in smoking cessation services and what are their chances of success in quitting smoking? *“Between April 2019 and March 2020, in stop smoking services in England, a vaping product was used in 5.2% of quit attempts, either alone, concurrently or consecutively in combination with licensed medication. Consistent with the findings of our previous reports, the highest quit rates were observed when the quit attempt involved the use of a licensed medicine and a vaping product consecutively (74.1%). Quit rates with a vaping product and licensed medication concurrently (60.0%), a vaping product alone (59.7%) and varenicline alone (59.4%) were similar. Few stop smoking services offer vaping products to support a quit attempt. A consistent approach to the use of vaping products should be pursued by all stop smoking services. Further research into the barriers and enablers to using vaping products as part of a supported quit attempt is needed.* An ASH survey found that only 11% of local smoking cessation services offer vaping products to smokers who want to try quitting.

¹⁹⁶ <https://ash.org.uk/information-and-resources/fact-sheets/health/smoking-and-mental-health/>

¹⁹⁷ See among others <https://www.kcl.ac.uk/ioppn/depts/addictions/people/profiles/DrDebbieRobson> and her talk at the e-cigarette summit in 2019: 'Widening access to e-cigarettes for people with mental health and/or substance use problems'.
¹⁹⁸https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/962221/Vaping_in_England_evidence_update_February_2021.pdf

L'evidence update de PHE comprend également de nouvelles recherches sur la e-cigarette en tant qu'outil de sevrage tabagique, plus précisément des preuves ajoutées après le « *E cigarettes and heated tobacco products evidence rapport* '199 de 2018. La recherche est résumée comme suit : « *Three systematic reviews and meta analyses consistently found that vaping products that contain nicotine are more effective for helping people stop smoking than NRT. This finding is supported by 2 non-randomised studies that included NRT as a comparison group. Quit rates from one recently published RCT to assess the feasibility of providing vaping products to people discharged from a residential substance misuse service, were comparable to those of people provided with NRT. There were inconsistencies between effect estimates from each of the 3 meta analytical reviews about whether vaping products with nicotine are more effective than those without nicotine or behavioural support, though the effect estimates were strengthened, in favour of vaping products containing nicotine, when studies at high risk of bias were excluded. Quit rates among the non randomised studies, most of which were single group before and after studies and therefore inherently biased, ranged from 7 to 36 % in participants with a clinical condition (mental illness, substance misuse, HIV/AIDS) and 11 to 62 % in non-clinical participants* ».

Quelles sont les implications de cette recherche supplémentaire, selon PHE ? « *Studies continue to show that tens of thousands of smokers stopped as a result of vaping in 2017, similar to estimates in previous years. Compared to our 2018 report, there is stronger evidence in this year's report that nicotine vaping products are effective for smoking cessation and reduction. As suggested in our previous reports, combining vaping products (the most popular source of support used by people making a quitting in the general population), with stop smoking service support (which is the most effective type of support), should be an option available to all people who want to quit smoking. Local authorities should continue to fund and provide stop smoking services and all stop smoking services should have a consistent approach to the use of vaping products*».

More research needed on some issues, report says

: « *Further research is needed to assess whether smokers who use stop smoking services and vaping products differ from smokers who use the services and other smoking cessation aids. Further research is needed into the barriers and enablers to using vaping products as part of a supported quit attempt in stop smoking services. More studies are needed which include newer types of vaping products that have better nicotine delivery* ».

Le rapport contient un commentaire important sur les RCT et leur différence avec la « vraie vie » : « *As we have stated in previous reports, the strict inclusion and exclusion criteria of RCTs mean that they do not apply to many people in real-world clinical settings or people in the general population who smoke or vape. Most RCTs require strict adherence to particular intervention measures (for example, type, dose, duration and frequency) which also does not reflect what happens in real life. Vaping technology has become more sophisticated and varied, and the people who vape have become more heterogeneous. So, new and flexible ways of conducting observational studies and RCTs are needed to allow for user experimentation (for example trial and error of different types of vaping products, allowing for changes in preferences over time)* ».

199 <https://www.gov.uk/government/publications/e-cigarettes-and-heated-tobacco-products-evidence-review>, cf. from p. 149.

Numerous studies appear on certain aspects of the e-cigarette as a smoking cessation tool: the regular and frequent use of the e-cigarette is associated with smoking cessation, infrequent use is not. Several studies point in this direction . E-cigarettes can also play a role in preventing relapses²⁰¹ .

« *Cigarette smoking is commonly viewed as a chronic, relapsing problem requiring long term, repeated attention and multiple quit attempts. Yet the question of whether e-cigarettes may assist with cessation is often examined with a binary, single event, "all or nothing" lens.*

There may be advantages of using e-cigarettes within a relapse prevention/recovery of smoking abstinence framework when more adaptively used in targeted, individually tailored situations. This presentation will discuss potential approaches of how e-cigarettes can be used in sequential quit attempts to promote abstinence following smoking lapses; the potential role of transitions in self-identity away from being a "smoker"; and research designs to maximize more targeted and tailored approaches to help identify a role for e cigarettes »

²⁰² . Other research on relapse indicates: " *There is an increased risk of smoking relapse among users of e-cigarettes, which may be explained by long-term former smokers. The main uncertainty is whether there is a difference in the risk according to e cigarette exposure frequency. The popularity of e-cigarettes among former smokers is growing. In this scenario, our results point to their great potential to increase the frequency of relapse to conventional smoking, besides moving to the regular use of e-cigarettes.* »

203

We will not go into details. However, we will briefly address the problem or challenge of dual use. According to the latest **Health Survey** (not a clinical study), 75 % of vapers still smoke conventional tobacco. The higher the level of education, less this dual use of e-cigarettes and tobacco is observed. Dual use is also higher among novice vapers (87%) than among those who have been using e-cigarettes for longer and are experienced users (72%), but the latter figure remains high.

According to the latest Tobacco Survey conducted by the Foundation against Cancer (2021), 1 in 4 vapers have completely switched (in 2020, they were 17%). All the others combine the e-cigarette with other tobacco products (69%, 75% in 2020), 6% have never used other tobacco products (8% in 2020). Among those who vape on a weekly basis, the majority are *dual users* (in all age categories).

The recent **Eurobarometer** also shows that dual use is high in Europe:

« *Three in ten smokers or ex-smokers who use or have used e-cigarettes or heated tobacco products say these products helped them to stop smoking tobacco completely, and more than a quarter say they reduced consumption but did not stop. Against this backdrop, it can be observed that large majorities of e-cigarette and heated tobacco product users are 'dual users', i.e. their use of these products comes on top of their traditional tobacco product consumption. A consistent share (27 %) of current users of e-cigarette or heated tobacco*

200 Cf. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6037106/>, <https://pubmed.ncbi.nlm.nih.gov/28802179/>, <https://pubmed.ncbi.nlm.nih.gov/29574448/>, <https://pubmed.ncbi.nlm.nih.gov/31298296/>, <https://pubmed.ncbi.nlm.nih.gov/32939555/>

²⁰¹ <https://harmreductionjournal.biomedcentral.com/articles/10.1186/s12954-018-0237-7>, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6938007/>, <https://www.e-cigarette-summit.us.com/seminar/robin-mermelstein/>

²⁰² See this conference: <https://www.e-cigarette-summit.us.com/seminar/robin-mermelstein/>

²⁰³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8078138/>

products have attempted to quit, with, once again, a large majority doing so without seeking any assistance »

²⁰⁴

With appropriate political support, information campaigns and education of smokers on the relative dangers of e-cigarettes, dual use can be thwarted.

This shows the development in a country like the UK. Should dual use be seen as a challenge? The challenge: how to better inform the smoker and motivate him to choose to use only the e-cigarette? Do dual users think that cutting down on smoking is also good for your health? The Health Survey shows that nearly one in three smokers who use e-cigarettes do so to smoke less.

In some countries, dual use is decreasing: • In France, the

number of daily smokers among vapers fell sharply between 2014 and 2017: from 64.5% to 40%. The ex-smokers group

among vapers has increased (from 23.5% to 49.5%) (Pasquereau et al., 2019).

- Au Royaume-Uni, les chiffres les plus récents disent ceci: *Nearly two thirds of current vapers are ex-smokers (64.6 %), and the proportion continues to grow, while the proportion who also smoke (known as dual users) has fallen to 30.5 % in 2021 ».*

²⁰⁵ La récente Evidence Update de PHE (2021) en fait état : « *The proportion of vapers who also smoke has declined since 2012, from 74 % to 38 % in the ASH Adult (note: chiffres de 2020) and from 92 % to 51 % in the STS survey. The discrepancy is likely due to different definitions of smoking status »*

²⁰⁶

Une étude anglaise (Jackson et al, 2019) le démontre également : « *In England, dual use of e-cigarettes is not associated with reduced overall quit rates compared with exclusive smoking or dual use of NRT. However, dual use of e-cigarettes is associated with a slightly higher quit attempt rate than exclusive smoking but lower than dual use of NRT »*

²⁰⁷

Arrêter de fumer est difficile pour beaucoup de gens. De manière quelque peu inquiétante, le récent Eurobaromètre indique que seuls 53 % des fumeurs actuels déclarent avoir essayé d'arrêter de fumer à un moment donné. Il y a plus d'intention d'arrêter chez les doubles utilisateurs : « *Among the dual users, i.e. they use these products on top of their traditional tobacco product consumption, more than six in ten (62 % compared with 53 % for the overall current smokers) have at some point attempted to stop. Most of those attempts took place more than a year ago, with more than one in four (42 % compared with 38 %) answering this. A fifth (20 % compared with 15 %) have attempted to give up smoking in the last 12 months. Conversely, less than four in ten (39 % compared with 49 %) have never tried to quit smoking. Among those dual users, those smoking both traditional tobacco products and*

e-cigarettes are the respondents with the higher level of attempt to quit smoking: overall 68 % have at some point attempted to stop, a fourth (25 %) in the last 12 months and a 43 % more than a year ago ».

²⁰⁴ <https://europa.eu/eurobarometer/surveys/detail/2240>

²⁰⁵ <https://ash.org.uk/wp-content/uploads/2021/06/Use-of-e-cigarettes-vapes-among-adults-in-Great-Britain-2021.pdf>

²⁰⁶ <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-february-2021/vaping-in-england-2021-evidence-update-summary>

²⁰⁷ <https://pubmed.ncbi.nlm.nih.gov/31841827/>

8.2.3. Potential of the e-cigarette for our country?

The two main challenges for the next decade are:

- The **number of smokers** must decrease more rapidly. According to the latest survey of cigarettes in Belgium (the figure is 14 million daily smokers in Belgium, health, who together smoke 21 million cigarettes per day (the figure is 14 million daily smokers in Belgium, health, who together smoke 21 million cigarettes per day)).
- **Strong emphasis must be placed on tobacco-related health inequalities** in every tobacco policy. Low-skilled and socially vulnerable people, in particular, continue to smoke today.

The Health Survey (Gisle et al., 2018) also zooms in on the latter issue: more educated people score higher on all indicators, as smoking is strongly associated with lower socio-economic status (SES). The authors do not even want to talk about a gradient: "There is no real socio-economic gradient in tobacco consumption, but rather a social gap: among the most educated people, there are significantly fewer smokers (15.3%) and daily smokers (10.1%) than in the three least educated categories". The average number of cigarettes smoked and the percentage of heavy smokers also decrease as the level of education increases (see also 7.2).

If we look at smoking cessation aids for low-skilled smokers, we see what :

- A minority of smokers find the path to the best quit aid.
smoking available: tobacco specialist.
- Low-educated and vulnerable groups are generally less able to find the way to help with smoking cessation²⁰⁹ .
- In our country, smokers make too few attempts to quit smoking and smokers with low SES make even less (Health Survey).
- Certain age groups (twenties, thirties, forties) are more difficult to achieve with the smoking cessation offer.
- Some of these groups seem to be interested in e-cigarettes (for example, the young adults and people with a secondary education diploma - cf. health survey).

In our country, the tobacco specialist offers the highest quality smoking cessation aid, but in Flanders only a few thousand smokers make use of this offer each year. Promoting the use of a tobacco specialist was at the center of a campaign launched by the Flemish authorities in 2019,²¹⁰ which assumed that " 66% of smokers want to quit, but only 2% use a tobacco specialist ", and that those who are accompanied multiply by three or four their chances of success.

The majority of ex-smokers have quit smoking on their own, not just here, but around the world. According to the Health Survey, a large majority of both smokers

²⁰⁸ ²⁰⁸ https://www.sciensano.be/sites/default/files/ta_rapport2_his2018_nl_v3.pdf

²⁰⁹ See among others <https://www.tabaknee.nl/dossiers/laagopgeleiden-en-roken/item/1932-2-hulpverlening-schiet-tekort-bij-low-skilled-smoker-1932> .

²¹⁰ <https://www.zorg-en-gezondheid.be/stoppen-met-roken-tot-4-maal-meer-kans-op-succes-via-begeleiding> .

(65.2%) than ex-smokers (84.0%) do not use a specific method. Respondents often refer to their will, their character, the support of those around them or certain circumstances that led them to (try to) quit smoking. Perhaps the vast majority of smokers will continue to quit unaided in the future (Chapman and MacKenzie, 2010).²¹¹ The recent Eurobarometer²¹²

also shows that more than three-quarters (76%) of people who quit or tried to quit did not seek help. This study found that the most commonly used smoking cessation aids were NRTs and e-cigarettes (13% and 11% of people who quit or tried, respectively). Only 6% of smokers sought help from smoking cessation services (such as quit helplines) or medical assistance.

When it comes to achieving demographic goals, clinical and individual support therefore plays a rather modest role. The best aid for quitting smoking - clinical treatment (individual therapy or group therapy by the tobacco specialist) - has relatively high efficacy at the individual level, but low impact on the population due to its small reach. Population-oriented tobacco reduction interventions - health education through mass media campaigns,

tobacco legislation - are less effective, but have a much wider reach, which increases their impact on the population (Willemsen, 2010). The measures proposed in the past to increase the impact of smoking cessation aids on the population are as follows: raising awareness among smokers of the fact that their perception of smoking cessation aids is wrong (in order to lower the threshold), correcting erroneous perceptions on the role of willpower and motivation in smokers, strengthen the role of health professionals by directing smokers towards smoking cessation aids. Ten years ago, Willemsen's study and commentaries mentioned that the Internet (because of its wide reach) could perhaps favorably influence the population impact of evidence-based smoking cessation offers.

An interesting question is whether the e-cigarette can be a smoking cessation tool with a greater impact on the population in our country. In the report "Tobacco Consumption"

²¹³ the latest Health Survey presents a figure of the six main smoking cessation methods used by smokers and ex-smokers in our country (and ticked by at least 2% of those concerned). " *The methods are identical in daily smokers (who have relapsed) and ex-smokers (who no longer smoke), but in different proportions. The vast majority of both daily smokers (65.2%) and ex-smokers (84.0%) do not use a specific method. Respondents often refer to their will, their character, the support of those around them or certain circumstances that led them to (try to) quit smoking.*

A number of daily smokers also report using electronic cigarettes (19.8%), conventional nicotine substitutes (patches, stickers, etc.)

²¹¹ There is very little research in the field of tobacco control on smokers who quit smoking without assistance. In the past, Simon Chapman (University of Sydney) has repeatedly attempted to highlight this fact and advocated that this fact should be further investigated in smokers so that smoking cessation aid based on evidence can learn from it. See for example <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000216>. He advocates against medicalizing and "psychologizing" (unilaterally) smoking cessation and believes that the masses of smokers who quit without help should not be discouraged by the message that they will not succeed without help.

²¹² <https://feditobxl.be/nl/2021/03/eurobarometer-attitudes-of-europeans-towards-tobacco-and-electronic-cigarettes/>

²¹³ https://www.sciensano.be/sites/default/files/ta_rapport2_his2018_nl_v3.pdf

(13.5%) and drugs (Zyban, Champix, etc.) (7.7%). Ex-smokers declare, although in lesser proportions, the following methods used: drugs (5.6%), nicotine substitutes (4.7%) and electronic cigarettes (3.8%)”.

In the Health Survey, one in five daily smokers declares having already used the e-cigarette as an aid. It is most often used as a smoking cessation aid by men and by the 15-34 age group, but it is little used from the age of 55. It is also used more as a smoking cessation agent by smokers with a higher education diploma. In some groups, e-cigarettes appear to be on the rise as a smoking cessation agent. The authors of this report underline the "normalization" of smoking cessation and are rather negative with regard to the transition to vaping: " 77.5% of smokers who have already tried to quit (whether they succeeded or not) did not use any specific means. For 67% of them (n=370), it is a recent attempt (< 1 year) to quit smoking, precisely a period during which a support program would be useful. Similarly, few of them use a tobacco specialist (1.7%), a general practitioner (1.2%) or the services of "TabacStop" (0%). The use of drugs (5.4%) or conventional nicotine substitutes (11.0%) is also unpopular. On the other hand, 26.9% of them have switched to electronic cigarettes, hoping that this is only a transition phase. Survey data on how (former) smokers try/have tried to quit demonstrates that there is still a lot of work to be done to 'normalize' and encourage smoking cessation support and to help smokers who want to quit smoking in order to reduce the risk of relapse and increase the chances of success. Quitting smoking without help is associated with a strong character, of which the ex-smoker is proud.

On the other hand, quitting smoking with help is often seen as a weakness or lack of willpower, which gives help a negative connotation. This is obviously not the message we are trying to convey" (p. 30).

The Tobacco Survey conducted by the Foundation against Cancer (2021) shows that nearly 7 out of 10 smokers who tried to quit did so on their own, that 14% used nicotine substitutes and 11% used e-cigarettes with nicotine²¹⁴ .

The report "Usage of electronic cigarettes" (Health Survey)²¹⁵ which, like the report "Use of tobacco" was published in 2020, indicates the following about the use of e-cigarettes according to socio-economic differences: " The experimentation with e-cigarettes in Belgium more widely affects people from upper secondary education (20.5%) compared to those from less educated backgrounds (9.4% among those without a diploma or primary school) or from higher education (13.7%). Current users are also more concentrated among people from secondary education classes (4.5% to 6.3%) compared to only 2.1% to 2.8% among the least educated and the most educated”.

An increase in e-cigarette users among men and among young people and young adults is observed.

²¹⁴ https://www.kanker.be/sites/default/files/def_ipsos_rapport_rookenquete_2021_nl_-_pg_99.pdf

²¹⁵ https://www.sciensano.be/sites/default/files/ec_rapport2_his2018_nl_v3.pdf

A prerequisite for achieving population impact is that there must be many quit attempts. Efforts to provide professional help to smokers only make sense in a population of smokers who make many quit attempts (Zhu, 2012). Promoting the use of smoking cessation aids should therefore preferably also aim to increase the number of quit attempts.²¹⁶ In our country, one challenge is precisely the fact that smokers make too few quit attempts. Figures from the Health Survey show that for 6 out of 10 smokers, the last attempt to quit was more than a year ago. Smokers with low SES also make fewer quit attempts than smokers with high SES.

However, many smokers want to quit: 73.5%. There is a contradiction here: wanting to stop but making too few attempts to stop.

The e-cigarette is undoubtedly able to combine the best of both worlds:

- It can be combined with the best smoking cessation aid (tobacco specialist, anti-smoking medication).
- It can persuade smokers who do not want to go to a tobacco specialist or who have already tried other means of quitting smoking, encourage smokers who do not have the explicit intention of quitting to do so, contribute to the gradual cessation of smoking (during a period of dual use), help smokers who have quit to avoid relapses, etc. It can also target the mass of less qualified and younger groups of smokers, who are difficult to reach by the recognized smoking cessation offer and potentially have an impact on the population, as is already the case today in France and UK.

Une étude récente de la KULeuven sur l'utilisation de la e-cigarette dans le cadre des offres du tabacologue démontre ce qui suit : « *One third of all participants (n = 244) achieved smoking abstinence 7 months after the quit date, with e-cigarette users having higher chances to be smoking abstinent at the final session compared to NRT users. Point prevalence abstinence rates across all follow-up measurements, however, as well as continuous and prolonged smoking abstinence, were similar in e-cigarette users and in clients having chosen a commonly recommended (or no) smoking cessation aid. No differences were obtained between smoking cessation aids with respect to product use and*

experiences. Conclusions: People who smoke and choose e-cigarettes in the context of smoking cessation treatment by tobacco counselors show similar if not higher smoking cessation rates compared to those choosing other evidence-based (or no) smoking cessation aids »

217

In his book on quitting smoking, Professor Robert West²¹⁸ states that quitting smoking is different for everyone and that there is no *single* way to quit smoking. It is very attentive to what the smoker wants and does and relies on the philosophy "I

²¹⁶ In later research on increasing smoking cessation at the population level, Zhu states: "Finally, it suggests that the field of cessation has focused so much on developing and promoting interventions to improve smokers' odds of success that it has largely neglected to investigate how to get more smokers to try to quit and to try more frequently. Future research should examine whether increasing the rate of quit attempts would be key to improving the population cessation rate." - <https://tobaccocontrol.bmj.com/content/21/2/110.short> 217 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7931336/?utm_source=nieuwsbrief&utm_medium=email&utm_campaign=Nieuwsbrief%20tabak%20maart&utm_content=2021

²¹⁸ West is a globally recognized authority on smoking cessation and smoking cessation research, and is attached to University College London as a psychologist. His book on smoking cessation "No tobacco! - Find your method to permanently quit smoking" has also been translated into French.

advise, but you decide. In Flanders, the *Vlaams Consortium Tabak* (*Vlaams Instituut Gezond Leven, Vereniging voor Respiratoire Gezondheidszorg en Tuberculosebestrijding* (VRGT), *Kom op tegen Kanker* (KOTK) and STK) recently updated an existing text on smoking cessation²¹⁹. This text is intended to serve as a support for professionals in the care and social assistance sector, municipalities, businesses, etc. and answers the following question: what can we say about quitting smoking to the smokers we meet? The text lists six methods and tools that can benefit smokers: the tobacco specialist, Tabacstop, smoking cessation drugs, the general practitioner and the pharmacist, the e-cigarette with nicotine and Allen Carr.

It is possible that the e-cigarette plays a role at the population level as its acceptance and market penetration seem to be increasing, at least in countries where it is easily accessible and where legislation does not discourage or prohibit its use. Data from the previous Eurobarometer (Special Eurobarometer 429) suggests, after extrapolation to the whole European population, that there are more than six million ex-smokers in Europe who say that e-cigarettes have helped them to quit smoking (and that current use of e-cigarettes is seen almost exclusively among smokers) (Farsalinos et al., 2016).

If the e-cigarette is to have a greater impact on the population over time, it may be necessary to counteract the overly negative image and perception among smokers and the misperception of the substance nicotine itself (compared to smoked tobacco).

The recent Eurobarometer shows that the vast majority of people with little or no experience of e-cigarettes (70%) do not think that e-cigarettes can help smokers quit. Only 20% of this group think they can help. In the United Kingdom it is 51%, perhaps because the authorities play an encouraging role there.

The Eurobarometer underlines that this one-sided image could in particular be due to poor knowledge of the difference between the effects of nicotine and the carcinogenic substances present in tobacco smoke.

In **France**, half of the population is convinced that e-cigarettes are just as harmful or more harmful than conventional cigarettes. Daily smokers believe that vaping is more harmful than cigarettes.

In **New Zealand**, 47% of people surveyed in a *Health Promotion Agency* (HPA) study think e-cigarettes are less harmful than cigarettes, but 28% find them equally or more harmful. and 24% say they don't know. Conclusion of this study: *"The current findings provide an overview of the use and*

perceptions of e-cigarettes among current and ex-smokers in New Zealand. Together, they suggest some important challenges for public health messaging in relation to e-cigarettes, including the need to: i) further encourage their use as a tool to quit smoking completely; and ii) provide smokers with clear and accurate information about the relative harms of e-cigarettes and cigarettes" (Guiney et al., 2019).

Today in the **United States**, most Americans believe that e-cigarettes are as or more harmful than regular tobacco cigarettes. These figures are based on the

²¹⁹ <https://www.gezondleven.be/themas/tabak/stoppen-met-roken/welke-boodschap-geven-aan-rokers>

data from the HINTS220 survey . Compared to the 2014 and 2017 measures, the responses " *more harmful* " and " *much more harmful* " score much higher in the latest 2020 data (perhaps heavily influenced by "EVALI" in 2019 in the United States) . Some voices from the *Tobacco Harm Reduction* describe this situation as

" *shocking* " and this tendency of " *disgrace* "

221

The Tobacco Survey conducted by the **Foundation against Cancer** reveals that " *the majority of vapers are still convinced that vaping is less harmful* ". 58% believe that e-cigarettes are less harmful than other tobacco products, 38% that they are as harmful and 4% that they are more harmful²²² . However, the same survey shows that the perception of smokers and e-cigarette users on the harmfulness of e-cigarettes is completely reversed. This perception has not changed. Only 36% think that e-cigarettes are less harmful than other tobacco products. 55% think both are equally harmful and 9% think e-cigarettes are more harmful.

In **the UK** - a country strongly committed to e-cigarettes - the negative perception is also growing. Last year it was reported the following: " *The proportion of smokers correctly believing vaping is less harmful than smoking has fallen from 48% last year, to 39% this year. This does not include the 1% of smokers who think vaping*

is harmless ". This annual survey, carried out for ASH-UK, also shows that, for the first time, the number of vapers in the United Kingdom fell in 2020: this figure fell from 7.1% to 6.3% of the adult population. (today there are 3.2 million vapers).

PHE's latest *Evidence Updates* (2021) shows that only 29% of current smokers think vaping is less harmful than smoking, 38% think they are equally dangerous, 18% don't know and 15% think vaping is more harmful.

Accurate knowledge of the relative risk of vaping is not widespread among smokers, even in a country like the UK. As early as March 2020, the UK government issued a press release on " *false fears preventing smokers from using e-cigarettes to quit* ": " *Over half of smokers believe nicotine vaping products are equally or more harmful than smoking despite US vaping deaths being caused by substances banned in UK.* " ²²³ In this press release, it is emphasized once again: " *E cigarettes are much less harmful than tobacco but are not completely safe. They contain significantly less harmful chemicals which cause diseases related to smoking but the long term impact of using e-cigarettes will remain unknown for some time* ".

Socio-economic status (SES) is once again a factor in the perception of e-cigarettes: poorly educated and vulnerable groups are the least aware of the relative harmfulness of e-cigarettes (Pasquereau et al., 2019) . Maybe that's why they think quitting smoking doesn't matter so much?

It appears from the Evidence update of PHE (2021) that misperceptions about e-cigarettes are again more frequent among smokers of low socio-economic level

²²⁰ https://hints.cancer.gov/view-questions-topics/question-details.aspx?red=1&qid=1282&PK_Cycle=8

²²¹ <https://clivebates.com/e-cigarette-risk-perceptions-an-american-crime-scene/#more-6801>

²²² https://www.kanker.be/sites/default/files/def_ipsos_rapport_rookenquete_2021_nl_pg_99.pdf

²²³ <https://www.gov.uk/government/news/false-fears-preventing-smokers-from-using-e-cigarettes-to-quit>

économique (ouvriers qualifiés et non qualifiés et chômeurs). Le rapport mentionne également ce lien entre le SSE et l'utilisation de la e-cigarette : « *A greater emphasis needs to be placed on how best to communicate evidence of relative harm to smokers so that they can consider all the options available to them to quit smoking completely. Vaping is more common among more disadvantaged adult groups in society. This mirrors smoking prevalence, and research should continue to explore the effect this has on health inequalities* ».

8.3. Young people and non-smokers

Many of the institutions mentioned above that highlight the potential of e-cigarettes in the context of smoking cessation at the same time draw attention to the need for good protection of minors. In this chapter, we will examine youth vaping behavior, the relationship between vaping and smoking at home, and the discussion of flavorings in e-cigarettes.

8.3.1. Use of e-cigarettes

Dans un briefing (2020)²²⁴, l'OMS fait le point sur les tendances de l'utilisation des e cigarettes chez les adultes et les jeunes : « *The proportion of adults who currently (defined as at least once in the last month) used EN&NNDS in the two main world markets for these products, the United States of America and the European Union (EU), was 3.2 % in 2018 and 2 % in 2017 respectively. Highest prevalence of use among EU countries in 2018 was in the United Kingdom (England), at 6.2 %. In New Zealand, 3.8 % of adults currently used EN&NNDS in 2017–2018. Additional data from nine countries indicate that in most, no more than 4 % of adults used EN&NNDS regularly between 2017 and 2018. Very few countries have trend data. The proportion of current adult users of EN&NNDS in the United States has remained stable since 2014 (at 3.7 %) and in the EU since 2015 (2 %). In Canada, past 30-*

day use and daily use of EN&NNDS among adults remained stable in the period between 2013 and 2017. Only New Zealand shows a clear increase of use of EN&NNDS among adults, from 1.4 % in 2015–2016 to 3.8 % in 2017–2018 and 4.7 % in 2018–2019. Most EN&NNDS users are or were smokers ».

Regarding the number of young people who regularly use EN&NNDS, the WHO indicates, among other things, that the figure for this group is higher than for adults:

« *Data on the current use of EN&NNDS among young people aged 13–15 years from 22 countries indicate that the proportion using EN&NNDS regularly is higher than among their adult counterparts. Figures for young people ranged from 0.7 % in Japan to 18.4 % in Ukraine between 2017 and 2019, with a median country value of 8.1 %. Between 2008 and 2015, ever using EN&NNDS among young people increased in Poland, New Zealand, the Republic of Korea and the United States, decreased in Canada and Italy, and remained stable in the United Kingdom. Current use of EN&NNDS among 11–18-year-olds in the United States increased from 2017 to 2018 while remaining stable in the United Kingdom. In 2019, 1.6 % of 11–18-year-olds in the United Kingdom used EN&NNDS more than once a week, compared to 1.7 % in 2018. In Canada, past 30-day use of EN&NNDS among young people in grades 7–9 was 5.4 % in 2016–2017, which was not significantly different from use*

²²⁴ https://www.euro.who.int/_data/assets/pdf_file/0009/443673/Electronic-nicotine-and-non-nicotine-delivery-systems-brief-eng.pdf

in 2014–2015. A recent study comparing the change in EN&NNDS use among 16–19-year olds in Canada, the United Kingdom (England) and the United States between 2017 and 2018 confirmed the increase of EN&NNDS use in Canada and the United States and the stability in the United Kingdom (England) for use during the past 30 days and past week ».

En ce qui concerne l'utilisation actuelle des jeunes non-fumeurs, l'OMS indique ceci : « *Data from the United States show that in 2017, 0.8 % of all 11–18-year-olds who had never smoked a cigarette before were using EN&NNDS regularly (at least once in the last 10 days). In 2018, the proportion increased to 2.4 %. In the United Kingdom (England), however, 0.8 % of young people aged 11–18 years who had never smoked were currently using EN&NNDS. Weekly use of EN&NNDS among never-smokers aged 17 and 18 years was 0 % in 2016 and 2017 and 0.2 % in 2018. The recent study comparing the change in EN&NNDS use among 16–19-year-olds in Canada, the United Kingdom (England) and the United States between 2017 and 2018 confirmed the increasing number of never-smokers using EN&NNDS during the past 30 days and the past week in Canada and the United States, while the figure did not change in the United Kingdom (England)* ». Les tableaux et les références sont disponibles dans le document.

La « Canadian Tobacco & Nicotine Survey, 2020-21 »²²⁵ indique que « *vaping rates have stabilized in Canada between 2019 and 2020* » en dat « *one-fifth of Canadian vapers are teenagers* ». En ce qui concerne les habitudes d'utilisation des jeunes : « *For vaping, about one in seven (14 %) of those who had ever used these products were using them daily in the fall/winter of 2020-2021. In this case, however, the pattern is reversed in comparison with smoking: it is the younger generation who had much higher rates of experimentation than older Canadians. Just more than one in ten adults (13 %) had ever tried vaping, compared with two-fifths of youth and young adults (40 %)* ».

In countries like the **United States and Canada**, e-cigarettes are less regulated than in Europe, which may play a role in e-cigarette use among young people.

Par exemple, la teneur en nicotine autorisée n'y est pas limitée comme dans les États membres de l'Union européenne. « *Health Canada has identified the availability of high nicotine-concentration vaping products in the Canadian market since 2018 as one of the key factors that have contributed to the rapid rise in youth vaping.* » (...) « *The objective of the Nicotine Concentration in Vaping Products Regulations (the Regulations) is to protect young persons from inducements to use vaping products by lowering the concentration of nicotine to a maximum of 20 mg/mL. This is expected to contribute to reducing their appeal to youth* ».

226

It appears from population surveys in the **UK, France, Belgium, Germany, the EU**, etc. that vaping among non-smokers is rare. Vaping is most common among current smokers and ex-smokers. Frequent or daily vaping in people who have never smoked or who have smoked only a few cigarettes in their lifetime is a relatively rare phenomenon.

225 <http://www.smoke-free.ca/SUAP/2021/CTNS-2020-results.pdf>

226 <https://gazette.gc.ca/rp-pr/p2/2021/2021-06-23/html/sor-dors123-eng.html>

In **France**, the report of the Barometer of Public Health France 2017 points out: " *In 2017, in metropolitan France, vapers aged 18 to 75 have almost all had experience with tobacco, as current smokers or ex-smokers* " .²²⁷ (Pasquereau et al., 2019).

Au **Royaume-Uni**, on observe des tendances similaires (2020): " *Only 0.3 % of never smokers are current vapers (amounting to 2.9 % of vapers), down from 0.8 % in 2019.* " (2020) 228. The latest *evidence update* from PHE (2021) indicates that the prevalence of vaping among never smokers is between 0.3% and 0.6 %²²⁹ . The 2020 Eurobarometer shows that 98% of current vapers were previously smokers²³⁰

The latest Health Survey (**Sciensano**) demonstrates the following: " *The e-cigarette is used at all ages, especially between 15 and 54; it is more popular among men and appeals more to young people and middle-class people (secondary school graduates). Almost nine out of ten users smoked before vaping, and three-quarters combine electronic cigarettes with traditional smoking.* (p. 6) (...) " *It should be noted that nearly 90% of electronic cigarette users have already smoked before, which may explain the choice of e-liquids containing nicotine* " (p. 25)

²³¹ . The Cancer Foundation (FCC) Tobacco Survey (2019) shows that smokers who start vaping out of curiosity and who have never smoked before quickly quit vaping.

Of those who start vaping but have never smoked before, 91% quit again. 7% of them use e-cigarettes less than once a week and 2% daily (= 1 person in the survey or 1.53 %)²³² . The most recent Tobacco Survey conducted by the Cancer Foundation (2021) states the following: " *There are almost no non-smokers who start vaping at least once a week* "

233

This Cancer Foundation (FCC, 2021) smoking survey also shows that the number of users who vape²³⁴ at least once a week in the 20-30 age bracket has increased since 2018 age 18-24: from 4

% (2019) to 8% (2020) to 10% (2021) and age group 25-34 years: from 7% (2018) to 10% (2020) to 12% (2021). Between 2020 and 2021, there is a slight increase in these groups

227

<https://www.santepubliquefrance.fr/recherche/#search=BAROM%C3%88TRE%20DE%20SANT%C3%89%20PUBLIQUE%20FRANCE%202017%20USAGE%20DE%20LA%20CIGARETTE%20C3%89LECTRONIQUE,%20TABAGISME%20ET%20OPIONS%20DES%2018-75%20YEARS>

²²⁸ <https://www.drugsandalcohol.ie/33211/1/Use-of-e-cigarettes-vapes-among-adults-in-Great-Britain-2020.pdf>

²²⁹ <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-february-2021/vaping-in-england-2021-evidence-update-summary#vaping-among-adults>

²³⁰ <https://ethra.co/news/70-eurobarometer-2021>

²³¹ https://www.sciensano.be/sites/default/files/ec_report_2018_fr_v3.pdf . See also page 19: " *Among vapers, 88.4% declare that they smoked tobacco before trying the e-cigarette for the first time, while 11.7% of them did not smoke (and are therefore "first-time users" of the e-cigarette).* "

²³² https://www.kanker.be/sites/default/files/rookenquete_rapport_2.pdf

²³³ https://www.kanker.be/sites/default/files/def_ipsos_rapport_rookenquete_2021_nl_pg_99.pdf

²³⁴ 'Steam at least weekly' is based on the question below, where options 4 and 5 are taken together for set steam at least weekly.

Question: What is the applicable situation for you?

- 1: I have never used an electronic cigarette
- 2: I tried an electronic cigarette once, but I don't use it anymore.
- 3: I use electronic cigarettes less than once a week
- 4: I don't use electronic cigarettes every day, but at least once a week.
- 5: I use electronic cigarettes every day

of age which is not significant. The increase in use between 2018 and 2021 is significant.

If we take a closer look at the use of e-cigarettes by young people, the Health Survey shows that the main form of use by young people is experimentation. " *Most experiments with the e-cigarette do not seem to lead to its regular use, and daily use remains relatively limited to date* " (p.

6)(...). " *Young people experimented with electronic cigarettes more often (25.4%) and used them more often during the survey (5.5%). It is true that only 0.6% of young people are daily vapers. (p. 25),* But this is also stated: " *Among vapers aged 15 and older, 11.6% had never smoked before. Among young people (15-24 years), a third of vapers (33.5%) have not smoked before*" (p. 6)²³⁵ . Ongoing monitoring is therefore necessary, according to the authors. They also explain why in the report:

- " *Notwithstanding, young people are more likely than their elders to use e-cigarettes outside the context of previous smoking (33.5% compared to 5.6%-12.0% among the oldest) and less likely to maintain concomitant smoking (54.7% of vapers aged 15-24 smoke compared to 75.5% among all vapers). This tends to attest to the independent appeal of e-products vis-à-vis tobacco among the younger generation.* (p. 25)
- Young people cite the experience of pleasure as the main reason for using e-cigarettes. Half of young users are already " *advanced*" users (≥ 1 year).
- Nearly two-thirds of users choose liquids containing nicotine, an addictive ingredient.
- The vast majority of users also use a recently developed type of e-cigarette. This new e-cigarette delivers nicotine much faster than the first generation of e-cigarettes, " *but nicotine absorption can affect brain development before the age of 25*".

In our country, the **Leerlingenbevraging de la Vereniging voor alcohol- en andere** ²³⁶ provides figures on the use of e-cigarettes by young people. **drugproblems** (VAD)

In 2019, for the first time, the *Leerlingenbevraging*, a survey conducted by VAD ²³⁷ measured the use of e-cigarettes among young Flemings. 23% of students have already used an e-cigarette. 17% did so last year, 6.6% last month. A majority of the 17% of users in the past year, or 11%, indicate that they currently no longer vape (have quit within the past 12 months). Among recent users (6.6%), most (3.7%) indicate that they do so occasionally. 2.1% of students regularly use e-cigarettes A small proportion of all students use e-cigarettes daily (0.7%).

Among students who used e-cigarettes in the last 30 days, those without nicotine were used the most (54.6%). Nearly a quarter of them use e

²³⁵ However, it should be noted that the use of electronic cigarettes in this age group of 15-24 years is also low: 0.6% daily use, 5% occasional use, 20% have stopped use it and 75% have never used it. See: https://sas.sciensano.be/SASStoredProcess/quest?_program=HISIA/SP/selectmod2018&module=ecigaret

²³⁶ <https://www.vad.be/onderzoek/vad-leerlingenbevraging>

²³⁷ <https://www.vad.be/onderzoek/vad-leerlingenbevraging>

cigarettes both with and without nicotine (23.5%) and more than one in five recent users use only e-cigarettes with nicotine (21.9%). In the health survey, these figures differ slightly (but the age group is wider): 36% of 15-24 year olds use liquids without nicotine, 37% of liquids containing mainly nicotine.

The *Leerlingenbevraging 2020* conducted with pupils shows no increase in the use of e-cigarettes compared to the previous school year. Over the past year, one in six students have used e-cigarettes but a large majority have also stopped experimenting with them again. The number of occasional, regular and daily users is small. Compared to the previous school year, the use of e-cigarettes with nicotine has increased. The age at which people start vaping seems to be similar to that of smoking.

Based on these figures, it can be concluded that the use of e-cigarettes is currently not on the rise among young Flemings. It is mainly of experimentation, and few people remain "faithful" to the e-cigarette thereafter.

In the UK, the tobacco control organization ASH states that the most common reason given by young people for trying an e-cigarette is indeed: "I must have tried it". The situation is similar in the *National Youth Tobacco Survey* (NYTS), a questionnaire offered each year to young Americans.

Many alarming reports on the use of e-cigarettes by young people refer to the United States. The fact that the figures for e-cigarette use among young people and young adults in our country are not as alarming today is perhaps due to our legislation. It protects young people better than American legislation (among others, in Europe, the nicotine content of e-cigarettes is legally limited, but from a more general point of view, e-cigarettes are also covered by legislation on tobacco in our country).

However, vigilance is still required when it comes to young people and vaping. In the United Kingdom, the most e-cigarette-friendly country in Europe, the following is said: "*In conclusion, data from the 2021 ASH YouGov Smokefree youth GB survey suggests that while some young people experiment with e-cigarettes, particularly those who have tried smoking, regular use remains low. Likelihood of trying or currently using e-cigarettes increases with*

age and smoking status. However, continued surveillance is needed »

238

8.3.2. Relationship between vaping and smoking in young people

Is the e-cigarette a springboard to traditional tobacco for young people? The "gateway" hypothesis examines whether there is a causal relationship between starting to vape (without being a smoker) and later starting to smoke and becoming a regular smoker (when without start vaping, you would not have started smoking or become a regular smoker). We list the different positions and arguments.

²³⁸ <https://ash.org.uk/wp-content/uploads/2021/07/Use-of-e-cigarettes-among-young-people-in-Great-Britain-2021.pdf>

There is a correlation between vaping and smoking among young people, as demonstrated by the *Leerlingenbevraging* of the Flemish VAD: young people who smoke more also use e-cigarettes more (and vice versa). The 2019 results showed that, as with smoking, there is a clear difference in vaping behavior between students in stream A and those in stream B. In the former, 8.1% have already vaped, in the second, it is almost twice as much (15.1%). There is also a clear difference in the superstructure: pupils in technical secondary education (EST) and (even more so) in vocational secondary education (ESP) use

more e-cigarettes than students in general secondary education (ESG). These proportions persist in the other prevalences and frequencies. Regular use is significantly higher in ESP-type education (6.3%) than in EST-type education (3.4%) and ESG-type education (0.6%). The 2020 *Leerlingenbevraging* again showed that young people who smoke more also use more e-cigarettes: boys more than girls, ESP and EST students more than ESG students.

In France, the 2019 Public Health Barometer shows that in the group of young people who have already smoked and vaped, a majority started with conventional cigarettes (Pasquereau et al., 2019).

In the UK, tobacco control organization ASH and PHE came to the conclusion in 2020 that vaping is rare among young people who have never smoked.

« *Current vaping prevalence (weekly or less than weekly) among young people in England has remained reasonably steady with the best recent estimates putting it at 6 % of 11 to 15-year-olds in 2018 and 5 % of 11 to 18-year-olds in 2019. Older children are more likely to vape. Current use among 11-year-olds was estimated at less than 1 % in 2018, compared with 11 % of 15-year-olds. Current vaping is mainly concentrated in young people who have experience of smoking. Less than 1 % of young people who have never smoked are current vapers* »

239240

The latest PHE *Evidence Update* (2021)²⁴¹ demonstrates, among other things, the following:

« *ASH-Youth survey data (11 to 18 year olds) showed:*

- *smoking prevalence (including those who smoked sometimes or more than once a week) in March 2020 was 6.7 % (compared with 6.3 % in March 2019) and has changed little since 2015 when it was 7.1 %*
- *little change in levels of vaping over the last few years with current vaping (at least once per month) prevalence being 4.8 % in March 2020, the same as in March 2019*

The ITC Youth survey data (16 to 19 year olds) showed:

- *smoking prevalence at 6.2 % (defined as smoking more than 100 cigarettes in their life and having smoked in the past 30 days)*
- *current vaping prevalence at 7.7 % (defined as vaping on more than 10 days in their lifetime and having vaped in the past 30 days)”.*

²³⁹ <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-march-2020/vaping-in-england-2020-evidence-update-summary>

²⁴⁰ See also: <https://ash.org.uk/wp-content/uploads/2019/06/ASH-Factsheet-Youth-E-cigarette-Use-2019.pdf>

²⁴¹ <https://www.gov.uk/government/publications/vaping-in-england-evidence-update-february-2021/vaping-in-england-2021-evidence-update-summary>

(...) *“Most young people who had never smoked had also never vaped. Between 0.8 % and 1.3 % of young people who had never smoked were current vapers.”*

(...) *More 11 to 18 year olds who had tried vaping said they had:*

- *smoked first (45.4 %)*
- *vaped before they smoked (20.6 %)*
- *tried a vaping product and never tried smoking (28.9 %)*”.

The alarming presentation of the figures available in the United States on young people and the permanent description (in the United States) of the situation as an “epidemic” are also criticized. At the 2019 *E-cigarette Summit*, Professor Jarvis of *the University College of London* refuted the gateway theory in his analysis of the US NYTS investigation of 2018242.

According to him, the NYTS shows that the most young people

who have used e-cigarettes in the past 30 days have also used conventional cigarettes in the past. Only 1% of young people who have never smoked are regular users of e-cigarettes. According to Jarvis, the data also shows that the age at which young people start smoking is lower than the age at which they start smoking e-cigarettes. He concludes that the NYTS data does not support the fear that a new generation of addicts is coming because of the e-cigarette. An update to his article²⁴³ concludes: *“While use of e-cigarettes in US high-school students*

increased sharply between 2017 and 2019, frequent use and signs of e-cigarette dependence remained rare in students who had only ever used e-cigarettes and never any other tobacco product”.

The **NASEM** study (2018) concludes on the association of vaping and smoking in young people as follows:

- *« Conclusion 16-1. There is substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults.*
- *Conclusion 16-2. Among youth and young adult e-cigarette users who ever use combustible tobacco cigarettes, there is moderate evidence that e-cigarette use increases the frequency and intensity of subsequent combustible tobacco cigarette smoking.*
- *Conclusion 16-3. Among youth and young adult e-cigarette users who ever use combustible tobacco cigarettes, there is limited evidence that e-cigarette use increases, in the near term, the duration of subsequent combustible tobacco cigarette smoking »*

244

Dans « *The e-cigarette debate : what counts as evidence ?* » (Fairchild et al, 2019)²⁴⁵ on discute de la distinction entre NASEM et PHE : « *NASEM concluded, “There is substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults.” The committee identified 9 studies that met the evidentiary bar. For the analysis of the relationship between e-cigarette use and smoking over the past 30 days, only 2 studies qualified. While the report did note contradictory data, it determined*

²⁴² Voir « Epidemic of nicotine addiction? What does the National Youth Tobacco Survey reveal about high school e-cigarette use in the USA? », delivered at the E-cigarette Summit 2019 in London, <https://vimeo.com/373899455> and see <https://www.qeios.com/read/745076.2>

²⁴³ <https://www.qeios.com/read/745076.5>

²⁴⁴ <https://www.nap.edu/resource/24952/012318ecigaretteConclusionsbyOutcome.pdf>

²⁴⁵ <https://ajph.aphapublications.org/doi/10.2105/AJPH.2019.305107>

that observational or ecological evidence could not provide a conclusive refutation of the risk to children. Only randomized controlled trials could meet that bar. Conclusive proof, for NASEM, was the standard when it came to vulnerable populations like children." (...) "For the PHE, the evidence could not be read as providing proof that e-cigarettes were serving as a gateway to tobacco for young people. "Despite some experimentation with these devices among never smokers, e-cigarettes are attracting very few young people who have never smoked into regular use." Linda Bauld, one of the report's authors, was unambiguous in calling the impact on youth "negligible." Indeed, studies suggest that England's focus on smokers will have an impact on youth uptake: adult smoking represents a risk factor for youth uptake".

The WHO concludes in a recent e-cigarette briefing (2020)²⁴⁶ that there is a clear relationship between smoking and vaping among young people, but that so far it has not been proven. It was a causal relationship: " *There is moderate evidence that young never-smokers who experiment with ENDS are at least twice more likely to experiment with smoking later. The data available so far do not, however, prove that this evident association is causal. While some authors believe that ENDS use and smoking are initiated independently of each other as the result of a common latent propensity to risky*

behaviour, others think that the similarity between ENDS use and smoking facilitates the trajectory from one product to the other within a social learning framework."

Le Scientific Committee on Health, Environmental and Emerging Risks (SCHEER)²⁴⁷ de la Commission européenne conclut dans son rapport final: « *Regarding the role of electronic cigarettes as a gateway to smoking/the initiation of smoking, particularly for young people, the SCHEER concludes that there is moderate evidence that electronic cigarettes are a gateway to smoking for young people* ».

The **French High Council of Health** states in its recent opinion on e-cigarettes:

" *The scientific data are rather in favor of the initiating role of SEDEN in the consumption of tobacco in adolescents. However, the studies are not without bias and to our knowledge no cohort has been conducted in France to answer this question. In 2016, the opinion of the HCSP^[2] indicated that "(...) the electronic cigarette (...) could constitute a gateway to smoking. This risk would be counterbalanced by the fact that the electronic cigarette could delay the onset of smoking". The summary of the NAS ^[34] and the additional bibliography compiled by the HCSP do not allow us to question the first proposition ("could constitute a*

*gateway to smoking"). The conditional used in 2016 is still valid due to the methodological limits of the studies and the questionable transposability of foreign results to a French context. On the other hand, the literature does not support the second proposition ("electronic cigarettes could delay the onset of smoking."), which was based at the time on the opinion of stakeholders". After analyzing the issue, the French HCS presents a diagram to indicate the relationship between the use of electronic cigarettes and tobacco among young people: " *The relationships between SEDEN and tobacco are therefore complex and multiple hypotheses have been put forward for explain. The following diagram (Figure 3) summarizes and illustrates these assumptions (not**

²⁴⁶ https://www.euro.who.int/_data/assets/pdf_file/0009/443673/Electronic-nicotine-and-non-nicotine-delivery-systems-brief-eng.pdf

²⁴⁷ https://ec.europa.eu/health/system/files/2021-04/scheer_o_017_0.pdf

mutually exclusive). It summarizes the factors that can explain the consumption of tobacco and/or SEDEN, the factors that can explain the relationship between these two consumptions, as well as the moderators, which are external factors that can modify these relationships in one direction or the other .

248

Researchers from the University of California San Diego (Pierce et al., 2021), based on data from the **Population Assessment of Tobacco and Health** (PATH study) conclude the following: *“Trying e-cigarettes and multiple other tobacco products before age 18 years is strongly associated with later daily cigarette smoking. The recent large increase in e-cigarette use will likely reverse the decline in cigarette smoking among US young adults ».*

Une analyse de la littérature (méta-analyse) financée par la *British Heart Foundation* et *Cancer Research UK* et réalisée par l'université de Bristol (Khouja et al., 2020)²⁴⁹ conclut qu'il existe une association entre l'utilisation de la e-cigarette chez les non-fumeurs et le tabagisme ultérieur, mais que les résultats ne permettent pas de conclure à un effet de passerelle. *« Although the association between e-cigarette use among non-smokers and subsequent smoking appears strong, the available evidence is limited by the reliance on self-report measures of smoking history without biochemical verification. None of the studies included negative controls which would provide stronger evidence for whether the association may be causal. Much of the evidence also failed to consider the nicotine content of e-liquids used by non-smokers meaning it is difficult to make conclusions about whether nicotine is the mechanism driving this association. » (...)* *“In conclusion, there is a strong consistent association in observational studies between e-cigarette use among non-smokers and later smoking. However, findings from published studies do not provide clear evidence that this is explained by a gateway effect rather than shared common causes of both e cigarette use and smoking. This emphasises the need for a scientific forum to discuss the evidence to date and directions for future research. Future research should consider including relevant potential confounders, such as better measures of impulsivity and other measures of propensity to risk taking, and objective measures of smoking status in order to better explore the potential role of e-cigarettes as a gateway to smoking. Studies that explore the genetic underpinnings of these behaviours and use negative control outcomes may also help improve our understanding of the association between e-cigarette use and later smoking. A scoping review, including qualitative evidence, could provide a clearer understanding of the why e-cigarette use is associated with later smoking. Importantly, any recommendations regarding e-cigarette regulations to limit the burden of future smoking must consider the potential beneficial impact of e-cigarette use on smoking cessation ».*

The following studies are also interesting to better understand the relationship between vaping and smoking among young people. A review (Chan et al., 2020) concludes that there is a relationship, but that causality cannot be established from the studies concerned: *“ There is a longitudinal association between adolescent vaping and smoking initiation; however, the evidence is limited by publication bias, high sample attrition and inadequate adjustment for potential confounders ”*

250

²⁴⁸ <https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=1138>, cf. p. 28

²⁴⁹ <https://tobaccocontrol.bmj.com/content/30/1/8>

²⁵⁰ <https://pubmed.ncbi.nlm.nih.gov/32888234/>

A study by Sooyong & Selya (2020) examines the effect of "having ever smoked an e-cigarette on having ever smoked", "having ever smoked an e-cigarette on smoking at current time", "current e-cigarette use on having ever smoked", and "current e-cigarette use on current smoking". The study looked at 14 risk factors that may be associated with smoking and vaping, such as alcohol and drug use and having friends who smoke. Conclusion: "E-cigarette use does not appear to be associated with current, continued smoking. Instead, the apparent relationship between e-cigarette use and current conventional smoking is fully explained by shared risk factors, thus failing to support claims that e-cigarettes have a causal effect on concurrent conventional smoking among youth. E-cigarette use has a remaining association with lifetime cigarette smoking after propensity score adjustment; however, future research is needed to determine whether this is a causal relationship or merely reflects unmeasured confounding." » E-cigarette use is not associated with current (continuing) smoking. According to this study, the relationship between the two can be explained entirely by common risk factors. There is no causal effect of e-cigarette use on current youth smoking. Ever e-cigarette use and current e-cigarette use further increase the likelihood of smoking a conventional cigarette (but more research is needed to determine if a causal link exists). In summary, vaping increases the likelihood that adolescents will try cigarettes but not become (regular) smokers.

A recent study (Sun et al, 2021) states that "prospective studies have consistently reported a strong association between e-cigarette use and subsequent cigarette smoking, but many failed to adjust for important risk factors". L'étude conclut ce qui suit : « Among adolescent never cigarette smokers, those who had ever used e-cigarettes at baseline, compared with never e-cigarette users, exhibited modest or non-significant increases in subsequent past 12-month or past 30-day smoking when adjusting for behavioral risk factors

» 251

A study carried out by the University of Maastricht (Martinelli et al, 2021) with young Dutch and Flemish people concludes the following: "Our study replicated the positive relation between e-cigarette use and tobacco smoking in both directions for adolescents. This may mean that the gateway works in two directions, that e-cigarette and tobacco use share common risk factors, or that both mechanisms apply". The conclusions speak of a "gateway", but isn't it rather a positive relationship between vaping and smoking and between smoking and vaping? Here are some comments on the study by the researchers themselves (to be found on the university's website). T. Martinelli of the IVO Research Institute, lead author of the scientific paper: "Although previous studies have often claimed that e-cigarette use is a 'stepping stone' to youth smoking, this new

study paints a more nuanced picture. Young people who start out with tobacco are also more likely to start using e-cigarettes later.

One explanation could be that a certain group of young people are more inclined to try different means (like e-cigarettes and tobacco) and that the order in which they try them does not necessarily matter". Professor G. Nagelhout, from

²⁵¹ <https://academic.oup.com/ntr/advance-article/doi/10.1093/ntr/ntab243/6432620>

Maastricht University and the IVO Research Institute, states the following: " *Our results do not allow us to state with certainty that electronic cigarettes are the cause of young people's initiation to tobacco* ".

If a gateway effect had a substantial impact on youth smoking prevalence, since the introduction of e-cigarettes to the market, youth smoking rates should have increased again. However, this figure is falling (still) in our country²⁵² and in Europe (see the figures from the *Health Behavior in School-aged Children* HBCS), but also in other Western countries such as the United States. In the United States, moreover, the decline has been accentuated as e-cigarettes have become more popular. "The inverse relationship between vaping and smoking was robust across different data sets for both youth and young adults and for current and more established smoking. While trying electronic cigarettes may causally increase smoking among some youth, the aggregate effect at the population level appears to be negligible given the reduction in smoking initiation during the period of vaping's ancestry" (Levy et al., 2019). The 2021 National Youth Tobacco Survey (NYTS), released in March 2022, shows that youth smoking continues to decline . On average, 1.5% of high school students have smoked a cigarette in the past 30 days. Over the past decade, youth smoking has declined by 90% in the United States (this decline accelerated during the period of popularity of e-cigarettes among young people). The use of e-cigarettes by young people has also decreased significantly since 2019 ²⁵⁴

In New Zealand, daily consumption of cigarettes and e-cigarettes is low among young people; in 2019, the daily consumption of e-cigarettes among non-smokers was "very low". Students from certain schools ("middle and lower class schools") or students who belong to other risk groups are more likely to be daily smokers or vapers (Walker et al., 2020).

If you look at very recent figures for teenagers, young adults and adults in New Zealand, the trend seems to be that with falling smoking figures comes a rise in e-use figures. -cigarettes²⁵⁵ . In New Zealand, e-cigarette use has increased, while smoking has continued to decline over the past six years. Is it the result of the combination of good implementation of tobacco control policies based on FCTC measures and the impact of e-cigarettes that has turned young people and adults away from cigarettes

classics (tobacco)?

A study published in *The Lancet* (2020) concludes as follows on the potential replacement role of the e-cigarette: *The overall decline in smoking over the past 6 years in New Zealand youth suggests that e-cigarettes might be displacing smoking. Ongoing monitoring will be*

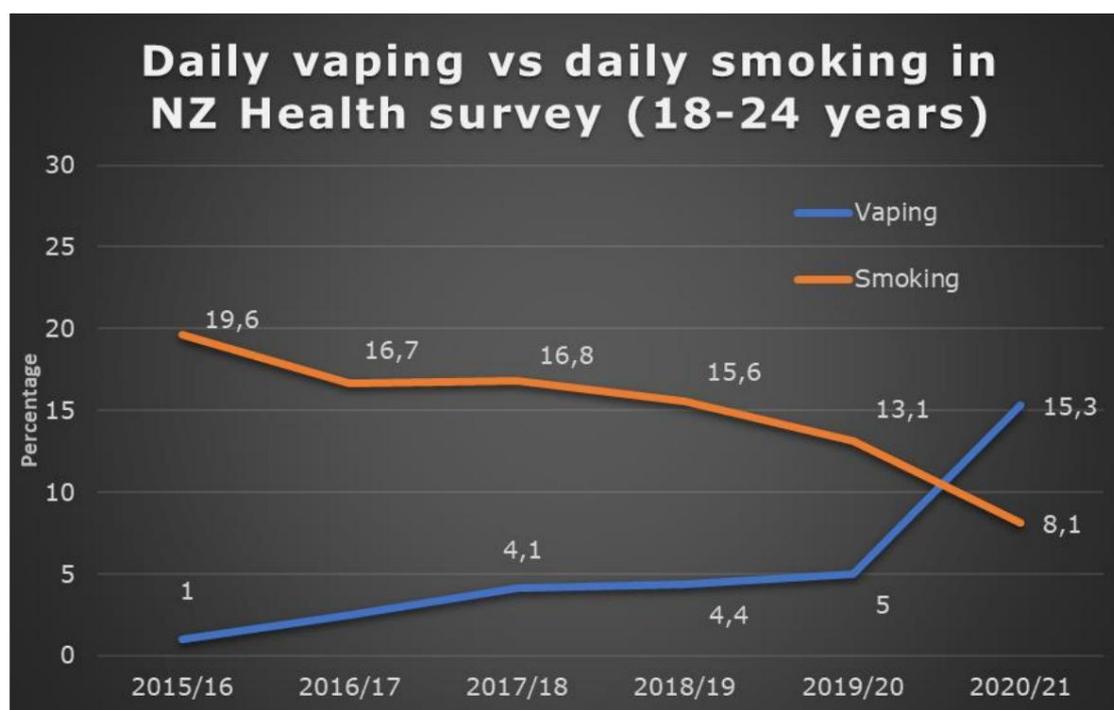
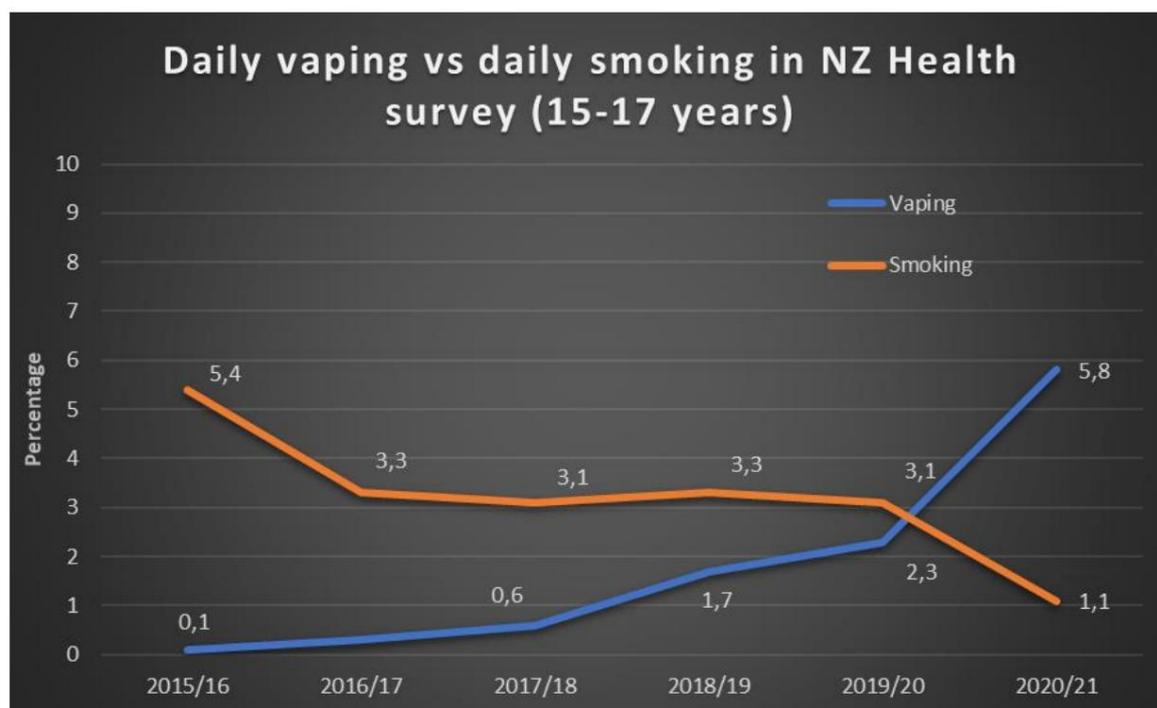
²⁵² See the HBCS studies: <https://www.jongeren-en-gezondheid.ugent.be/>. See also the general report presented by the VAD last year, which illustrates an evolution of smoking among young Flemish people over the last 20 school years: https://www.vad.be/assets/Syntheserapport_VAD-leerlingenbevraging_2000-2019.

²⁵³ https://www.cdc.gov/mmwr/volumes/71/ss/ss7105a1.htm?s_cid=ss7105a1_w

²⁵⁴ https://www.cdc.gov/mmwr/volumes/71/ss/ss7105a1.htm?s_cid=ss7105a1_w

²⁵⁵ <https://www.health.govt.nz/publication/annual-update-key-results-2020-21-new-zealand-health-survey>

important to determine whether the liberalisation of e-cigarette availability and marketing in New Zealand has any effect on long-term patterns of daily e-cigarette and cigarette use.”²⁵⁶



Will this trend manifest itself elsewhere in the near future? And how to estimate such an evolution?

A recent American study also suggests that vaping has replaced smoking among young people: “Youth e-cigarette use has increased rapidly, with high prevalence among

²⁵⁶ [https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667\(19\)30241-5/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(19)30241-5/fulltext). See also the statement of ASH New Zealand: <https://www.ash.org.nz/e-cigarettes-displacing-youth-smoking-in-new-zealand>

nonsmoking youth. However, the decline in current smoking among 12th graders has accelerated since e-cigarettes have become available. E-cigarette use is largely concentrated among youth who share characteristics with smokers of the pre-vaping era, suggesting e-cigarettes may have replaced cigarette smoking »

257

In New Zealand, a comprehensive Youth Health Survey (2021) also indicates that “ a significant proportion of New Zealand adolescents, many of whom have never smoked, use nicotine-containing e-cigarettes regularly”. The conclusions that the authors formulate with regard to this evolution: “ Vaping is less harmful than smoking, but it is not harmless. Public health action is needed to support young non-smokers to remain

smokefree and vape-free.”

258

Whether (broader) risk behaviors are included in the analysis of the relationship between vaping and youth smoking – including the strong association with more specific smoking behaviors and/or cannabis use and/or drinking - then it is interesting to explore how these behaviors relate to mental well-being. “ Perceived stress predicted use and poly use of e-cigarettes, hookahs, cigarettes, and cigars in adolescence ”

259

A study establishes links between mental health and single use of e-cigarettes, single use of tobacco and mixed use. “Relative to conventional cigarette only users, e-cigarette only users reported lower levels of internalizing mental health syndromes and traits.

Depression, panic disorder, and inability to experience pleasure (i.e., anhedonia) were higher in e-cigarette only users vs. non-users. For externalizing mental health and anhedonia, comorbidity was lowest in non-users, moderate in single-product users

(conventional or e-cigarette), and highest in dual users. Adolescent e-cigarette use is characterized by emotional problems midway between non-use and conventional cigarette

use. Dual use is associated with pervasive psychiatric comorbidity »

260

. With the caution that is necessary, one could argue that young people with more externalizing problems (usually associated with impulsiveness, which also implies greater curiosity, desire or audacity to take more risks, etc., by example ADHD) are more likely to use both products.

For the group that is consistently described in the addiction literature as being more prone to use, strengthening a number of mental skills (emotion regulation, impulse control) may make sense, in combination with an environment which (in a non-prescriptive way) leaves room for stimulating activities that feed curiosity and are not linked to substances (in other words, which provide an alternative offer). This issue needs to be investigated further.

A study of a slightly older group of university students who had never used an e-cigarette concluded that “ this study provides initial support for a scale to

257 <https://academic.oup.com/ntr/article-abstract/23/11/1958/6276227?redirectedFrom=fulltext>

258 <https://onlinelibrary.wiley.com/doi/full/10.1111/1753-6405.13169>

259 <https://www.sciencedirect.com/science/article/abs/pii/S0022395616307361>

260 https://www.sciencedirect.com/science/article/abs/pii/S002239561530008X?casa_token=dbBIT-phFxUAAAAA:5q0tq63S1fW6Q03c24v-jkHZYsGjppAKgg7uHi5iX2byH87Jxggope7Zw4jo-lmGitGEIFf2 et <https://pediatrics.aappublications.org/content/144/1/e20182935>

assess what motives abstainers may have to initiate e-cigarette use. Results indicated that coping motives may be indicators of readiness to initiate e-cigarettes". Les résultats importants: "Analyses revealed three factors of abstention motives (avoiding health outcomes, low incentive to initiate, and concerns regarding social approval of use) and three factors of initiation motives (tobacco alternatives, social reasons, and coping with negative emotions). When demographics were controlled for, only coping motives significantly positively related to abstainers' willingness and intentions for future e-cigarette initiation.

Furthermore, only the avoiding health outcomes abstention motive was positively related to participants' perceived vulnerability to the negative health effects of e-cigarettes » ²⁶¹

At a recent e-cigarette summit in the United States (2021), J. Pearson (University of Nevada) gave a lecture titled "Adolescent substance use: more than e" to better understand the complex issue of consumption of substance substances (alcohol, nicotine, cannabis, etc.) have. Research shows that adolescents who regularly use various

a higher risk of poor school performance, psychosocial problems, risky sexual behavior and criminal problems. Message: it is not enough to focus on a single substance (e.g. nicotine use by young people), we must also include this broader framework.

8.3.3. Flavors

A big discussion today is about flavors in e-liquids.

Regarding the role of flavors in the initiation and use of e-cigarettes, the WHO states the following: "E-liquids for EN&NNDS are marketed in more than 15,000 unique flavours.

Flavours are classified in two big groups: tobacco flavours, and those that impart a strong non-tobacco smell or taste. The latter are considered so-called characterizing flavours, the main categories of which are menthol/ mint, nuts, spices, coffee/tea, alcohol, other beverages, fruit, candy and other sweets. Flavours are one of the most appealing features of EN&NNDS and have been described as the major motivation for ENDS use by young people. They can alter expectations and reward from EN&NNDS, including nicotine effects.

Advertisements on e-liquid containers and vendor websites frequently contain images and descriptions of flavours that convey appealing product sensation. Flavours seem to play a part in promoting the switch from combustible tobacco products to EN&NNDS. They also play an important role in increasing uptake of EN&NNDS among young people, noticeably more significantly than among adults. The use of flavoured e-liquids is generally higher among young people and young adults than in older adults »

²⁶³ . This briefing formulates the recommendation suivante: « limiting the levels and number of specific flavours allowed in EN&NNDS to reduce initiation by young people ».

In the "WHO-study group on tobacco regulation report" (2021)²⁶⁴, the "discussion" section summarizes the debate as follows: "The use of flavors in nicotine and tobacco products is controversial, as they have been clearly shown to contribute to the use and appeal of these products, particularly among young people. ENDS products continue to be a

²⁶¹ <https://pubmed.ncbi.nlm.nih.gov/34762040/>

²⁶² <https://vimeo.com/showcase/9170785>

²⁶³ https://www.euro.who.int/_data/assets/pdf_file/0009/443673/Electronic-nicotine-and-non-nicotine-delivery-systems-brief-eng.pdf

²⁶⁴ <https://www.who.int/publications/i/item/9789240022720>, cf. chapter 9.

major concern, as their popularity is growing. A major feature of their appeal is the wide variety of flavours, which promote experimentation and prolonged use. Additionally, emerging evidence suggests that flavours may contribute to the toxicity of newer products such as ENDS in unique ways. Increased use of tobacco and nicotine due to flavours increases the burden on public health; however, flavours might be used to reduce the burden, as some adult smokers have reported that the flavours in products like ENDS contribute to their efforts to stop or reduce cigarette use. Policy-makers should consider this aspect when regulating flavours in tobacco products. Regulation of flavouring in tobacco products should be a priority in all regulatory approaches to limit the spread and progression of nicotine and tobacco use and to reduce use of combustible tobacco products ».

Le rapport formule les recommandations politiques suivantes : « A piecemeal approach to regulating flavoured nicotine and tobacco products will not turn the tide of the tobacco epidemic. A multi-pronged combination of various policy tools with a panoramic view of all nicotine and tobacco product use will help health agencies to address the issue of flavoured products. ENDS could be used as an opportunity to increase the regulation of all tobacco

products to achieve the ultimate objective of nicotine- and tobacco-free future generations.

Policies on flavours in novel and emerging nicotine and tobacco products should include the following. • Where flavours are not banned, their regulation in nicotine and tobacco products

should be consistent globally; i.e. the availability of flavours should be regulated similarly for all nicotine and tobacco products rather than for each product. • Research should be conducted on the possible role of characterizing flavours in products like ENDS or HTPs in helping smokers to quit ».

Another WHO report entitled “ WHO report on the global tobacco epidemic 2021: 265 examines in more detail e-cigarettes and addressing new and emerging products ”

aromas and gives an overview of the policies implemented in the countries. In addition to WHO Director-General Dr. Tedros Adhanom Ghebreyesus, Michael R. Bloomberg of *Bloomberg Philanthropies* wrote a foreword to this report. As part of Bloomberg's sponsorship of the WHO, questions are asked by experts in the

tobacco-related harm reduction .

Flavors are the subject of debate in many countries. In the neighboring Netherlands, it has been decided to only allow tobacco flavors in the future. The RIVM has published an opinion on the subject²⁶⁷ .

“ The authorities want to make electronic cigarettes less attractive, especially for young people. As certain flavors (sweet, fruity) favor their use, the authorities have decided that only tobacco-flavoured electronic cigarettes can be put on the market in the future. The RIVM has conducted research on flavoring substances currently in use and proposes to limit the number of authorized flavoring substances to 23 substances that taste like tobacco, alone or in combination. However, the RIVM warns: “ Adults also use e-cigarettes as a smoking cessation aid. In the Netherlands, most e-cigarette users are (ex-)smokers. Smokers (and ex

²⁶⁵ <https://www.who.int/publications/i/item/9789240032095>

²⁶⁶ See in this regard, among others, <https://clivebates.com/holding-the-bloomberg-anti-vaping-propaganda-complex-to-account/> in

²⁶⁷ <https://www.rivm.nl/nieuws/rivm-advies-beperk-smaakstoffen-voor-e-sigaret-tot-23-met-alleen-tabaksmak>

smokers) adults and young non-smokers particularly like sweet and fruity. If only tobacco flavors are allowed, the electronic cigarette may lose its appeal as an aid. It can also mean that users will start adding flavorings themselves. This is possible with the aromas which are available separately. The RIVM advises the Ministry to take this into account when drafting the new rules”.

Regarding the intention of the Netherlands to ban all tastes except tobacco, 24 experts reacted from the point of view of reducing the risks associated with tobacco²⁶⁸. An important argument is that aromas other than tobacco taste play a role in the vaping behavior of adult smokers, including in smoking cessation.

The latest Tobacco Survey conducted by the Cancer Foundation (2021) shows that 52% of current e-cigarette users prefer fruit flavors (a significant increase from 2020, when the figure was 39%). After menthol or mint flavoring, tobacco flavoring comes in third place (26% in 2021, 32% in 2020)

269

A recent systematic review by four English universities (November 2021)²⁷⁰ examines 58 studies - summing up the opinions and experiences of over 500,000

mineurs - et conclut ceci : « Flavours may be an important motivator for e-cigarette uptake, but the role of flavours in tobacco smoking uptake or cessation is unclear. The quality of the evidence on use of e-cigarette flavours by young people is low overall.” Le professeur C.

Notley (Université d'East Anglia) discute son étude dans ces commentaires: *“We found that flavoured e-liquids are an important aspect of vaping that young people enjoy. This suggests that flavoured products may encourage young people to switch away from harmful tobacco smoking towards less harmful vaping. Flavours may be an important motivator for e-cigarette uptake – but we found no evidence that using flavoured e-liquids attracted young people to go on to take up tobacco smoking. And we also found no adverse effects or harm caused by using liquid vape flavours. However, there is also a need to monitor flavour use to ensure that young people who have never smoked are not attracted to taking up vaping. Ensuring the continued availability of a range of e-liquid flavours is likely to be important in encouraging young people who smoke to switch to vaping as a less harmful alternative »*

271

The debate on flavors is linked to that on communication and marketing aimed at young people. A number of views from the e-cigarette-friendly UK are relevant here.

Flavors play a role in marketing e-cigarettes to young people. According to the smoking cessation organization ASH-UK (2019), the problem is twofold: the large amount of flavorings and the way they are presented via " *packaging, labeling and branding* " which influence children's choices (use of brightly colored packaging, " *sweet names* " (references to candies), cartoon characters

²⁶⁸ <https://www.internetconsultatie.nl/smaakjes/reactie/bf5d0c59-b4bb-41c0-b521-9167659326c3>

²⁶⁹ https://www.kanker.be/sites/default/files/def_ipsos_rapport_rookenquete_2021_nl_-_pg_99.pdf b

²⁷⁰ <https://onlinelibrary.wiley.com/doi/full/10.1111/add.15723>

²⁷¹ <https://www.eurekalert.org/news-releases/934914> + see. also a PowerPoint on study and flavoring presented at a recent UK e-cigarette summit – 2021 (<https://www.e-cigarette-summit.co.uk/>) : <https://www.e-cigarette-summit.co.uk/wp-content/uploads/sites/82/2020/11/Caitlin-Notley.pdf>

anime, etc.)²⁷². Marketing can also be done in other ways, for example through channels used by young people (social media, etc.). This may also apply to other nicotine products that target younger users (among others).

The University of Stirling has conducted research on e-cigarette marketing in the United Kingdom and found that " *e-cigarette marketing regulations can be improved* " 273
la question « what should government do ? », le rapport « E-cigarette marketing in the UK » répond ce qui suit : « *E-cigarette advertising should be primarily targeted at and appealing to people who smoke. It should never target people who have never smoked, especially young people. Regulation on e-cigarette advertising should limit people who neither smoke nor vape, and youth especially, from noticing and being attracted to e-cigarette advertising. It should also allow adverts to effectively target people who smoke to encourage them to quit. Our findings suggest that despite relatively good compliance with the regulations, the current rules may not be sufficiently achieving these aims* ». L'étude constate que les fumeurs ne are not sufficiently well informed (" *We need better targeting to adults who smoke to encourages the switch to vaping and support smoking cessation*" is in a box on p. 8). At the same time, the report notes that young people are now noticing e-cigarette marketing more through authorized channels in the UK than they are noticing e-cigarette marketing on websites and media social issues, which represents a challenge in terms of regulations, and that the marketing of e-cigarettes is « *appealing is to more than a third of young people* » et que « *young people increasingly believe e-cigarette marketing is targeted at people who don't smoke* ».

Cancer Research UK's recommendations to the UK authorities based on this report are as follows:

- « *Ensure e-cigarette adverts appeal to the intended target audience and are addressing barriers to switching* »
- "Reduce appeal to youth" ("More research should be commissioned to better understand what regulations would be most effective at limiting the appeal of e cigarette adverts to youth. Further guidance on the use of imagery and the depiction of people in e-cigarette adverts is also needed.")
- "Improve consumer protection messages" ("E-cigarette adverts should be required to specify that e-cigarettes should only be used by current or former smokers as an alternative to smoking.")
- "Better monitor e-cigarette advertising to promote compliance – especially on social media».

In our country, advertising for e-cigarettes is not allowed, but when it comes to possible other forms of marketing aimed at young people (packaging, appearance, channels such as social media, etc.), vigilance is required.

²⁷² See D. Arnott, Director of ASH-UK speaking at the 2019 UK E-Cigarette Summit: <https://www.e-cigarette-summit.co.uk/seminar/strengths-and-weaknesses-of-the-tpd-and-what-comes-next/>. Specific examples of problematic marketing use (based on flavor references) were given during this lecture. It would be interesting to know what that is in the UK and how and to what extent our own market is affected by marketing to children and young people. <https://www.stir.ac.uk/research/hub/publication/1713630>

²⁷³

IX ANNEX 2 - Proposed additional health warnings and messages on package inserts

The appendices are provided for information purposes and their content does not in any way engage the responsibility of the CSS.

Proposals for additional health warnings²⁷⁴

The warnings should be easily understood by less educated smokers. There are organizations that can provide expert advice on this to ensure the suggested warnings are understood²⁷⁵. In the UK, research is already underway on the wording of additional health warnings²⁷⁶.

- Never use oil-based e-liquids, it's dangerous.
- Alternating between vaping and smoking offers little or no benefit to health. health, so quit smoking.
- Do you need help to quit smoking or vaping? Tabakstop.be or 0800 111 00 or tabakoloog.be
- When you vape, no tobacco is burned and therefore fewer harmful substances are released compared to smoking tobacco. Vaping is therefore less harmful health than smoking.
- Do not buy e-cigarettes on the Internet. It is illegal and unreliable.
- The e-cigarette is much less harmful than tobacco, but it is also not 100% safe or healthy. It is best to use them only to quit smoking.

- The long term effects of using this product are not known.
- Do not throw this product in the trash, but take it to the container park.

Text proposals for inserts (for cigarettes, rolling tobacco, cigarillos, etc. and e-cigarettes)

²⁷⁴

Insert texts should be easily understood by less educated smokers. There are organizations that can provide expert advice on this so that the proposed texts are well understood. Ideally, the texts should be supplemented with pictograms, which increases readability.

- **Stop smoking tobacco completely.** Avoid dual use (= smoking and vape at a time), because as a smoker you will hardly get any health benefit from it. • The use of nicotine alone (vaping) is less harmful for adults than smoking. In the case of smoking, nicotine is also used, but with

²⁷⁴ These proposed health warnings should be reformulated to meet the needs of light smokers. qualified (this should be checked with organizations specializing in language suitable for these groups).

²⁷⁵ See in particular (in Flanders): <https://www.wablieft.be/nl/tekstadvies>, <https://www.duidelijketaal.be/>, <https://www.weliswaar.be/10-redenen-om-laagdrempelig-te-communiceren>, <https://schrijfassistent.be/splash.php>.

²⁷⁶ <https://harmreductionjournal.biomedcentral.com/articles/10.1186/s12954-021-00540-1>

the deadly and carcinogenic substances present in tobacco and tobacco smoke. **Vaping is therefore preferable to continuing to smoke.** But it's also best to quit vaping because we don't know what the long-term effects will be. We don't know what the effect of the ingredients/flavors is when inhaled. Just because the flavors have been deemed safe as a food flavoring does not mean they are safe for pulmonary ingestion (i.e. inhalation via vaping).

- **Stopping vaping** also requires an effort (because the addiction to nicotine remains) but a vaper can be guided in this process by a tobacco specialist. If quitting vaping is not (yet) possible, it is better to continue vaping than to start smoking tobacco again. An e-cigarette with nicotine can be combined with behavioral support (tabacologist or Tabakstop) or with other nicotine substitutes (for example patches with

nicotine) when quitting smoking. However, for smokers who are reluctant to follow a smoking cessation consultation, try to quit smoking (by themselves) with the help of an e-cigarette is a much better option than continuing to smoke.

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XI Composition of the working group

The composition of the Bureau and the College as well as the list of experts appointed by royal decree can be found on the CSS website ([page: About us](#)).

All the experts took part *in the working group in their personal capacity* . Their general declarations of interests as well as those of the members of the Bureau and of the College can be consulted on the CSS website ([page: conflicts of interest](#)).

The following experts participated in the preparation and approval of the opinion. The working group was chaired by **Luc PUSSEMIER and Kristiaan NACKAERTS** and the scientific secretariat was provided by Muriel BALTES.

BAEYENS Frank	Psychology	KULeuven
BARHDADI Sophia	Chemistry, additives, contaminants	Sciensano
BIZEL Pierre	Smoking prevention, lifestyle Observatory of	Health, Hainaut
BODO Martial	Psychology, tabacology	The table
DE DUVE Martin	Public health, addiction, prevention, health promotion	Health Universe
DECONINCK Eric	Chemistry, additives, contaminants	Sciensano
DOM Geert	Psychiatry	UA, CAPRI
GABRIELS Suzanne	Psychology, tobacco and tobacco prevention	foundation against cancer
HENDRICKX Stefaan	Tobacco prevention, tobacco science, health promotion, health inequalities	Flemish Institute Healthy To live
LARDON Philip	Oncology, physiology	UAntwerp
Stephane LECLERCQ	Public health, risk reduction	Fedito BXL
MATTHYS Frieda	Psychiatry, behavioral medicine UZ Brussel	
NACKAERTS Kristiaan	Pneumology	KULeuven
PUSSEMIER Luc	Chemistry, additives, contaminants	EX-DOE
WHAT Dirk	Tobacco	foundation against cancer
VAN HAL Guido	Smoking prevention	UAntwerp and Center for Cancer detection
FROM LAREBEKE	Toxicology, carcinogenesis and prevention	ex-UGent
ARSCHODT Nicolas	cancer primary	

The following administrations and/or ministerial cabinets were heard:

Mathieu Capouet	Tobacco policy	SPF APF- Tobacco cell
REMUE Eline	Electronic cigarette, notification tobacco products	SPF APF- Tobacco cell

The translation was done externally.

About the Superior Health Council (CSS)

The Superior Health Council is a federal advisory body whose secretariat is provided by the Federal Public Health, Food Chain Safety and Environment Service. It was founded in 1849 and provides scientific advice relating to public health to the Ministers of Public Health and the Environment, their administrations and a few agencies.

These opinions are issued on request or on their own initiative. The CSS endeavors to indicate to political decision-makers the path to follow in terms of public health on the basis of the most recent scientific knowledge.

In addition to its internal secretariat made up of around 25 employees, the Council calls on a large network of more than 500 experts (university professors, employees of scientific institutions, actors in the field, etc.), among whom 300 are appointed by royal decree as a Council expert. Experts meet in multidisciplinary working groups to draft opinions.

As an official body, the Superior Health Council considers it essential to guarantee the neutrality and impartiality of the scientific opinions it delivers. To this end, it has adopted a structure, rules and procedures to respond effectively to these needs at each stage of the advice process. The key stages in this matter are the preliminary analysis of the request, the appointment of experts within the working groups, the application of a system for managing potential conflicts of interest (based on declarations of interest, an examination of possible conflicts, and an Ethics Committee) and the final validation of the opinions by the College (decision-making body of the CSS, made up of 30 members from the *pool* of appointed experts). This coherent whole must allow the issuing of opinions based on the most cutting-edge scientific expertise available and this, with the greatest possible impartiality.

After validation by the College, the opinions are sent to the applicant and to the Minister of Public Health and are made public on the website (www.hgr-css.be). A number of them are also communicated to the press and to the relevant target groups (professionals from the healthcare sector, universities, politicians, consumer associations, etc.).

If you wish to stay informed of the activities and publications of the CSS, you can send an email to the following address: info.hgr-css@health.belgium.be.

www.css-hgr.be



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