# Impact Assessment – Unlicensed Nicotine Containing Products

This impact assessment is intended to support the UK's position in EU negotiations on the regulation of Nicotine Containing Products, which is currently being considered along with changes to the Tobacco Products Directive.

## *Key Conclusions*

- Problems exist with the manufactured quality of e-cigarettes currently on the UK market.
- There are uncertainties about the long term safety of using currently marketed e-cigarettes. These concerns are not addressed by the regulatory framework in which these products currently sit.
- However, as yet there is an absence of scientific evidence that shows long term harm to health is occurring in reality because of product safety.
- There are plausible theories that link the use of currently marketed e-cigarettes in smokers' quit attempts to lost opportunities for successful smoking cessation.
- However, as yet there is no clinical evidence that suggests currently marketed e-cigarettes are less effective as aids to smoking cessation than licensed Nicotine Replacement Therapies or, potentially, e-cigarettes that might become licensed under medicines regulations.
- Our estimated annualised costs to a single UK e-cigarette importer for complying with medicines regulation range from £87,000 to £266,000.
- This range could increase by several tens of thousands of pounds if additional animal and human trials are required because MHRA assessors have substantial concerns about the safety of particular e-cigarette substances or delivery mechanisms.
- The value of the health gains associated with a single successful quit attempt is very substantial – The Department of Health estimates it to be £74,000.
- The orders of magnitude of our estimated compliance costs suggests that a policy of licensing e-cigarettes would have to create very few additional successful quit attempts for the policy's benefits to justify its costs.
- However, if such a policy restricted the accessibility of e-cigarettes on the UK market, the number of successful quit attempts could decline, in which case the policy would be a costly failure unless there were substantial countervailing benefits from improved long term safety.
- The concept of accessibility extends to pricing. There are concerns that licensing e-cigarettes could deprive future consumers of price reductions that would otherwise have occurred without licensing.
- These latter points underline the importance of choosing and designing policy interventions that minimise reductions in e-cigarette accessibility.

## *Problems under consideration*

### *Definition of Nicotine Containing Products (NCPs)*

1. For the purposes of this IA, NCPs include products that contain levels of nicotine that have a measureable effect on the body. Tobacco products are excluded because they are subject to separate, specific legislation.

### *Current Regulation of NCPs*

2. The specific NCPs that are of concern are those that are not currently licensed under medicines regulations. By far the most common types of these products are e-cigarettes - a heterogeneous collection of electrical devices that resemble cigarettes and produce a vapour that is inhaled. In most cases the vapour is produced by heating a volatile liquid, using a small internal battery for power. The liquid[1] – and hence the vapour - may contain flavouring and/or nicotine, among other substances. We are only interested in e-cigarettes that contain nicotine, and we have adopted the term Electronic Nicotine Delivery Systems (ENDS) to describe these particular products.

3. There are also a range of other products that fall into the relevant unlicensed NCP sub-category, including hand gels, lip balms, and lollipops. The collective term that we have used in this IA for all the products of concern is Unlicensed Nicotine Containing Products (UNCPs).

4. UNCPs that make no medicinal claim are currently regulated under the "catch-all" of the General Product Safety Regulations and the Chemicals (Hazard Information and Packaging for Supply) Regulations 2002 (CHIP). (There are a number of additional legislative requirements relating to the electrical safety.) These Regulations allow products to be removed from the market in response to safety concerns, including misleading labelling. But a product is not likely to be considered unsafe by virtue of the inherent risk associated with use of the product so it is unlikely that risks associated with nicotine could be taken into account.

5. Currently, any NCP that makes a medicinal claim is considered by the Medicines and Healthcare products Regulatory Agency (MHRA) to be a medicinal product. NCP suppliers who do not make medicinal claims for their products do not currently need to comply with medicines regulation.

6. The forms of NCP that are licensed under medicines regulation (called Nicotine Replacement Therapies – NRTs – such as gums, patches and inhalator) have specific medical uses for relieving craving and nicotine withdrawal symptoms associated with tobacco dependence. NRTs are medically indicated to aid smokers wishing to quit or reduce consumption prior

[1] Analyses of electronic cigarette cartridge contents and vapour demonstrate that the primary components are propylene glycol, glycerine and nicotine. Many other additives such as flavours and contaminants have been detected.

to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them.

***Supply of UNCPs***

7. We believe that there are several hundred companies offering e-cigarettes for sale in the UK, mostly operating via websites, although the number of retail outlets is increasing and now includes major supermarkets. The majority of companies source from China (accounting for 70% of electronic cigarettes manufactured in the world) and other parts of Asia. One company in the UK is known to be developing UK manufacturing capability, and there is growing interest amongst other companies. The WHO predicts that by 2050, the NCP market will be equivalent in value to the tobacco products market.

***Use of UNCPs***

8. There is currently no strong evidence to suggest that NCPs are used by non-smokers or that use of NCPs acts as a gateway to smoking[2].

9. Use of UNCPs among smokers can be categorised according the intention behind the use:

- Category 1. To reduce cravings and withdrawal symptoms as part of smoking quit strategies
- Category 2. As a direct substitute for smoked tobacco products in order to reduce harm to health. In contrast to Category 1 use, these smokers have no specific intention of overcoming their nicotine addiction
- Category 3. To relieve nicotine cravings in public and work environments where smoking is not permitted.

10. Available data suggest that most smokers who use UNCPs (between 83% and 92%) fall into categories 1 and 2 [3].

11. Current evidence on the size of the NCP market in the UK suggests more than 7% of all UK smokers (around 700,000 people) are now regularly using electronic cigarettes in some form[4]. It is estimated that electronic cigarettes are now being used more than any single form of nicotine replacement therapy product.

12. There is good evidence that use of NRTs increases the chances of successful quit attempts[5]. Although scientific evidence on the precise processes that lead to this increased quit rate under NRTs is not available, it seems plausible to speculate that use of NRTs to effect a controlled and

[2] Refer to section 3 of the CHM EWG paper "Current use of electronic cigarettes"
[3] Refer to section 3 of the CHM EWG paper "Current use of electronic cigarettes"
[4] See footnote 4
[5] For instance, a Cochrane Review of 132 trials found that NRT increased the chances of stopping smoking by 50 to 70% compared with placebo or non-NRT groups. "Nicotine Replacement Therapy for Smoking Cessation (Review)" The Cochrane Library 2008, Issue 3.

gradual reduction in nicotine consumption is important. UNCPs such as ENDS that allow smokers to reduce their nicotine consumption in this controlled way may therefore be useful aids to smoking cessation.

13. Consuming these UNCPs tells consumers nothing about long term safety and possible long-latency health effects of using these products. Without assistance from trusted third party information providers, consumers are therefore left unsure whether the benefits of using UNCPs outweigh the risks.

14. The UK market for unlicensed NCPs is expected to be worth around £100m in 2014. By comparison, the existing licensed NRT market was worth £110m in 2012.

15. ENDS use seems to be increasing quickly. In a large GB population survey, in 2010, 9% of smokers reported ever having used electronic cigarettes. By 2012 this had risen to 22%.

***Concerns about UNCPs***

16. Concerns about UNCPs and ENDSs in particular fall into six categories:

- Problems with manufacturing quality and standards
- The existence of contaminants in the solutions that contain nicotine
- Uncertainty about the long term health effects of the substances used to create the inhaled ENDS vapour .
- Barriers to UNCP trade across the European single market.
- UNCPs marketing and product characteristics (eg introduction of flavours) may attract young people.
- ENDS could be marketed in a way that ultimately promotes smoking.

17. Evidence on the manufacturing quality and standards of ENDS suggests that there are deficiencies[6], giving rise, in particular, to concerns about the inconsistencies in the strength of nicotine delivery and the existence of contaminants.

18. Laboratory analysis indicates that the strength of nicotine delivery from ENDS is not standardised across brands, can be at variance to claims made on labelling, and can even be inconsistent between refill cartridges for the same brand. Almost all of the ENDS so far tested have shown these problems[7].

19. Further laboratory analysis has shown detectable levels of contaminants, including known carcinogens and toxic chemicals[8].

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[6] These are summarised in the CHM EWG paper “Quality, safety and efficacy of unlicensed NCPs” paper.

[7] In the UK, product sampling was based on share of the market, and hence the sampling crudely reflected the prevalence of these problems in the UK.

[8] These are summarised in the CHM EWG paper “Quality, safety and efficacy of unlicensed NCPs” paper.

Contaminants of various types were found in all cases where they were looked for, and were not stated on the product labelling. Evidence suggests that the contaminants are mainly present because of poor manufacturing practices[9].

20. The concern over the long term health effects of ENDS vapour is one of uncertainty. We do not know whether inhaling the labelled substances is safe in the long term. Furthermore, some of the labelled substances undergo chemical change as a result of the heating process, and the safety of these derived chemicals is uncertain.

21. The problem of free movement of ENDS within the European single market exists because approximately half of the member states regulate ENDSs under medicines regulations, while several others rely on consumer protection regulation. We have no information on the costs caused by this problem[10].

22. The 2012 EU IA that covers proposals for UNCP regulation[11] suggests that UNCP marketing and product characteristics may attract young people. However, although this may be true, the IA does not present any evidence on the extent of the problem or, more importantly, the harm that it may be doing to young people.

23. The concern that ENDS may be promoted in a way that ultimately encourages smoking is so far mostly hypothetical.

***Consumers and UNCPs***

24. The usual starting point for consumer policy is that, unless governments have overwhelming safety concerns, consumers should be free to decide for themselves whether the benefits from consuming a product outweigh the costs and risks. However, a problem occurs if consumers do not have sufficient information to make sensible judgements.

25. The problem gets worse if consumers perceive that suppliers are deliberately withholding relevant information about the quality, effectiveness and safety of the products. This can lead to mistrust and a market that does not reward suppliers who provide higher quality products. This situation is most likely to occur with "credence goods"[12] such as pharmaceuticals, where,

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[9] Sampling revealed no correlation between contaminants and nicotine levels, suggesting that the presence of contaminants is not an inevitable by-product of the techniques used to extract or produce nicotine. Some contaminants are related to the use of impure nicotine, propylene glycol and glycerine solutions. Other constituents are probably related to flavours and others appear related to plasticizers and other leachable and/or extractable compounds involved in the packaging and manufacture of the products. Others are related to the battery components. And others to the thermal decomposition of the excipients.

[10] The 2012 EU impact assessment that covers the NCP issue provided no quantitative analysis of the problem.

[11] http://ec.europa.eu/health/tobacco/docs/com_2012_788_ia_en.pdf

[12] Credence goods are products whose beneficial effects are difficult for the consumer to recognise for themselves. This might be because the effects are subtle, can be difficult to

without the intervention of a trusted third party, high quality suppliers find difficulty in convincing potential consumers of the superior quality of their products. The result is usually a dysfunctional market that serves neither high quality suppliers nor consumers well.

26. Applying these ideas to the current situation with UNCPs suggests the following:

- Smokers who use ENDS can lack reliable information and/or reassurance on how well products will meet their needs. The problem may be particularly bad for smokers who use ENDSs (and perhaps other UNCPs) in their quit attempts because precise knowledge of consistency of nicotine dosage may be important in ensuring the controlled reduction in nicotine consumption that may increase the chances of successful smoking cessation.

- All ENDS users lack information and/or reassurance on the long term safety of consuming ENDS. This problem is caused by uncertainty about the long term safety of inhaling ENDS vapour and by manufacturing processes that allow unlabelled contaminants into the products.

- There is some evidence that new producers of higher quality products are looking for ways to differentiate their products from lower quality products already on the market. MHRA is expecting a marketing authorisation application from a new ENDS manufacturer. This development suggests that the current market for unlicensed products does not help producers of higher quality products differentiate their products. However, it is clear that licensing products under medicines regulation already provides a solution for these producers.

- There is also some evidence[13] that consumers are wary of ENDS sold over the internet and, in particular, have concerns about the quality of the products. This is possibly a general problem with perceptions about internet sales rather than a specific problem with perceptions about ENDS.

### *Evidence of harm to consumers*

27. Although there is evidence that informational problems exist, the harm that these problems cause can only be measured in terms of loss of welfare to the people who use the products.

28. While contaminants in ENDS have been identified, and the long term health effects of inhaling ENDS vapour are unknown, so far there is an absence of evidence that shows that these problems create significant harm to health.

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distinguish from other factors such as co-morbidity, or because the effects are only felt over the long term.

[13] http://www.mhra.gov.uk/Publications/Consultations/Medicinesconsultations/MLXs/CON065617

29. There is also uncertainty about the long term effects of nicotine consumption, although it is worth noting that any risk is likely to be very small compared with smoking.

30. There is currently an absence of empirical evidence of non-health harm, such as a loss of consumer welfare from widespread mis-selling of NCPs. However, because the strength of nicotine delivery is not always accurately reported on product labels, it seems reasonable to assume that some products do not meet some consumers' expectations, and therefore these consumers are ultimately dissatisfied with their purchases.

31. A significant harm caused by ENDS may be the creation of missed opportunities for successful smoking cessation. As noted previously, the lack of accurate information on the nicotine dosage of ENDS may hamper smokers' attempts to overcome their nicotine addiction because a controlled reduction in nicotine intake becomes difficult. Note however that there is no direct clinical evidence that links use of ENDS to reduced chances of smoking cessation compared with the use of currently licensed products.

32. The harm caused by ENDS depends on what the individuals attempting to quit would have used in the absence of ENDS. If they would not have used any nicotine containing product, then at worst, ENDS use would have little effect on the chances of successful smoking cessation, and at best would increase the chances. If however, individuals would have used licensed products (NRTs) instead of ENDS, then the picture is unclear – as noted above we have no direct trial evidence that indicates that ENDS are more or less effective than NRTs.

33. Unfortunately, we have no evidence on what aspiring quitters would have used in the absence ENDS.

34. There is one further concern over the effect of poor dosage control in UNCPs. If smokers use poor quality UNCPs and fail in their quit attempts, they may gain the impression that all NCPs (including NRTs) are equally ineffective. This is likely to adversely affect the chances of successful future quit attempts.

35. The costs to individuals of continued smoking are very substantial. In 2010, the Department of Health estimated that each successful quit attempt saves 1.24 life years[14]. The corollary of this is that each unsuccessful attempt *costs* 1.24 life years[15]. The Department's standard value of a life year is

[14] This estimate was produced for the Department's impact assessment of the Prohibition of Display of Tobacco Products at the Point of Sale in England https://www.gov.uk/government/publications/impact-assessment-on-the-prohibition-of-display-of-tobacco-products-at-the-point-of-sale-in-england
The estimate took into account the average age and the sex of people attempting to quit, as well as the chances of successful future quit attempts.

[15] This assumes that an unsuccessful quit attempt in the current period does not influence the probability of successful quit attempts in future periods.

£60,000. The overall value of the lost life years per failed quit attempt is therefore £74,000.

## *Rationale for intervention*

36. The primary rationale for UK government intervention would be to reduce harm to public health, principally by overcoming the safety, efficacy and quality information and reassurance deficiencies that adversely affect consumers. Such information and reassurance are types of public good, which are usually undersupplied by unregulated markets.

37. An additional rationale for intervention at the EU level would be to promote the free movement of UNCPs throughout the EU single market. Only government can act to remove the barriers that currently impede the free movement of UNCPs.

38. A final rationale for intervention would be to preclude the possibility that ENDS are marketed and advertised in ways that attract young people and/or promote smoking.

## *Policy objectives*

39. The overarching aim is to reduce potential harm and costs to current and potential UNCP consumers. We believe that this aim could be supported by achieving the following objectives.

Objective 1. UNCP users have reliable information on the nicotine dosage delivered by UNCPs .

Objective 2. UNCP users have credible reassurance that consumption of UNCPs will not significantly harm their health in the long term.

Objective 3. UNCPs that pose unacceptable health risks to consumers can be denied market access or removed from the market if new safety concerns arise.

Objective 4. Free movement of NCPs within the European single market.

Objective 5. ENDS advertising and product characteristics do not attract young people or promote smoking generally.

The final objective is included to ensure proportionate and targeted policy making:

Objective 6. The benefits of all interventions justify their costs, and that interventions are well targeted at solving the problems indentified in this IA, without creating unjustified burdens on business and consumers, and perverse incentives for smokers.

## *Description and assessment of options*

40. This section describes the options that were included in the EU's Impact Assessment (see footnote 11 for a link to the EU IA). It also qualitatively assesses how well each option would meet the Policy Objectives identified in the previous section.

Option 0 – do nothing

41. This option would continue to rely on existing regulation in each of the member states. In the UK, this would mean continuing to use European and domestic consumer protection provisions.

42. How well would this option meet our objectives?

Objective 1. It is possible that over time, standards of nicotine dosage could develop within the UNCP industry without government intervention. However, standards have yet to emerge in the seven years that ENDSs have been available. It is also a moot point over how consistently industry would apply standards if they emerged.

Objective 2. It seems unlikely that, unprompted, the industry would gather sufficient safety data on long term health effects to be able to provide credible reassurance to consumers. However it seems likely that in an increasingly competitive market, higher standards of manufacturing quality will emerge and thereby address some of the long term safety concerns.

Objective 3. This objective would also not be met by the "do nothing" option. Given our conclusion that, unprompted, the UNCP industry would be unlikely to gather sufficient safety data, there would be little basis on which to deny or remove market access for UNCPs that pose long term health hazards.

Objective 4. Freedom of movement in the European single market would not be achieved through the "do nothing" option

Objective 5. The "do nothing" option would not achieve the objective of controlling product characteristics and advertising.

Objective 6. Doing nothing implies no incremental costs and benefits, and hence this objective becomes irrelevant.

Option 1 – Subject UNCPs to labelling and ingredients requirements under the Tobacco Products Directive

43. Under this option, UNCPs placed on the market would be subject to:

- Adapted health warnings (e.g. that the product contains nicotine, and has not been tested for safety, quality or efficacy),

- Ingredients reporting
- A prohibition on marketing UNCPs that have characterising flavours (menthol and other flavouring designed to enhance the enjoyment of inhalation).

Objective 1. In line with our reasoning under the "do nothing" option, we believe that Option 1 would not meet this objective

Objective 2. Although Option 1 would effectively introduce a "buyer beware" warning, it would not provide consumers with reassurance that their long term health would not be seriously affected by consuming UNCPs.

Objective 3. Option 1 would not provide any additional data on long term health and hence would not improve the situation with regard to denying market access to unsafe UNCPs.

Objective 4. Option 1 would not meet the objective of free movement of UNCPs within the European single market.

Objective 5. Option 1 could presumably be adapted to fully meet concerns about young people and potential smokers.

Objective 6. Although the cost of this option to UNCP suppliers would be minimal, it seems the benefits would also be minimal.

<u>Option 2 – Establish a new authorisation scheme for UNCPs under the Tobacco Products Directive</u>

44. Under this option only UNCPs that have been authorised under a new authorisation procedure for assessing risks and benefits would be allowed to be placed on the market. Otherwise, placing a UNCP on the market would be prohibited. The authorisation procedure would also cover labelling and additives control.

Objective 1. It is not clear that Option 2, as envisaged by the EU, would ensure that manufacturing and industry standards would deliver reliable information on nicotine dosage to UNCP consumers. However, such a requirement could presumably be designed into option 2 to meet this objective.

Objective 2. Option 2 would provide consumers with reassurance over long term health implications of consuming UNCPs.

Objective 3. Although Option 2 would provide the information required to deny market access to unsafe UNCPs, it is not clear that it would deliver post marketing safety vigilance that could trigger the removal of unsafe UNCP from the market.

Objective 4. Unless EEA member states that currently regulate all NCPs under medicines regulation were to drop these requirements for ENDSs and other currently unlicensed NCPs, Option 2 would not meet the objective of free movement of UNCPs within the European single market.

Objective 5. Option 2 could presumably be easily adapted to fully meet concerns about young people and potential smokers.

Objective 6. The balance of costs and benefits for Option 2 is unclear. There may be scope for designing a targeted scheme that meets most of the policy objectives without imposing unjustified costs for business. However, the scheme would create costs for governments in establishing and operating a new regulatory system.

Option 3 - Subject NCPs over a certain nicotine threshold to the medicinal products' legislation and the remaining NCPs to labelling requirements

45. NCPs with a nicotine level over a certain threshold would only be allowed to be placed on the market if they have been authorised as medicinal products on the basis of their quality, safety and efficacy, and with a positive risk/benefit balance under medicinal products legislation. NCPs with nicotine levels below this threshold will be subject to an adapted health warning. The nicotine threshold could be established by considering the nicotine content of medicinal products (NRTs) for smoking cessation that have already received a market authorisation under the medicinal products' legislation. It is not, however, clear if this approach is scientifically or legally justified, and how the level is set needs further exploration.

Objective 1 – Consumers would have accurate information on nicotine dosage delivered by the now licensed NCPs and how effectively and quickly the nicotine is likely to be absorbed.

Objective 2 – Consumers would have reassurance about long term health risks but only for those products that are above the nicotine threshold. As noted in footnote 3, laboratory analysis of products has so far revealed no correlation between nicotine and contaminant levels. Furthermore, we believe the substances used to create the ENDS vapour will not be any different for products above and below the threshold. There is therefore no reason to believe that products below the threshold might not pose long term health hazards to consumers.

Objective 3 – Option 3 would provide effective mechanisms for identifying unsafe products and thereby denying or removing market access for products above the threshold. Potentially unsafe products below the threshold would continue to be marketed.

Objective 4. Option 3 would achieve freedom of movement within the European single market for products above the threshold. The situation for products below the threshold would be unclear.

Objective 5. Option 3 would fully meet concerns about young people and potential smokers.

Objective 6. Option 3 would create substantial costs for EU and UK businesses. A rough analysis of these costs is provided in the next section. Judging whether the benefits to consumers would justify the costs is currently very difficult because of our poor state of knowledge of the harms and other costs that UNCPs and ENDSs in particular currently impose on consumers.

46. Some media attention has recently been paid to the possibility that bringing ENDSs into the scope of medicines regulation might increase the price of these products to the extent that consumers might switch back to smoking in order to relieve their nicotine cravings. By analogy with what has happened in the market for Nicotine Replacement Therapies, this argument seems to be flawed. Anecdotal evidence suggests that NRTs are priced at a level that is equivalent to the "price" of smoking cigarettes. Although this might indicate that competition in this sector is not strong (otherwise you might expect prices to be lower than the equivalent price of smoking), it does indicate that tobacco pricing places a significant upper bound constraint on NRT pricing, even though NRTs are subject to substantial costs of licensing. There seems to be no reason to believe that the same would not be true of licensed ENDSs.

47. There is however another concern about ENDS pricing and the effects of bringing these products into scope of medicines regulations. The market for unlicensed ENDS seems to be maturing, with greater availability and competition between suppliers. In time, we would expect prices to drop below current levels (which anecdotal evidence suggests are equivalent to the price of smoking), making using ENDS yet more attractive than smoking. Licensing ENDS is likely to erect a barrier to entry into the market, thus limiting the competition and innovation that would otherwise have driven prices downwards. By itself this would represent a reduction in consumer welfare but if additionally it means that fewer smokers switch to ENDS than otherwise have been the case, then it is possible that the health losses would be significant.

<u>Option 4 - Subject all NCP to the medicinal products' legislation</u>

48. Only NCP that are authorised as medicinal products on the basis of their quality, safety and efficacy, and with a positive risk/benefit balance would be allowed to be placed on the market. Otherwise, the placing on the market of NCP would be prohibited.

49. Option 4 would meet the policy objectives in the same way as option 3, although it would additionally remove uncertainty about harm to public healthy and barriers to trade that would remain under Option 3 for NCPs below the nicotine threshold. Bringing more products into scope would mean that Option 4 would have higher regulatory costs compared with Option 3.

## *Costs of bringing currently unlicensed NCPs into scope of medicinal products regulation*

50. The greatest uncertainty in estimating the UK costs of bringing UNCPs within scope of medicines regulation is the number of UK firms that would apply for marketing authorisations (MAs). The number could conceivably range from zero (in which case all UK supply would come from MA holders in other EU member states) to several tens of firms.

51. To abstract from this uncertainty and provide an illustration of potential costs, we have estimated the direct costs that would be borne by a single UK firm wishing to import an ENDS product from a non-EU source. Such an importer would have to acquire and maintain a Marketing Authorisation (MA), a Manufacturer's/Importer's Authorisation (MIA), and as part of the MA, satisfy requirements for on-going monitoring of product safety and effectiveness once the product is on the market (pharmacovigilance). Distributing ENDS in the UK would also require a Wholesale Dealer Licence.

| | One-off | Annual Recurring | Present Value | Annualised |
|---|---|---|---|---|
| Marketing Authorisation costs | | | | |
| Lower estimate | £215,000 | £1,000 | £222,000 | £26,000 |
| Upper estimate | £350,000 | £1,000 | £357,000 | £41,000 |
| Manufacturer's Import Authorisation costs | | | | |
| Lower estimate | £23,000 | £39,000 | £322,000 | £37,000 |
| Upper estimate | £23,000 | £190,000 | £1,467,000 | £170,000 |
| Wholesale Dealer Licence costs | | | | |
| Lower estimate | £4,000 | £9,000 | £70,000 | £8,000 |
| Upper estimate | £7,000 | £43,000 | £331,000 | £38,000 |
| Pharmacovigilance costs | | | | |
| Estimate | £10,000 | £16,000 | £150,000 | £17,000 |
| **TOTAL** | | | | |
| **Lower estimate** | **£252,000** | **£65,000** | **£747,000** | **£87,000** |
| **Upper estimate** | **£390,000** | **£249,000** | **£2,288,000** | **£266,000** |

52. Our estimates are presented as broad ranges to reflect our considerable uncertainty over the individual circumstances of any particular firm (for example, size of operation and existing MA experience) and over the cost of the pre-clinical trials that would be needed to support an MA application (this information is often treated as confidential by MA holders). The evidence and assumptions behind our estimates are summarised in the Annex.

53. Note that we have not included the costs of achieving Good Manufacturing Practice (GMP). Currently all manufacturing is conducted outside the EU and we have assumed that in the first instance, the foreign manufacturers would bear the costs of achieving GMP.

54. We have also assumed that any production that might be established within the EU in the future would bear similar costs of achieving relevant

manufacturing standards regardless of whether the UNCPs come into the scope of medicines regulations or not[16].

55. It is likely that foreign manufacturers, EU MA holders, and all other participants in the supply chain would seek to pass their incremental costs onto their buyers, and ultimately to consumers. The extent to which UK consumers would bear the incremental costs is a moot point. Pricing of NCPs seems to be constrained at the upper bound by the pricing of tobacco products, and hence to a considerable extent, we would not expect NCP consumers to suffer from substantial price increases after policy implementation. Nevertheless, bringing currently unlicensed NCPs into scope of medicines regulation is likely to introduce considerable barriers to market entry, which could limit competition and hence deprive consumers of price reductions that would otherwise occur under the "do nothing" option.

56. Although in the long term we would not expect owners of the capital invested in the manufacture and supply of NCPs to suffer losses, there would likely be short term transitional losses for some stakeholders, not least current importers of UNCPs who would be unwilling to invest in gaining the necessary authorisations and licenses. However, it seems likely that these stakeholders would be able to redeploy their capital and expertise quickly to other activities, and hence their losses would be limited.

The possibility of additional MA costs

57. Our MA cost estimates assume that applicants would not have to conduct expensive animal and post-market-authorisation human clinical trials to satisfy MHRA that the risks to health from long term inhalation of ENDS vapour are acceptable. However, this may not be the case and MHRA assessors might ask for these additional trials. The one-off costs of conducting these additional trials would probably run into several hundreds of thousands of pounds.

Putting the costs into context

58. From a UK societal perspective, our estimated costs of compliance lack meaning unless they can be put into the context of the possible benefits the policy might bring. The lack of direct evidence of the safety and efficacy of licensed versus non-licensed NCPs (discussed in previous sections of this IA) means that we can not estimate these benefits directly. However, we can calculate the number of additional successful smoking quit attempts a year that the proposed policy intervention would need to generate in order for the benefits to justify the costs. On the costs side, we have used our estimated annualised[17] cost range of £87,000 to £266,000. On the benefits side, we have used the estimated value of the health benefits gained from a successful quit attempt. We reported this figure as £74,000 in paragraph 35.

[16] The robustness of this assumption will need to be examined in future versions of this IA
[17] Annualisation is effectively a way of averaging one-off and recurring costs across a number of years – ten in this case

59. The calculation reveals that very few additional successful quit attempts would be needed in order to justify the costs borne by a single UK MA holder. Given the uncertainty of our estimates, we think that the precise result (between 1 and 3 additional successful quit attempts a year) is much less important than the orders of magnitude of our estimates. These suggest that the policy would only need to be marginally successful (generate very few additional successful quit attempts) for it to be justified.

60. However the reverse might also be true. The policy might only need to be marginally unsuccessful for it to be considered a costly failure. If the design and implementation of the policy has the effect of reducing access to NCPs (particularly ENDS) then it is possible that the number of successful quit attempts could decline. If there were no substantial countervailing health gains from improvements in safety, the policy's overall impact could be highly negative.

## *Annex. Costs of Compliance*

This annex gives the assumptions and evidence that we have used to estimate the costs that one UK ENDS importing firm would incur if UNCPs were to come into scope of medicines regulation. At this early stage there is considerable uncertainty about exact costs, and hence the contribution of this costing exercise is to establish the relevant orders of magnitude. Stakeholders should therefore not rely on these cost estimates for planning purposes.

### *Marketing Authorisation costs*

One-off costs:

- Preparing dossier - £30,000 (MHRA estimate)
- Pharmaceutical development studies for product quality - £10,000 to £50,000 (MHRA estimate)
- Batch manufacture (pilot scale) and stability studies - £10,000 to £50,000 (MHRA estimate)
- Quality/non-clinical studies (genotoxicity studies of impurities , analysis of vapour constituents, extractables and leachables) - £46,000 to £90,000 (Industry estimate – excludes phys chem tests)
- In-vivo pharmacokinetic studies and/or supporting efficacy studies - £90,000 to £130,000 (Industry estimate)
- MHRA fee for abridged complex application - £28,780

Recurring costs:

- Annual periodic fee - £452
- Annual GSL periodic fee - £452
- Variation fees – not estimated (likely to be of the same order of magnitude as other fees)

### *Manufacturer/Import Authorisation*

One-off costs:

- Costs of preparing application - £10,000 (MHRA estimate)
- MHRA fee - £3,027
- Establishing testing facilities – £10,000 (MHRA estimate)

Recurring costs:

- Re-testing products after import
    - Number of batches per year – 6 to 24 (MHRA assumption)
    - Cost per batch - £1,000 to £3,000 (MHRA estimate)
- Inspection of manufacturers site
    - MHRA cost per day - £2,500
    - Number of days – 5 (MHRA estimate)
    - Travel and accommodation - £6,000 (MHRA estimate)
    - Frequency – every two years (MHRA assumption)

- Inspection of UK site
    - MHRA fees - £3,000 (MHRA estimate)
    - Firm's hosting staff costs - £6,000 (MHRA estimate)
    - Frequency – every two years (MHRA assumption)
- Qualified person
    - Full time salary - £60,000 to £80,000 (MHRA estimate)
    - Non salary staff costs – 30% (MHRA estimate)
    - Full time equivalent – 25% to 100% (MHRA assumption)

***Pharmacovigilance***

One-off costs:

- Service provider to establish PhV systems - £9,800 (Industry estimate)

Recurring costs:

- Annual service provider costs - £12,900 (Industry estimate)
- Inspection costs
    - MHRA fees - £5,000 (MHRA estimate)
    - Inspection hosting costs - £5,000 (MHRA estimate)
    - Frequency – every 3 years (MHRA assumption)

***Wholesale dealing***

One-off costs:

- Application for Wholesale Dealer's Licence
    - Application fee - £1,754
    - Initial inspection fee - £1,882
    - Internal staff costs for application - £48 (MHRA estimate)
    - Inspection hosting costs - £242 (MHRA estimate)
- Temperature monitoring equipment - £100 to £3,000

Recurring costs

- Subsequent inspections
    - MHRA fee - £1,882
    - Inspection hosting costs - £242 (MHRA estimate)
    - Frequency – every 3.5 years
- Variations – not estimated (likely to be significantly less than £1,000 a year)
- Compliance with Good Distribution Practice
    - Responsible person - £7,000 to £39,000 per year (MHRA estimate)
    - Other staff training - £363 to £847 (MHRA estimate)
    - Temperature mapping - £200 to £3,000 every two years