

The Honorable Margaret Hamburg, Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: FDA Regulation of E-Cigarettes

Dear Commissioner Hamburg,

The following quote is taken from the Strategic Plan for Regulatory Science page on FDA.gov¹, “The core responsibility of FDA is to protect consumers by applying the best possible science to its regulatory activities.” We write to you today to urge you to uphold this ideal in the coming electronic cigarette regulation. However, in order to act upon the best possible science, it is integral to acknowledge and incorporate the fact that e-cigarettes are several orders of magnitude safer than cigarettes.

Scientific thinking is characterized by critical objectivity, and to apply the best possible science it is essential to divorce yourself from ideology, bias and emotion. Electronic cigarettes suffer from the absence of this style of thinking in many who oppose the technology. Despite the fact that most people are well aware that heating a nicotine-infused liquid to the point of vaporization isn't the same as combusting toxin-laden tobacco, many still suggest that they should be treated in the same way from a regulatory perspective.

This viewpoint is driven by nothing other than ideology, fear and a perverted application of the precautionary principle. E-cigarettes represent a shining beacon of hope in the battle against needless smoking-related deaths, and crushing the industry with tobacco-like regulation would extinguish the only remaining option for many smokers who are unable to quit using previously-available methods.

E-Cigarettes Are Exponentially Safer

According to the CDC², there are over 440,000 deaths annually in the U.S. from cigarette smoking. These deaths come from a plethora of cancers as well as cardiovascular and respiratory diseases, but the primary drug smokers are looking for – nicotine – is not the culprit. Instead, smoking represents chugging down a concoction of thousands of chemicals (including 70 known carcinogens³) which are entirely unnecessary.

You will be undoubtedly familiar with the harm reduction approach – having worked to promote needle exchange programs during your time as the Commissioner of the New York City Department of Health and Mental Hygiene – and are well-aware that what appears to be unseemly may actually be a blessing when you think realistically. Just like blood-borne viruses are curbed through the provision of a needle exchange program, smoking-related morbidity and mortality can be curbed through the proliferation of electronic cigarettes.

One of the core tenets of the anti-e-cigarette argument is that there is insufficient evidence as to the contents of the vapor and their long-term safety. However, there is considerable evidence of

¹ Food and Drug Administration (2013), Advancing Regulatory Science: Moving Regulatory Science into the 21st Century – <http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm267719.htm>

² Centers for Disease Control and Prevention (2013), Tobacco-Related Mortality - http://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/tobacco_related_mortality/

³ Centers for Disease Control and Prevention (2011), Chemicals in Tobacco Smoke – http://www.cdc.gov/tobacco/data_statistics/sgr/2010/consumer_booklet/chemicals_smoke/

the contents of e-cigarette vapor, as demonstrated by a recent systematic review⁴ of the body of data on the topic conducted by Igor Burstyn, PhD of Drexel University's School of Public Health. This gathered the data from over 9,000 measurements of the contents and quantities of the components of the vapor, and compared them with accepted maximum safe exposure thresholds.

The findings were unambiguous; the trace levels of toxicants in e-cigarette vapor rarely exceeded 1 percent of the occupational maximum safe exposure limits. It's also worth noting that these same toxicants are found in similar quantities in FDA-approved gums, patches⁵ and inhalers. A specific study⁶ included in the review came from Dr. Maciej Goniewicz *et. al.* (from the Department of Health Behavior, Roswell Park Cancer Institute), which compared levels of specific toxicants and carcinogens in e-cigarettes with those from a cigarette and an approved nicotine inhaler. The researchers found that the measured chemicals were only present in e-cigarettes in 9 to 450 times smaller quantities than in cigarettes, and comparable ones to the nicotine inhaler. Additionally, studies in animals have provided evidence for the long-term safety of inhaled nicotine⁷ and propylene glycol⁸ (the core component of e-cigarette vapor). Additionally, toxicological studies have found that e-cigarette vapor is many times less toxic to cells in comparison to cigarette smoke^{9,10}. There is no dispute; based on everything we know, e-cigarettes are dramatically safer than cigarettes.

The FDA's analysis found traces of tobacco-specific nitrosamines in electronic cigarette liquid, but even this finding shows the sheer magnitude of the disparity between the safety of electronic cigarettes and tobacco cigarettes. Comparison¹¹ shows that tobacco cigarettes contain up to 1,400 times more tobacco-specific nitrosamines than the FDA detected. Regulating e-cigarettes under the rules established for tobacco cigarettes would be like regulating codeine-containing cough medicine under the same guidelines as heroin.

Advertising and "Appealing to Youth"

The Attorneys General's letter focused primarily on the misguided notion that e-cigarettes are appealing to the youth. Flavor-names are paraded like suspects, the superficially-shocking CDC National Youth Tobacco Survey results are repeated and irrelevant branding decisions are targeted.

⁴ Burstyn, I (2013), Peering through the mist: What does the chemistry of contaminants in electronic cigarettes tell us about health risks? Drexel University School of Public Health, Philadelphia, PA - <http://publichealth.drexel.edu/~media/Files/publichealth/ms08.pdf>

⁵ Siegel, M (2009), Comparison of Carcinogen Levels Shows that Electronic Cigarettes are Much Safer Than Conventional Ones, *The Rest of the Story* - <http://tobaccoanalysis.blogspot.co.uk/2009/07/comparison.html>

⁶ Goniewicz, M. *et. al.* (2013) Levels of Selected Carcinogens and Toxicants in Vapour From Electronic Cigarettes, *Tobacco Control*, doi:10.1136/tobaccocontrol-2012-050859-
<http://tobaccocontrol.bmj.com/content/early/2013/03/05/tobaccocontrol-2012-050859.abstract>

⁷ Waldum, H. L. *et. al.* (1996), Long-term effects of inhaled nicotine, *Life sci.* 58 (16) p. 1339 – 46
<http://www.ncbi.nlm.nih.gov/pubmed/8614291>

⁸ Robertson, O. H. *et. al.* (1947) Tests for the chronic toxicity of propylene glycol and triethylene glycol on monkeys and rats by vapour inhalation and oral administration, *J Pharmacol Exp Ther September* 91:52-76 -
<http://jpet.aspetjournals.org/content/91/1/52.abstract>

⁹ Farsalinos, K.E. *et. al.* (2013) Comparison of the cytotoxic potential of cigarette smoke and electronic cigarette vapour extract on cultured myocardial cells. *Int. J. Environ. Res. Public Health* 10, no. 10: 5146-5162. -
<http://www.ncbi.nlm.nih.gov/pubmed/24135821>

¹⁰ Romagna, G. *et. al.* (2013) Cytotoxicity evaluation of electronic cigarette vapor extract on cultured mammalian fibroblasts (ClearStream-LIFE): comparison with tobacco cigarette smoke extract. *Inhal Toxicol.* 25(6):354-61. - <http://www.ncbi.nlm.nih.gov/pubmed/23742112>

¹¹ See footnote 5.



Qualitative research has shown that the variety of flavors available is one of the major contributors to the “hobby element” which has made e-cigarette so popular with smokers¹². People do not socially discuss nicotine gum flavors, but they readily share tips and information about the myriad small businesses offering wide ranges of “e-liquid” flavors. Chocolate-flavored nicotine induces fear if you’re working under the unsupported assumption that e-cigarettes are targeting youths, but for the intended market it is a crucial factor in the efficacy and acceptability of a potentially life-saving product.

The CDC data¹³ is offered as “evidence” of this assumed “targeting” of youth, with one in ten high school students having tried an e-cigarette in 2012. In 2011, the survey found that 18.1 percent of high school students had tried a cigarette in the previous 30 days¹⁴, whereas for e-cigarettes in 2012, 2.8 percent of high school students had tried one in the previous 30 days (2.2 percent of whom had also smoked a cigarette). For any objective observer, the comparatively large numbers of teenagers smoking cigarettes should be the primary concern, since e-cigarette use is still extremely uncommon with non-smoking youth. In addition, the more recent survey classed experimentation with e-cigs in the past 30 days as “current use,” which leads to misleading statistics¹⁵.

In addition, a recent survey found that e-cigarettes do not serve as a “gateway” to smoking¹⁶, as was alleged in press statements at the time of the CDC survey. The researchers surveyed 1,300 college students and were only able to find *one* who had used e-cigarettes before transitioning to smoking.

With these facts in mind, allegations from the Attorneys General that flavors such as chocolate and the use of cartoon animals or video game characters on packaging fall into perspective. As difficult as it clearly is for some to accept, adults *do like* sweet, fruity flavors and *do sometimes* play video games. Moreover, in addition to the numerous states with bans on sales of e-cigarettes to minors, the vast majority of manufacturers impose the same rule themselves. There is no serious dispute on the issue of banning e-cigarettes sales to minors – it is a reasonable step – but arguments based on the fabricated notion that e-cigarette companies are “targeting” children are an inadequate reason to severely limit the appeal of the products to their intended market.

The issue of the advertising e-cigarettes is closely-related, and there is no justification for tobacco-like restrictions. Tobacco cigarettes are a dangerous product, and if marketing is “successful” around one half of those buyers will later die as a result¹⁷. Although long-term evidence isn’t yet available (by nature of their recent emergence) on e-cigarettes, the best existing scientific data provides no reason whatsoever to assume long-term danger. E-cigarettes are much,

¹² Barbeau, A., Burda, J. and Siegel, M. (2013). Perceived Efficacy of E-Cigarette Versus Nicotine Replacement Therapy Among Successful E-Cigarette Users: A Qualitative Approach. *Addiction Science & Clinical Practice* 2013, 8:5 – <http://www.ascpjournals.org/content/8/1/5>

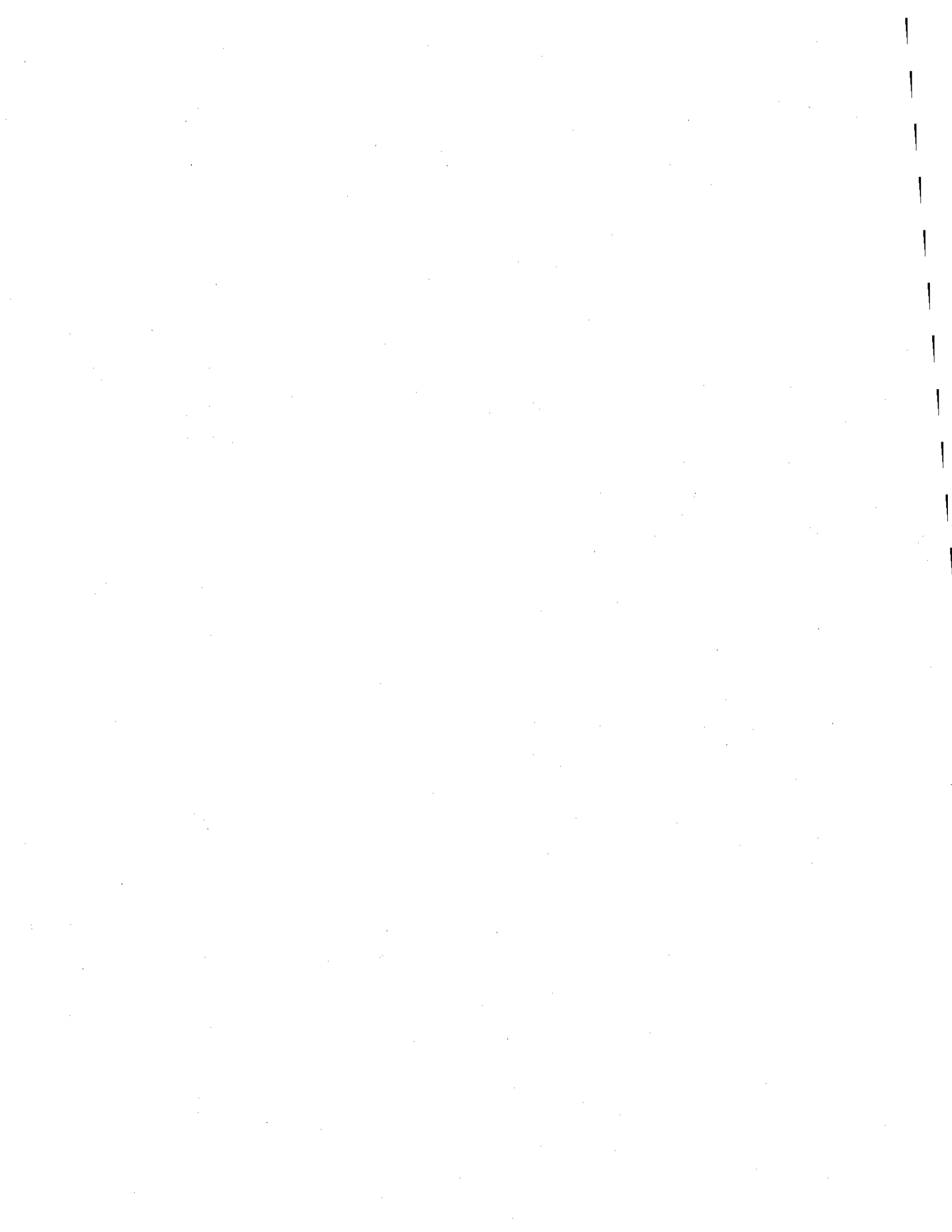
¹³ Corey, C. *et al.*, Centers for Disease Control and Prevention (2013). Notes from the Field: Electronic Cigarette Use Among Middle and High School Students – United States, 2011-2012 – September 6, 2013 / 62(35);729-730 – <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6235a6.htm>

¹⁴ Centers for Disease Control and Prevention (2013). Youth and Tobacco Use - http://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/#estimates

¹⁵ Siegel, M. (2013). Electronic Cigarette Experimentation Increases Among Youth, But Use Among Nonsmokers Remains Low and Regular Use Rates Are Still Unknown, *The Rest of the Story* – <http://tobaccoanalysis.blogspot.co.uk/2013/09/electronic-cigarette-experimentation.html>

¹⁶ Goodman, B. (2013) E-Cigarettes May Not be Gateway to Smoking: Study, *Health* - <http://news.health.com/2013/10/29/e-cigarettes-may-not-be-gateway-to-smoking-study/>

¹⁷ World Health Organization (2013). Tobacco Fact Sheet - <http://www.who.int/mediacentre/factsheets/fs339/en/>



much safer than tobacco cigarettes, so identical marketing restrictions are unnecessary and detrimental to emerging businesses.

Regulate Lightly to Protect Public Health

The e-cigarette industry is largely composed of startup businesses; independent entities with limited financial resources which contribute to the appealing diversity in e-cigarettes and their accessories. Overly stringent regulations would crush these businesses under the increased financial burden, thus reducing the variety of available products and limiting the efficacy of e-cigarettes as a reduced harm alternative.

The EU's recent rejection of proposals to regulate e-cigarettes as medicines reflects this priority; it allows the industry to thrive and continue to be effective. However, even imposing tobacco-like restrictions is needlessly impacting the burgeoning businesses, given the fact that the two products don't even lie on the same scale in terms of risks.

It is reasonable to establish manufacturing standards to ensure that the products are accurately labeled, the actual nicotine content doesn't drastically differ from the stated concentration and that they are produced in an environment free from sources of contamination. Keeping in mind that even unregulated e-cigarettes are considerably safer than cigarettes, it is essential that these standards be achievable by the majority of manufacturers (including small businesses) as to not needlessly impact on the appeal of something with the potential to save millions of lives. Regulatory frameworks copied from medicines or tobacco products are inapplicable, because e-cigs make no therapeutic claim and contain no tobacco.

Without the ideological urge to demonize anything vaguely resembling smoking, irrational fear of the fabricated "intentions" of the industry and the overly precautionary desire to impose crippling restrictions *just in case* the sum of the evidence on e-cigs to date is entirely incorrect, regulatory science can thrive. And that science speaks clearly: e-cigarettes pose little (if any) danger to users – making them orders of magnitude safer than cigarettes – and hold significant promise for reducing the staggering death toll produced by smoking.

We urge the FDA to recognize these facts and refuse to regulate a new, life-saving product under guidelines designed for one that is undeniably fatal.

Very respectfully yours,



Dr. Riccardo Polosa, MD, PhD

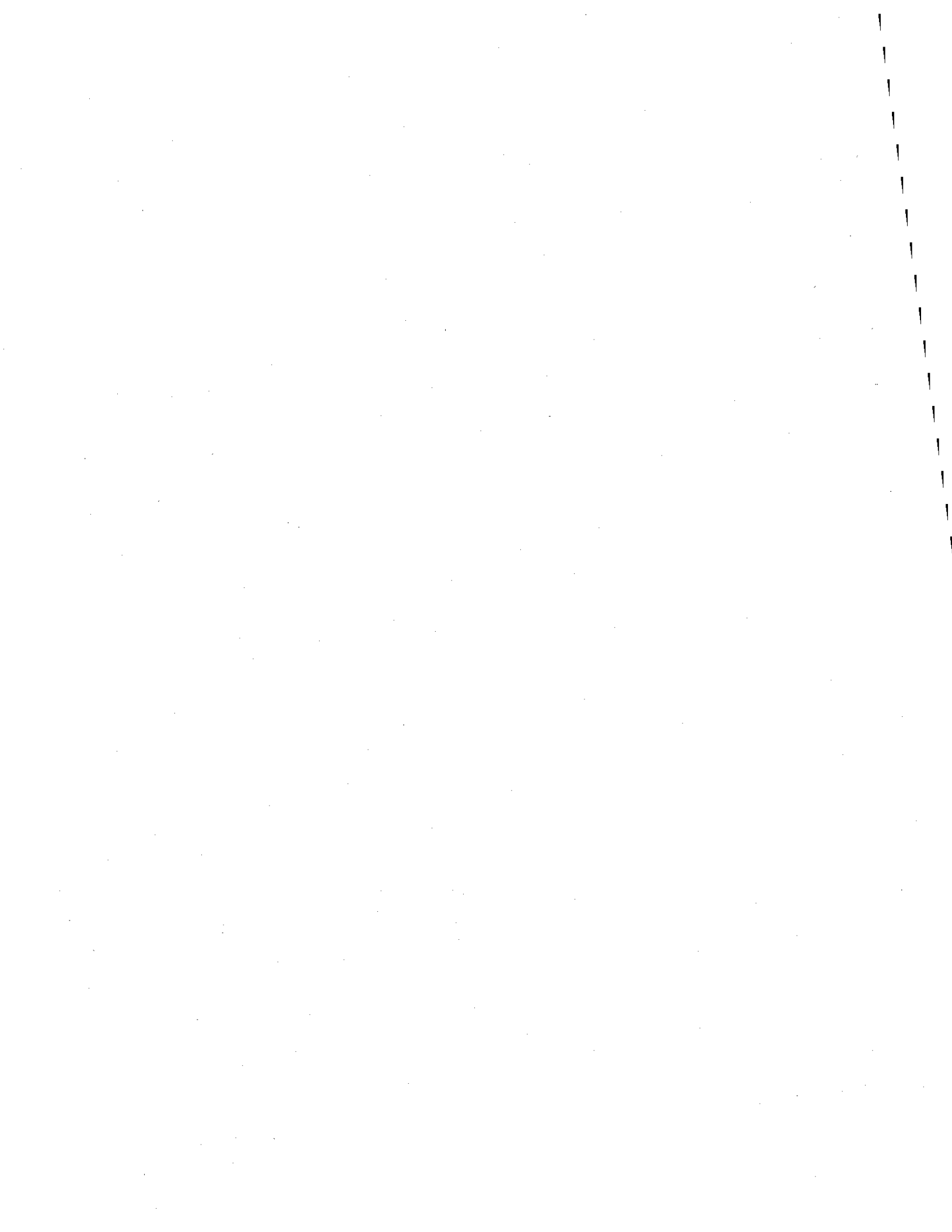
Director, Institute of Internal Medicine
and Clinical Immunology, University
of Catalina.



Dr. Konstantinos Farsalinos, MD,

Researcher, Onassis Cardiac Surgery
Center, Greece

Researcher, Medical Imaging Research
Center, University Hospital Gathuisberg,
Belgium



DocuSigned by:
Christopher Snowden
D68C25DD6A084EB
christopher snowdon

Institute of Economic Affairs

DocuSigned by:
L. Dawkins
EE61C8CCE250489
L. Dawkins

University of East London

^{DS}
VS

Professor Gerry Stimson,
Director, Knowledge - Action - Change

