

# Science and Technology Committee

## Oral evidence: [E-cigarettes](#), HC 505

Tuesday 27 February 2018

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[Watch the meeting](#)

Members present: Stephen Metcalfe (in the Chair); Bill Grant; Darren Jones; Damien Moore; Martin Whitfield.

Questions 133 - 216

### Witnesses

**I:** Dr Ian Jones, Vice-President, Reduced-Risk Products, Japan Tobacco International; Dr Chris Proctor, Chief Scientific Officer, British American Tobacco; Dr Moira Gilchrist, Vice-President, Scientific and Public Communications, Philip Morris Limited; and Dr Grant O'Connell, Regulatory and Scientific Affairs, Fontem Ventures.

**II:** Professor David Harrison, Chair of the UK Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC); and Dr Lynne Dawkins, Associate Professor, Centre for Addictive Behaviours Research, London South Bank University.

Written evidence from witnesses:

- [Japan Tobacco International](#)
- [British American Tobacco](#)
- [Philip Morris Limited](#)
- [Fontem Ventures](#)
- [Centre for Addictive Behaviours Research, London South Bank University](#)



## Examination of witnesses

Witnesses: Dr Ian Jones, Dr Chris Proctor, Dr Moira Gilchrist and Dr Grant O'Connell.

Q133 **Chair:** Good morning; welcome. Thank you for joining us for this evidence session on e-cigarettes and alternative smoking products. For the record, will you introduce yourselves and tell us which organisations you represent this morning?

**Dr Gilchrist:** I am Dr Moira Gilchrist, vice-president of scientific and public communications at Philip Morris International.

**Dr Jones:** Good morning. My name is Dr Ian Jones. I am vice-president of reduced-risk products science at Japan Tobacco International. Before that, I was an anatomical neuropharmacologist at the University of Bath.

**Dr Proctor:** I am Chris Proctor, chief scientific officer at British American Tobacco.

**Dr O'Connell:** Good morning. I am Dr Grant O'Connell, vice-president of corporate affairs at Fontem Ventures, a subsidiary of Imperial Brands.

Q134 **Chair:** We are looking at e-cigarettes and heat-not-burn. I would like to focus first on e-cigarettes. Will you each tell us briefly what research your companies have undertaken on the health impacts of e-cigarettes and what your findings have been?

**Dr Gilchrist:** We have been working quite hard on a range of different alternative smoke-free products within our portfolio. We have been looking initially at some of the e-cigarette science around the toxicology of the carrier agents used in the most common electronic cigarette products—propylene glycol, vegetable glycerine and nicotine—to understand how that may affect the toxicology of e-cigarettes in general.

That has been our focus to start with. For our new product, which is on the market currently here in the United Kingdom, we are going through a very full assessment programme to understand its health effects relative to combustible cigarettes. We are looking not just at chemistry but at toxicology and systems toxicology. Ultimately, we will do clinical studies. We are not quite there yet, but that is what we are working on for electronic cigarettes.

**Dr Jones:** For us, it is very similar. We have a mixture of what we call the fundamental science—looking at, for example, the effect of different coil materials on the vapour chemistry and different propylene glycol-glycerol ratios—and assessments of products that we have on the market, such as our Logic range of products, for which we conduct chemical and in vitro toxicological tests. At the moment, we are conducting short-term clinical tests on those products in the USA.



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**Dr Proctor:** We have done a lot on e-cigarettes. In 2015<sup>1</sup>, we were the first of the tobacco companies to enter the e-cigarette market, with Vype. Since that time, we have been doing chemical, toxicological and clinical studies on Vype and our other e-cigarettes.

The research is very similar to that which Public Health England reviewed. You find far fewer toxicants in the emissions from e-cigarettes, and the toxicological impact of those emissions is much lower than with cigarette smoking. We are about to start a one-year-long clinical study, which will include an e-cigarette, that will look at both biomarkers of exposure to toxicants and biological effect markers, to see what the longer-term risks may be.

**Dr O'Connell:** At Fontem Ventures, we manufacture and market the vaping brand blu. We take a systematic approach to the science around our products. If we look at the aerosol chemistry of the blu portfolio, we see that it has a very simple chemical composition compared with conventional cigarette smoke, which results in minimal biological responses in traditional toxicology assays. We are most encouraged by our clinical research with the blu product. We were able to demonstrate that, over just five days, smokers switching to blu had significant reductions in harmful chemicals in their blood and urine, which was largely indistinguishable from that of smokers who quit cold turkey over five days. We are now into the phase of our clinical research around the blu portfolio.

Q135 **Chair:** What is the scale of the research you are doing? You have talked about clinical trials and testing, and a one-year-long trial, but what is the size of the cohort you are working with?

**Dr Proctor:** Our clinical study is a big one, with over 1,000 people. The study has several arms. It will compare people who quit smoking for a year—in that arm, we have 800 people—with people who switch from smoking to either our tobacco-heating product, glo, or one of our electronic cigarettes. To do a year-long study, you need a large starting population, to ensure you get enough people at the end of the study to do the analysis for the biomarkers of exposure and biological effect.

Q136 **Chair:** Would anyone else like to comment on the scale of their research?

**Dr Gilchrist:** I can talk to the work we are doing on heated tobacco products, because that is furthest advanced in the assessment we are doing. We are doing large-scale clinical studies, similar to the one that Dr Proctor described, looking at the effect of switching to our IQOS product, which is a heated tobacco product, over the course of a year. Again, we have about 1,000 participants in that study. We are looking at the impact compared with stopping smoking altogether. We will release data from the first six months of that study shortly.

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<sup>1</sup> Correction by witness: The year was 2013.



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The other clinical studies we have done are very encouraging. We have done a three-month study looking at the same types of markers we are looking at in the year-long study. As my colleague said, the results show that, for the duration of the study, the reduction in biomarkers of exposure to harmful chemicals comes close to that seen in those who stop smoking altogether. That is very encouraging.

**Dr Jones:** It is similar from our side. For our e-cigarettes, we are in the middle of a short-term clinical study—a week-long study. That has hundreds, rather than thousands, because the drop-out rate is lower over a shorter period of time.

**Dr O'Connell:** We recently published one of the first long-term clinical studies, over two years. As Dr Jones said, we have some drop-outs. Our study looked at 209 smokers switching to an e-vapour product.

Q137 **Chair:** Did you say 290?

**Dr O'Connell:** I said 209. The results showed that, after two years of use of this product in the real world, there were no safety concerns with the product. It was very well tolerated by the smokers.

Q138 **Chair:** You said that some of the trials have up to 1,000 people. Is 1,000 a big enough sample group to make sure you understand the impact it will have on different types of people within that group?

**Dr Gilchrist:** Our statisticians looked at this for a long time when designing the study, to understand the impact of people dropping out over time. We also wanted to ensure that we could capture the impact of dual use, for example, because that is a concern. We need to understand whether there is a decrease in effect when people are dual-using. The preference is that people switch completely to these products, but we need to understand what the impact of dual-using with combustible cigarettes would be.

We are also looking at different age groups, as well as gender, to see whether there are any differences. We will be able to do that with the sample size we have.

**Dr Jones:** Our approach is very similar. We conduct what are called power calculations prior to conducting such studies. It depends on the question you are asking. If you want to detect the difference, there is a statistical method to determine the sufficient sample size you need to detect that difference.

**Dr Proctor:** My answer will be slightly different. We can look at what the Royal College of Physicians and Public Health England have said on the relative risks of e-cigarettes. They believe that they are 95%, or more than 95%, less risky than smoking, but that there is a need for both product standards and long-term research. In that long-term research, the year-long studies may not be enough, because biomarkers of biological effect change quite slowly. Eventually there need to be cohorts



of people who are followed for much longer periods than that. That is why ensuring that we are getting feedback from safety reports on e-cigarette use is good comfort as we go along that journey. Eventually, there will need to be longer-term epidemiological studies to determine exactly what the relative risks of e-cigarettes are, compared with other products.

**Q139 Chair:** You have talked about the Public Health England reports and the 95% figure. First, what does 95% mean? Can you quantify that for the public outside? Secondly, what are your own findings about the safety differences between conventional cigarettes and e-cigarettes?

**Dr Proctor:** That is a great question. It is now well acknowledged that there is a risk continuum, where cigarette smoking is by far the most risky tobacco and nicotine product, and nicotine replacement therapy is the least risky. You have that continuum. The only other thing that we can place with accuracy on that continuum is Snus, the Swedish oral tobacco, because there has been long-term epidemiology. If cigarettes are here and NRT is there, it is at about the 90% or 95% mark, as the Royal College of Physicians has said.

With e-cigarettes, we are really at educated conjecture, because we do not have that epidemiology. You cannot pinpoint with accuracy exactly where they should sit, but they have far fewer toxic emissions than cigarette smoke. Most of the things that are formed in cigarette smoke that are known to be harmful chemicals are absent in e-cigarettes, but some chemicals are still there. You get some thermal breakdown from things like propylene glycol and glycerol, which may cause some risk.

The data that we have are pretty much consistent with where Public Health England is coming down on this. It is saying, "We think that it should be even better than 95%, but there is still a residual risk of 4% to 5%. Those risks can be minimised if we introduce proper product standards. We also need to do long-term epidemiological research to be sure that that is happening across all people."

**Dr Gilchrist:** One of the things we understand from our research is that the burning of tobacco is causing the main issues associated with smoking-related diseases. The moment you have a product where you are not introducing the burning of tobacco, you are likely to have a very significant reduction in health risks. As Dr Proctor said, quantifying that risk will take longer-term epidemiological studies. We have started those types of studies for our heated tobacco product that is on the market in Japan. We have seen a large amount of switching of smokers in those studies. We are looking at the impact on disease-risk reduction over the long term. That will begin to help us to quantify the percentage of risk reduction compared with ongoing smoking. Right now, as Chris said, we are really making a conjecture about what that may be, but all the signs point in the right direction, to a very significant reduction in risk.

**Dr O'Connell:** I agree with Dr Proctor. It is quite difficult just now accurately to quantify an exact percentage figure. However, what Public



Health England tried to do with the 95% figure was communicate to smokers the magnitude of risk reduction and how less harmful electronic vaping products are. It was a way of communicating to smokers in easy-to-understand language. The message is not getting through, particularly in the UK, where an increasing number of smokers believe that e-vapour products are as harmful as, or more harmful than, conventional cigarettes. There is a huge communication challenge in the UK to get that public health message across.

**Q140 Chair:** We may well come back to that. As you have touched on it, will you explain why you think that is the case? Who is driving that, or failing to communicate the potential health benefits?

**Dr O'Connell:** At least in part, it is the tobacco products directive, which captures e-vapour products. In many cases, it fails to distinguish between tobacco-containing and non-tobacco-containing products. Many of the restrictions within the TPD correspond to those on conventional tobacco products. The TPD does not take into account the scientific evidence base that supports vaping products, either. Essentially, we have a conflation of tobacco and e-vapour products, which sends the wrong message to smokers.

**Q141 Darren Jones:** Are you saying that the public are misinformed about the difference because of the TPD? Surely the public do not really know what the TPD is.

**Dr O'Connell:** No. If we look at advertising, for example, within the TPD, a number of the restrictions that apply to conventional cigarettes also apply to e-vapour products. The message that that sends is that they are one of a kind, from the regulatory perspective. The misreporting of scientific studies, and their subsequent presentation in the media, is also a serious contributor to this. That is having a measurable impact on consumer confidence, which urgently needs to be addressed.

**Q142 Chair:** I have one final question, before I pass over to Bill Grant. Another inquiry that we are conducting is into research integrity. One of the concerns is that not all the findings of particular research projects are published. Will you publish all the findings, not just the ones that support the stance you are taking at the start?

**Dr Proctor:** Yes. It is important, particularly for the clinical studies, that you register your studies before you even start to do them, so that people can see that a study is being done and have very good transparency. They can then say, "The study has been done, but it has not been published. Why has it not been published?" or, "No, it has been published." We have already registered the one-year-long clinical trial. We have explained exactly what we are going to do, where it is being done and that we will publish as soon as we get to the end of it.

**Dr Jones:** We also utilise our science website, where we put not only our published studies but conference proceedings and other scientific data that we have collated. Those are not only for scientists—but also tailored



for lay audiences, to try to explain to the general public the science behind these products.

**Dr Gilchrist:** We are also taking an approach that involves transparently sharing all our research—not just peer-reviewed publications but the source data—so that scientists themselves can take the data and come to their own conclusions. We are doing that because we understand that there are enormous questions about research integrity because of the history of the industry. People are asking questions all the time—the same sorts of questions that I asked before I joined the company. I came from the pharmaceutical industry; I worked in Cancer Research UK. I had big questions about whether science coming from the tobacco industry could really be credible. We have made a concerted effort to ensure that we are following all the correct standards, good clinical practice and good laboratory practices, and that we are publishing and sharing the data, so that people do not have to rely on trust and can verify our data for themselves.

**Dr O'Connell:** At Imperial and at Fontem, we are committed to transparent research. We regularly present our findings at conferences, where we seek dialogue with other scientists and critique of our work, which helps to strengthen it when we are working to develop other studies. We frequently publish our research in the peer-reviewed literature. That is all available on those scientific websites as well. We hope to have dialogue and questions from the scientific community on our research.

Q143 **Bill Grant:** What testing has been done on the effect of devices in relation to different temperatures, different nicotine strengths and what are described as different puffing habits? Taking all those together, what research, testing or studies have been done? Do any of those factors make any significant difference to, or have any significant impact on, the health of the user?

**Dr Proctor:** In the context of vaping products such as e-cigarettes, temperature can make a difference. If the thing is overpowered and the coil in the system gets too hot, you get thermal breakdown of glycerol and propylene glycol, which can create toxic aldehydes. That is another reason why we really need to make sure we have good product standards in this space. If e-cigarettes overheat, you will get some of those toxic compounds coming through.

The British Standards Institution was the first to start setting standards on this. Now that has gone to European level, at CEN, and is going to international level. It will be a really important area, to make sure that people can have confidence that, whatever e-cigarette they are using, the temperature is being controlled. We will talk about tobacco-heating products later. It is also the case there that the higher the temperature, the more toxicants you get, so you need to control temperature in tobacco-heating products.



The second issue in your question was nicotine strength. We have done some topography on this, looking at the way in which people use the product at different nicotine strengths. With cigarette smoking, you get compensation. If people have lower nicotine, they overpuff to get nicotine back up. That looks to be happening less in the studies that we have done; it is less of an issue there. Temperature is definitely something that needs to be looked after.

**Dr Jones:** I would second that. Our studies also show temperature to be one of the critical variables—not only for e-cigarettes, but for the heated tobacco products we will talk about later.

The other consideration is material selection. There was a paper last week looking at metal ions in vapour. Making sure that you are using the right material for the coil, for example, to ensure that metal ions are not migrating to vapour, is a critical consideration. What goes into the device is as important as how it functions.

**Dr O'Connell:** Regarding the thermal breakdown of products, temperature—making sure that the liquid is not overheating—is clearly a very important consideration. Our research has shown that good fluid dynamics within the system are equally important, to ensure that we have good flow of the liquid to the wick and the coil, and good vapour generation. Through the learnings that we have got from our research, we have engineered out the old sponge-and-cartomiser system, where you have a sponge full of liquid. When you squeeze it, the fluid dries out, so you are left with a dry substance. We have moved to free-flow technology to overcome that, so we are reducing the thermal breakdown issues with our product.

Q144 **Bill Grant:** Does the free-flow technology—this sounds like a terrible question—make the puffing easier? Is there less resistance to the user when they are endeavouring to inhale?

**Dr O'Connell:** The idea is that a consistent vapour should be delivered to the vaper, to make it a nicer experience for them.

On the second point—nicotine—you have Dr Lynne Dawkins presenting to the Committee after this. She has done some very nice work looking at the effects of different nicotine levels on puffing topographies. It will be quite interesting to hear about that from her.

**Dr Gilchrist:** One of the calls that I have as a scientist is to ensure that smokers here in the United Kingdom can access better information about the range of different smoke-free products that are alternatives to cigarettes. To ensure that consumers are getting the right information, it is critically important that there are standards. There must be standards to ensure that companies are using the right materials and have heating technology under control in a wide variety of different use scenarios, so that when a smoker uses an e-cigarette product or a heated tobacco product, they are always inhaling what the manufacture says they are





going to inhale. Standards can play a critical role in helping to ensure that consumers have a safe product and can be informed about the relative health risk in an accurate way.

Q145 **Bill Grant:** May I take the panel to toxicity of the products, or harmful by-products generated by them? How do they compare against nicotine replacement therapies, such as gums and patches? Have you done a benchmarking exercise or a comparator on the toxicity?

**Dr Proctor:** Nicotine replacement therapies are designed to be medicinal and have very low levels of toxicant exposure. On the risk continuum, you know that cigarettes are up here and nicotine replacement therapy is right down at the bottom. The Royal College of Physicians did a very good review of the safety of nicotine replacement therapy a couple of years ago.

Both vapour products and tobacco-heating products will have additional risks compared with that; we just do not know exactly what the level is. Public Health England has estimated where it should be—a residual risk of 5% or lower for vapour products. We will not really know for a bit longer, but there is likely to be some additional risk. If you compare them with NRT, it is probably relatively similar. If you compare them with cigarettes, it is very different, for both vapour products and tobacco-heating products, in terms of the likely risks that they present.

**Dr O'Connell:** At Imperial Brands and Fontem Ventures, we published a clinical study in 2005 that compared an e-vapour product with NRT. We were interested in looking at the safety profile of the vapour product relative to the NRT product. We found that the vaping product had a very similar short-term safety profile to the NRT product. We also found that the e-vapour product in the study was able to reduce smoking desire and nicotine withdrawal symptoms more than the NRT product. It was able not only to deliver nicotine in the same way as an NRT, but to provide some of the behavioural and sensorial aspects of the smoking experience. The e-vapour product in that study was very well tolerated and looked to be a suitable alternative for smokers.

**Dr Jones:** We are in the process of conducting a clinical trial addressing this exact question. It is too early to share the data yet, as we have not finished the study. Once we have, I will be very happy to share the data with the Committee.

**Dr Gilchrist:** We recognise that the best thing that a smoker can do is stop using tobacco or nicotine products altogether. We have not necessarily focused on the risk profile of our portfolio of smokeless products versus nicotine replacement therapy, because the focus has been on showing the difference compared with ongoing smoking. Here in the United Kingdom, 7.6 million people are still using combustible cigarettes daily. The public health emergency is that we should encourage all of those either to quit tobacco and nicotine altogether or to



switch to a product that is a better choice than continuing to smoke. That is the focus we have had.

Q146 **Bill Grant:** As an ex-smoker, I am pleased to have got that question, and the next question relates to the fact that I am ex-fire officer. The question is around evidence in America, where some of these devices exploded and were a fire risk. That has been noted and recorded in the United States. Is there any evidence of recorded events such as the ignition of devices? Have you as producers or engaging manufacturers adapted the devices to combat, to reduce or, hopefully, to eliminate that risk? Is it a real risk?

**Dr Gilchrist:** It is a risk. With any battery-controlled product, there is a risk of fire. We take that risk very seriously and have done a lot of engineering work to put protective systems around the batteries in our products. For example, for our heated tobacco product, we have been very successful. We have shipped more than 12 million kits worldwide and have never had a battery problem. Standards can help to ensure that there is consumer protection. It is perfectly possible from an engineering perspective to put the right controls in place.

**Dr Jones:** In Europe, we have quite rigorous battery standards. There is a lot of investment from us in making sure that the batteries that we source meet those standards. The problem is that some of the batteries that are available do not comply with the European battery safety standards. We ensure that they do by having vent protection, so if there is a failure they vent properly when they are transported. The critical thing is to make sure that the batteries that are used in products meet the existing standards.

**Dr Proctor:** Clearly, standards are critical, but you need to get good consumer information out there, too. In our vaping business last year, we had about 2,000 consumer complaints. Around 50 of them were related to batteries. Even with that relatively small number of complaints, quite often people were using the wrong chargers on the batteries. Health England was probably very correct in saying that this could be a risk. It looks to be relatively small, but you need to get great consumer information out there to make sure that people use the product as intended—with the charger—and do not add to the risks of a battery being set on fire.

**Dr O'Connell:** In its report a couple of weeks ago, Public Health England highlighted the fact that there is low incidence of this in the UK, but we take it very seriously. We should follow the manufacturer's instructions, using the correct charger and not charging overnight. There is a real need for product standards in this area around battery safety. In our products, we use lithium-ion batteries, which have protection circuits—integrated circuits—to stop short-circuiting. There are venting mechanisms to stop the build-up of gases.



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We find that a number of products on the market do not comply with those standards. We also find that people connect the wrong coil to the wrong battery, so that there is short-circuiting, fire and explosion. There is a real need for battery standards in this area.

The other issue we face is that, as responsible manufacturers who are complying with battery standards and striving to have high-quality products, we are often perceived as having poor-performing products, because we have in-built safety factors in our batteries that mean that they are not operating at maximum power. You can think of it as a bridge that is designed to hold a 10-tonne lorry, but could actually hold 50 tonnes. There is a safety factor built into our products that some of the other devices that are perceived to be more powerful do not have. We are competitively disadvantaged in that space for having high-quality products.

**Q147 Bill Grant:** We are an innovative nation, and there is a risk that we may tamper with some of these heat-not-burn products. Is there any evidence of people changing not the design criteria but the intended outcome criteria of the device? Is there evidence that people enrich or enhance the product mischievously?

**Dr Gilchrist:** I will start with our heated tobacco product, IQOS. We took this concern very seriously. We know that human beings—not just here in the United Kingdom, but anywhere in the world—can be very innovative. We set out to ensure that we minimised, to the extent that we possibly could, the ways in which people could adjust what the device would deliver. We have encrypted the software, for example, so that we believe that it is impossible for somebody to hack the device. We have employed professional hackers to try to overcome the protections we have put in place. We are aware that ingenuity and technical ability increases over time, so we are continuing to monitor that, to make sure that there is no way the user can do something to change the delivery of the device.

We are doing that because we know that the precise temperature at which we heat the tobacco is very important in ensuring that we reduce the level of harmful and potentially harmful chemicals that are produced. It is not in our interest to allow somebody to be able to adjust that, because then you do not have the reductions that are so important for the longer-term risk reduction. The focus is on making sure that there are controls in place and that the user cannot interfere with them in a way that may be harmful to the product and the user.

**Dr Jones:** Our current heated tobacco product is what we call a closed system. The product comes pre-filled, so the user does not have to fill it. Think of it like a cartomiser e-cigarette. We do not have an open system where the consumer puts in his own consumable. That is how we control it. To date, we have not seen any evidence of consumers trying to manipulate our heated tobacco product.



**Dr Proctor:** Closed systems are interesting. Our tobacco-heating product is another closed system—so are our vaping products, where you buy the cartridge and it is all sealed in. In vaping products, there are clearly some people who are modifying their own, particularly in open systems. The solution to that requires innovation from a technological point of view. We are still on a journey with vaping products to needing greater choice and more innovation in the sector. That is why, in R and D in Southampton, we have been bringing in technologies from other companies, such as Dyson. We are having them join us to figure out what the next generation of vaping products will be. That innovation can get out there only with a lot of energy and support to come up with the next generation, which will be less able to be tampered with because there will be no need, as it is satisfying all the consumer's needs.

Innovation in the space will continue to be critical on both the tobacco-heating products side and the vaping side, as will more choice. That is really where we are coming to. Not everyone is going to switch to a vaping product. Some will want a tobacco-heating product. Some would like oral tobacco products, rather than smoking. A range of innovations across the whole space will be really important. It gets rid of the temptation to tamper if you have the satisfying product in the first place.

**Dr Gilchrist:** Dr Proctor makes a very important point, particularly for the United Kingdom. We have seen a plateauing in the number of smokers who are switching to electronic cigarettes over time. Something like 800,000 people switched in 2015. Last year, it was something like 100,000. The risk is that we have reached the maximum potential of electronic cigarettes. I hope that that is not the case, but it shows that there is room for all sorts of different product innovations in the smoke-free product area. As a company, we are working to ensure that we are offering choice and different types of technology that can suit each smoker's needs.

Q148 **Bill Grant:** Dr Proctor, you said you are still on a journey. What direction is that journey taking? Could you answer very briefly? I know that I have taken up a lot of time. What is the journey for these devices?

**Dr Proctor:** They are on a journey in two ways: first, to be more satisfying; and, secondly, to be safer. That is where we are going. The coil and wick that are used in most e-cigarettes will become outmoded. There will be new ways in which you create a vapour without the breakdown of glycerol and propylene glycol, but with greater satisfaction for the consumer.

**Dr O'Connell:** May I add something in response to your question on modifications? At blu, we have engineered out the foreseeable modifications. We have unique proprietary screw threads and our pod system. The topic of thermal breakdown and the dry-puff conditions we heard about from Dr Polosa a few weeks ago at the Committee are quite important. Future innovations in the e-vapour category are looking to remove the heat source entirely. We could see the generation of an



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aerosol through high-vibration ultrasonic vibrations or through pressure systems, such as a deodorant can. There are innovations coming through all the time.

Q149 **Bill Grant:** It is evolving.

**Dr O'Connell:** Yes. We would like the regulation to encourage and foster that innovation, so that we can give the smokers what they are after.

**Chair:** That is very good. Before I go to Martin, may I ask Darren to make a tiny intervention?

Q150 **Darren Jones:** I was interested in the point about hacking. Does that mean that these devices are connected to people's mobile phones, in order for there to be a connection? If so, what data are being collected, and why?

**Dr Gilchrist:** In some of the more recent devices that we have, there is what we call Bluetooth capability. That is intended to help smokers to make the switch. We know that when smokers first start switching to our heated tobacco product, for example, there is a period of natural adaptation that has to occur. You do not turn to being able to use the product from one day to the next.

We use the Bluetooth capability to count the number of sticks that the smoker is using, for example, and to remind them to do things like cleaning, which they do not have to do when they are simply taking a cigarette out of a pack and lighting it. It is to encourage them to do the steps that are required and are innate to the technology.

We also use it to remind them to do things like order product, so that they do not run out and have to go back to combustible cigarettes—to coach them through the adaptation period and to encourage them to use only the heated tobacco product, not combustible cigarettes. That is the focus of that type of technology.

**Chair:** To ensure that we get the most out of this session, I encourage colleagues to keep their questions tight and focused. I also encourage you to keep your answers as concise as possible. If you do not, we will run out of time, unfortunately, as often happens, and will not get everything we want. Martin will be an exemplar on this.

Q151 **Martin Whitfield:** I will make it very short and succinct. To turn the question slightly on its head, do you think that there is a risk that e-cigarettes will do the opposite, by renormalising smoking and taking non-smokers on the wrong-way trip? I will take your views first—apparently, very short and succinct views.

**Dr Jones:** My very short and succinct answer is that the data to date suggest otherwise—that, if anything, e-cigarettes are a gateway out of smoking.



**Dr Gilchrist:** For heated tobacco products, which are the focus of much of our research, we see very little interest from people who are non-smokers, particularly in younger age groups. Young adults are not at all interested in these products—potentially, because they contain tobacco, which is somewhat off-putting for non-smokers. Of course, we understand that this is an area we need to be very mindful of and concerned about. It is an area we need to monitor in a post-market environment, to survey and to check, but, so far, the data we have to hand show exactly what Dr Jones has said—that these types of products are a gateway out of smoking, not a gateway into it.

**Dr Proctor:** That is absolutely true. We should be absolutely clear that these are nicotine products, so they should be only for adults. They will still be addictive. Therefore, all the protections to ensure that young people do not use them should be in place. In the UK, we should be comforted by the fact that we have very good surveys going on, particularly through people like Action on Smoking and Health, that are looking at the situation as it changes year by year. So far, it looks like the vaping products are not a gateway into smoking. Those surveys should continue, so that we can keep an eye on the situation.

**Dr O'Connell:** It is a legitimate question to raise, but we are very encouraged by the UK data, which show that never-smokers' use of these products is around 1%, which is comparable to never-smokers' use of NRT in the UK.

On young people, in particular, one of the largest surveys that was ever conducted across the UK—it looked at 60,000 pupils, including data from Scotland and Wales—found that use of vaping products was negligible, and that regular use was confined to those pupils who already smoked. We are very confident that these products are getting into the hands of adult smokers only.

Q152 **Martin Whitfield:** As you say, those conclusions are based on research from a variety of sources.

How do you go about designing the marketing of this? What inputs do you have to appeal to a very specific type of customer, the smoker—ideally, the smoker who wants to give up? How do you go about doing that through marketing?

**Dr Gilchrist:** I am a scientist; I am absolutely not a marketing expert. I can give you a broad view. We are very interested in ensuring we have the opportunity to have targeted communications to smokers. We are not interested in broad communication opportunities; we are interested in attracting the right users—smokers who would otherwise continue to use cigarettes. Pack inserts in conventional cigarette packs are one example of that. Unfortunately, we cannot do that here in the United Kingdom, because of the laws that exist. We believe that that would be a tremendous opportunity to talk only to smokers, to tell them about the existence of new smoke-free products. That would be a very simple thing



to do here in the United Kingdom that would allow marketing to exactly the right audience and not to the wrong audience.

**Dr Jones:** I would second that hidden caveat; I am also a scientist. My understanding is that, as Moira has said, targeted marketing is not permitted at this point in time. That would certainly help, whether it was via pack inserts or via direct communications to smokers and vapers.

**Dr Proctor:** With our Vype e-cigarette brand, for example, we make sure that it is all adult verified when people are on the website. Through the company we use, you have to have a passport number or a register of enrolment number, so you know that you will have adults only on that site. Currently, since TPD was brought in and the law was changed, you cannot give any proper communication on the website related to the risks, even though you have already caught someone who is clearly an adult. Oddly, you can do some advertising on billboards, but you cannot do it on the site, where you already have a clear target audience. That was not the case before TPD came in. The Advertising Association set good, sensible rules for that, but those have gone backwards a bit. It will certainly help if we start to look at that again later.

**Dr O'Connell:** We should be clear that these products are for adult consumers only. I am not a marketer either, but it is very clear from Imperial that we want as many smokers as possible to transition to our portfolio of vaping products. To ensure that our products do not get into the hands of and are not marketed to under-18s, we employ age verification systems on our website as well. We have an international marketing standard we expect all colleagues and markets to follow and to adhere to.

Q153 **Martin Whitfield:** Are there any other changes to the current regulations that you think would assist? You have mentioned inserts and targeting of specific groups. Is there anything else that concerns you and is preventing you from achieving transition?

**Dr Gilchrist:** The way I would look at it, as a scientist, would be to say, "What opportunities are there to provide accurate scientific information to men and women who smoke, in order that they can make an informed choice?" Anything in the regulation that can help that can only be a good thing in encouraging smokers either to stop using tobacco and nicotine products altogether or to switch to products that are clearly a better choice than continuing to smoke.

**Dr Jones:** I would second that.

**Dr Proctor:** On the communications side, there is definitely more that could be done. The TPD also sets some standards both for the volume of a tank that you can use and for the amount of nicotine that you can use in it. Those should probably be looked at again. They were set on a precautionary basis, quite quickly, as those laws were coming in, so it would probably be worth looking at them again.



We are at the beginning of trying to figure out what the regulatory regime around the heated tobacco product space should be. I think that it should be a separate category. If we agree that these are reduced risk, because they do not burn the tobacco and do not create any cigarette smoke, we need to consider what the various regimes that we set there should be—on advertising, on excise rates and on how we establish what makes a tobacco-heated product. At the moment, they are under novel tobacco products, but there is more to be done to carve that out as a category.

Q154 **Martin Whitfield:** May I come in on that before you respond further? Are you still of the view that the precautionary nature of the regulations—that foundation—is right?

**Dr Proctor:** Yes. The TPD regulations, as they apply to vaping products, were reasonably proportionate. Vaping has moved very quickly, in about five or six years, and the regulations came quite early in what was happening. Naturally, they were cautious, because no one really knew what was happening with the marketplace or with the safety of the products. We know more even now, two or three years later, through the various surveys that go on. We could look at the regulations again and say, "Have they been set exactly right? Are there some things that we should be able to tweak to give a bit more commercial freedom, to encourage use of the products more and to encourage innovation in that category, because it still has a journey to go?"

Q155 **Martin Whitfield:** Even before the epidemiological studies can possibly be made.

**Dr Proctor:** The epidemiological studies are needed for precision on what the relative risk is, but we now have a lot of evidence that suggests that these products are safer than smoking. Public Health England, the Royal College of Physicians and the data we have collected are pretty indicative that they are going to sit somewhere different from where cigarette smoking is. If public policy is to try to encourage people to switch from smoking to these less risky products, we probably need to look at how we encourage that in various different regulatory regimes.

**Dr O'Connell:** The concern that we have with the TPD for the regulation of vaping products is that it was bolted on to tobacco product regulation. We believe that regulation should foster innovation in this category and should be based on compliance with robust product quality, safety and manufacturing standards, alongside a responsible marketing approach that ensures youth protection. That is the angle we would come from.

We are concerned about some elements of the TPD. As Dr Proctor said, the arbitrary limits on nicotine strengths and bottle sizes are a concern. We are also concerned about the length of the notification process, because it inhibits the ability to bring these innovative products to market sooner. One of the features of this category is innovation.





Regarding advertising, the Royal College of Physicians noted that these products should be promoted widely to smokers. We would like to see greater advertising freedoms, so that we can communicate our brands to smokers and communicate the value proposition and the innovation of our products—essentially, so that we can compete with the established tobacco brands.

Q156 **Damien Moore:** Should vaping liquids not containing nicotine be subject to the same regulations as vaping liquids containing nicotine?

**Dr Jones:** Yes, we believe they should. Consumers are still inhaling the vapour from these liquids. We are also seeing—I believe, in the UK—what are called short fills, where consumers buy a small bottle of nicotine-containing liquid and add it to an unregulated bottle of zero-nicotine flavoured liquid. For me, as a scientist, that is a concern, because we do not know what is in that zero-nicotine flavoured liquid combination. Based on the principles of consumer protection, I think that zero-nicotine liquids should be regulated in the same way.

**Dr Proctor:** My understanding is that they are not at the moment—they are more under the general consumer safety approach. With Vype, we sell zero-nicotine closed cartridges, as well as 18 mg per millilitre cartridges. We apply the same stewardship standards to those, so we are looking at what happens when they are used in the product. Maybe there is a reason why they should be regulated differently, but the consequence of that regulation should not be that there are laxer product standards for them, as they are still generating emissions that people are inhaling. There is a balancing act there, to ensure that we do not see untoward things happen with the zero-nicotine liquids.

**Dr O'Connell:** We would echo what Dr Jones just said. These liquids are designed to be inhaled. Therefore, they should be subject to the same rigorous standards as the nicotine-containing products. Some members of the UK trade association have done some testing on these short-fill liquids. They have found some undesirable chemicals that would be prohibited in the nicotine-containing liquids, so we definitely think that that should be looked at. The French have said that the TPD will apply equally to nicotine-containing and non-nicotine-containing liquids; the Dutch are also looking at this. We think that, if the liquid is intended for vaping, it should be subject to the same stewardship and standards as nicotine-containing liquid.

Q157 **Damien Moore:** You are saying that there should be the same, not laxer, regulation.

**Dr O'Connell:** We would apply the same standards.

Q158 **Darren Jones:** Do any of you smoke e-cigarettes?

**Dr Proctor:** I do occasionally.

Q159 **Darren Jones:** Do you have a favourite flavour?



**Dr Proctor:** Yes.

Q160 **Darren Jones:** Which one?

**Dr Proctor:** I am not sure that there are any e-cigarettes without flavours. I tend to choose mint.

Q161 **Darren Jones:** One of the things we grappled with in a previous hearing was the research into the consequences of the flavourings in e-cigarettes. Would anyone like to answer on the research into that and the possible health consequences of the flavouring specifically, as opposed to the nicotine or the carrier agents?

**Dr Gilchrist:** Maybe I can start, as it is linked a bit to the question you asked about the Bluetooth technology. There is an adaptation period smokers need to go through. Flavours can play an important role in helping them to adapt to this new type of product. While some products are close to the taste and flavour of cigarettes, they are not the same. We believe that flavours are important in helping that adaptation. Nevertheless, we are taking extreme care to ensure that the flavours that we put into our products are toxicologically appropriate. We go through a very long toxicological screening process before we approve a flavour for use in a given product type. We think that it is important that we can have flavoured products, because they help smokers to make the transition, and to make it more quickly than perhaps they would with unflavoured products.

Some of the concerns about flavouring are more about the marketing of those flavours—how they are described and how they are characterised to vulnerable populations, such as youth. Clearly, that can be regulated, but flavours are helpful and necessary to help smokers, the intended audience for these products, to make the switch in as short a time as possible.

**Dr Jones:** I would echo that. This is one area where I believe that TPD2 had done a good job. In the notification process, we have to provide the scientific information on the flavours and individual ingredients that we add to the e-liquids and to defend the use of those ingredients, not only at a qualitative level—what they are—but also at the quantitative level: how much of each ingredient we add. That is one of the things that I am pleased to see from TPD2. It is forcing manufacturers to know what they are putting into their e-liquids. I am not sure that, prior to TPD2, everyone knew particularly what was going in.

**Dr Proctor:** There is more that can be done on flavours. There are clearly some flavours that are already blacklisted. There is a compound called diacetyl, which can lead to lung problems. That is on a blacklist, but we know that there are some other flavours that can break down to that compound. When we find that, we publish that research, but it needs to get into a product standard that is then enforced. If flavours are done correctly, they should not add to the toxicological burden of the vaping



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device. We have done testing with and without flavours, and you do not see a change in the toxicological profile, but some could change it. We need to be careful and to have proper standards in place and in force, to make sure that you do not get flavours that could cause health problems.

**Dr O'Connell:** It is a good question. You asked, "What is your favourite flavour?" What we find with vapers is something called flavour fatigue. Flavour variability is incredibly important for vapers. A recent study suggested that 64% of vapers change their flavours daily, so this mix-and-match and availability is essential for this category.

We see that flavours are important in attracting smokers to the category and retaining them, to prevent relapse. That does not detract from concerns about flavours potentially being attractive to children. We would say that there should not be blanket bans on flavours per se, but responsible marketing approaches. We would be very happy to discuss an appropriate naming convention for e-liquids. The bubble gums and cotton candies are unacceptable, for example.

From a toxicology perspective, we have professional toxicologists at Imperial and Fontem who are looking at every single ingredient that is used in our liquids. We have 100% disclosure of the ingredients in our liquids. They can do risk assessments to determine the appropriate levels in use in our products. We mandate that all the flavour houses we work with disclose that information to us.

Q162 **Darren Jones:** Am I right in assuming that there is a market of providers outside the tobacco companies that are producing the non-nicotine versions of these flavouring liquids? If so, as an extension to the previous question, do you have concerns around the toxicological assessment of the flavourings by those companies when they are making those liquids?

**Dr Proctor:** We do. In my labs, I have professional toxicologists who spend their lives looking at these things, but I am sure that a lot of the manufacturers do not have access to that. That is why I think that declaration of ingredients was important in TPD2. We need to move a step forward, to make sure not only that that is being checked and that declarations are accurate, but that we start to weed out some of the things that may be of toxicological concern.

**Dr Jones:** In my experience, when I have spoken to some of the SMEs in the area, there is a misunderstanding about what a flavour is. Some think that, when they buy cherry flavour from their supplier, that is the ingredient. In fact, there may be 10 or 20 ingredients that make up that cherry flavour. Therefore, there also needs to be a bit of education about what flavours are. That means coming back to each single ingredient, to understand what it is and whether it is suitable for purpose.

Q163 **Darren Jones:** Lastly, is there anything from a public policy or regulatory perspective that would improve the blacklisting process for



flavours that might have a toxicological impact? Are you happy with the system as it is today?

**Dr Proctor:** No; there is more. We have basic standards in place. The work that is being done now at international level and at European level, through CEN, will give more precision. It is looking at both device safety and emissions safety. When that process is finished—it should be finished in 2018—and it comes back into us, we have to get some kind of enforcement regime around it, too, to make sure that if there is a growing blacklist we are checking against it to ensure that those ingredients are not in any of the flavours in the marketplace.

Q164 **Darren Jones:** Does that mean that there is no enforcement today, as a voluntary blacklist?

**Dr Proctor:** It is voluntary disclosure. I do not know whether the MHRA has sufficient resources to look through that or to check whether it is correct. We also need to have a big enough blacklist. We have a very simple blacklist at the moment, which needs to grow to include some of the compounds. We must then ensure that the enforcement agency has enough resource to be able to look at that and to make sure that we do not have those products on the market.

**Dr O'Connell:** The issue regarding whether some liquids already contain these chemicals is that in the absence of product standards, particularly around testing methods, you are comparing apples with pears. There is not one standard method. One lab will use method A and one will use method B, so you might not detect the chemical. We agree that strict enforcement of product standards is absolutely essential. We believe that that would form the basis of a bespoke regulatory framework for these products.

Q165 **Martin Whitfield:** I know we have had some contributions about heat-not-burn, but will you specifically explain, according to the research, the main difference between cigarette smoking and heat-not-burn?

**Dr Gilchrist:** Perhaps I will start, as I think we are probably furthest ahead in our development and assessment of heated tobacco products.

Tobacco in a combustible cigarette burns at anywhere between 600 °C and 900 °C—so, at a very high temperature. It is that high temperature that causes the production of the vast majority of the harmful chemicals that appear in cigarette smoke.

When we are heating tobacco, we are heating it at much lower temperatures. In our IQOS device, the maximum temperature that the tobacco can reach is 350 °C, which is well below the temperature where combustion may start to happen. The consequence of that is that we get a very significant reduction in harmful chemicals—a 90% to 95% reduction in harmful and potentially harmful chemicals.



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We have taken that onwards from the laboratory. We have looked at toxicological studies, too. There, we see a greater than 90% reduction in toxicity compared with cigarette smoke in standard tests. We have also done something called systems toxicology, which looks at the very mechanisms by which smoking-related diseases are caused in the body. There again, there is a tenfold reduction in the impact on those disease mechanisms for our heated tobacco products compared with cigarette smoke.

We have gone on and done clinical studies in adult smokers. We have completed eight clinical studies so far. We see that smokers are exposed to much lower levels of those harmful chemicals. In fact, they are exposed to levels that come close to the levels seen in smokers who stop smoking for the duration of the study. We have so far completed two studies over three months, which is very encouraging.

We also see things called clinical risk markers, which show that you are at an increased risk of having one of the smoking-related diseases. They all move, even in that short period of only three months, which is very short for a health outcome. They move in the same direction as the smokers who quit during the study.

Ongoing now is the year-long study to which I alluded at the beginning. We will have six months of data released quite shortly, where we are looking at those clinical risk markers over the longer term. We are hopeful we will see encouraging results, as we have seen with all the studies we have done.

As a scientist, I would say, "Don't focus on the fact that it is tobacco, because it is not tobacco that is causing the smoking-related diseases; it is the fact that it is combusted in cigarettes that causes the issue."

The products are not risk free. They deliver nicotine, and they deliver some residual levels of harmful chemicals, but those levels are much reduced compared with cigarette smoke.

**Dr Jones:** When we have looked at heated tobacco, temperature seems to be the key. We have looked at a number of devices that heat at different temperatures. There appears to be a correlation between temperature and what we would call vapour complexity, or the reduction in harmful constituent vapour, and toxicological activity.

The interesting thing is that no combustion is the key. Once you remove the combustion, it is almost like walking off a cliff. There is a correlation, but it is down in the 90s—between 90 and 99. The big difference is just that difference between combustion and no combustion. Then, when you go from 350 °C down to almost room temperature, that is in the 90s, but there is a slight positive correlation.

**Dr Proctor:** Not all heated tobacco products are the same. We presented to the Committee on Toxicity on a product called iFuse—a hybrid that



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performs very much like an e-cigarette, but it has a tobacco cap in it. That warms to about 30 °C to 40 °C, so you get pretty much the same emissions that you will get from an e-cigarette from that.

In our glo product, which only heats up to 240 °C, you are getting no combustion, and you are getting that reduction in the chemical emissions, which then translates, when you do clinical studies, through reductions in biomarkers of exposure.

**Dr O'Connell:** Unlike e-cigarettes and vaping products, heated tobacco products contain tobacco, so there is a fundamental difference in these product categories. Unlike for the e-vapour product category, where a substantial independent scientific evidence base supports these products in tobacco harm reduction, there is a lack of independent studies for the heated tobacco products.

The research seems to show—and our own research would confirm—that the emissions in heated tobacco products are significantly reduced. Public Health England acknowledged that at the Committee on Toxicology. Whether that translates into a reduction in risk remains to be seen.

**Dr Gilchrist:** Another thing that we look at as scientists is not just this reduction in harmful chemicals and the ultimate impact that they may have on health, which we believe will be very significant; we also need to look at whether smokers can switch to this product. We believe that heated tobacco products play an important role for many smokers, because the taste and flavour is much closer to the flavour of combustible cigarettes than e-vapour products can currently achieve.

We see very significant levels of complete switching to our IQOS products—around 70% of purchasers of the product are switching completely and are not dual using. That is an important factor when you look at what the longer-term health outcomes could be. Eliminating the use of combustible cigarettes for each and every smoker is the most important thing.

We see two pillars to the success of a product. The reduction in risk is very significant. Then, there is the ability of smokers to switch, and switch completely and not use combustible cigarettes.

**Dr Proctor:** I agree with Moira. We need a range of products in this space. Vaping has a really important part to play; tobacco-heating products have, and all tobacco products have, too.

When I started I was talking about the epidemiology. We have all the products that we know are much less risky than smoking that are currently prohibited under the TPD. Expanding that range across and giving smokers choices to move to something that we have determined as being less risky—they have different characteristics and different rituals, or they may have similar ones, which is sometimes a driving force for people switching and staying. You have not just nicotine equivalency



but also ritual equivalency, with some of the sensations they have got used to over many years of smoking, and these would be built into some of these innovative products.

Q166 **Martin Whitfield:** Where are the big gaps in the research with heat-not-burn?

**Dr Gilchrist:** Dr O'Connell mentioned independent research. We believe that independent studies on our products are extremely important. The product is new. It has only really been on the market for a couple of years. It is unrealistic to expect that there will be lots of studies already completed, because scientific studies take time. Nevertheless, an increasing number of studies are coming into the scientific literature. Interestingly, there was a conference last week at the Society for Research on Nicotine and Tobacco, where a number of scientific studies on the IQOS product were presented. There was a toxicology study, and BAT has done a clinical study including our product. The results are so far all going in the same direction as the results that we have had. We encourage more—we would really like to see more here in the United Kingdom, because the scientific base here is fantastic. We would encourage that. It will take time. So far, things look very encouraging.

**Dr Jones:** There is a biological plausibility. Theoretically, these products should have a modicum of risk reduction because they are not combusting the products.

We have heard much about electronic cigarette standards. These products also need standards put around them, particularly to ensure that the products are not combusting the tobacco under any particular use conditions. A definition of "no combustion" is quite an interesting one, scientifically.

Q167 **Martin Whitfield:** But they require regulatory approval, do they not? Does that restrict, or do you find that there are boundaries to doing research? I was thinking more of behavioural research and stuff, rather than mid-product research.

**Dr Gilchrist:** No—I would not say it is a boundary. This is really important. We have taken the scientific approach that we have taken over the past decade, because it made scientific sense. We are using the information that we developed according to the principles that are used in the pharmaceutical industry, and we are sharing that scientific information with regulators. It makes perfect sense. There needs to be oversight. It is important for consumer confidence, so smokers can be assured that people have looked at the science and not just the companies. It is a very important process to go through. We are going through this process in the United States right now.

Q168 **Martin Whitfield:** What you are suggesting, Dr Jones, is that perhaps that should extend more to the actual product itself, to ensure that the manufacturing standards are high.



**Dr Jones:** I think they should be complementary—there should be a complementary approach.

**Dr O'Connell:** From the research that we have done on heated tobacco, we see that the tobacco blend of the tobacco consumable and the temperature of the device greatly influence the emissions. What we have in this category is not homogeneous. There are different ignition sources and heating systems, too. That is slightly different in the vaping category, where the principles are basically the same.

Q169 **Martin Whitfield:** So, it is fundamental that the potential health impact is sensitive to the heat and the type of combustion that is used.

**Dr Gilchrist:** To add to what Dr Jones said, the most important thing is not combusting. We see a very dramatic reduction as soon as you eliminate combustion. Then, you are working in the—

Q170 **Martin Whitfield:** In the 10%.

**Dr Gilchrist:** Exactly—10%.

**Dr Proctor:** There are clear scientific tests that you can apply to show that you have combustion. We have published a five-step scientific process to show, for example, that you are not getting chemicals such as carbon monoxide or oxides of nitrogen being formed from combustion, and other things, looking at before and after.

That is kind of an easy thing to put into a product standard—saying that a product range can be identified as something that heats but does not burn the tobacco.

Q171 **Martin Whitfield:** So, is there an agreement on what is combustion—to turn your question around, Dr Jones?

**Dr Jones:** There is a scientific definition of what combustion is—the oxidative reaction. It is a matter of demonstrating, particularly in a tobacco matrix. As Dr Proctor says, you almost have to go through this five-step process, looking for reaction products of combustion. As PMI has done, you can look to see if the device works in a nitrogen atmosphere, in the absence of oxygen. It is like a weight of evidence: no one study on its own will demonstrate it, but if you do several studies and put them together—

Q172 **Martin Whitfield:** But agreement could be reached on what amounts to combustion.

**Dr Gilchrist:** Absolutely.

**Dr Proctor:** These are simple studies. They are not long-term, complicated clinical studies. They are simple laboratory studies that can be applied.





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**Dr Gilchrist:** We have shared our data on lack of combustion with a number of combustion experts across the globe, one of whom was responsible for defining the fire safety protocols on the space shuttle. We have had experts look at the type of evidence that would be required, and it is essentially the type of studies that Dr Proctor mentioned. These are not rocket science; they are simple to do, and they can provide a helpful basis for product standards.

**Dr O'Connell:** Looking at the development of policy around heated tobacco, we see in the combustion studies that it is very important to have independent verification of those studies to confirm what our colleagues are finding.

**Chair:** We have approximately 10 minutes left of this session, and two questions to get through. If you could keep yours to five minutes, Bill, that would be great.

Q173 **Bill Grant:** Noting the regulatory framework, should heat-not-burn products be treated in the same way as conventional cigarettes, or does such a grouping fail to recognise the clearly differing health impacts?

**Dr Proctor:** I think they should be separated. Because we are not burning, it is clearly a different product. It is currently under the novel tobacco products, and we need to see what that actually means. It should not be treated as cigarettes; it needs to be treated separately.

**Dr Jones:** I agree. I think they should be recognised as a sub-category on their own, as heated tobacco products.

Q174 **Bill Grant:** Is that the general consensus?

**Dr Gilchrist:** I think the most important thing is differentiating from combustible cigarettes. The range of smoke-free products currently available need to be treated differently from cigarettes when it comes to regulation and standards, and when it comes to communication opportunities.

The UK is fairly unique in the way it is looking at tobacco policy. It is science led—which, as a scientist, I think is very encouraging. You are in a position here to be able, ultimately, to eliminate the use of combustible cigarettes. We as a company stand ready to discuss with the Government when that could be and what triggers would need to be in place for us, as scientists, to be comfortable that there would not be unintended consequences to making a firm date for stopping the sales of cigarettes—for example, introducing all sorts of different smoke-free products that comply with standards and that are a better choice than continuing to smoke and, say, having 50% of smokers already having switched to them. I think we would be in a position to sit down with Government and agree on the time when we can stop selling combustible cigarettes. The UK is probably one of the most advanced countries in the world that could be in a position to do that in a very short space of time, which is really encouraging.



**Dr O'Connell:** Unlike the e-vapour product category, which has had public health endorsement—from the royal college, from Public Health England and from Cancer Research UK—no regulator or public health body has yet concluded that heated tobacco products reduce risk. To that end, we believe that they should be regulated alongside their traditional counterparts until such time.

**Dr Proctor:** When the Committee of Toxicity reviewed the data from both Philip Morris and myself, it believed that tobacco e-products were likely to be less risky than conventional cigarettes. On the data it has so far, the committee has said that it could not precisely put them in a place compared with e-cigarettes or NRT.

Q175 **Bill Grant:** So, it remains to be proved or peer reviewed that they are accurate, but you think that will evolve in time.

Moving on, Public Health England recently had a report on alternative smoking products, suggesting that e-cigarettes be made available on prescription as a cessation or stop-smoking treatment. Would you agree?

**Dr Proctor:** To make this really short—yes.

**Bill Grant:** This could be like “The X Factor.”

**Dr Gilchrist:** We would agree with any measure that can help smokers to switch if they are not going to quit altogether. Any measure that can help them switch to an alternative, smoke-free product is important.

**Dr O'Connell:** We would support the wide availability of e-vaping products to smokers, whether that is by the medicinal route or through the consumer route. We support a twin-track regulatory approach.

From our experience, I should add that smokers do not see themselves as patients. The innovation and product availability is one of the key features for the smoker in this category.

Q176 **Bill Grant:** On a similar theme, and perhaps linked to business or funding stream opportunities for companies—and this brings in marketing—do you have any plans to apply for a medicines licence for any of your e-cigarette or heat-not-burn products, to make them available on prescription via general practitioners? Do you see that as a way forward?

**Dr Proctor:** We have had to license applications, both for a product called Voke and for a product called e-Voke. That was some time ago. We got to a place where we decided that we needed to focus on our vape brand, Vype, and to bring these tobacco-heating products to market. We are not currently doing that through the medical licence route.

**Dr Jones:** We looked at it. The concern that we have, other than the cost, is mainly about the time. These products are innovating and changing so fast—if you run for a medicinal licence approval, you essentially freeze the product at the start, and you have to have the



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same product at the end. By that time, particularly in today's environment, the other products have evolved so fast that your product is out of date by the time you reach the other end.

**Dr O'Connell:** I echo what Dr Jones has said. We had some constructive dialogue with the MHRA to explore this. We would say that there needs to be a fast-track process if this is going to be explored. By the time you get the licence and market the product, the technology is redundant. There is also the issue of reduction in consumer choice and flavours, which needs to be explored.

Q177 **Bill Grant:** Am I sensing that as a "Not now, unless the criteria change"? Is that what I am picking up?

**Dr Gilchrist:** We are continually looking at it. We do not have a firm plan as yet. What Dr Jones mentioned regarding innovation is one of the key factors in making the decision. We will certainly continue to monitor how we think we could use that route to bring products to smokers.

Q178 **Bill Grant:** This is a wicked question, but do you see a financial incentive for your companies to go down that particular route for the distribution of your product?

**Dr Gilchrist:** I do not think it is necessarily a financial incentive. The regulatory review is important. We are availing ourselves of the regulatory process in the United States at the moment. That is not a medicines regulation, but it is a very well-prescribed regulatory route, which means that the regulator is looking at our science and is coming to a decision about it. That is what we would encourage in any other country: some way to have regulatory authorisation so that consumers can be confident about any information about the product and its relative risk.

Q179 **Bill Grant:** Consumers and, potentially, GPs could be confident about that.

**Dr Gilchrist:** They could be—absolutely.

**Dr Jones:** Likewise, I do not think there is a financial factor behind it. I think it is more a case of opening up another avenue by which consumers could have access to these products.

**Dr Proctor:** I agree.

Q180 **Chair:** Will you confirm whether any of your products would have to be medically licensed before a GP could prescribe them?

**Dr Gilchrist:** I am not super clear about that. Unfortunately, I do not live in the United Kingdom any more—I live abroad. I am fairly aware of the regulation, although I am not super clear about it. I think there are two roles that a physician can play in the life of a smoker. First, there is the prescription route. Then, there is the lifestyle advice route. What Public Health England has done here in the UK has been extremely important



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for physicians for the latter. Helping them to give smokers the right lifestyle advice about the choices they are making and to give them information about electronic cigarettes and heated tobacco products in that kind of format is important. It might be just as important, if not more so, than the medicinal route.

**Dr Jones:** I have a similar understanding. I apologise, as I, too, now live abroad, but the lifestyle choice or guidance—stop-smoking services in the UK—are advising people who wish to stop smoking to try e-cigarettes if they want to do so. My understanding is that, for prescription, that would have to be for a medicinal purpose.

Q181 **Chair:** I suppose it is about cost, too.

**Dr Jones:** Yes. TPD2 says that electronic cigarettes for medicinal purposes should be subject to MHRA licensing.

**Dr O'Connell:** The British Medical Association's position at the end of last year was significant. Following a review of the evidence, it came out as very supportive of the category and its great potential.

On the whole medicinal topic, if we consider the UK vaping population, we have 3 million vapers—former smokers and current smokers—of whom half have switched to vaping. That has not cost a penny to the taxpayer. That is quite a significant public health achievement.

Q182 **Darren Jones:** I have two quick questions. First, will you explain to the Committee what the different profitability would be from combustible cigarettes, e-cigarettes, heat-not-burn—what that might look like for you now and in the future?

Secondly, have you made any representations or expressed any views on excise duty regulation around e-cigarettes and heat-not-burn?

**Dr Gilchrist:** I am a scientist, so I am absolutely not an expert in fiscal matters, nor on profitability—as my husband will attest.

To take the last question first, on excise tax: in general, as a scientist, I would say that it makes sense for excise tax to match risk, so high-risk products should have high tax and low-risk products should have low tax. On a very simple basis, that is how I would look at it.

On profitability, I will probably be told that it is commercially confidential, but if the Committee felt it important we could offer some information in confidentiality. I am certainly not an expert in that area.

**Dr Jones:** Likewise, I am not an expert, but I am very happy to take that question back to my colleagues in the office and to ask them to submit something on profitability to the Committee.

On excise tax, I understand that, in the UK, e-cigarettes are already subject to VAT. We do not believe that there is any need to do anything in addition to that. As I say, we believe that heated tobacco products



should be subject to their own bespoke taxation under tobacco products that is commensurate with their risk or risk reduction potential.

**Dr Proctor:** I am not an expert, but I am going to say something anyway. My understanding is that, last year, our revenue from next-generation products was about 2%, and we are expecting it to be 3% to 5% this year. We have an ambition for it to be at 30% by 2030, and 50% by 2050. It is an evolving thing. That is only going to happen if we continue to innovate and get the regulatory opportunity to bring these new products to market.

On the question of excise, yes, we made representations in relation to tobacco-heating products. We think they should be under a different regime from that of cigarettes—weight based and at a lower rate than for cigarettes. For e-cigarettes and vaping products, we think VAT is enough.

Q183 **Darren Jones:** Feel free to say that you will need to check, but you talk about revenue. What about profitability between the different products?

**Dr Proctor:** That is where you've got me, as a non-expert.

**Darren Jones:** That is all right.

**Dr O'Connell:** Similarly, I am a scientist. What I would say from the Imperial side is that the money from the tobacco business generates the funds to invest into the NGP side of the business. As we get more smokers to switch to blu and our vaping products, Imperial will transition, and the NGP part of the business will become a bigger material part.

Regarding excise, we are clear that vaping products do not contain tobacco, and they should therefore not be excised as tobacco. It is important that the affordability of these products is maintained, so that we can get more smokers to transition.

Regarding heated tobacco and excise, Imperial and Fontem set out their views to the Treasury in response to the written consultation—I think that was just before Christmas. From our perspective, in the absence of public health endorsement of the heated tobacco category, we believe that heated tobacco should be taxed alongside traditional, conventional cigarettes.

**Darren Jones:** For the purposes of this Committee, we are primarily interested in the scientific basis of policy, but it is interesting to understand the commercial drivers around it, and whether there are any competitive drivers to the arguments you are making, perhaps between different products. That was very useful—thank you—but if you want to write to the Committee with further information afterwards, I am sure we will be happy to receive it.

**Chair:** Thank you very much indeed for your very open and insightful answers this morning.

That brings the first session to an end. We will move straight on to our second panel, but we do appreciate your attendance today.

## Examination of witnesses

Witnesses: Professor David Harrison and Dr Lynne Dawkins.

Q184 **Chair:** Good morning, and welcome. Thank you very much indeed for joining us for this second panel session this morning on our inquiry into e-cigarettes and reduced-risk tobacco products.

For the record, will you state who you are and which organisations you represent this morning?

**Dr Dawkins:** I am Dr Lynne Dawkins. I am an associate professor at the centre for addictive behaviours research at London South Bank University. I am an experimental psychologist. I have been working in nicotine and tobacco research for more than 20 years now, and on e-cigarettes since 2009.

**Professor Harrison:** I am David Harrison. I am a professor at the University of St Andrews, in pathology, and also in Edinburgh. I am here on behalf of the Committee on Carcinogenicity, which is a sister committee to the Committee on Toxicity, which we have already heard about. My general interest is experimental cancer biology.

Q185 **Chair:** Thank you, and welcome. Professor Harrison, may I start with you? You have mentioned the Committee on Toxicology. What have been the findings of the committee, or what work has it done, on e-cigarettes and heat-not-burn products?

**Professor Harrison:** There are three related committees: on toxicity, which is the one that we are talking about; on carcinogenicity, which is particularly on cancer; and on mutagenicity, which is on things that cause mutations. They have worked together, and they have completed a piece of work on heat-not-burn. They are just beginning to look in depth at e-cigarettes. They do not have conclusions, although they have gathered some evidence on that.

Starting with heat-not-burn, we would agree with many of the conclusions that we have already heard, regarding standardisation, methodology and so on.

On two of the big ones, one question is, "What is the importance of the combustion of tobacco?" The other is on the centrality of nicotine. Those are interesting. On combustion, we know that tobacco is a group 1 carcinogen—it causes cancer, whether or not you burn it. It is likely that anything that has tobacco in it will be somewhere between those two.

Combustion is extremely important. We reviewed that at length, and we found that, overall, there was a 90% to 95% reduction in cancer-causing chemicals. Some disappeared altogether, and some were reduced by only



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a half. There is clearly an interest in what is happening at the chemical level.

Nicotine is clearly important. Dr Dawkins is an acknowledged expert in addiction. Of course, many of the chemicals that are causing cancer are not nicotine. In the case of e-cigarettes and the work that is beginning on that, there are other things that are ingested or inhaled—particles, including metals, solvents and flavourings as we have heard—that we need to assess, too.

As regards conclusions on heat-not-burn, the COT has recognised that there is a risk. We do not know the answers. The committee's job is not to advise, other than to say that there is a risk. It cannot be quantified, although it appears to be less than from burning cigarettes, but the effect of that is not known.

On e-cigarettes, it is just beginning, but it is a broader look than just nicotine—it is particles, metals and volatile organic compounds. It is a more complex ask, in a sense, to look at that.

Q186 **Chair:** On heat-not-burn, what are the potential harmful compounds? Are they readily identifiable?

**Professor Harrison:** They are. We have heard from the companies, and they have done extensive studies. They have not found anything new, which is important. It is exactly the same chemicals that you would find in cigarette smoke—combustion. Some of those chemicals do not require combustion to be available, such as nitrosamines. The combustion is about the quantity of chemical released, and they shift the balance, but the chemicals are essentially the same as other chemicals you would expect from cigarette smoking, which have the potential to cause mutations and, ultimately, cancer.

Q187 **Chair:** Welcome, Dr Dawkins. We are going to come on to your experiments with different-strength e-cigarettes a little later. You highlight that, the more someone consumes e-cigarettes—as a general point—the more formaldehyde-type chemical they absorb. Why is that a problem? How does the risk compare with that from conventional cigarettes?

**Dr Dawkins:** I will start by saying that, compared with conventional cigarettes, the levels are much lower. We have not done an exact comparison, but they are much lower.

We have looked at formaldehyde in two ways. First, we have looked at a biomarker of formaldehyde in the urine of participants. We have also looked at formaldehyde and other aldehydes that are known human carcinogens in the aerosol. What we have done, uniquely, is to capture the puffing patterns that vapers engage in when they use different strengths of nicotine e-liquids, and then to replicate those puffing patterns with that same device and the same nicotine concentrations to



generate the aerosol and then trap it to analyse the potentially harmful compounds.

There are two levels. There is the biomarker work, which is quite novel, and it is not a very well-validated assay, so we would like to see it replicated. Then, there is the more robust, well-validated formaldehyde found in the aerosol. Again, the levels are lower than in tobacco smoke.

Q188 **Chair:** Correct me if I am wrong, but aldehyde—formaldehyde—is carcinogenic, so any absorption of it is potentially risky.

**Dr Dawkins:** Yes. Formaldehyde and acetaldehyde are known human carcinogens, but it is the dose that is important. We do not know at this stage—perhaps others do, but I am not sure if there is a cut-off at which point we can say that a certain level will translate into the development of cancer. We do not know, over the longer term, what levels of repeated exposure will have an impact on health risk.

Q189 **Chair:** One of the features of e-cigarettes and heat-not-burn products is the difference among individual products in the amount of voltage, energy or power that they generate, and therefore the temperature at which substances are heated. Has the work of either of you looked at the differing effect of temperature on both groups of products?

**Dr Dawkins:** We know that aldehydes are formed when the solvents in e-liquid are overheated—the vegetable glycerine and the propylene glycol. There have been reports that extremely high levels of aldehydes can be found when the liquid is overheated. It has also been argued that, under normal circumstances, vapers would be able to detect that overheating: they experience an aversive taste, so they would avoid using under those conditions.

It comes back to the importance of using realistic ways of vaping. In our work, we have looked at two different things. We have looked at nicotine concentrations in e-liquid. In another study, we have allowed users to adjust the power in some conditions or to keep it fixed in others.

There is an interaction between the two. When vapers are given a lower nicotine concentration e-liquid and are allowed to adjust the power, they increase the power, and that is then associated with an increase in aldehyde exposure.

**Professor Harrison:** As I have said before, the COT is just beginning to look at e-cigarettes, but many of the third and fourth-generation devices have very little literature published. Many of the early studies on the first and second-generation devices did not specify voltage or temperature, so there is a real dearth of information. Even where you have that information, it is not always easy to compare between studies. As Dr Dawkins is saying, there is work emerging that temperature is a factor.





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On heat-not-burn, going from 350° C down to 30° C, we know that there is no combustion on both settings, but, as I have said, you will still be releasing some potentially harmful chemicals, albeit in smaller amounts.

Actually, those comparative studies have not been done, or, if they have been done, the methodology is so disparate that it is very difficult to compare one study with another.

Q190 **Chair:** So, there is still a lot of work to do in that area.

**Professor Harrison:** Yes.

Q191 **Chair:** Who should be doing that work?

**Professor Harrison:** Much of it should probably be done by industry. Some of the data that COT reviewed was top rate in quality and academic excellence—it was absolutely first rate—but, clearly, public reassurance may require at least some of that at least to be confirmed outwith industry.

Q192 **Chair:** One of the features of conventional cigarettes is second-hand smoke—the trail that drifts off—which led to greater control over where one may smoke cigarettes. Have you done any work on the potential of second-hand vapour, smoke or however you wish to describe it from these two types of product?

**Professor Harrison:** Again, it is early days but, reviewing the literature on e-cigarettes, some studies in closed rooms would show as much nicotine or perhaps half as much nicotine in the air from an e-cigarette as from a conventional cigarette. There is a significant exposure, potentially. Again, it is very difficult to comment on how real that is, because of methodology.

Metal particles have been detected in ambient air. One of the areas that COT is looking at is bystander effects. With e-cigarettes or with heat-not-burn, there is a similar issue. Everything is reduced compared with cigarette smoke, but bystander effects are something to be aware of. One would expect, however, that the dose would be commensurately less than for cigarettes.

**Dr Dawkins:** My understanding from reading the literature—this is not something in which I have a great deal of expertise—is that the nicotine levels found in the aerosol of electronic cigarettes dissipate quicker and generally at much lower levels than for tobacco cigarettes.

The studies that I have read show that, generally, levels of potentially harmful compounds were below the occupational safety levels in vape shops. There has not been a huge amount of research done in that area.

**Professor Harrison:** There is a huge spread, and the trouble with detecting very small amounts is that you tend to collect samples, and the collection itself changes the balance of what you then find. It is a real mess of an area.



**Dr Dawkins:** It would be useful to do work on other individuals who live with vapers and to examine biomarkers of exposure in those individuals.

**Chair:** Thank you—that is useful.

Q193 **Damien Moore:** Dr Dawkins, in your written submission you tell us about your experiments with having e-cigarettes with different nicotine strengths, and how that influences users' puffing behaviour. Will you briefly recap for us the essential conclusions from those studies?

**Dr Dawkins:** We have done a couple of studies, both in the lab and outside the lab, using real-world puffing patterns.

We were interested in what happens when vapers switch to using lower nicotine concentration e-liquid. Using an experimental design, we allocated people to use a high level on one occasion and a lower level on another occasion: 24 mg/ml versus 6 mg/ml, for example. We measured their puffing patterns. In one study, we measured nicotine delivery. We looked at the subjective effects of satisfaction and craving reduction. We then mimicked those puffing patterns under the low and high nicotine e-liquid conditions in a separate laboratory, using the same device to generate aerosol to look at the carbonyl compounds in the aerosol.

We found—both in the laboratory condition and outside over a longer duration of four weeks—that using a lower nicotine concentration e-liquid in the same device resulted in compensatory behaviour. This is commonly seen with tobacco smokers when they switch to using lower nicotine yield cigarettes. Vapers will increase their puff number and their puff duration, and they consume a great deal more e-liquid.

In the second study, where we allowed vapers either to keep the power fixed or to be able to adjust it as they saw fit, under certain conditions 70% adjusted the power upwards when they were using a low nicotine concentration, and only 30% did so with a high concentration. We saw that, on average, when people are using a lower nicotine concentration, they compensate both in their puffing behaviour and by changing the power on the device—by increasing the power. A combination of those two things seems to be associated with greater exposure to carbonyl.

The key message is not to encourage vapers to switch to using lower nicotine concentrations. In fact—perhaps counterintuitively—using a higher nicotine concentration might result in less puffing. The nicotine delivery still seems to be much better with the higher nicotine concentration.

Q194 **Damien Moore:** Professor Harrison, has the Committee on Toxicity done any evaluation of the effect of different puffing patterns in response to different nicotine strengths?

**Professor Harrison:** It has not. Dr Dawkins is leading the field in this respect. There is very little published work on that. The belief is probably that stronger nicotine strength will reduce puffing, and that is being



experimentally confirmed, but COT has not formally reviewed any reviews on that subject.

Q195 **Damien Moore:** Is there any evidence on what strength of e-cigarettes or heat-not-burn products is most likely to help those trying to give up conventional cigarettes?

**Dr Dawkins:** It is quite difficult to answer whether there is a direct effect from nicotine content. I cannot say so much about heat-not-burn, but, particularly with e-cigarettes, the nicotine delivery depends on the user behaviour, on the propylene glycol to vegetable glycerine ratio, on the flavourings, on the device type, on the power and on so many other things.

However, having said that, and with those caveats in mind, there is some evidence to suggest that higher levels of nicotine are better for quitting. Dr Farsalinos in Greece asked vapers about this, and they reported that they had to use high concentrations to quit, but then they reduced over time.

My colleague Catherine Kimber, who was one of the co-authors on our submission, has also shown that higher levels of nicotine, compared with a low level and using the same device, were associated with better craving relief and with better quitting over six months—so, more people were able to quit with the high nicotine concentration e-liquid. That was a study of only 70 smokers, so more is obviously needed.

We can also look at the evidence from nicotine mediations—from nicotine replacement therapy. Nicotine is clearly important because hundreds of randomised control trials have shown that nicotine-containing NRT is better than placebo. There is also evidence that using a combination of nicotine replacement therapy products—a patch and gum or a lozenge—can increase cessation success.

**Professor Harrison:** I do not think that data exist for heat-not-burn. In fact, one of the issues with heat-not-burn is that, when we talk about these reductions, what are we actually comparing? It tends to be standardising the amount of nicotine consumed. In fact, with these numbers that we have heard about, where anything from 40% to 95% of chemicals are reduced, that is on the basis of assuming a standardisation to the normal cigarette, whatever that is. We do not have evidence going beyond that to say what would be a suitable replacement.

Q196 **Damien Moore:** The 20 mg/ml cap on e-cigarettes comes from the EU directive. What scope is there for changing that after Brexit?

**Dr Dawkins:** I think that is for you to say rather than me. First, there is no rationale for that cap. I think it was mentioned earlier that there was not so much evidence around at the time when article 20 of the TPD was being created. It seems arbitrary to me. There is no evidence for increased harms of nicotine with levels above 20 mg/ml. In the absence of that evidence, and in the light of research by our group showing that if



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you reduce you compensate, that is costly financially, as you are using more e-liquid, and it may also come with a health cost if increased exposure translates to long-term health risk.

I have a number of other points to make on this. At the time of the TPD, just before implementation, Action on Smoking and Health conducted a survey of the number of people using above 20 mg/ml. It was 9% at the time—a minority, but still a significant number of people.

These are vapers, and we should remember that we also want to appeal to smokers. For smokers, higher levels are likely to be important.

The ASH study also showed that half of smokers who had tried electronic cigarettes did not find them satisfying and did not find that they reduced their craving, so they gave up using them. For those smokers who are transitioning, higher levels of nicotine may be quite attractive.

High levels of nicotine are not necessary in the more sophisticated devices—the high-power modular systems—which may be why, over time, vapers are reducing the nicotine concentration in their e-liquid. But not everybody wants to use these large devices with higher power and lots of vapour.

In another study that we conducted, where we asked smokers which device they would use if they had a choice—a small cigarette-like device or a fountain-pen-like device—50% said they would prefer to use the smaller cigarette-like device. Many people want a discreet device and do not want lots of vapour, and because those types of devices are less powerful they aerosolise the solution less effectively. You need the higher nicotine concentrations.

I also think that, in general, the cap on nicotine concentrations is sending the wrong message—that nicotine is problematic and addictive. Further to that, you slap a health warning on e-cigarettes that says, “Nicotine is a highly addictive substance.” That is sending the wrong message—that it is nicotine that is the problem. It is smoking that is the problem, not nicotine.

Q197 **Chair:** Although nicotine is a highly addictive product.

**Dr Dawkins:** The addiction relates to the delivery mechanism. Addiction delivered from a tobacco cigarette is, indeed, highly addictive. It is the speed of the delivery. Cigarette smoking is the fastest way of delivering nicotine. Other compounds are added to tobacco to facilitate nicotine delivery. There is a chemical known as a monoamine oxidase inhibitor, which stops dopamine, a brain chemical responsible for reward, from being broken down, so there are other factors in tobacco smoke alongside the nicotine delivery that maintain and facilitate addiction.

Q198 **Chair:** I want to make this absolutely clear. The pattern among established vapers is of starting high and then dropping down. Is there any additional health benefit from reducing the amount of nicotine in the



liquid you use, or is it a perceived health benefit?

**Dr Dawkins:** I think this is a perceived benefit. This is anecdotal evidence from my discussions with vapers: "I am trying to wean myself off nicotine. I don't want to transfer to another product. It's still maintaining the addiction." A couple of studies, one by Jean-François Etter and an unpublished study that we conducted, showed that, over time, although vapers reduced the nicotine concentration in their e-liquid, their cotinine levels—which is a marker for nicotine intake—remained very stable. This is consistent with what we have shown in the lab: that people compensate—they just puff more, they puff longer and they use more liquid. I would not say that there is any health benefit.

Q199 **Chair:** For someone vaping with no nicotine in a liquid and with a high content, is there any additional health benefit?

**Dr Dawkins:** The nicotine is not the harmful component. Obviously, vaping is less harmful than smoking. Any harms appear to be associated with the flavours and the heating of the solvents.

Q200 **Martin Whitfield:** What is the harmful effect of nicotine on the human body?

**Dr Dawkins:** Nicotine is a mild stimulant, so it has an effect on blood pressure and heart rate, but, for most individuals, this does not seem to be problematic. That is why nicotine is licensed as a medicine by the MHRA in nicotine replacement therapy products—and, indeed, is safe for use in pregnancy.

There is some literature that nicotine might be harmful to the developing brain in adolescence, but those findings come almost exclusively from animal research, so it is very difficult to extrapolate from that to humans. We do not see any evidence that there are lots of adolescents with difficulties from using nicotine. It is difficult, because it is hard to isolate the nicotine from the smoking.

**Professor Harrison:** The nicotine in animal experiments that we have heard about tends to be in a large dose. There is some evidence, for example, that mice may metabolise nicotine differently. There are recent studies suggesting that e-cigarettes are therefore dangerous, but that may be mouse-specific—so we should stop mice using e-cigarettes.

There is evidence of acute injury to the lining of blood vessels, for example, and there is some evidence—it is not that strong—that nicotine can be damaging to people who already have cardiac failure. Actually, I think these are fairly marginal compared with the real damage related to cigarettes, which is tobacco. In particular, it is mixtures, not a single chemical. Nicotine may be a part of that, but it is those other chemicals that are doing the heavy work.

Q201 **Martin Whitfield:** Do you think we know all we need to know about the effect of nicotine on the human body? We always want to know more, but



are you satisfied that we know enough for you to have answered in the way you have about nicotine compared with tobacco, with the multitude of chemicals and the mix that is in there?

**Dr Dawkins:** I think there is still work to be done there. The effects of nicotine have been conflated with smoking for so long, and I think there may be different effects, depending on the nature of the delivery. That is all I could say on that—I am not an expert in that area.

**Professor Harrison:** I think that is probably true. If nicotine is encouraging you to engage in habits that expose you to other toxic substances, yes, we should be doing more work, but the body of evidence is that nicotine is not by any means the most harmful product.

Q202 **Martin Whitfield:** You compare nicotine patches and gums; you suggest that people might use one or more. Is the academic interest—I suppose that is how I want to phrase this—in the nicotine hit or the amount of nicotine, when you are talking about low nicotine requiring more frequent puffs? The nicotine is a guide, I suppose, to the body's desires, so the high nicotine satisfies quicker—therefore there is less; therefore, inherently, it is less damaging. Is that a true conclusion of what you are saying?

**Dr Dawkins:** Absolutely.

Q203 **Martin Whitfield:** Are your concerns with regard to e-cigarettes actually as much to do with all the other materials involved—the metals, the particulates and things like that? Is that where the potential long-term dangers lie?

**Professor Harrison:** The Committee on Toxicity wants to address that, as it is the new part of the picture. There is so much known about nicotine, but it is the potential for metals, solvents and flavourings that have previously been used but never inhaled—that is where the interest with e-cigarette risk assessment lies.

Q204 **Martin Whitfield:** That is where the risk assessment comes from.

**Dr Dawkins:** I agree.

**Martin Whitfield:** You agree. I have gone as far as I can go with this, then.

Q205 **Darren Jones:** I have two final small questions. Am I right in suggesting that the bulk of the evidence on e-cigarettes and heat-not-burn is focused on in vitro and mice testing, and that we are just starting to get into the clinical studies with real people? Is that right?

**Professor Harrison:** The big challenge with epidemiology is that it is long term. It can take 20 years to get lung cancer if you smoke. The real studies and the real-world difference is going to be, "Will we be able to tell in 20 years?" We are trying to model from what we know that even very small exposure—a small number of cigarettes smoked—can make a



difference in large epidemiological studies. There is parallel work trying to model this. If we have reduced the number of chemicals, have we reduced the risk? The message is that animal experiments do not give a very good guide. Just because we have taken out half or three quarters of the chemicals, that does not necessarily mean that we have taken out half or three quarters of the risk. The only way to find that is through real-world experience. That is tough, and it takes time.

**Q206 Darren Jones:** So there are no risks in an overemphasis on non-clinical trials, beyond the ones that we cannot control, as they just take a long time to do.

**Professor Harrison:** There are other risks, and there are potential biomarkers—we have heard the term before—that might say something is going to happen. They tend to be fairly low sensitivity when it comes to long-term consequences. There are real challenges in gathering the data prospectively.

**Q207 Darren Jones:** I assume that, on the behavioural side, it is a slightly different story, because you are doing behavioural studies with people.

**Dr Dawkins:** Yes.

**Q208 Darren Jones:** Is there a restriction, therefore, on the conclusions that you can make on the behavioural side, because you are waiting for the epidemiological studies on the toxicology side to catch up?

**Dr Dawkins:** On the behavioural side, we can inform the lab-based studies by saying, “This is the way people use”—albeit there is huge variation in the way people use, because it depends on the device, the vehicle, the nicotine concentration and so on. There have been so many studies that have made conclusions based on unrealistic set-ups and unrealistic puffing patterns. That is where behaviour can inform the lab-based work.

**Q209 Darren Jones:** Do you find that your conclusions are doing that?

**Dr Dawkins:** It is early days. We have only recently published these, and our second paper is still under review—although hopefully it will be out soon. It is early days, but we need to make this more widely known, and hopefully this will happen.

**Q210 Darren Jones:** That sounded very diplomatic, but a message has gone out to look at your behavioural studies when doing clinical studies.

**Professor Harrison:** The speakers before all talked about the need for standardisation. That is not just devices—some of the earlier ones were pretty ropey. People were inhaling lead, for example. There is a real need for standardisation. For experimental design, it is essential that that is described. Otherwise, data are well-nigh meaningless, because they have no relevance to the real world and cannot be compared with anything else. People make claims that are either scaremongering or falsely



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reassuring with no real validity. Standardisation is a very important message to come out from this.

Q211 **Darren Jones:** Yes—that is quite important.

Lastly, if you had a blank cheque from the research councils, what would be the top areas of research, where there are gaps today in e-cigarettes and heat-not-burns, on which you would like to spend that money?

**Professor Harrison:** Would you like to spend some money first?

**Dr Dawkins:** Yes, I can start.

**Darren Jones:** Hypothetically, I should add.

**Dr Dawkins:** Long-term longitudinal studies will give us the best indicator of long-term health outcomes. That would take a lot of money, because there would be 20-plus years over which we would be looking at actual health outcomes. Obviously, we cannot wait that long—we need to have a bit more of an idea now.

The second area would be flavourings, because research has already shown that there can be huge variations in levels of potentially harmful compounds, depending on the flavour. But it is not just the flavour. We have also found different levels of aldehydes in the same flavour from different batches, so it is not the flavour per se—this goes back to a point that was made earlier—but the various compounds that make up that flavour. They may be present in one batch but not another batch, so I am sorry, but it is even more complicated than just flavourings.

Q212 **Darren Jones:** You may not know the answer, but do we make flavours in this country, or do we import them?

**Dr Dawkins:** I think they can be made in this country, and they can be imported.

Q213 **Darren Jones:** Are they subject to normal chemical regulations—the REACH chemical regulations?

**Dr Dawkins:** I am not sure.

**Professor Harrison:** They will be assessed, so they will go through that process. Flavourings are being looked at EU-wide at the minute.

Q214 **Darren Jones:** Regarding your answer, Professor Harrison, on the blank cheque.

**Professor Harrison:** Yes—I would like to spend some money.

Q215 **Darren Jones:** So—the key gaps: what would you spend the money on?

**Professor Harrison:** Some money on standardisation—the standardisation of the research. The UK Government have invested heavily in systems biology, and one of the previous speakers referred to systems toxicology, which PMI in particular has done. That is basically





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computational modelling—taking information and using it in a dynamic sense to try to make predictive models so that you can tell after two years that something is happening, rather than waiting for 20 years. A lot of money is being spent on that, so targeting some additional funding there would be useful.

Then, there is the longer-term epidemiology. That is not without its challenges, because people may start and stop. They may smoke cigarettes sometimes, and they may use heat-not-burn sometimes. There is increasing evidence, particularly from the far east, that even one or two cigarettes a day, if you do big enough studies, will show a risk of lung cancer. If you take an average as being 20, that is a 95% reduction, and cigarette smoking might still increase the rate of lung cancer. That puts it into perspective that, if there are 40,000 people a year dying in this country, 400 would be 1%, so 2,000 would be 5%.

On the long-term epidemiology studies—it is not just saying, “Well, there is no risk, so let’s go for it.” It is saying, “This may be the best thing to do, but that does not mean that these are risk free.”

**Chair:** Thank you very much indeed. Your answers and your attendance today are very much appreciated. Thank you for joining us.

**Dr Dawkins:** Do I have time for one final point?

**Chair:** Please—yes.

**Dr Dawkins:** I wish to pick up on the point that Moira made earlier about the plateau in the number of people taking up e-cigarettes. Much research is on current vapers. They are probably okay—they have made the switch. We need to concentrate on smokers. Why are smokers not making the switch? Why are half of those smokers who have tried electronic cigarettes not fully transitioning? This may be partly due to the nicotine concentrations, and it may be partly due to the health messages, but we need to make them as attractive as possible to smokers. That means having a variety of different products—one size does not fit all—and having different concentrations of nicotine available.

Q216 **Chair:** Professor Harrison, is there anything further that you would like to say?

**Professor Harrison:** That is a great way to have job creation for risk managers, but I absolutely agree. If we are going to use this as a strategy, it has to be diverse and appropriate for different people.

**Chair:** Again, thank you both for joining us.