Mr Ismail Sabri Yaakob,
Prime Minister of Malaysia,
Prime Minister's Office Main Block,
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Federal Government Administrative Centre
62502 Putrajaya
MALAYSIA

19th July 2022

Your Excellency, Honourable Minister,

Proposed prohibition of sale of cigarettes, tobacco or vape products to those born after 2005

Please find attached a letter sent to the offices of the Prime Minister, Minister of Health and Minister of Finance of Malaysia.

As an international group of health leaders, from the EU, North and South America, Africa and Asia, we are long-standing experts and advocates for public health and tobacco control. We support the WHO Framework on Tobacco Control (FCTC) and Article 1(d) of the FCTC[1], which states "tobacco control" means a range of supply, demand and harm reduction strategies that aim to improve the health of a population by eliminating or reducing their consumption of tobacco products and exposure to tobacco smoke "

We have provided brief biographies: see 'About the Authors', as well as a list of 'References'.

We are prompted to offer our comments following the 14th July 2022 local press report on the cabinet approval of the draft proposed Tobacco and Smoking Control Bill, which contains provisions to prohibit the sale of cigarettes, tobacco and vape products to those born after 2005[2].

As long-term tobacco control advocates, we applaud your government's efforts to strengthen the prevention and control of combustible tobacco-related disease and premature death. However, if the prohibition were to be extended to non-combustible, reduced risk products, such as ENDS, we fear that there would be unintended consequences for those smokers who cannot or will not quit smoking. We would rather urge the Malaysian Government to regulate with a regulatory framework that is proportionate to the product's relative risk profile to tobacco. See below under '*Regulating for net public health benefit*'.

In our comments, we refer to such devices as Electronic Nicotine Delivery Systems (ENDS). However, similar considerations apply to all smoke-free nicotine products – electronic cigarettes, heated tobacco products, smokeless tobacco or snus, and oral nicotine pouches. The critical issue for public health is whether the product involves combustion and inhalation of smoke, which is the primary cause of disease and premature death. Smoke-free nicotine products have the

potential to drive out smoking and completely revolutionise the tobacco market and tobacco industry.

We therefore urge the government of Malaysia not to prohibit smoke free nicotine-based alternatives to combustible cigarettes and to employ evidence-based regulation to help protect the health of Malaysia's 32.67 million people. 40% of Malaysian men still consume combustible cigarettes. The Malaysia government should support smokers by encouraging a mass switch from high-risk cigarettes to low-risk ENDS and accelerating the end of the epidemic of smoking-related disease.

Regulating for net public health benefit

We would like to encourage your government to establish evidence-based tobacco control and harm reduction policies, which would deliver net public health benefit for the people of Malaysia. To this end, regarding non-combustible nicotine-based alternatives, we need to emphasise two important qualities:

(1) they do not involve combustion and so do not create products of combustion, and
(2) to an increasing extent, they can replace smoking for many smokers.

Because almost all of the harm associated with tobacco/nicotine use arises from exposure to smoke, not nicotine, then these products are likely, beyond any reasonable doubt, to be much less harmful than smoking (90-100% less harmful depending on product and regulatory standards). The fact that they appeal to smokers as satisfactory alternatives to smoking offers the potential for major changes in the way people use nicotine with great health benefits as a result.

- Instead of prohibition, a new regulatory regime could specify age restrictions, product standards, labelling, marketing and use restrictions as appropriate. There is an opportunity for Malaysia to gain from experience in the United Kingdom, European Union and elsewhere, where there are many valuable lessons to learn.

- The effect of the proposed prohibitive regulatory regime denies Malaysia smokers access to much lower risk products and has the unintended effect of protecting the cigarette trade and incumbent business interests of the major tobacco companies – even though these companies are trying to switch to marketing lower risk products. There is no justification for this.

- We urge the Government of Malaysia to embrace tobacco harm reduction in Malaysia’s approach to tobacco control and create the appropriate regulatory and fiscal framework to allow low-risk products to displace smoking in the consumer market for nicotine. This would meet the demands of people who cannot or do not wish to quit completely, but with much less cancer, cardiovascular and respiratory disease as a result. The current

consultation and intention to amend critical regulations provide an opportunity to start that process.

Specifically regarding ENDS; any policy making in this area should recognise three fundamental characteristics:

1. While not necessarily without risks, it is clear beyond reasonable doubt that ENDS are much less harmful to health than cigarettes. *See Section 1.*

2. ENDS contribute to smoking cessation or displace cigarettes among people who would otherwise take up smoking, including young people. *See Section 2.*

3. ENDS are economic substitutes for cigarettes. Increases in costs or regulatory burdens on ENDS are likely to decrease demand for ENDS but also increase demand for cigarettes. *See Section 3.*

Evidence for the three characteristics listed above is described briefly in the following three sections of this response and supported by a scientific paper included in Appendix 1. This paper is the work of fifteen past presidents of the scholarly society, the Society for Research on Nicotine and Tobacco. It includes some of the foremost experts in the world[3].

The danger of unintended consequences

Because cigarettes are much more harmful than ENDS, it will only take a slight rise in smoking to offset any public health benefit from reduced ENDS use arising from ENDS prohibition or excessive regulation. The critical issue is the interaction of demand for ENDS with demand for much more harmful cigarettes. This is not a new idea: the Royal College of Physicians (London) expressed this clearly in its 2016 report[4]: … if [a risk-averse, precautionary] approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer-friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it causes harm by perpetuating smoking. Getting this balance right is difficult. If a proposed prohibition on ENDS were to be considered, it would certainly not "get this balance right" or even recognize that a balance is necessary. Prohibition or excessive regulation of ENDS without considering the effects on smoking could easily lead to a net increase in harm to public health by "perpetuating smoking" or stimulating black market activity.

Policy implications

Finally, we briefly consider policy implications in Section 4, calling for a risk-proportionate approach to regulation and use of ENDS to address the health problems caused by cigarettes. In a risk-proportionate approach, the highest risk products face the most stringent regulation, and low-risk alternatives face fewer and lighter restrictions. Prohibitions are the worst possible policy option: denying law-abiding smokers much safer options; creating black markets; increasing criminality and corruption; and creating new burdens on law enforcement. ENDS should be used

to drive down smoking, the dominant form of tobacco use in Malaysia. ENDS should be seen as an opportunity, not a risk.

Section 1: ENDS are much less harmful than cigarettes

The most crucial insight is that smoking is the problem. Smoking accounts for 98 per cent of the global burden of tobacco-related mortality[5,6]. Inhalation of products of combustion – the toxic tar and gases created in the burning tip of a cigarette – is the primary cause of harm, not nicotine itself. As Professor Michael Russell famously explained in 1976[7]: People smoke for nicotine, but they die from the tar. Their risk of lung cancer and bronchitis might be more quickly and effectively reduced if attention were focused on how to reduce their tar intake, irrespective of nicotine intake. In this statement, Russell lays the ground for tobacco harm reduction: reducing exposure to the toxic tar from cigarette smoke without quitting nicotine as well. This allows smokers an easier path to smoke-free status and means more will be able and willing to take it. Forty-six years later, ENDS make this possible in a format that works for consumers through a compact, efficient device that operates below the temperature at which combustion can occur but delivers a satisfactory nicotine dose through an inhaled aerosol ("vapour").

There is no real doubt that ENDS are much less risky than cigarettes. Many of the toxicants in tobacco smoke are either not present at detectable levels or present at much lower levels than in cigarette smoke. The most convincing evidence comes from biomarker data (measurement of toxicants in the blood, saliva or urine of users and non-users). In 2018, independent experts for Public Health England reviewed the biomarker data and concluded[8]: Vaping poses only a small fraction of the risks of smoking and switching completely from smoking to vaping conveys substantial health benefits over continued smoking. Based on current knowledge, stating that vaping is at least 95% less harmful than smoking remains a good way to communicate the large difference in relative risk unambiguously so that more smokers are encouraged to make the switch from smoking to vaping. It should be noted that this does not mean e-cigarettes are safe.

The United States National Academies of Science, Engineering and Medicine concluded[9]: Laboratory tests of e-cigarette ingredients, in vitro toxicological tests, and short-term human studies suggest that e-cigarettes are likely to be far less harmful than combustible tobacco cigarettes.

A more detailed discussion of the health impacts of e-cigarettes compared to cigarettes forms part of a recent paper by fifteen past presidents of the independent Society of Research on Nicotine and Tobacco (SRNT)[10]. These authors, some of the world's leading authorities, summarise the safety case as
follows: Many scientists have concluded that vaping is likely substantially less dangerous than smoking because of the following:

- The number of chemicals in cigarette smoke, greater than 7000, exceeds that of e-cigarettes aerosol by 2 orders of magnitude.

- Among potentially toxic substances common to both products, cigarette smoke generally contains substantially larger quantities than e-cigarette aerosol. However, e-cigarette aerosol contains some substances not found in cigarette smoke.
- Biomarkers reflecting exposure to toxic substances are present at much higher levels in exclusive cigarette smokers than in exclusive vapers, and studies of smokers who switch to e-cigarettes find decreases in toxicant exposures.

Tests of lung and vascular function indicate improvement in cigarette smokers who switch to e-cigarettes. Exclusive users of e-cigarettes (most being former smokers) report fewer respiratory symptoms than do cigarette smokers and dual users. The SRNT past presidents' paper was published in the American Journal of Public Health and is appended as Appendix 1. Citations for the statements above can be accessed via the paper.

Section 2: ENDS help smokers quit and displace smoking

2.1 Adult smoking cessation

There is considerable converging evidence from multiple sources, including randomised controlled trials, observational studies, population trends, and market data, that people use ENDS to quit smoking, cut down, transition to smoke-free status over time, or as a diversion from smoking in the first place. The evidence for ENDS as a substitute for cigarettes and a driver of smoking cessation comes from multiple sources, each with its strengths and weaknesses, but taken together make a strong case – and more robust than the conventional smoking cessation treatments. The British smoking cessation expert, Professor Robert West, summarised the state of evidence in a 2019 presentation[11]. The link to Professor West's whole presentation is provided in the endnote. The following provides an overview of studies that support the evidence framework articulated in Professor West's presentation.

• Randomised controlled trials: Several recent trials show positive results[12,13]. The most substantial clinical trial to date showed e-cigarettes with approximately twice the smoking cessation efficacy of NRT[14]. There is an accumulating evidence base: the Cochrane Review, which provides a world-renowned synthesis of clinical trial evidence, concluded in September 2021[15]: Nicotine e-cigarettes probably do help people to stop smoking for at least six months. They probably work better than nicotine replacement therapy and nicotine-free e-cigarettes. They may work better than no support, or behavioural support alone, and they may not be associated with serious unwanted effects The Cochrane Review restricts its evidence reviews to clinical trial evidence. But a range of evidence from other sources strengthens the support for ENDS for smoking cessation:

• Observational data: There is evidence that smokers who use e-cigarettes are more likely to quit smoking than those who do not[16,17].

• Population trends: There is evidence that smoking cessation activity also increases as the prevalence of e-cigarette uses increases in a population[18,19,20,21].

• Modelling studies: Modelling studies based on the experience show substantial public health potential even when parameterised with sceptical assumptions[22,23].

• Testimonials: Thousands of users provide compelling reports of quitting smoking with ENDS[24].

2.2 Dual use is part of a positive transition

Some claim that the "dual use" of ENDS and cigarettes is problematic. However, it is better understood as a part of a transition pathway from exclusive smoking to exclusive ENDS use – not everyone switches immediately[25,26,27]. In Britain, the proportion of ENDS users who are dual users has fallen steadily from two thirds in 2014 to less than one-third in 2021, suggesting a steady migration from dual use to exclusive use of ENDS[28]. The evidence also suggests that vaping encourages smoking cessation in smokers who were not otherwise interested in quitting smoking. These smokers become what is known as "Accidental quitters"[29,30].

2.3 Diversion of young people from smoking

Again, the evidence points to interactions between ENDS use and cigarettes among adolescents, with ENDS functioning as a diversion from smoking for adolescents[30,31,32]. This is consistent with observed US adolescent population trends, which have seen a sharp decline in smoking as ENDS use has risen[33,34]. US and UK data show that the most intensive adolescent use of ENDS is among those most likely to smoke[35,36,37]. There is little evidence of dependence in ENDS users who are never smokers, and these users generally use ENDS infrequently[38]. The US high school past-30-day vaping rate fell from 27.5% in 2019[39] to just 11.3% in 2021[40]. This rapid change suggests there is a core of more intense users who would otherwise be smoking (and who likely benefit from vaping) and a broader group of experimental or frivolous 'party' users that justify less public health concern.

2.4 Looking at all the evidence

Taken as a whole, the evidence makes a compelling case that smoke-free alternatives to cigarettes displace smoking. The Tobacco Treatment Network of the SRNT recently argued[41]: Strategies used for combustible product cessation may be adapted for novel products, and treatment recommendations for tobacco use disorder should be made within the context of a harm reduction framework wherein alternative product use may be the desired outcome. A further discussion of the smoking cessation evidence is summarised in the letter from fifteen past presidents of SRNT[10], which is also appended at Appendix 1. The authors conclude: "Although not the final word, the totality of the evidence indicates that frequent vaping increases adult smoking cessation. Smokers unable to quit smoking with evidence-based cessation methods should be well informed about the relative risks of vaping and smoking and vaping's potential to help them quit smoking".

Section 3: ENDS function as substitutes for cigarettes

It is not uncommon for two goods to function as economic substitutes if they represent different forms of similar consumption in competition: tea and coffee, beef and lamb, or rice and pasta. This means that the price of one product will affect the demand for the other through a positive 'cross-elasticity'. It also means that regulation that suppresses demand for one product will increase demand for the substitute product. Evidence is emerging that ENDS use displaces smoking and promotes smoking cessation (see section 2 above). Further evidence for substitution comes from analyses of the effects of measures to control ENDS use. Evidence suggests e-liquid flavour bans[42], e-cigarette advertising bans[43], and access restrictions[44] may increase cigarette smoking. However, the most direct and relevant evidence comes from studies of the demand response to ENDS taxes that have been imposed. The World Health Organisation argues that[45]: ENDS/ENNDS and cigarettes are substitutes – higher cigarette prices are associated with increased ENDS/ENNDS sales. A significant body of literature broadly supports WHO's assertion[46,47,48,49,50,51,52,53,54,55,56]. Substitution effects make a significant difference to the overall public health consequences of regulation. The fact that ENDS and cigarettes are economic substitutes should be a central consideration in ENDS regulatory policy because this is the mechanism by which prohibition or excessive regulation of ENDS is likely to do more harm than good.

Section 4: Consequences for policy

4.1 The policy of prohibition and the risks of unintended harmful consequences

In our experience, governments should reject prohibitions or anticipate numerous perverse consequences. The arguments against ENDS prohibition are well established[57]. They are based on the experience of prohibition of illicit drugs[58], alcohol[59], and tobacco[60,61,62,63]. It is almost impossible to suppress demand for a recreational stimulant like nicotine. Many people will wish to use nicotine products that do not have the severe health impacts of cigarettes and other combustibles.

A prohibition does not make the banned products disappear. A prohibition changes how the products are supplied, who supplies them, and at what price. Over time, this demand for ENDS products would be met through cross-border trade, internet sales, and ultimately more established criminal networks with aggravated risks of bribery and corruption. It is also likely that young people would play a significant role in the illicit supply chain. A further consideration is the behavioural responses to a prohibition of ENDS. This could take the form of illicit manufacture and sale of ENDS in Malaysia, cross-border trade by which foreign producers undermine law-abiding Malaysia producers, an increase in DIY home mixing or formation of informal supply chains, and various possible workarounds. Many of the likely behavioural responses create

significant additional risks compared to a well-regulated lawful market. A better strategy would be to allow legally available ENDS products to compete with cigarettes rather than to create a regulatory protection for the cigarette trade.

4.2 Adopt risk proportionate regulation

The most effective approach will be to abandon prohibition in favour of "risk-proportionate" regulation. This is not a novel idea but reflects the standard regulatory practice of imposing burdens and restrictions that reflect the voluntary and involuntary risks to those most directly affected. In a risk-proportionate approach, the main regulatory levers are applied differentially. The most stringent and restrictive regulation would be applied to the most harmful products, cigarettes. Regulation of the smoke-free alternatives would focus on consumer protection (i.e., benefits to the consumer) and control of uptake by adolescents where this does not cause significant harm to adult smokers.

Section 5: Conclusion

The primary goal of the Malaysia tobacco policy should be to prevent and control tobacco-related excess mortality and morbidity. In practice, this means reducing smoking as deeply and rapidly as possible. Tobacco harm reduction provides a fast-acting, market-based strategy for reducing smoking and eliminating most smoking-related risks. The regulation of ENDS and other smoke-free products should always be considered as part of a regulatory system that covers all the nicotine products, both smoked and smoke-free. The aim should be to encourage the migration from high-risk to low-risk products and support positive behaviour change. Regulators should take great care to avoid the perverse consequences of prohibitions and use regulation instead. Risk-proportionate regulation provides a robust basis for controlling the consumer nicotine market and creates strong incentives that support public health.

About the authors

- **Delon Human** (France, South Africa) M.B.Ch.B., M.Prax.Med, MFGP, DCH, MBA is a physician qualified in family medicine and child health, with an MBA from the Edinburgh Business School. He is a published author and health care consultant specializing in global health strategy, harm reduction and health communication. He has been active in tobacco control for decades, including advocacy for taxes on combustible tobacco to drive down consumer demand. He has acted as adviser to WHO Director-Generals and UN Secretary-General Ban Ki Moon. Formerly, he was Secretary General of the World Medical Association (WMA), the global representative body for physicians and thereafter Secretary General of the International Food and Beverage Alliance (IFBA). He is a fellow of the Russian and Romanian Academies of Medical Sciences. Delon has been involved in harm reduction in tobacco and nicotine, alcohol and drugs for the last 25 years. In clinical medicine, his work focused on tobacco cessation programs, while in medical politics, the development of the FCTC. He was Chair of the coordinating committee for NGOs in preparation of World No Tobacco Day 1999. He authored the book "Wise Nicotine".

- **Karl Fagerström** was born in Sweden 1946. He studied at the University of Uppsala and graduated as a licensed clinical psychologist 1975. At that time, he started a smoking cessation clinic and invented the Fagerstrom Test for Cigarette Dependence. In 1981 he got his Ph.D. on a dissertation about nicotine dependence and smoking cessation. In the end of the seventies and early eighties he served as the editor-in-chief for the Scandinavian Journal for Behaviour Therapy. From 1983 through 1997 he worked for Pharmacia & Upjohn as Director of Scientific Information for Nicotine Replacement Products. He has worked with the nicotine gum Nicorette since 1975 and has been contributing to NRT developments such as patch, spray, pouch, and inhaler. Ever since 1975 to 2010 he has been working clinically part-time. From 1997 to 2008 he worked with his private research clinic where he studied various drugs intended for treating nicotine dependence. Currently he works with his own private consultancy (Fagerström Consulting). He is a founding member of the Society for Research on Nicotine and Tobacco and currently a Deputy Editor of the Nicotine & Tobacco Research. He started the European SRNT affiliate in 1999 of which he was been the president up to 2003. His main research contributions have been in the fields of Behaviour Medicine, Tobacco, and Nicotine with 170 peer reviewed publications of which he is the first author of 100. The current main interests are on understanding the positive effects of nicotine and reducing harm and exposure to tobacco toxins among all those who cannot give up smoking. He was awarded the WHO medal 1999 for outstanding work in tobacco control. Recently he was announced to be the recipient of the 2013 Award on Clinical Science from the Society for Research on Tobacco and Nicotine.

- **Francis P. Crawley** (Belgium) is the Executive Director of the Good Clinical Practice Alliance – Europe in Brussels, Belgium. He is the co-founder and a Steering Committee

member of the Strategic Initiative for Developing Capacity in Ethical Review. He is a philosopher specialized in ethical, legal, and regulatory issues in health research, teaching at several European, Asian, and Middle East universities. He is the past Secretary General, Ethics Officer, and Chairman of the Ethics Working Party at the European Forum for Good Clinical Practice. He has acted as an author or expert for the leading international and European research ethics and GCP guidelines, as well as for several guidelines in Asia, Africa, the Americas, and Europe. Amongst other things, he is the committee chairman of the WHO guidelines on ethics committees and data monitoring committees; and was a member of the Scientific Advisory Committee for the World Health Organization's International Clinical Trials Registry Platform (ICTRP). He also served for four years on the UNAIDS Ethical Review Committee.

- **Heino Stöver (Germany)** is a social scientist, PhD, and Professor of Social Scientific Addiction Research at the Frankfurt University of Applied Sciences in Germany, Faculty of Health and Social Work. Since 1987 he has been director of the Archive and Documentation Centre for Drug Literature and Research at the University of Bremen. He is the president of the national umbrella organisation working on harm reduction for drug users, called akzept e.V. (Bundesverband für akzeptierende Drogenarbeit und humane Drogenpolitik. Since 2009 he has been the director of the "Institute of Addiction Research". Heino Stöver's main fields of research and project development expertise is health promotion for vulnerable and marginalized groups, drug services, prison health care and related health issues (especially HIV/AIDS, Hepatitis C, drug dependence, and gender issues), and the potential of e-cigarettes. His international research and consultancy expertise includes working as a consultant for the European Commission, United Nations Office on Drugs and Crime (UNODC), World Health Organization (WHO), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), International Committee of the Red Cross (ICRC) and Open Society Institute (OSI) in various contexts. He has published several articles in peer reviewed international journals and books on preventing and treating infectious diseases adequately (HIV/AIDS, hepatitis, STIs, and TB), opioid substitution programmes (including the provision of heroin) in the community and in prisons, and general health care issues. He is co-founder of the International Journal of Prisoner Health.

- **Kgosi Letlape** (South Africa) is a Physician and President of the Africa Harm Reduction Alliance (AHRA). Dr Kgosi Letlape MD FCS (Ophth) SA, MBBS is an ophthalmologist by training, and a past President of the World Medical Association (WMA). He is the current President of the Africa Medical Association (AMA). Dr Letlape is the current President and co-founder of the Africa Harm Reduction Alliance (AHRA), which aims to create awareness and educate people about the need to reduce harm and promote well-being. Other positions Dr Letlape has held include serving as past President of the Health Professions Council of South Africa (HPCSA) and former Chairman of the Board of the South African Medical Association (SAMA). In 1988, he was admitted as a fellow of the College of Surgeons of South Africa in 1988, and as a fellow of ophthalmology of the Royal College of Surgeons of Edinburgh. From 2002 to 2013, he served as the Executive Director

of the Tshepang Trust. This not-for-profit organisation was established at the behest of the late South African president Nelson Mandela. It received funding from the US Presidential Emergency Program for AIDS relief – via the Centers for Disease Control and Prevention (CDC). The Trust collaborated with state hospitals, pioneering the provision of treatment for HIV and AIDS patients. Dr Letlape is an outspoken advocate of universal access to health care and harm reduction.

- **Scott D. Ballin (USA)** has spent more than 40 years involved in issues related to tobacco and public health. He has worked on a spectrum of tobacco and nicotine issues ranging from labeling reforms on cigarettes and smokeless tobacco products to U.S. Food and Drug Administration (FDA) regulation of tobacco, excise taxes, clean indoor air laws and tobacco agriculture reforms. For more than 10 years, he served as the American Heart Association's vice president and legislative counsel, as well as a steering committee member and two-time chairman of the Coalition on Smoking or Health, which was the first truly active national coalition in the tobacco control movement. Ballin served on the steering committee of the Alliance for Health Economic and Agriculture Development (AHEAD), an organization formed to bring parties together to work for the enactment of recommendations contained in a presidential report, "Tobacco at a Crossroads." In recent years, he has worked as an advisor to the University of Virginia on a series of dialogues— "The Morven Dialogues"— on tobacco, nicotine, and harm reduction, and he also served as a consultant and advisor to the Food and Drug Law Institute's tobacco conferences in 2016 and 2017. He has authored a series of white papers on tobacco harm reduction, and he has given expert testimony before the U.S. Congress and the FDA on numerous occasions. Ballin is a graduate of the Georgetown University School of Foreign Service and a graduate of the George Mason University Antonin Scalia School of Law in Arlington, Virginia, USA.

- **John R. "Jack" Fowle III, PhD DABT (USA)** Principal of Science to Inform, LLC, consulting on the use of science to inform decisions. Until 2012, Board-certified toxicologist Jack served in a variety of scientific leadership roles at EPA. His last posting was the Deputy Director of the US EPA Health Effects Division in the Office of Pesticide Programs (OPP), where he was responsible for directing the health risk assessment activities supporting the re-registration of existing pesticides. He managed the integration of new computational and in vitro toxicology alternative to animal testing toxicological approaches into OPP's human health risk assessments. Before OPP he was Director of EPA's Neurotoxicology Division, as well as Assistant Laboratory Director, at the National Health and Environmental Effects Research Lab (NHEERL) developing alternatives to animal approaches and establishing the Agency's comp tox program. He has also served as the Science Advisor to US Senator Daniel Patrick Moynihan on a variety of science policy issues. He currently serves on the Board of Directors for the Institute for In Vitro Sciences (IIVS), as well as the Center for Alternatives to Animal Testing (CAAT) at the Johns Hopkins University. He is President of the Board of Trustees for the Evidence Based Toxicology Consortium also, at the Johns Hopkins University that focuses on the development and application of evidence-based approaches to better inform risk

decisions, and he is President of the American Society for Cellular and Computational Toxicology (ASCCT), as well as Past President of SOT's In Vitro and Alternative Methods Specialty section.

- **Giovanni Li Volti (Italy)** is full professor of Biochemistry at the University of Catania, and current elected Director of the Center of Excellence for the acceleration of Harm Reduction (CoEHAR) at the same University. Soon after the graduation in Medicine and Surgery at the University of Catania, he attended the Department of Pharmacology at the New York Medical College, and in 2005 he obtained the title of PhD in Pediatric Sciences at the University of Catania. With more than 250 peer reviewed publication, his main research fields concern the study of oxidative stress, chronic degenerative diseases and biomarkers. He is the Principal Investigator of the Replica project, an international ring trial aiming at replicating the most relevant published research in inflammation induced by exposure to the aerosol of electronic cigarettes and THP to provide independent validation.

- **Riccardo Polosa** (Italy) is the Founder of the Center of Excellence for the Acceleration of HArm Reduction (CoEHAR) at the University of Catania. Full Professor of Internal Medicine at the same University with specialist role as a Respiratory Physician, Clinical Immunologist, Allergist and Rheumatologist, Polosa is Founder of the Institute of Internal and Emergency Medicine at the main teaching hospital of the University of Catania where he coordinates a large staff of senior physicians, young residents, nurses and administrative clerks. He is also Founder of the University Center for Tobacco Research, where contracted research staff conducts high profile clinical and behavioural research and Honorary Professor of Medicine at University of Southampton, UK. An internationally recognized leader in the field of clinical bronchoprovocation (airway-challenge studies) and tobacco harm reduction, he has published more than 350 peer-reviewed articles and books, mainly on respiratory medicine, clinical immunology, and tobacco addiction. After many years of service as President of the Italian Anti-Smoking League (LIAF: Lega Italiana Anti Fumo), he now serves as its Chief Scientific Advisor. He is also Convenor for the Working Group on "Requirements and test methods for emissions of electronic cigarettes", within the European Committee for Standardization (CEN/TC 437).

- **Aldo Eugenio Calogero (Italy)** is Full Professor of Endocrinology at the University of Catania and Director of the Division of Andrology and Endocrinology at the University Teaching Hospital. He published more than 800 articles and abstracts, of which 385 are original articles published in peer-reviewed journals. Since 2014, he has held the position of Deputy Director of the Department of Clinical and Experimental Medicine of the University of Catania. Founding member of the CoEHAR, in addition to the clinical activity in Endocrinology and Andrology, he began to take an interest in different aspects of male infertility, including studies to evaluate the role of male accessory gland infections/inflammations, environmental pollutants, diabetes mellitus, and cigarette

smoke on both conventional and biofunctional sperm parameters, which have led to the development of strategies to prevent the onset of male infertility.

- **Venera Tomaselli (Italy)** is Associate professor of Social Statistics at the University of Catania. Graduated in Political Sciences and with a PhD in "Sociology and Research Methods", she is Component member of the Presidium of Quality of the University of Catania and Founding member of the CoEHAR. Her research activity is focused on Multivariate and Multidimensional Statistics, Multi-level Models, Meta-Analysis Models,, Network Analysis, Big Data and Data Mining, Accuracy Measures for Demoscopic Surveys and Opinion Polls, applied in different scientific areas, especially Biomedical research and Clinical experimental studies. She is the Principal Investigator of the Troina study, which evaluated the possible correlations between smoking and COVID-19.

- **Massimo Caruso (Italy)** is a researcher and assistant professor of Biochemistry at the University of Catania, and Co-PI of the Replica project. With a degree in Biological Sciences and a PhD in Respiratory Diseases, he distinguished himself at the American Academy of Asthma, Allergy and Immunology for his studies on delayed hypersensitivity reactions to drugs, winning the Fellow in Training International Travel grant Scholarship for two years. His research activity has been focused on the biomarkers of asthma and in particular the phenotype of smoking asthmatics, with the study of biomarkers of cell damage induced by cigarette smoke and "smoke-free" electronic device's aerosol as an alternative to tobacco smoke. He is a member of the CoEHAR.

- **Simone Ronsisvalle (Italy)** is a researcher and assistant professor of Pharmaceutical Chemistry at the University of Catania. With a degree Pharmaceutical Chemistry and Technology and a PhD in Pharmaceutical Sciences, he is a member of the CoEHAR. His scientific activity concern the design, synthesis, characterization, study of structure / activity relationships and the optimization of compounds of pharmaceutical interest, especially neuroprotective agents, immune modulators and anti-inflammatory, diagnostic and antitumor potentials agents. He is currently involved in the evaluation of toxic, irritant, and carcinogenic compounds in cigarette smoke and other nicotine delivery devices.

Appendix 1

Communication to the American Journal of Public Health by fifteen past presidents of the Society for Research on Nicotine and Tobacco (SRNT), August 2021: 10.2105/AJPH.2021.306416

Balancing Consideration of the Risks and Benefits of E-Cigarettes

David J. K. Balfour, DSc, Neal L. Benowitz, MD, Suzanne M. Colby, PhD, Dorothy K.

Hatsukami, PhD, Harry A. Lando, PhD, Scott J. Leischow, PhD, Caryn Lerman, PhD, Robin J. Mermelstein, PhD, Raymond Niaura, PhD, Kenneth A. Perkins, PhD, Ovide F. Pomerleau, PhD, Nancy A. Rigotti, MD, Gary E. Swan, PhD, Kenneth E. Warner, PhD, and Robert West, PhD. (Am J Public Health. Published online ahead of print August 19, 2021:e1–e12. https://doi.org/10.2105/AJPH.2021.306416)
(Link to the article)

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