IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of:	Adam Bowen et al.	
U.S. Patent No.:	12,156,533	Attorney Docket No. 58718-0002IP1
Issue Date:	December 3, 2024	
Appl. Serial No.:	17/171,976	
Filing Date:	February 9, 2021	
Title:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF	

DECLARATION OF MARTIN WENSLEY

I currently hold the opinions set expressed in this declaration. But my analysis may continue, and I may acquire additional information and/or attain supplemental insights that may result in added observations.

I declare that all statements made herein on my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Date: NOV 26th 2025

By: Martin Wensley

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I, Martin Wensley, declare that:

I. INTRODUCTION AND SCOPE OF WORK

1. I have been retained on behalf of NJOY LLC and NJOY Holdings (collectively, "Petitioner") to offer technical opinions related to U.S. Patent No. 12,156,533 ("the '533") (EX1001). I understand that Petitioner is requesting that the Patent Trial and Appeal Board ("Board") institute an *Inter Partes* Review ("IPR") proceeding of the '533 patent.

2. I have been asked to provide my independent analysis of the '533 patent in light of the prior art publications cited in this Declaration.

3. I am not and never have been, an employee of Petitioner. I received no compensation for this Declaration beyond my normal hourly compensation based on my time actually spent analyzing the '533 patent, the prior art publications cited below, and issues related thereto, and I will not receive any added compensation based on the outcome of any IPR or other proceeding involving the '533 patent.

II. QUALIFICATIONS AND BACKGROUND INFORMATION

4. My qualifications are summarized here and explained in more detail in my curriculum vitae, which is attached as Appendix A to this Declaration.

5. I have spent more than 30 years as an engineer. In 1980, I obtained my Bachelor's degree in Physics from the University of California at Santa Cruz. I

started my career working in architectural design and construction management in my own firm. When my brother founded an aerospace firm, TDG Aerospace, I transitioned into an engineering role at that firm in 1990.

6. From 1990 to 1995, I was Vice President of Engineering at TDG Aerospace. While there, I helped create the NoFOD de-icing system for commercial jets. The NoFOD system is a thin second skin applied to the wings of an aircraft, made up of a resistive heater and honeycomb insulation, using a Nomex material, between two layers of aluminum. The system helped to prevent the build-up of wing ice, which would otherwise degrade wing performance and potentially disable rear mounted engines should ice break off.

7. From 1995 to 2000, I was Vice President of Research and Development at Techniquip. I was responsible for the development of optical instruments for medical and industrial purposes. This included work on electrical control and measurement systems for optical instruments.

8. My work over the last 20 years has largely focused on respiratory drug delivery systems. I first became involved in this field with Molecular Delivery Corporation, where I was its first employee. Within a year, Molecular Delivery Corporation merged with Alexza Pharmaceuticals (Alexza).

9. Between 2000 and 2009, I was Head of Device Technology at Alexza. I developed respiratory drug delivery technology and spearheaded research into fundamental methods to aerosolize pharmaceuticals.

10. During my time at Alexza, I worked on a variety of heaters for pharmaceuticals. These included chemical heaters and electrical heaters (both of the resistive and inductive kind). While there were electrical heaters available off the shelf, we also designed some in-house. For example, we designed the Staccato device for pharmaceutical use during my time at Alexza. The multi-dose form with a 25-segment electrical heater had up to 25 doses of drug compound coated onto individual metal substrates in a resistive heating system that is heated upon application of battery-supplied electrical current. The disposable single dose form had a metal substrate that heated through an exothermic chemical reaction.

11. While at Alexza, I was also involved in designing a small aerosol device to deliver fentanyl to canines and we built an inductive heater for that device from scratch. We wanted to create a 60-100 nanometer-sized aerosol from a very thin layer of pharmaceutical. In order to achieve that, a thin layer of the pharmaceutical, which had been coated onto a one-time use strip of stainless steel, was moved through the alternating magnetic field so that we could heat up small portions of the pharmaceutical sequentially and quickly. We chose an induction

heating system because it was impractical in that situation to try to electrically connect the moving heating zone on the stainless-steel strip.

12. Also at Alexza, I was involved in designing a large device capable of generating large amounts of aerosol that could be used to carry out toxicological studies. In this case, we bought an inductive heater off the shelf and built the device around it. The material that we wanted to heat up and aerosolize was coated onto a stainless-steel film that moved through the heating area (the magnetic field generation coils). Like the device I described in the preceding paragraph, that device also relied on induction heating because it was not practical to electrically connect the moving stainless-steel film.

13. The technology in the Staccato system (described at paragraph 10 above) was later adapted for nicotine delivery through the respiratory tract. Alexza had been looking at nicotine for some time, including vaporization and use of nicotine solids, and I was very involved in the project. During my time at Alexza, I worked with a separate team on the formulation of nicotine into various salts and metal complexes in order to stabilize the nicotine for use in the Alexza technology. Specifically, my work included examining how these various salts and metal complexes interacted with heater elements and the vaporization of the compounds.

14. Between 2009 and 2011, I worked as Head of Device Technology at Cyprus Bioscience, a pharmaceutical company. Cyprus Bioscience licensed Alexza's work on nicotine delivery related to the Staccato system, and I continued my work on the project. Our goal was to provide an inhalation device for nicotine replacement therapy. Using a heater array similar to that of the multi-dose form of the Staccato device, we heated a film of nicotine salt on a heating element.

15. In 2011, I co-founded E Nicotine Technology and was its Chief Technology Officer. Between 2011 and 2015, I managed the development of new drug delivery devices to treat cigarette addiction. For example, I oversaw many aspects of the technology development, including clinical trial materials, intellectual property, and product development.

16. Fontem Ventures (owned by Imperial Brands, formerly Imperial Tobacco) later acquired E Nicotine Technology and I took on the role as Director of Engineering. Between 2015 and 2018, my work included leading efforts in researching aerosol generation technology, as well as engineering the development of aerosol generation devices for respiratory drug delivery. My work at Fontem further included serving as technical lead for a nicotine replacement therapy in the UK as part of the approval process by the Medicines and Healthcare products Regulatory Agency (MHRA). I later became Research Manager at Fontem

between February 2018 and July 2018 and in that role, I managed the development of novel products and formulations to replace conventional combustible cigarettes.

17. As a result of my education and experience, I have expertise in physics, mechanical engineering, thermodynamics, heater technology, and aerosol delivery. My career has mostly focused on developing handheld drug delivery devices. Leveraging my experience in this field, I formed my own consulting business in 2019. I am now the Founder and Chief Executive Officer of Airja, a medical device company specializing in respiratory drug delivery devices and products. Airja is developing products to produce precise condensation aerosols in pharmaceutical and recreational markets (such as nicotine and cannabinoids).

18. My curriculum vitae, included as Appendix A to this declaration, includes a list of publications on which I am a named author. Additionally, it includes a list of patents that I am a named inventor or co-inventor on, including a number of patents related to drug/aerosol delivery devices. It contains further details regarding my experience, education, publications, and other qualifications to render an expert opinion in connection with this proceeding.

19. In writing this Declaration, I have considered the following my own knowledge and experience, including my work experience in the fields of drug and

aerosol delivery devices. In addition, I have analyzed the following publications and materials, in addition to other materials I cite in my declaration:

- U.S. Patent No. 12,156,533 (EX1001), and its accompanying prosecution history (EX1002)
- U.S. Patent Application Publication 2014/0000638 to Sebastian et al. ("Sebastian") (EX1004)
- U.S. Patent Application Publication 2006/0018840 to Lechuga-Ballesteros et al. ("Lechuga-Ballesteros") (EX1005)
- EP 0283672 to Lawson et al. ("Lawson") (EX1006)
- Bauer et al., "Introduction to Chemistry," 2nd. Ed., The McGraw-Hill Companies, Inc. (2010) ("Bauer") (EX1007)
- Duell et al., "Nicotine in tobacco product aerosols: 'It's déjà vu all over again,'" Tob. Control, (2020) 29:656-662 ("Duell") (EX1008)
- Declaration of Dr. Steven Byrn (EX1009)
- Caldwell et al., "A Systematic Review of Nicotine by Inhalation: Is There a Role for the Inhaled Route?," Nicotine Tob. Res., (2012) 14(10):1127-1139 (EX1010)
- Blackman, et al., "Chemistry," 2nd. Ed., John Wiley & Sons Australia, Ltd. (2012) (EX1011)
- Goniewicz et al., "Nicotine Levels in Electronic Cigarettes," Nicotine Tob. Res., (2013) 15(1):158-166 (EX1012)
- Bertholon et al., "Electronic Cigarettes: A Short Review," Respiration, (2013) 86:433-438 (EX1013)
- Modi et al., "US Tobacco," UBS Investment Research (2012) (EX1014)

- Tianrong Chen, "Chemical Evaluation of Electronic Cigarettes," Tob. Control, (2014) 23:ii11-ii17 (EX1015)
- Stahl & Wermuth (Eds.), "Handbook of Pharmaceutical Salts: Properties, Selection, and Use: Chapter 7 – A Procedure for Salt Selection and Optimization," (2002), 161-189 (EX1016)
- Gupta et al., "Salts of Therapeutic Agents: Chemical, Physicochemical, and Biological Considerations," Molecules, (2018) 23(7):1719 (EX1017)
- Cruz-Cabez, "Acid-base crystalline complexes and the pKa rule," CrystEngComm, (2012) 114:6362-6365 (EX1018)

20. Counsel has informed me that I should consider these materials through the lens of one of ordinary skill in the art related to the '533 patent at the time of the earliest possible priority date of the '533 patent, and I have done so during my review of these materials. I have been informed by Counsel to use the date of May 6, 2013 as the Priority Date.

21. My opinions, as explained below, are based on my education, experience, and expertise in the fields relating to the '533 patent. Unless otherwise stated, my testimony below refers to the knowledge of one of ordinary skill in the art as of the earliest possible priority date. Any figures that appear within this document have been prepared with the assistance of Counsel and reflect my understanding of the '533 patent and the prior art discussed below.

III. LEVEL OF ORDINARY SKILL IN THE ART

22. A person of ordinary skill in the art ("POSITA") of the '533 patent at the time of invention would have at least (i) a bachelor's degree in chemistry, physics, or a related discipline and three years' experience in design and implementation of aerosol delivery systems and the formulation of their consumables, or (ii) an equivalent combination of education and/or work experience.

23. Based on my experiences, I believe that I am qualified to opine as to the knowledge and level of skill of one of ordinary skill in the art at the time of the invention of the '533 patent and what such a person would have understood at that time, and the state of the art during that time

IV. CLAIM CONSTRUCTION

24. In making this Declaration, I have been asked to consider the terms found in the claims of the '533 Patent according to the plain and ordinary meaning standard applied in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) for how those terms would have been understood by a POSITA at the time of the claimed invention.

V. OVERVIEW OF CONCLUSIONS FORMED

25. This Declaration explains the conclusions that I have formed based on my analysis. To summarize those conclusions, based on my knowledge and experience and my review of the prior art listed above, it is my opinion that:

- each and every limitation of claims 1-8 and 10 are found in Sebastian; and
- each and every limitation of claims 1-10 are found in Sebastian, when considered in view of the teachings of Lechuga-Ballesteros.

VI. TECHNOLOGY BACKGROUND AND SUMMARY OF THE '533 PATENT

A. Technology Overview

26. The '533 patent generally relates to formulations used in electronic cigarettes, which are often also referred to as "e-cigarettes." I will use these terms interchangeably here. Below, I give a brief overview of what e-cigarettes are, discuss some basic principles governing nicotine chemistry within e-cigarettes, and provide some historical context for the use of nicotine salts in cigarettes, which dates back to the 1900's in traditional (or conventional) cigarettes.

1. E-Cigarettes

27. Like traditional cigarettes, the purpose of e-cigarettes is to deliver nicotine and flavoring compounds to consumers through inhalation of a material

created by heating a nicotine-containing material. EX1012, 1; EX1013, 3. Traditional cigarettes delivered nicotine by combusting tobacco. Combusting the tobacco produces smoke containing nicotine, however, that smoke also contains harmful chemical byproducts, including tar and carbon monoxide. In contrast, e-cigarettes were designed to provide nicotine to a consumer through an aerosol form by ***vaporizing*** nicotine rather than combusting tobacco. Thus, e-cigarettes are able to bypass many of the harmful byproducts associated with smoking. EX1013, 2; EX1014, 3.

28. E-cigarettes generally consist of a reservoir or cartridge designed to hold a liquid formulation that contains nicotine, a heating element designed to aerosolize the nicotine-containing liquid (which can be flavored), a sensor to activate the heating element, a battery, and a mouthpiece. EX1013, 2-3; EX1012, 1; EX1004, [0010]-[0012], [0048], [0051], [0057].

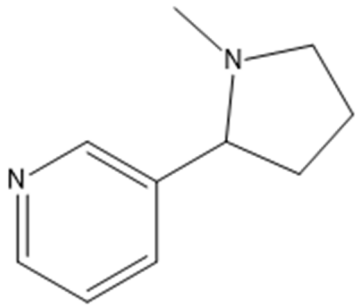
29. Since their introduction in the early 2000's, e-cigarettes have grown significantly in popularity. This rise of e-cigarettes has been driven both by consumers seeking alternatives that pose less risk than combustible tobacco and by the desire for more customizable, convenient, and socially-acceptable nicotine delivery methods. *See, e.g.*, EX1014, 7; EX1015, 1.

30. In modern e-cigarettes, aerosolized liquids are known to include nicotine salts. Nicotine salts are produced by combining what is commonly referred to in the industry as "free base" nicotine with an acid, the chemistry of which I touch on further below. EX1008, 2 (Fig. 1). By adding organic acid to the e-cigarette formulation, the proportion of free base nicotine is reduced depending on factors such as the ratio of organic acid to nicotine. *See, e.g.*, EX1008, 2 (Fig. 1).

31. In fact, the tobacco industry has been well aware of nicotine salts for decades. The benefits of nicotine salts were appreciated not only in traditional combustible cigarette products, but also in early e-cigarette formulations, as I discuss in more detail below. EX1006, 1:25-27; EX1008, 1, 5-6.

2. Nicotine Chemistry

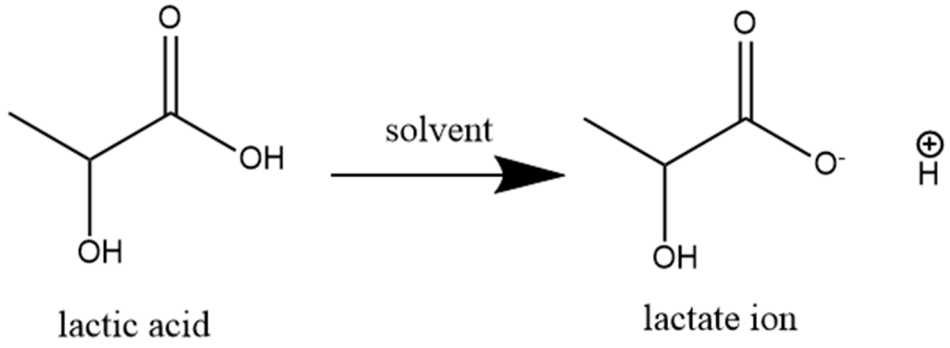
32. Nicotine is a naturally occurring alkaloid compound that is found primarily in tobacco plants. EX1007, 210; EX1008, 5. I have provided the chemical structure of nicotine below:



"free base" nicotine

See EX1007, 210. Nicotine is classified as a base because it contains two nitrogen ("N") atoms that can receive a proton (i.e. can be protonated). I note that in the unprotonated form I show above, nicotine is often referred to within the tobacco industry as "free base" nicotine. All that means is that the nicotine is "free" in the sense that it is not associated with a proton from an acid. EX1008, 1; EX1005, [0023]. It was well known in the industry that, in this form, nicotine is more volatile and more readily vaporized, but can be harsh when inhaled. EX1008, 1, 5; EX1005, [0062].

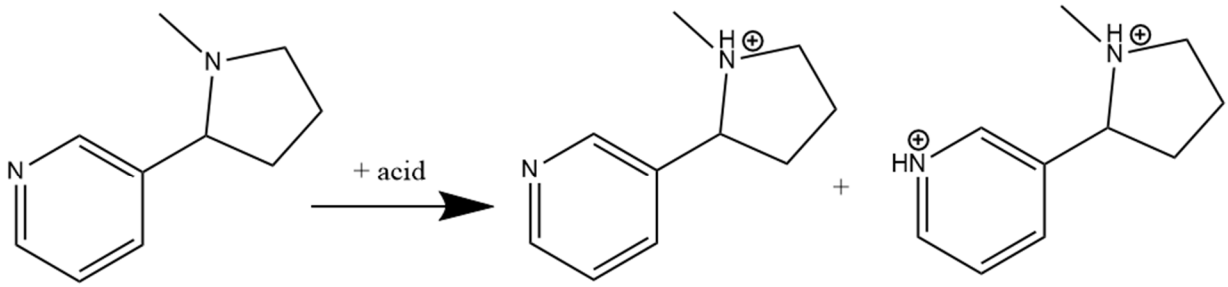
33. At a high level, a nicotine salt forms when nicotine is exposed to and reacts with an acid, such as benzoic acid or lactic acid. Let's take lactic acid as an example. Lactic acid can dissociate into a negatively-charged form, creating a lactate ion and a corresponding hydrogen molecule, which has a positive charge, as I show below:



lactic acid lactate ion

See EX1007, 206; EX1009, ¶ 33.

34. When free base nicotine[1] is exposed to an acid, it reacts with the released positively-charged hydrogen molecules of the acid, resulting in positively-charged ionic forms of nicotine:



"free base" nicotine monoprotonated nicotine diprotonated nicotine

See EX1008, 2; EX1009, ¶ 34. I note that this reaction is expressly acknowledged by the '533 patent itself, which confirms that protonated nicotine can exist with

[1] As I noted above, we in the industry commonly refer to unprotonated nicotine as "free base" nicotine, and I will use these two terms interchangeably in my Declaration.

both a single charged nitrogen ("monoprotonated") or two charged nitrogens ("diprotonated"). *See* EX1001, 12:65-13:2; EX1008, 2; EX1009, ¶ 34.

35. When lactic acid and "free base" nicotine are present together in a solvent, I understand that the lactic acid will release a positively-charged hydrogen molecule, leaving a negatively-charged lactate ion. The released hydrogen molecule is now available and will react with nicotine to produce a positively-charged nicotine ion. I understand that the opposing charges lead the negatively-charged lactate ion and the positively-charged hydrogen ion to interact and form a salt, i.e., nicotine lactate. EX1009, ¶ 35; *see also* EX1008, 2 (Fig. 1) (showing chemical reaction between nicotine and benzoic acid to form a nicotine salt). I understand that additional details regarding the chemistry of this salt formation have been provided by Dr. Stephen Byrn, in a declaration (EX1009). I understand that Dr. Byrn has over fifty years of experience as a chemist, and I rely in part on his opinions and declaration where cited here.

36. Thus, I understand that salt formation occurs as a fundamental reaction between an acid and a base. In my view, an acid interacting with a base to form a salt, like nicotine lactate, appears to be nothing new. I understand that knowledge of this chemistry has in fact been around for centuries. EX1007, 140-141; EX1009, ¶¶ 19-20.

3. History of Nicotine Salts in Cigarettes

37. The delivery of nicotine using nicotine salts was widely known and dates back to the 1900's in conventional cigarettes. EX1008, 5-6. In fact, the shift in the use of free base nicotine to nicotine salt (i.e. with protonated nicotine) in electronic cigarettes has been described as "déjà vu all over again." Indeed, a 2019 article ("Duell") described that it had long been appreciated that in addition to nicotine, tobacco contained "leaf sugars" that were "precursors of tobacco-smoke organic acids." EX1008, 5. These were "generally lost during slow air curing" performed in the 1600's, resulting in cigarettes containing high proportions of free base nicotine (denoted as "α_{fb}" in the article). EX1008, 5; *see also* EX1008, 5 (Duell quoting 1974 article stating "[t]he presence of ***unprotonated [i.e. free base] nicotine*** in the smoke of French cigarettes and the observation that French smokers of black tobacco inhale less frequently than smokers in England and the USA…support our hypothesis that the pH is a determining factor in the 'inhalability' of tobacco smoke.").[2]

38. In the 1850s, "flue-cured" tobacco was developed, and was shown to produce "a noticeably milder smoke" because it "remain[ed] high in leaf sugars so

[2] All emphasis added herein unless otherwise noted.

that the resulting smoke contain[ed] numerous organic acids." EX1008, 5. Furthermore, citing an article ***from 1909***, Duell provided direct evidence that the "role of acids in converting nicotine to a ***protonated, 'salt' form*** in tobacco smoke has long been understood." EX1008, 6. The 1909 article stated:

> Apparently the only possible explanation of this pronounced effect on the sharpness of the smoke is that in the presence of the citric acid the nicotine ***enters the smoke in the form of a salt*** rather than in the free state, and thereby ***loses its pungency while still exerting the usual physiological effect***.

EX1008, 6.[3]

39. The appreciation of the benefits of nicotine salts can be found elsewhere as well. For example, in the 1980's, a salt solution was applied to the "filler material" of the conventional cigarette such that the nicotine salt resulted in "improved tobacco taste, strength and smoking satisfaction…while avoiding undesirable off-tastes" when smoked. EX1006, 3:25-27. Indeed, the tobacco industry has long appreciated the benefits of nicotine salts to deliver nicotine.

[3] I note that citric acid is an organic acid, and is identified as one both by the '533 patent specification and Lechuga-Ballesteros. *See* EX1001, 14:42-64 (identifying "nicotine citrate" as an organic acid "used in the salt formation"), Figs. 3-5, (experiments using "nicotine citrate"), 30:57-65 (identifying "citric acid" as "organic acid"); EX1005, [0042], cl. 9.

40. To demonstrate the clear parallels between the transitions to the use of nicotine salts in conventional cigarettes and e-cigarettes, Duell created a comparison graphic showing the transition from free base nicotine to nicotine salts in each kind of cigarette, reproduced below. EX1008, 5 (Fig. 3). In this graphic, the proportion of free base nicotine to nicotine salt is shown on the horizontal axis, with 1 being 100% free base nicotine and 0 being 100% nicotine salt. EX1008, 5 (Fig. 3). Looking first at conventional cigarettes, the top wavy line tracks the transition from the use of "air-cured" nicotine in the 1600s on the right, associated with a higher fraction of free base nicotine (α_{fb} ~0.5-0.9), to "flue-cured" nicotine in the 1850s on the left, with a much lower fraction of free base nicotine (α_{fb} < 0.1). EX1008, 5 (Fig. 3). As noted previously, this lower fraction of free base nicotine was observed because of the nicotine "leaf sugars" that were organic acid precursors. EX1008, 5.

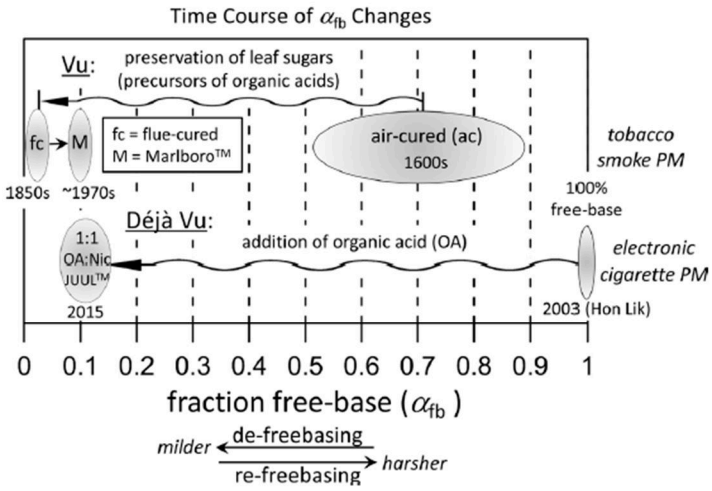


Figure 3 A visual representation of the historical changes in α_{fb} in tobacco smoke PM (top) in comparison to how electronic cigarette fluids and their associated aerosols have been changed (bottom). fc, flue-cured; α_{fb}, fraction of nicotine in the free-base form; M, Marlboro; Nic, nicotine; OA, organic acid; PM, particulate matter.

EX1008, 5. Meanwhile, the transition from nicotine free base to nicotine salts in electronic cigarettes is shown by the bottom wavy line. The first e-cigarettes, introduced in 2003, used exclusively free base nicotine ($\alpha_{fb} = 1$). EX1008, 5 (Fig. 3). Over time, there was a transition to the "addition of organic acid (OA)," i.e. use of nicotine salts. EX1008, 5 (Fig. 3). Duell shows the Juul product as an example, which used a "1:1" (or equimolar) ratio of organic acid ("OA") to nicotine ("Nic"), resulting in very little free base nicotine (α_{fb} ~0.1). EX1008, 5 (Fig. 3). Duell therefore concluded that "[t]he chemistry changes during the rapid evolution of e-cigarettes closely parallel the events that occurred during the centuries-long development of smoked tobacco." EX1008, 5.

41. Thus, while I understand that the Patent Owner argued that nicotine salts showed "surprising benefits" (EX1002, 285), the shared histories of conventional cigarettes and e-cigarettes show that the use of nicotine salts was neither new nor surprising. EX1008, 5-6.

B. Summary of the '533 Patent

42. The '533 patent is titled, "Nicotine Salt Formulations for Aerosol Devices and Methods Thereof." EX1001. I understand that the '533 patent describes nicotine-salt formulations used in e-cigarettes and other vaporizing devices and discloses certain nicotine salt formulations. It also compares the properties of these formulations to those of free base nicotine. Describing what was already known in the industry, the '533 patent references a well-established fact that "formulations comprising a nicotine salt…cause faster and more significant rise [in heart rate] when compared with a nicotine freebase formulation with the same amount of nicotine by weight." EX1001, 22:42-45. I understand that this conclusion is based on pharmacokinetic blood plasma testing purporting to show that nicotine salt formulations yield comparable or higher rates of nicotine uptake in the blood. *See, e.g.*, EX1001, 27:5-64, Figs. 4-6.

43. Further, I note that the '533 patent stated that the "increased heart rate" was "theoretically approaching or theoretically comparable to that of a traditional burned cigarette," which purportedly "has not been demonstrated or

identified in other electronic cigarette devices." EX1001, 22:58-61; *see also* EX1001, 24:14-22.

C. Prosecution History of the '533 Patent

44. I understand that U.S. Patent Application No. 17/171,976 was filed on February 9, 2021, which issued as the '533 patent on December 3, 2024. *See* EX1002. When originally submitted, what is now Claim 1 covered "a salt of nicotine and benzoic acid in a liquid carrier." *See* EX1002, 167. I understand that all claims were rejected as obvious based on the combination of Sebastian (EX1004) in view of Lechuga-Ballesteros (EX1005). EX1002, 207-216.

45. To overcome Sebastian, I understand the applicant asserted that "Sebastian describes formulations that contain nicotine in the form of nicotine free base, which is consistent with the knowledge in the art at the time that nicotine free base was the preferred form for delivery of nicotine in an electronic cigarette." EX1002, 285. The applicant also argued that there was no motivation to modify the formulation in Sebastian based on Lechuga-Ballesteros "because the devices and the formulations are not interchangeable." EX1002, 286.

46. I understand that the Examiner then withdrew the rejection based on Sebastian and referenced applicant's arguments about the lack of motivation to modify Sebastian "persuasive as it pertains to the ***electronic cigarette*** claim[.]" EX1002, 314. However, the Examiner cited Lechuga-Ballesteros again and issued

a new rejection of the ***cartridge*** claim based on this reference alone. EX1002, 308-313. I understand that this means the Examiner found Lechuga-Ballesteros disclosed all of the features of the cartridge claimed by the applicant. EX1002, 308-313.

47. I note that because the Examiner found the electronic cigarette claim allowable, the applicant amended the cartridge claim to cover an "***electronic cigarette*** cartridge," *See* EX1002, 313; EX1002, 377. After this amendment by the applicant, the Examiner issued a Notice of Allowance. EX1002, 396-403.

48. I further understand that after the claims were allowed, the applicant requested that prosecution be re-opened and broadened claim 1 to also cover ***lactic acid*** ("a salt of nicotine and an organic acid in a liquid carrier, wherein the organic acid is benzoic acid ***or lactic acid***[.]"). EX1002, 498.

49. Upon re-opening prosecution, I understand the Examiner newly rejected the "electronic cigarette cartridge" claim, this time over Lawson. EX1006; *See* EX1002, 519-523. I understand that the Examiner found the "electronic cigarette" claim again allowable. EX1002, 523. In response, the applicant cancelled the "electronic cigarette cartridge" claim, (EX1002, 684), and the Examiner issued a second Notice of Allowance, (EX1002, 692-696).

VII. THE CHALLENGED CLAIMS ARE DISCLOSED BY THE PRIOR ART

A. [Ground 1] Sebastian Discloses Claims 1-8, 10

1. Overview of Sebastian

50. Sebastian is titled, "Reservoir and Heater System for Controllable Delivery of Multiple Aerosolizable Materials in an Electronic Smoking Article." EX1004. Sebastian describes that it was "desirable to provide a smoking article that can provide the sensations of cigarette, cigar, or pipe smoking, that does so without combusting tobacco, that does so without the need of a combustion heat source, and that does so without necessarily delivering considerable quantities of incomplete combustion and pyrolysis products." EX1004, [0008].

51. To that end, Sebastian goes on to describe an "electronic smoking article" that has the capability to generate an inhalable aerosol. *See, e.g.*, EX1004, Abstract, [0009]-[0010]. I note that Sebastian's electronic smoking article comprises a "cartridge" with "one or more reservoirs" that can store an "aerosol precursor composition" in liquid form. EX1004, [0069], [0116]. As I will discuss in more detail below, Sebastian further describes that this aerosol precursor composition can contain a combination of nicotine, organic acid, a liquid carrier, and other inhalable materials such as flavorants. EX1004, [0055]-[0057], [0059], [0061]. Sebastian contemplates using electrical energy to heat the liquid aerosol

precursor in the electronic smoking article until it is volatized (i.e., aerosolized) into an inhalable aerosol that can deliver the nicotine formulation to a consumer. EX1004, [0031], [0065].

2. Analysis

[1pre] An electronic cigarette comprising…

52. Sebastian discloses an electronic cigarette. I note that Sebastian explains that the "electronic smoking article" of "[t]he present invention provides articles that use ***electrical energy*** to heat a material (preferably without combusting the material to any significant degree) to form an inhalable substance, the articles being sufficiently compact to be considered 'hand-held' devices." EX1004, [0029].

53. Sebastian further explains that the term "smoking article" "is intended to mean an article that provides the taste and/or the sensation (e.g., hand-feel or mouth-feel) of ***smoking a cigarette***, cigar, or pipe without substantial combustion of any component of the article." EX1004, [0029]. I note that Sebastian is explicit here that the term "smoking" does not refer to generation of smoke, but instead "relates to the physical action of an individual in using the article—e.g., holding the article, drawing on one end of the article, and inhaling from the article." EX1004, [0029].

54. In my view, Sebastian's "electronic smoking article" is consistent with the '533 patent's description of its claimed "electronic cigarette." Specifically, I note that the '533 patent states that the term "electronic cigarette" "refers to an electronic inhaler that vaporizes a liquid solution into an aerosol mist, simulating the act of tobacco smoking." EX1001, 11:24-27. Thus, the claimed "electronic cigarette" appears similar in purpose to Sebastian's "electronic smoking article." Both the '533 patent's electronic cigarette and Sebastian's electronic smoking article are used to generate an inhalable aerosol by vaporizing a liquid solution containing nicotine to provide an experience that is similar to that of smoking a conventional or traditional cigarette.

55. I further note that, in addition to serving the same purpose, Sebastian's "electronic smoking article" is also similar in structure to the '533 patent's "electronic cigarette." The '533 patent describes an electronic cigarette as having "three essential components: a plastic cartridge that serves as a mouthpiece and a reservoir for liquid, an 'atomizer' that vaporizes the liquid, and a battery." EX1001, 11:31-35. And, as I discuss in more detail below, Sebastian's "electronic smoking article" likewise includes a cartridge that serves as both a mouthpiece and reservoir for liquid, an "aerosolization zone" within which the liquid is vaporized, and a battery. EX1004, [0011]-[0012], [0116].

56. A comparison of Figure 7 of the ’533 patent to Sebastian’s Figure 3 makes the similarity of these components readily apparent. Below, I have provided annotated versions of both figures. Both figures show a cartridge with a mouthpiece (red) and reservoir (blue), and a battery (yellow):

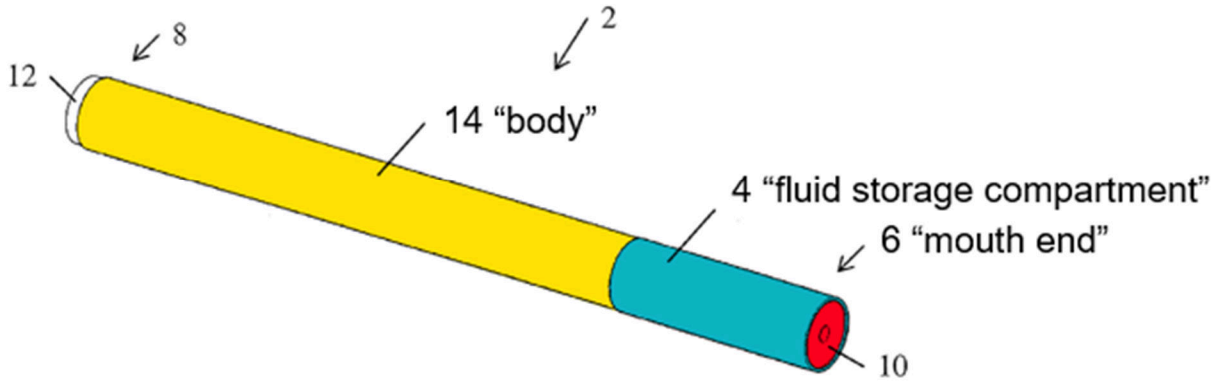


FIG. 7, ’533 Patent

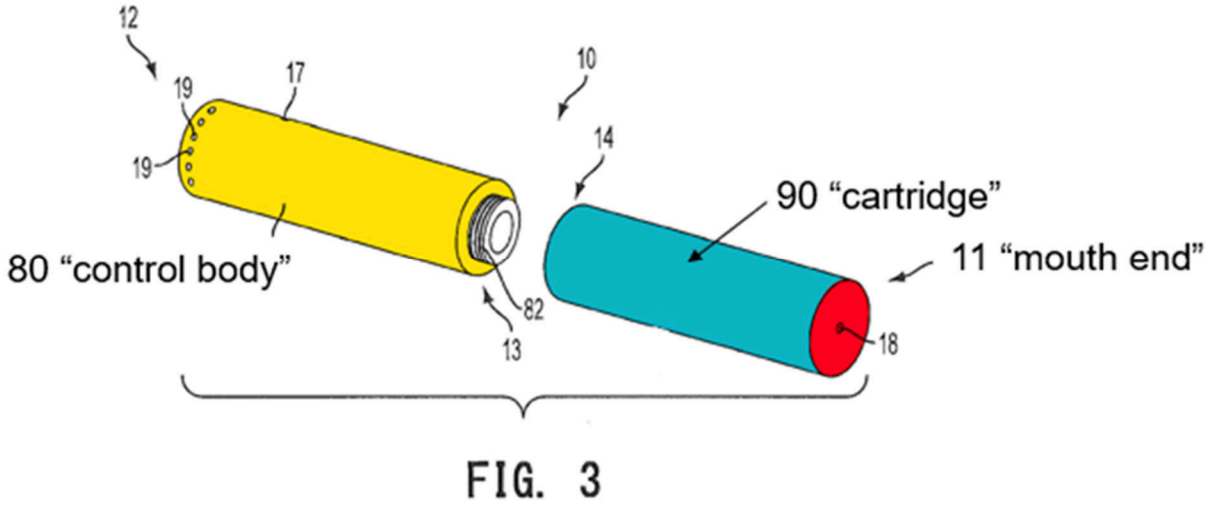


FIG. 3

FIG. 3, Sebastian

See EX1001, Fig. 7; EX1004, Fig. 3. Specifically, Figure 7 of the '533 patent (shown on top) depicts a "fluid storage compartment 4" having a "mouth end 6." EX1001, 17:10-15. I note that the '533 patent expressly states that "the fluid storage compartment 4 is replaceable ***as part of a replaceable cartridge***." EX1001, 17:29-31. Similarly, Figure 3 of Sebastian (shown on bottom) also depicts a "cartridge 90" with a "mouthend 11." EX1004, [0085], [0088]. Likewise, Figure 3 of Sebastian further depicts a "control body 80" that includes a "battery 40" (Figure 4, not shown here). EX1004, [0087]. In my view, this structure is identical to the '533 patent's "body 14" that also contains a battery. *See* EX1001, 17:21-23 ("the electronic cigarette comprises a rechargeable battery within a body 14 of the electronic cigarette").

57. My review of the prosecution history of the '533 patent further supports my opinion that Sebastian's "electronic smoking article" constitutes an "electronic cigarette." I note that the Examiner rejected the claims as obvious in part over Sebastian, finding that "Sebastian et al discloses an electronic smoking article (***i.e., electronic cigarette***) that provides for delivery of aerosolized components of a liquid aerosol precursor composition[.]" EX1002, 208. In addition, I see that the Examiner cited the same Figure 3 that I showed above and highlighted Sebastian's "control body 80" as "detachably connected to a cartridge

90…which houses the liquid composition, a distal end of which is inserted into the mouth of [a] user." EX1002, 208-209. The Examiner concluded—as I do—that Sebastian teaches the claimed electronic cigarette. EX1002, 208-209.

58. I note that rather than contending in response that Sebastian somehow does not disclose an electronic cigarette, the applicant expressly used the term "electronic cigarette" in connection with Sebastian. EX1002, 285-286 (arguing that Sebastian disclosed use of "nicotine free base," "consistent with the knowledge in the art at the time" that this "was the preferred form for delivery of nicotine ***in an electronic cigarette***"). In my view, in so arguing, the applicant effectively conceded that Sebastian disclosed an electronic cigarette.

59. Thus, in view of Sebastian's express disclosures and the prosecution history, I conclude that Sebastian teaches an electronic cigarette.

[1a] a cartridge,

60. Sebastian expressly discloses a cartridge. Sebastian states plainly that its electronic smoking article contains "a ***cartridge*** with a connecting end that engages the connecting end of the control body and with an opposing, mouthend." EX1004, [0068]. Sebastian additionally explains that its cartridge has a "mouth opening 18 at the mouthend 11 thereof to allow passage of air and entrained vapor (i.e., the components of the aerosol precursor composition in an inhalable form) from the cartridge to a consumer[.]" EX1004, [0088]; *see also* EX1004, Figs. 3-4.

61. In my view, Sebastian's "cartridge" is consistent with the '533 patent's description of a "cartridge." The '533 patent describes its cartridge "as a mouthpiece and a reservoir for liquid[.]" EX1001, 11:33-34. Similarly, Sebastian expressly states that "the interior cartridge space can include one or more reservoirs for storing a plurality of components of an aerosol precursor composition[.]" EX1004, [0116].

62. In addition, I note that the '533 patent explains that "the fluid storage compartment 4 is ***replaceable*** as part of a replaceable cartridge." EX1001, 17:29-31. Similarly, Sebastian describes that its "cartridge can comprise a shell containing one or more disposable components and having an end that removably attaches to the control body." EX1004, [0030]; *see also* EX1004, [0067] ("The first unit can comprise a distal end that engages the second unit and an opposing, proximate end that includes a mouthpiece (or simply the mouthend)….In preferred embodiments, the first unit can be disposable."), [0085] ("In specific embodiments, the control body can be referred to as being reusable, and the cartridge can be referred to as being disposable."), [0115]-[0116]. Based on what Sebastian expressly describes as its "cartridge," it is my opinion that the claimed "cartridge" is consistent with Sebastian's "cartridge."

63. A comparison of annotated Figure 7 from the ’533 patent and annotated Figure 3 from Sebastian makes the similarity of these components readily apparent:

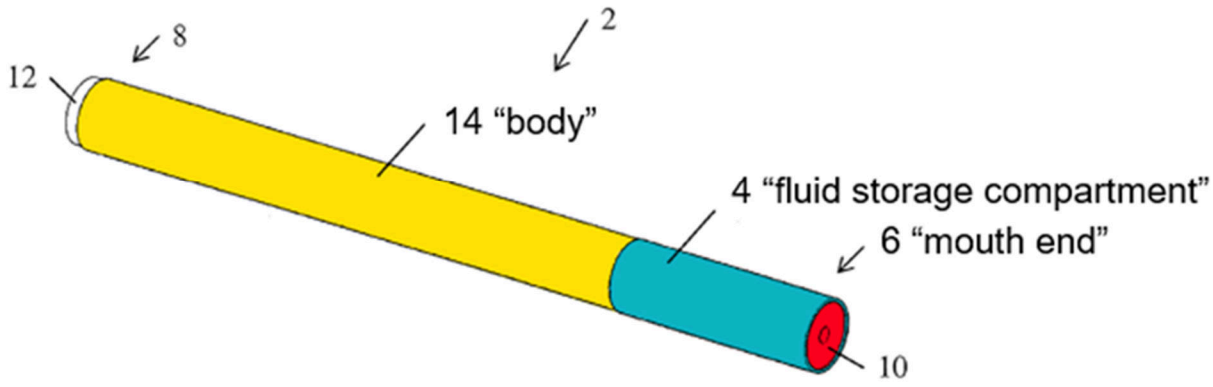


FIG. 7, ’533 Patent

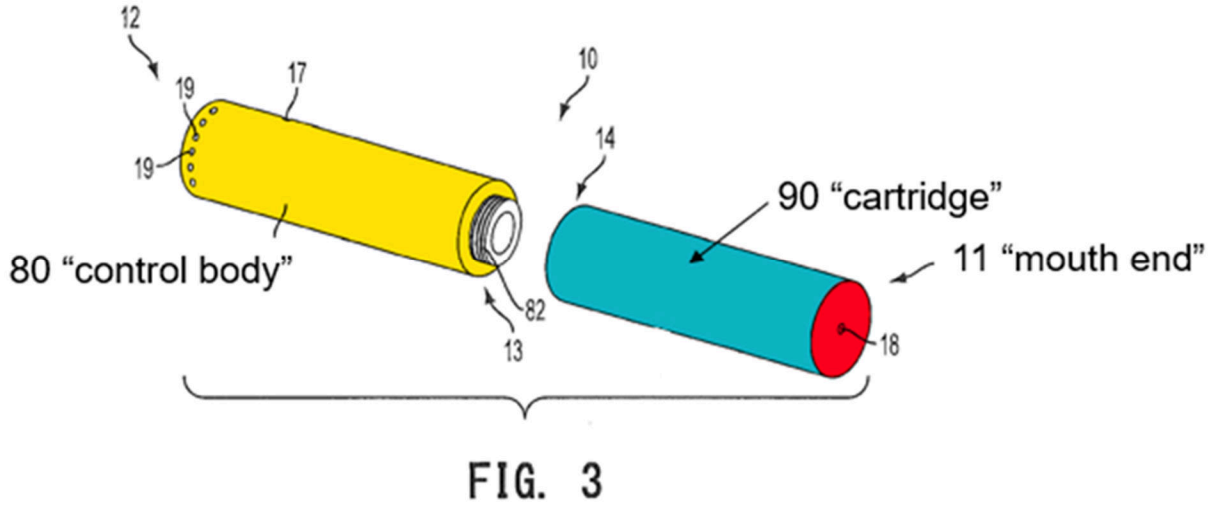


FIG. 3, Sebastian

See EX1001, Fig. 7; EX1004, Fig. 3. Sebastian (shown on top) discloses a "cartridge 90" with a "mouthend 11." EX1004, [0085], [0088]. It is my view that this is consistent with the "fluid storage compartment 4" having a "mouth end 6," of the cartridge in the '533 patent, as shown above in annotated Figure 7. EX1001, 17:10-15; *see also* EX1001, 17:29-31 (explaining "the fluid storage compartment 4 is replaceable ***as part of a replaceable cartridge***.").

64. In addition, my review of the prosecution history of the '533 patent further supports my opinion that Sebastian's "cartridge" describes the '533 patent's "cartridge." Specifically, I note that when the Examiner rejected all the claims based on Sebastian, he found that Sebastian's "cartridge" corresponded to the claimed cartridge. EX1002, 208-09. In response, the applicant did not dispute that Sebastian disclosed a cartridge. EX1002, 285-86.

65. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches a cartridge.

[1b] wherein the cartridge comprises a nicotine salt liquid formulation, wherein: (a) the nicotine salt liquid formulation comprises a salt of nicotine and an organic acid in a liquid carrier,

66. Sebastian discloses a nicotine salt liquid formulation comprised of a salt of nicotine and an organic acid in a liquid carrier. As I will discuss in turn below, Sebastian discloses both "a salt of nicotine and an organic acid" and that the salt is "in a liquid carrier."

i. Sebastian discloses "a salt of nicotine and an organic acid"

67. Specifically, I find that Sebastian discloses nicotine, the combination of nicotine with organic acid, and the necessary formation of a nicotine salt.

68. ***First,*** Sebastian expressly describes the inclusion of nicotine. EX1004 [0057]. For instance, Sebastian states that "liquid nicotine can be used" and additionally discloses that nicotine "can be included in the aerosol precursor or vapor precursor composition." EX1004, [0057]; *see also* EX1004, [0056] [0061] ("[a]s a non-limiting example, an aerosol precursor according to the invention can comprise…nicotine[.]").

69. ***Second,*** Sebastian expressly describes the combination of organic acids and nicotine. I note that Sebastian explains that "***[o]rganic acids particularly*** can be incorporated ***into the aerosol precursor*** to affect the flavor, sensation, or organoleptic properties of medicaments, ***such as nicotine***, that can be ***combined with the aerosol precursor***." EX1004, [0059]; *see also* EX1004, [0059] (identifying organic acids as "flavoring agents" that "can be combined with the aerosol-generating material if desired.").

70. Indeed, one of Sebastian's goals was to improve the "organoleptic properties" to "provide a smoking article that can provide the sensations of cigarette, cigar, or pipe smoking…without combusting tobacco," similar to the

'533 patent's goal of achieving "satisfaction" that is "more comparable to the satisfaction in an individual smoking a traditional cigarette." EX1004, [0008], [0059]; EX1001, 8:1-5; *see also* EX1001, 22:42-67.

71. ***Third,*** through its disclosure of a combination of nicotine and organic acid, it is my opinion that Sebastian discloses the creation of a "salt of nicotine and an organic acid." I note that the '533 patent itself discloses, "[n]icotine salts are formed by the addition of a suitable acid, including organic or inorganic acids." EX1001, 12:44-45; *see also* EX1001, 13:3-7 ("Nicotine salt formulations may be formed by adding a suitable acid to nicotine[.]"), 13:18-20 ("Nicotine salt formulations may be prepared by combining nicotine and a suitable acid in a carrier mixture, such as a mixture of propylene glycol and glycerin."). In my view, the '533 patent does not describe any specific or novel method of generating a nicotine salt. Instead, I note that there is an implicit recognition in the '533 patent that the mere addition of organic acid to nicotine in solution leads to salt formation. EX1001, 12:44-45, 13:3-20.

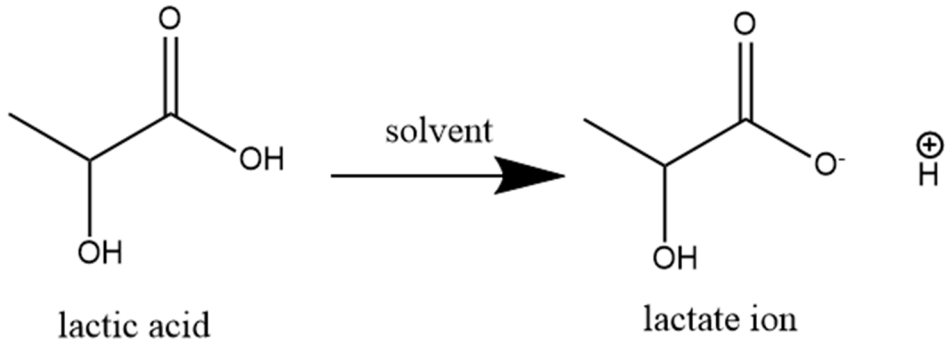
72. It is my opinion that Sebastian discloses this "salt" limitation as a matter of fundamental chemistry because the combination of an acid and a base will necessarily form a salt, in this case, nicotine salt. This is consistent with the '533 patent's disclosures. As I will discuss below, this understanding is supported

by fundamental chemistry concepts found in college-level chemistry textbooks and details shared by Dr. Byrn regarding the chemistry of nicotine salt formation.

a) Chemical principles dictate that Sebastian's formulation includes a salt

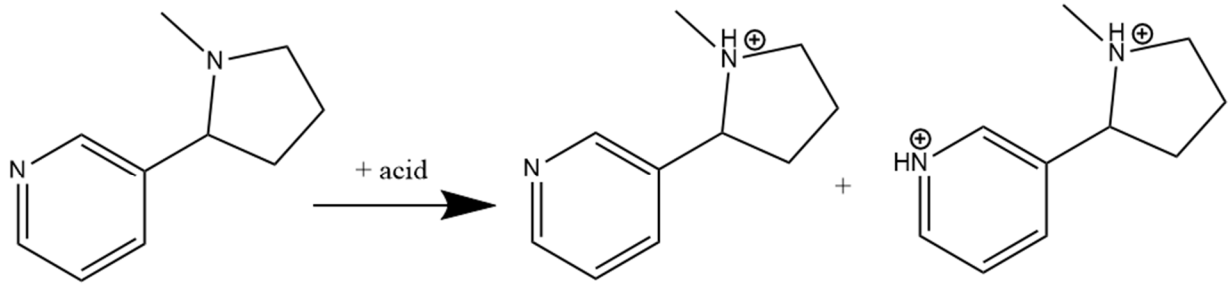
73. The formation of a salt in Sebastian is grounded in the inherent property of nicotine as a base and the reaction that occurs upon coming into contact with an acid such as lactic acid. EX1009, ¶¶ 19-20, 23-26, 32-35. In general, I understand that when an acid, such as lactic acid, and a base, such as nicotine, come into contact, a salt of the acid and base is ***necessarily*** formed because of the resulting reaction. EX1009, ¶¶ 19-22, 32-39; EX1016, 15; EX1017, 3; EX1018, 1; *see also* §VI.A.2, *supra*, incorporated by reference here.

74. The necessary formation of a salt can be illustrated using any one of the organic acids disclosed by Sebastian, including lactic acid. *See* EX1004, [0059]. Generally, in solution, lactic acid can dissociate into a negatively-charged form—the lactate ion—creating a lactate ion and releasing a corresponding hydrogen molecule, which has a positive charge, as I show below:



lactic acid lactate ion

EX1009, ¶ 33. When nicotine ($C_{10}H_{14}N_2$)—a base—is exposed to an acid, it will react with the free positively-charged hydrogen molecules, creating positively-charged ionic forms of nicotine:



"free base" nicotine monoprotonated nicotine diprotonated nicotine

EX1009, ¶ 34. I note that this reaction is expressly acknowledged by the '533 patent itself which confirms that protonated nicotine can exist with both a single charged nitrogen ("monoprotonated") or two charged nitrogens ("diprotonated"). *See* EX1001, 12:65-13:2; EX1008, 1-2; EX1009, ¶ 34.

75. Upon being present in solution together, I understand that the ***negatively***-charged lactate ions and the ***positively***-charged nicotine ions will attract

each other and interact due to their opposing charges. Fundamental chemical principles instruct that this interaction results in the formation of a salt, i.e., nicotine lactate. EX1009, ¶¶ 19-26, 32-39. Therefore, the formation of a salt ***necessarily*** occurs in Sebastian's aerosol precursor that contains lactic acid and nicotine together in a liquid as a result of the reaction between the two components. EX1009, ¶¶ 28-39.

76. It is my understanding that Sebastian also specifically discloses that in its formulations, "***organic acids***, such as levulinic acid, lactic acid, and pyruvic acid, ***can be included*** in the aerosol precursor ***with nicotine*** in amounts up to being ***equimolar*** (based on total organic acid content) with the nicotine." EX1004, [0059]; *see also* EX1004, [0059] (disclosing ratio of "about 0.5 moles of lactic acid per one mole of nicotine[.]"). It is my opinion that this statement further confirms that Sebastian contemplates and discloses a chemical reaction between nicotine and organic acid. "Equimolar" means present at equal molar concentrations, or amounts, i.e. a one-to-one (1:1) ratio. EX1009, ¶ 30.

77. A molar concentration is a reference to the fundamental chemistry concept of stoichiometry, which refers to the number of molecules of different reactants in a chemical reaction. "Equimolar" means that there is one molecule of acid for every molecule of nicotine—that is, every nicotine molecule has a

corresponding organic acid molecule with which it can react. EX1009, ¶ 30. Upon reading Sebastian, I understand that the express description of the specific stoichiometric ratios of organic acid to nicotine indicates a chemical reaction between organic acid and nicotine.

78. Upon comparing other disclosures in Sebastian, I note that Sebastian does not use stochiometric terms to discuss the concentrations of other components of its aerosol precursor composition relative to nicotine. For example, Sebastian only expresses concentrations of water or propylene glycol by weight percentage, and not in relation to the proportion of nicotine. *See, e.g.*, EX1004, [0061] ("the glycerol can be present in an amount of about 70% to about 90% by weight…the water can be present in an amount of about 10% to about 20% by weight[.]"). Therefore, it is my view that Sebastian's "up to equimolar" description distinctly contemplates a chemical reaction between nicotine and organic acid.

79. Thus, because the formation of a nicotine salt is the natural and necessary result flowing from nicotine and lactic acid being present together in Sebastian's aerosol precursor composition, it is my opinion that Sebastian discloses this limitation.

b) Chemistry textbooks and chemistry expert further demonstrate that Sebastian necessarily discloses a "nicotine salt"

80. The fundamental chemistry principles that explain why a nicotine salt necessarily forms in Sebastian are supported by reputable, college-level chemistry textbooks. For example, Bauer (EX1007) is a textbook titled "Introduction to Chemistry" published in 2010. I understand that it was designed to be used in a freshman-level Introductory Chemistry course requiring no chemistry prerequisite, and is intended for non-physical science majors in disciplines that do not require the rigor of a science major's General Chemistry course. I note that Bauer explains general chemistry principles underlying acid-base chemistry, including but not limited to the structures of lactic acid and nicotine, their properties as acids and bases, and how acids and bases react to form salts. EX1007, 61, 140-142, 206, 210.

81. With respect to the definition of acids and bases, I note that Bauer explains the "Brønsted-Lowry theory" which "defines an acid as any substance that can donate an H^+ ion to another substance" and "defines a base as any substance that can accept an H^+ ion from another substance." EX1007, 141. I note that Bauer's description of acids and bases is consistent with the '533 patent. For example, the '533 patent defines an "organic acid" as "an organic compound with

acidic properties (e.g., by Brønsted-Lowry definition, or Lewis definition)." EX1001, 11:6-8.

82. Furthermore, Bauer discloses the structures of both nicotine and lactic acid. Bauer classifies lactic acid as a carboxylic acid, noting that its "reactions often involve loss of H^+." *See* EX1007, 206. Meanwhile, Bauer classifies nicotine as an "amine," noting that "most amines act as bases due to the presence of an unshared electron pair on the nitrogen atom." EX1007, 210. Bauer further confirms that nicotine forms a base in the presence of water, and reacts with acids to form "salts." EX1007, 210; EX1009, ¶¶ 19-20.

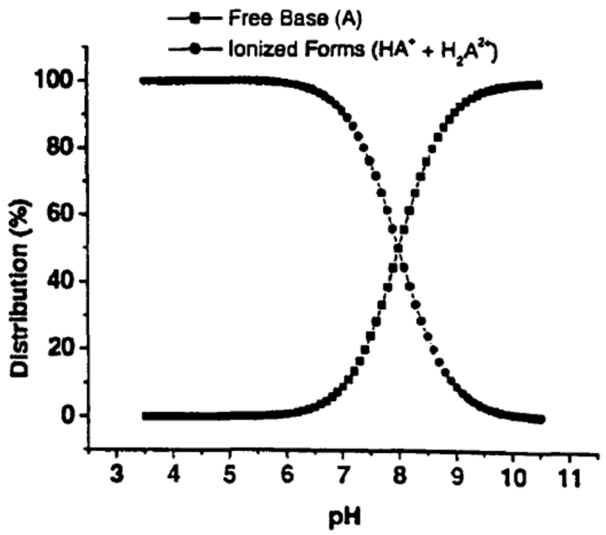
83. In addition to college-level textbooks, my opinion regarding the necessary formation of a nicotine salt in Sebastian is further confirmed by the opinions of Dr. Stephen Byrn, who I understand is a Ph.D. scientist with over 50 years of chemistry experience. *See* EX1009, ¶¶ 4-15. Based on my review of Dr. Byrn's opinions, I understand that lactic acid and nicotine, for example, possess inherent chemical characteristics—such as specific pK_a values—that reliably predict the formation of nicotine lactate—i.e., a salt—in Sebastian's aerosol precursor composition. EX1009, ¶¶ 21-27, 32-39; EX1011, 194-195. I note that Dr. Byrn, based on the well-established pK_a values of lactic acid and nicotine, and the difference in pK_a (ΔpK_a) between these two molecules, confirmed that

Sebastian's aerosol precursor composition contains nicotine lactate. EX1009, ¶¶ 36-39.

84. Dr. Byrn's opinions are consistent with my opinion that the interaction of lactic acid and nicotine in solution will necessarily result in the formation of nicotine lactate. EX1009, ¶¶ 32-39, 48. Specifically, Dr. Byrn also opined that lactic acid will dissociate into its ***negatively***-charged form in solution while nicotine will dissociate into its ***positively***-charged form, and these forms will attract and interact with each other to form a salt. EX1009, ¶¶ 32-35.

85. While I will not reiterate all of Dr. Byrn's explanation here, I note that Dr. Byrn describes how the specific chemical reaction between nicotine and lactic acid that results in salt formation is found in the record. While not express in the chemistry textbooks, Lechuga-Ballesteros shows experimental data demonstrating the specific formation of this salt, further corroborating my opinions here. EX1009, ¶¶ 40-47. For instance, the titration experiment disclosed in Lechuga-Ballesteros, which I will also discuss in more detail below, demonstrates in real time the formation of an "Ionized Form," i.e., a salt, when an acid is added to free base nicotine:

Figure 2B



EX1005, Fig. 2B. Dr. Byrn explains that this plot shows that the "Free Base (A)" curve begins with 100% free base at pH 11 (top right). EX1009, ¶¶ 41-43. At pH 11, there is no "ionized form," and thus no salt, present in the solution. As soon as the organic acid is added to the solution, however, a salt does form, and the nicotine is either monoprotonated ("HA^+") or diprotonated ("H_2A^{2+}"). EX1009, ¶ 43. Consequently, the pH of the solution decreases. I note that when sufficient acid is added to the solution to decrease the pH of the solution to 7, less than 10% free base nicotine is left in solution. EX1009, ¶ 44. Thus, in my view, a POSITA would understand that the other 90% of the nicotine is ionized, i.e., protonated, and forms a salt. EX1009, ¶ 44.

86. Therefore, for all of these reasons, Sebastian's disclosure of a nicotine salt is grounded in fundamental chemistry principles that are further supported by

college-level chemistry textbooks, additional corroborating record evidence, and Dr. Byrn's expert testimony.

ii. Sebastian discloses "in a liquid carrier"

87. Sebastian expressly discloses the nicotine salt in a liquid carrier. I note that Sebastian states that "the components for aerosolization (including aerosol formers and other inhalable materials) can be provided in liquid form in one or more reservoirs positioned sufficiently away from the resistive heating element to prevent premature aerosolization[.]" EX1004, [0051]. Sebastian also expressly provides that the "aerosol precursor compositions can include other liquid materials, such as water." EX1004, [0055]. Sebastian identifies several liquid carriers, disclosing that "aerosol precursor compositions can incorporate mixtures of glycerin and water, or mixtures of propylene glycol and water, or mixtures of propylene glycol and glycerin, or mixtures of propylene glycol, glycerin, and water." EX1004, [0055].

88. It is my opinion that Sebastian's disclosures are consistent with the '533 patent's description of a liquid carrier. Specifically, the '533 patent states, "[s]uitable carriers (e.g., a liquid solvent) for the nicotine salts described herein include a medium in which a nicotine salt is soluble at ambient conditions, such that the nicotine salt does not form a solid precipitate." EX1001, 11:44-47. I note

that the ’533 patent identifies the same liquid carriers as those disclosed by Sebastian, stating that “[e]xamples include, but are not limited to, glycerol, propylene glycol, trimethylene glycol, water, ethanol and the like, as well as combinations thereof.” EX1001, 11:47-50.

89. Based on my review of the prosecution history, I understand that the Examiner similarly found that Sebastian’s “aerosol precursor composition may include glycerol and/or propylene glycol (***read: liquid carrier***) in addition to a medicament, such as nicotine,” (EX1002, 209), and I note that the applicant did not argue otherwise. EX1002, 285-86.

90. Thus, in view of Sebastian’s express, inherent, and implicit disclosures, I conclude that Sebastian teaches “a salt of nicotine and an organic acid in a liquid carrier.”

[1c] the organic acid is benzoic acid or lactic acid;

91. Sebastian expressly discloses lactic acid. I note that Sebastian explicitly states that “organic acids, such as levulinic acid, ***lactic acid***, and pyruvic acid, can be included in the aerosol precursor with nicotine in amounts up to being equimolar (based on total organic acid content) with the nicotine.” EX1004, [0059]; *see also* EX1004, [0059] (aerosol precursor can include “about 0.1 to about 0.5 moles of lactic acid per one mole of nicotine”). Furthermore, I understand that

Sebastian's list of organic acids is non-exhaustive. EX1004, [0059] (identifying list of organic acids beginning with "e.g.").

92. Thus, in view of Sebastian's express disclosures, I conclude Sebastian teaches this limitation.

[1d] (b) the salt is present in an amount that forms a nicotine concentration of 0.5% (w/w) to 20% (w/w) in the nicotine salt liquid formulation;

93. Sebastian discloses nicotine concentrations within the claimed range of 0.5% to 20% by weight percentage. Specifically, I note that Sebastian expressly states that "nicotine can be present in amount of about 0.1% to about 5% by weight." EX1004, [0061]. In addition, Sebastian explains that "[f]lavors and the like (which can include medicaments, such as nicotine) can comprise up to about 10%, up to about 8%, or up to about 5% by weight of the aerosol precursor." EX1004, [0060].

94. These ranges disclosed by Sebastian fall within and around the claimed 5% to 20% range. I understand from counsel that a claimed range, such as the one claimed here, is sufficiently disclosed if the prior art describes a point within the range. It is evident that this is the case here. I also understand from counsel that even a partially overlapping range in the prior art will be considered to disclose the claimed range. Here, I note that there is clear overlap between the ranges disclosed by Sebastian and the claimed range. For example, I note that the

highest concentration of nicotine disclosed by Sebastian in one range is 5%, which is an ***order of magnitude greater*** than the claimed lower end of the range—i.e., 0.5% nicotine. *See* EX1001, 20:33-36.

95. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian discloses "the salt is present in an amount that forms a nicotine concentration of 0.5% (w/w) to 20% (w/w) in the nicotine salt liquid formulation."

[1e] (c) the liquid carrier comprises glycerol and propylene glycol; and…

96. Sebastian expressly describes the liquid aerosol precursor composition as comprising glycerol and propylene glycol. Specifically, I note that Sebastian states that an "aerosol precursor according to the invention can comprise ***glycerol, propylene glycol,*** water, nicotine, and one or more flavors." EX1004, [0061].

97. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches this limitation.

[1f] (d) the nicotine salt liquid formulation generates an inhalable aerosol upon heating in the electronic cigarette.

98. Sebastian expressly teaches a liquid aerosol precursor composition comprised of a salt of nicotine that becomes an inhalable aerosol upon heating. Specifically, I note that Sebastian expressly describes that its electronic smoking article "can comprise a heating member that heats an aerosol precursor component to produce an aerosol for inhalation by a user." EX1004, [0048]. Furthermore,

Sebastian discloses that "[w]hen the heating member heats the aerosol precursor component, an aerosol is…formed, released, or generated in a physical form suitable for inhalation by a consumer." EX1004, [0031].

99. Based on my review of the prosecution history, I understand that the Examiner concluded that Sebastian disclosed an electronic cigarette "that provides for delivery of aerosolized components of a liquid aerosol precursor composition to at least one heating element from which said aerosolized components are inhaled into the mouth of a user." EX1002, 208, 211-12. I also understand that the applicant did not argue that Sebastian failed to disclose either an electronic cigarette, as I discuss above for Element [1pre], or the generation of an inhalable aerosol upon heating the liquid formulation in an electronic cigarette. EX1002, 285-86; *see supra* §VII.A.2.[1pre].

100. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches "the nicotine salt liquid formulation generates an inhalable aerosol upon heating in the electronic cigarette."

[2] The electronic cigarette of claim 1, wherein the liquid carrier further comprises water.

101. Sebastian expressly describes that the liquid aerosol precursor composition further includes water. As I discussed previously, Sebastian discloses that "the aerosol precursor compositions can include other liquid materials, such as

water." EX1004, [0055]; *see also* EX1004, [0055] ("aerosol precursor compositions can incorporate mixtures of glycerin ***and water***, or mixtures of propylene glycol ***and water***, or mixtures of propylene glycol and glycerin, or mixtures of propylene glycol, glycerin, ***and water***."), [0061] ("an aerosol precursor according to the invention can comprise glycerol, propylene glycol, ***water***, nicotine, and one or more flavors.").

102. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches claim 2.

[3] The electronic cigarette of claim 1, wherein the salt is present in an amount that forms a nicotine concentration of 1% (w/w) to 18% (w/w) in the nicotine salt liquid formulation.

103. I conclude that Sebastian discloses the claimed range of nicotine concentrations in claim 3 for the same reasons I explained previously for Element [1d]. *See* §VII.A.2.[1d], *supra*. As discussed, I understand that by disclosing points within the claimed range and ranges that overlap with the claimed range, Sebastian discloses this claim.

[4] The electronic cigarette of claim 1, wherein the salt is present in an amount that forms a nicotine concentration of 3% (w/w) to 15% (w/w) in the nicotine salt liquid formulation.

104. I conclude that Sebastian discloses the claimed range of nicotine concentrations in claim 4 for the same reasons I explained previously for Element [1d]. *See* §VII.A.2.[1d], *supra*. As discussed, I understand that by disclosing

points within the claimed range and ranges that overlap with the claimed range, Sebastian discloses this claim.

[5] The electronic cigarette of claim 1, wherein the salt is present in an amount that forms a nicotine concentration of 4% (w/w) to 12% (w/w) in the nicotine salt liquid formulation.

105. I conclude that Sebastian discloses the claimed range of nicotine concentrations in claim 5 for the same reasons I explained previously for Element [1d]. *See* §VII.A.2.[1d], *supra*. As discussed, I understand that by disclosing points within the claimed range and ranges that overlap with the claimed range, Sebastian discloses this claim.

[6] The electronic cigarette of claim 1, wherein the nicotine salt liquid formulation further comprises a flavorant.

106. Sebastian expressly teaches that the aerosol precursor composition can comprise a flavorant. Sebastian states that "an aerosol precursor according to the invention can comprise…***one or more flavors***," (EX1004, [0061], and teaches that "[a] wide variety of types of flavoring agents, or materials that alter the sensory or organoleptic character or nature of the mainstream aerosol of the smoking article can be employed," (EX1004, [0059]; *see also* EX1004, [0059] ("The flavoring agents can be combined with the aerosol-generating material if desired.").

107. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches claim 6.

[7] The electronic cigarette of claim 1, wherein the nicotine salt liquid formulation further comprises one or more additional organic acids.

108. Sebastian expressly teaches that more than one organic acid can be included in the aerosol precursor composition. Sebastian states that "[a]ny combination of organic acids can be used." EX1004, [0059].

109. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches claim 7.

[8] The electronic cigarette of claim 1, wherein the cartridge is configured to serve as a mouthpiece and a reservoir, wherein the reservoir holds the nicotine salt liquid formulation.

110. Sebastian expressly discloses a cartridge that is configured to serve as a mouthpiece and a reservoir for the aerosol precursor composition. As I discussed previously, Sebastian expressly describes that its cartridge includes "a mouth opening 18 at the mouthend 11 thereof to allow passage of air and entrained vapor (i.e., the components of the aerosol precursor composition in an inhalable form) from the cartridge to a consumer during draw on the article 10." EX1004, [0088]. In addition, Sebastian expressly discloses that "the interior cartridge space can include one or more reservoirs for storing a plurality of components of an aerosol precursor composition." EX1004, [0116].

111. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches claim 8.

[10] The electronic cigarette of claim 1, wherein the organic acid is lactic acid.

112. Sebastian expressly discloses lactic acid. As I discussed above, Sebastian provides a non-exhaustive list of four organic acids, one of which is lactic acid. EX1004, [0059] (identifying levulinic acid, lactic acid, pyruvic acid, and succinic acid); *see also* §VII.A.2.[1c], *supra*.

113. Thus, in view of Sebastian's express disclosures, I conclude that Sebastian teaches claim 10.

B. [Ground 2] Sebastian in View of Lechuga-Ballesteros Discloses Claims 1-10

1. Overview of Lechuga-Ballesteros

114. Lechuga-Ballesteros is a patent application titled, "Aerosolizable Formulation Comprising Nicotine," published on January 26, 2006. EX1005. Lechuga-Ballesteros describes "Metered Dose Inhalers," or "MDIs," which can aerosolize and deliver nicotine to a consumer's lungs. EX1005, [0003], [0010]-[0012]. Lechuga-Ballesteros explains that it was "desirable to be able to deliver the nicotine in a manner that simulates the nicotine delivery of a cigarette." EX1005, [0010]. To that end, Lechuga-Ballesteros goes on to disclose an "aerosolizable formulation" that "comprises free-base nicotine; an organic acid, wherein (a) said organic acid is present in a mole ratio with said nicotine in a range of about 0.25:1 (organic acid:nicotine) to about 4:1 (organic acid:nicotine), (b) ***said***

organic acid and said free-base nicotine form a nicotine salt, and (c) an equivalent mixture of free-base nicotine and organic acid in water has a pH between about pH 3.0 and about pH 9.0; and a hydrofluoroalkane propellant." EX1005, [0012]; *see also* EX1005, [0013]-[0014].

115. I note that the primary organic acid disclosed and tested by Lechuga-Ballesteros was lactic acid, which was used to generate a salt of nicotine and lactic acid, i.e., nicotine lactate. *See* EX1005, [0023], [0084]. I further note that through testing, Lechuga-Ballesteros expressly disclosed that the "nicotine lactate solution had the most desirable combination of attributes." EX1005, [0084].

116. Indeed, through experiments comparing its nicotine salt formulation to free base nicotine formulations, Lechuga-Ballesteros found "that the formulation of the present invention provides a ***more palatable delivery*** of nicotine." EX1005, [0062]. Specifically, I understand that these findings included the result that "nicotine salt forms are less harsh and have a less unpleasant taste" and that the nicotine salt formulation "provides nicotine in an inhalable form that is ***more biocompatible than delivery of the free base*** and provides delivery of the nicotine in a pH range more acceptable to a subject, for example, a human." EX1005, [0062], [0067].

2. Motivation to Combine Teachings of Lechuga-Ballesteros to Sebastian

117. It is my opinion that, even if Sebastian alone is found to not disclose a nicotine salt—a conclusion contrary to the disclosures of Sebastian, as I discuss previously—a POSITA would nevertheless have found it obvious to incorporate a nicotine salt into Sebastian's liquid aerosol precursor composition based on the express teachings of Lechuga-Ballesteros, which expressly include the benefits of nicotine salts, and even further, the benefits of a nicotine lactate salt.

118. ***First,*** I note that a POSITA reading Sebastian would have had the goal of being able to offer aerosolized nicotine to a consumer while providing the "***taste and/or sensation*** (e.g., hand-feel or mouth-feel) ***of smoking a cigarette***, cigar, or pipe ***without substantial combustion*** of any component of the article." EX1004, [0029]. As such, it is my opinion that the same POSITA would have been motivated to look to the teachings of Lechuga-Ballesteros, as Lechuga-Ballesteros is also focused on providing nicotine in an aerosol form. Indeed, Lechuga-Ballesteros' objective was "nicotine penetration into the lungs that ***simulates the sensation*** normally provided by nicotine when ***delivered by smoking a cigarette*** yet ***without the disadvantages of inhalation of combustion products from tobacco***[.]" EX1005, [0070]; *see also* EX1005, [0010] ("It is further

desirable to be able to deliver the nicotine in a manner that ***simulates the nicotine delivery of a cigarette***").

119. To that end, it is my opinion that a POSITA would have recognized that Sebastian and Lechuga-Ballesteros both desired to simulate the sensation of smoking a cigarette through the inhalation of an aerosol which, in part, would replicate the delivery of nicotine to the central nervous system similar to that of a combustible cigarette. Additionally, by its nature the aerosol being inhaled would not include the combustion products that result from smoking cigarettes.

120. ***Second,*** it is my opinion that a POSITA reading Sebastian would have looked to Lechuga-Ballesteros because Lechuga-Ballesteros expressly discloses the superiority of nicotine salts over nicotine in free base form with respect to delivery properties and biocompatibility. Specifically, Lechuga-Ballesteros expressly describes that the "nicotine/organic acid formulation of the present invention (e.g., ***Nicotine Lactate*** formulation) was shown to have ***superior performance*** for the evaluated attributes than the Nicotine Free Base formulation." EX1005, [0055]; *see also* EX1005, [0057] ("results suggested that ***all of the nicotine lactate formulations were preferable*** to the nicotine propionate formulations, which were ***more preferable than the nicotine free base formulation***"). In addition, Lechuga-Ballesteros expressly discloses that "[i]t has

also been discovered that the formulation of the present invention ***provides a more palatable delivery*** of nicotine," noting that "[f]ree-base nicotine has a harsh, unpleasant taste." EX1005, [0062]. Furthermore, Lechuga-Ballesteros stated that "nicotine salt forms are ***less harsh*** and have a ***less unpleasant taste***" and do not lead to gastrointestinal upset as often as free base nicotine. EX1005, [0062].

121. I also highlight that Lechuga-Ballesteros supported its disclosure that nicotine lactate is superior with empirical data. *See, e.g.*, EX1004, [0073]-[0100] (Examples 1-6).

122. Looking first at Example 3, Lechuga-Ballesteros "evaluated further for properties related to aerosolized, pulmonary delivery of nicotine" including throat deposition of nicotine and the total nicotine dose delivered ("respirable dose"). EX1005, [0056]. Lechuga-Ballesteros found that the "nicotine lactate formulation…had lower throat deposition (~15% of total nicotine delivered dose) and provided a higher respirable dose (~72% of the total nicotine delivered dose) than the nicotine free base formulation." EX1005, [0087]; *see also* EX1005, [0086] (Table 3). In addition, Lechuga-Ballesteros taught that less throat deposition is preferred because it is associated with less irritation, as is a higher respirable dose of nicotine. EX1005, [0053]-[0054], [0056], [0087]. Furthermore, Lechuga-Ballesteros stated that its results "suggested better pulmonary delivery of

nicotine by the nicotine lactate formulation versus the nicotine free base formulation." EX1005, [0088].

123. Next, in Example 4, Lechuga-Ballesteros showed that its aerosolized nicotine lactate formulation provided nicotine in a more biocompatible form than free base nicotine. EX1005, [0067]. Specifically, Lechuga-Ballesteros found "that at an approximately 1.2:1 ratio (acid:nicotine) the majority of the nicotine free base was converted to the nicotine salt," meaning that "there is no dumping of strongly basic nicotine into the lungs, nor is there dumping of free acid into the lungs," but rather nicotine is "delivered as a salt comprising nicotine and the associated organic acid." EX1005, [0091]; *see also* EX1005, [0089]-[0090]. It is my opinion that a POSITA reading this disclosure would understand that the "no dumping" property of nicotine delivery in salt form was "a highly desirable feature" as the salt form "provides nicotine in an inhalable form that is ***more biocompatible*** than delivery of the free base and provides delivery of the nicotine ***in a pH range more acceptable*** to a subject, for example, a human." EX1005, [0091].

124. Therefore, based on the extensive empirical data supporting the superiority of nicotine salts over free base nicotine, it is my opinion that a POSITA reading Lechuga-Ballesteros would have been further motivated to incorporate a nicotine salt into Sebastian's liquid aerosol precursor composition to deliver

aerosolized nicotine in a more biocompatible form. As such, in my view, a POSITA would have been motivated to incorporate a nicotine lactate salt in Sebastian's liquid aerosol precursor composition.

125. ***Third,*** it is my opinion that the desirable delivery properties of nicotine salts were long known in the industry, and Lechuga-Ballesteros is just one example. Despite Patent Owner's contentions during prosecution that it had "surprisingly discovered" "the surprising benefits of formulating nicotine as a salt for delivery in an electronic cigarette" when "the common knowledge in the art at the time" was allegedly that "free base nicotine was preferred," (EX1002, 285), I note that the benefits of using a nicotine salt instead of free base nicotine were long known in the industry.

126. In fact, I further note that the superiority of nicotine salts over free base nicotine for nicotine delivery was so well-known that the shift in use to nicotine salts was described in the industry as "déjà vu all over again," as nicotine salts date back to at least the 1900's, if not before. EX1008, 1. As I noted previously in Section VI.A.3, Duell observed that the "role of acids in converting nicotine to a protonated, 'salt' form in tobacco smoke has long been understood," and quoted an article ***from 1909*** that stated:

> Apparently the only possible explanation of this pronounced effect on the sharpness of the smoke is that in the presence of the citric acid the nicotine ***enters the smoke in the form of a salt*** rather than in the free state, and thereby ***loses its pungency while still exerting the usual physiological effect***.

EX1008, 6.[4] In fact, to show the parallel development of the shift to nicotine salts over time between conventional cigarettes and e-cigarettes, the article's authors created a comparison showing the shift from free base nicotine to nicotine salts:

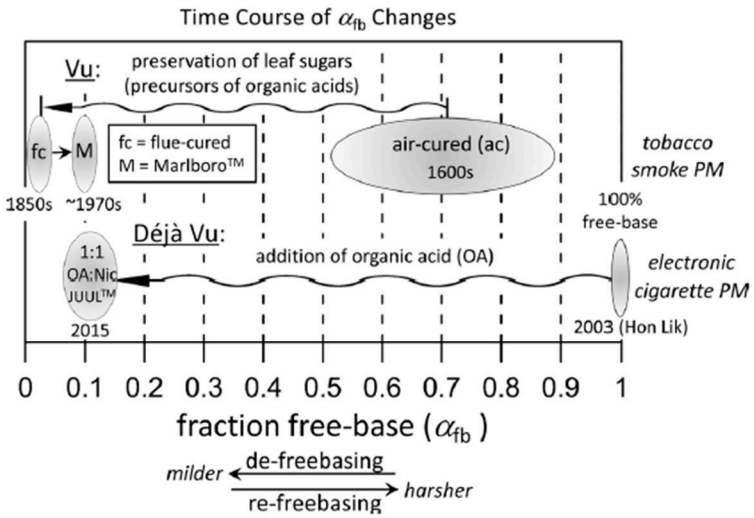


Figure 3 A visual representation of the historical changes in α_{fb} in tobacco smoke PM (top) in comparison to how electronic cigarette fluids and their associated aerosols have been changed (bottom). fc, flue-cured; α_{fb}, fraction of nicotine in the free-base form; M, Marlboro; Nic, nicotine; OA, organic acid; PM, particulate matter.

[4] I note that citric acid is an organic acid, and is identified as one both by the '533 patent specification and Lechuga-Ballesteros. *See* EX1001, 14:42-64 (identifying "nicotine citrate" as an organic acid "used in the salt formation"), Figs. 4-6, (experiments using "nicotine citrate"), 30:57-65 (identifying "citric acid" as "organic acid"); EX1005, [0042], cl. 9.

EX1008, 5; *see also* EX1008, 5 ("The chemistry changes during the rapid evolution of e-cigarettes closely parallel the events that occurred during the centuries-long development of smoked tobacco."). In this graphic, the proportion of free base nicotine to nicotine salt is shown on the horizontal axis, with 1 being 100% free base nicotine and 0 being 100% nicotine salt. EX1008, 5 (Fig. 3). As discussed previously in Section VI.A.3., the top wavy line shows the movement from "air-cured" nicotine in the 1600s on the right, which had a higher fraction of free base nicotine, to "flue-cured" nicotine in the 1850s on the left, with a lower fraction of free base nicotine due to the preservation of nicotine "leaf sugars" that were in fact preserved in the form of organic acid precursors. With respect to electronic cigarettes, the bottom wavy line shows the same movement from free base nicotine to the addition of organic acids, i.e. use of nicotine salts. EX1008, 5.

127. Based on my review of the prosecution history, I understand that the Examiner found that the claimed nicotine salt formulation was not novel. I further note that after the applicant added "lactic acid" to the claims, the Examiner rejected the claims as obvious over Lawson, a European patent related to conventional cigarettes that first published decades ago in 1988. EX1002, 519-523; EX1006, 1.

128. Lawson explained that at that time, tobacco with high nicotine content was available for use but was generally not preferred because "cigarettes having

high nicotine contents…generally have the propensity to yield unpalatable mainstream smoke which may be perceived as harsh or irritating to the mouth, nose and throat of the user." EX1006, 2:33-36.

129. Therefore, I understand that Lawson expressly taught incorporating "at least one salt provided from nicotine and an organic acid" to "improve the smoking character of such cigarettes so that their smoke is perceived as not being overly harsh or irritating." EX1006, 3:16-17, 2:37-38. In addition, Lawson disclosed "nicotine lactate" expressly as an exemplary nicotine salt. EX1006, 6:38-41.

130. Furthermore, I understand that Lawson described that the presence of a nicotine salt "provides improved tobacco taste, strength and smoking satisfaction as well as improved or maintained flavor characteristics to the aerosol during use of the article while avoiding undesirable off-tastes during use." EX1006, 3:25-27.

131. Based on my review of the prosecution history, I note that the Examiner found that Lawson, like Sebastian, disclosed every element of the claimed ***"cartridge"*** containing the nicotine salt formulation, including the nicotine salt claimed by the applicant. EX1002; 519-523. Therefore, it is my opinion that the prosecution history further supports the conclusion that nicotine salts—and

their desirable properties compared to free base nicotine—were well-known in the art long before the'533 patent, with Lawson being yet another example.

132. ***Fourth***, it is my understanding that during prosecution, the applicant contended that the ***manner*** of aerosolization (i.e., pressurized versus heated) would have dissuaded a POSITA from looking to Lechuga-Ballesteros and applying its express teachings regarding the superiority of aerosolized nicotine salt over aerosolized free base nicotine to Sebastian. EX1002, 285-290, 382-384. As a person of skill in the art who was working in this field at the time of the invention, I strongly disagree with this contention, as we had in fact been looking at references for many years prior that used MDIs to aerosolize nicotine compounds for use in technology that created aerosols via heating, as in e-cigarettes.

133. I understand from counsel that the prior art does not need to be physically combined in all respects to render the claimed invention obvious. I further understand that the Petitioner here is not arguing bodily incorporation of Lechuga-Ballestero's ***complete formulation*** in an e-cigarette. Specifically, while Lechuga-Ballesteros's MDI formulation contains a propellant, (*see, e.g.*, EX1005, [0049]), it is my opinion that a POSITA would certainly have understood that propellants would be inappropriate to use in a device relying on heating to achieve aerosolization, as Sebastian does.

134. However, this does not mean that a POSITA would have completely ignored Lechuga-Ballesteros's express disclosures explaining the superiority of aerosolized nicotine lactate over aerosolized free base nicotine, because these teachings apply directly to e-cigarette chemistry. EX1005, [0012], [0084]. Both Lechuga-Ballesteros and Sebastian provide the same end result—aerosolized nicotine. Therefore, in my view, it is irrelevant whether the aerosolization was achieved by pressure or by heat. EX1005, [0031] ("When the actuator is depressed a metered dose of the compound is aerosolized for inhalation"); EX1004, [0009] ("disclosed herein is a system that can transport and heat the various chemical compounds present in the aerosol precursor composition under controlled conditions so as to achieve a uniform puff chemistry.").

135. Indeed, I note that there is nothing in Lechuga-Ballesteros to suggest or indicate that the propellant affected or drove the superior delivery properties of nicotine lactate salt over free base nicotine in any way.

136. ***Finally***, to the extent that Patent Owner may argue that Lechuga-Ballesteros is not within the same field of invention as the '533 patent, such a contention is unfounded. Specifically, Lechuga-Ballesteros expressly describes the field of its invention as relating to "the delivery of alkaloids, such as nicotine, to the lungs of an individual." EX1005, [0002]. The '533 patent similarly states that

"described herein are nicotine salt formulations for use in an electronic cigarette, or the like, that provide a general satisfaction effect consistent with an ***efficient transfer of nicotine to the lungs*** of an individual[.]" EX1001, 8:22-26.

137. Additionally, I note that other prior art on the topic of nicotine delivery by inhalation from the same time period as Sebastian corroborates my opinion that Metered-Dose Inhalers ("MDIs")—like the one in Lechuga-Ballesteros—were viewed hand-in-hand with electronic cigarettes.

138. Specifically, in a 2012 review article titled "A Systematic Review of Nicotine by Inhalation: Is There a Role for the Inhaled Route?," the authors "systematically reviewed clinical trials of nicotine inhalation devices to identify technical insights that might lead to more effective therapeutic nicotine inhalers." EX1010, 1. The authors found that nicotine particles "can be made by (a) heating tobacco (by combustion [smoking] or electric heater)…(b) ***condensing and aggregating vaporized nicotine solutions by electric heater***…(c) aerosolizing nicotine solutions by bench-top nebulizer machines, (d) [pressurized metered-dose inhalers] pMDIs…(e) air classifiers…(f) capillary aerosol generators…and (g) novel devices[.]" EX1010, 5; *see also* EX1010, 4 (discussing MDIs immediately after electronic cigarettes). The authors found that "[o]f these devices, the pMDI is

currently the cheapest, most portable, and relatively simple and economically practical to manufacture on a large scale." EX1010, 5.

139. Therefore, this article demonstrates that at the time of the claimed invention, persons of skill in the art were actively considering MDI literature and electronic cigarette literature together.

140. In addition, it is my opinion that Lechuga-Ballesteros goes one step further than being in the same field of invention and addressing the same problem with respect to nicotine delivery as the '533 patent. Specifically, I note that Lechuga-Ballesteros even discloses the ***same solution*** to the problem, which is the use of a nicotine salt. Therefore, it is my view that any contention by Patent Owner that a POSITA would not look to Lechuga-Ballesteros runs contrary to the express disclosures of both Lechuga-Ballesteros and the '533 patent.

3. Reasonable Expectation of Success in Applying the Teachings of Lechuga-Ballesteros to Sebastian

141. Even if Sebastian is not determined to disclose a salt of nicotine and organic acid—which it does, as I discussed previously—it is my opinion that a POSITA would have had a reasonable expectation of success of incorporating a nicotine salt—particularly nicotine lactate—into Sebastian's liquid aerosol precursor composition due to the similarities between the liquid aerosol precursor compositions of Sebastian and Lechuga-Ballesteros.

142. ***First***, I note that Lechuga-Ballesteros and Sebastian describe similar methods of preparing a nicotine salt formulation. Specifically, in the titration experiment discussed previously, Lechuga-Ballesteros describes that "comparable amounts of nicotine and organic acid [were] combined in water[.]" EX1005, [0066], *see also* EX1005, [0089]. Likewise, nicotine, organic acid, and water are components of Sebastian's aerosol precursor composition. EX1004, [0055], [0060], [0061]. Therefore, given that Lechuga-Ballesteros discloses the creation of a nicotine lactate salt by the addition of nicotine and lactic acid to water, a POSITA would have reasonably expected nicotine lactate to also form in Sebastian because Sebastian also discloses combining nicotine, lactic acid, and water. EX1004, [0055], [0060], [0061].

143. ***Second***, I note that Lechuga-Ballesteros discloses liquid formulations in which the molar ratio of organic acid to nicotine is identical to that described in Sebastian. Specifically, Sebastian states that "organic acids, such as levulinic acid, lactic acid, and pyruvic acid, can be included in the aerosol precursor with nicotine in amounts ***up to being equimolar*** (based on total organic acid content) with the nicotine." EX1004, [0059]. As noted previously, "equimolar" means that the same number of molecules of nicotine are present as the number of molecules of organic acid. Lechuga-Ballesteros also discloses a molar ratio "preferably in a

range of about 1:1," which means that the nicotine and organic acid are present in stoichiometrically equal amounts. EX1005, [0040].

144. ***Third***, I understand that Sebastian's liquid aerosol precursor composition and Lechuga-Ballesteros's nicotine/organic acid formulation contain many of the same components, including solvents like propylene glycol, glycerol, and/or water. Specifically, Sebastian states that "an aerosol precursor according to the invention can comprise glycerol, propylene glycol, water, nicotine, and one or more flavors." EX1004, [0061]. Lechuga-Ballesteros similarly discloses that "an aerosolizable formulation comprises…(c) an equivalent mixture of free-base nicotine and organic acid in water," and further notes that "[a] number of suitable co-solvents can be used in the formulations of the present invention including…propylene glycol…[and] glycerol," and further that "[m]ixtures of two or more co-solvents may be used as well." EX1005, [0012], [0045].

145. ***Fourth***, it is evident that both Sebastian's liquid aerosol precursor composition and Lechuga-Ballesteros's nicotine lactate formulation were intended to be aerosolized and inhaled by a consumer. Specifically, Sebastian discloses that "the article is configured with a sufficient amount of the individual components of the aerosol precursor composition to function at a sufficient temperature for a sufficient time to release a desired content of aerosolized materials over a course of

use." EX1004, [0063]. Similarly, Lechuga-Ballesteros discloses that "a formulation comprising nicotine and organic acid is aerosolized and delivered to the respiratory tract of a user." EX1005, [0038].

146. Finally, as I discussed previously, I understand that Petitioner is not proposing to bodily incorporate Lechuga-Ballesteros's formulation into Sebastian's electronic smoking article. Instead, I note that Petitioner proposes the ***application*** of Lechuga-Ballesteros's teachings regarding the superiority of nicotine lactate salt over free base nicotine in aerosolized delivery. In view of this, any contention by Patent Owner that the presence of a propellant in Lechuga-Ballesteros's undermines a reasonable expectation of success is unfounded because Petitioner is not proposing incorporation of the propellant into Sebastian's liquid aerosol precursor composition. Therefore, it is my view that the presence of the propellant is irrelevant to the obviousness combination of Sebastian and Lechuga-Ballesteros.

147. Therefore, in view of the common disclosures between Sebastian and Lechuga-Ballesteros, it is my opinion that a POSITA would have a reasonable expectation of success in applying Lechuga-Ballestero's disclosures regarding its nicotine lactate salt to Sebastian's liquid aerosol precursor composition.

4. Analysis

[1pre] An electronic cigarette comprising…

148. Sebastian discloses an electronic cigarette for the reasons I explained previously. *See* §VII.A.2.[1pre], *supra*.

[1a] a cartridge,

149. Sebastian discloses a cartridge for the reasons I explained previously. *See* §VII.A.2.[1a], *supra*.

[1b] wherein the cartridge comprises a nicotine salt liquid formulation, wherein: (a) the nicotine salt liquid formulation comprises a salt of nicotine and an organic acid in a liquid carrier,

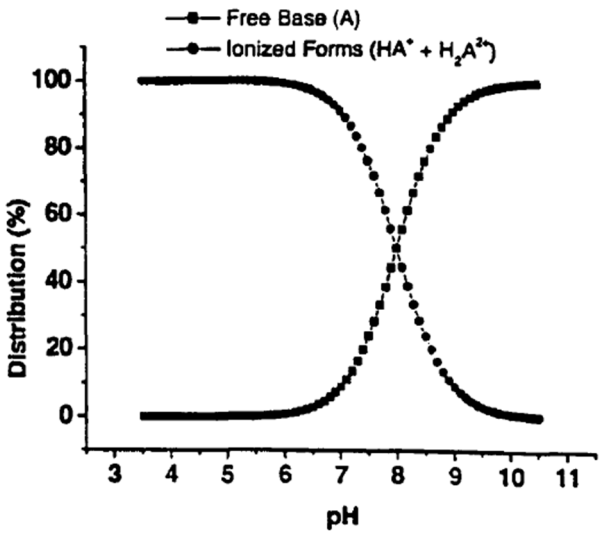
150. Both Sebastian and Lechuga-Ballesteros disclose a nicotine salt liquid formulation comprised of a salt of nicotine and an organic acid in a liquid carrier. As I discussed previously, Sebastian discloses a nicotine salt because it explicitly teaches combining nicotine and organic acid, which react and necessarily form a nicotine salt—a conclusion supported by fundamental chemical principles. *See* §VII.A.2.[1b], *supra*; EX1009, ¶¶ 19-20, 28-39.

151. Even if Sebastian is not found to disclose a nicotine salt, Lechuga-Ballesteros explicitly describes "an aerosolizable formulation [that] comprises ***free-base nicotine***; an ***organic acid***, wherein (a) said organic acid is present in a mole ratio with said nicotine in a range of about 0.25:1 (organic acid:nicotine) to about 4:1 (organic acid:nicotine), [and] (b) ***said organic acid and said free-base***

nicotine form a nicotine salt[.]" EX1005, [0012]; *see also* EX1005, [0013]-[0014]. In addition, Lechuga-Ballesteros goes beyond simply disclosing the formation of a nicotine salt; it goes one step further by describing the "superior performance" of nicotine salts over freebase nicotine and supporting its finding with empirical data, as I explained at length in Section VII.B.2-3, above.

152. Furthermore, it is my opinion that a POSITA would have, at minimum, understood that Lechuga-Ballesteros's express teaching to combine lactic acid and free base nicotine at a nearly equimolar molar ratio necessarily results in the generation of a salt. *See* EX1005, [0091] ("[t]he results of this experiment indicated that at an approximately 1.2:1 ratio (acid:nicotine) the ***majority of the nicotine free base was converted to the nicotine salt***"). In fact, to support this necessary formation of nicotine salt, Lechuga-Ballesteros even includes data showing how the salt is generated in real time:

Figure 2B



EX1005, Fig. 2B; *see also* EX1009, ¶¶ 40-47. In this titration curve, the "Free Base (A)" curve (squares) begins with 100% free base at pH 11. *See* EX1009, ¶¶ 41-43. At that point there is no salt, or "ionized form" present in the solution because organic acid has not been added yet. As soon as the organic acid[5] is added to the solution, a salt is formed, either monoprotonated ("HA^+") or diprotonated ("H_2A^{2+}"), and the pH of the solution decreases. *See* EX1009, ¶ 43; *see also* EX1011, 218-224. At an "equimolar" distribution of the two forms of nicotine—

[5] While Lechuga-Ballesteros does not specify the organic acid shown in Figure 2B, I understand that it is either the propionic acid or the lactic acid that was used to generate the nicotine titration curves in Figure 2A. *See* EX1005, Figs. 2A-2B, [0089]-[0091]. Given the similarities of the two acids at the 1.2:1 molar ratio identified in Example 4, (*see* [0091]), it is my view that a POSITA would expect the resulting percent distribution to likewise be highly similar.

i.e., 50% free base and 50% ionized salt form—the pH is ~8. When enough acid is added to the solution to decrease the pH of the solution to 7, less than 10% free base nicotine is left in solution. The other 90% of the solution is ionized, i.e., in salt form. *See* EX1009, ¶ 44.

153. Therefore, considering that Sebastian discloses including organic acid "in the aerosol precursor with nicotine in amounts ***up to being equimolar*** (based on total organic acid content) with the nicotine," it is my view that Lechuga-Ballesteros further corroborates that Sebastian requires no modification for a nicotine salt to form. EX1004, [0059]-[0061].

154. With respect to the "liquid carrier" limitation, I understand that Lechuga-Ballesteros discloses numerous examples of a "liquid carrier" and refers to them as "co-solvents" or "excipients." *See* EX1005, [0035]. Lechuga-Ballesteros identifies "[a] number of suitable co-solvents"—i.e., the claimed liquid carriers—such as propylene glycol and glycerol. EX1005, [0045].

155. Based on my review of the prosecution history, I understand that Patent Owner contended that its "liquid carrier" is somehow different from Lechuga-Ballesteros's "co-solvents." EX1002, 288-290. It is my opinion that Patent Owner's argument is undermined by its own specification which expressly discloses that "[s]uitable carriers (***e.g., a liquid solvent***) for the nicotine salts

described herein include a medium in which a nicotine salt is soluble at ambient conditions, such that the nicotine salt does not form a solid precipitate," going on to identify "glycerol" and "propylene glycol" specifically EX1001, 11:44-49.

156. Patent Owner's assertion is also unfounded because it ignores that both Lechuga-Ballesteros and Sebastian ***teach the exact same components*** claimed by Patent Owner as liquid carriers, including glycerol, propylene glycol, and water. EX1002, 288-289.

157. Finally, I understand that during prosecution, Patent Owner attempted to differentiate Lechuga-Ballesteros by arguing that ethanol is the preferred co-solvent in Lechuga-Ballesteros. EX1002, 288. Again, Patent Owner's argument is undercut by the '533 patent's specification which expressly discloses that "[e]xamples [of the liquid carrier] include, but are not limited to, glycerol, propylene glycol, trimethylene glycol, water, ***ethanol and the like***, as well as combinations thereof." EX1001, 11:47-50; *see also* EX1005, [0095]. Indeed, even if ethanol is one of the co-solvents disclosed by Lechuga-Ballesteros, the '533 patent's specification falls squarely within this disclosure.

158. Therefore, in view of Sebastian and Lechuga-Ballesteros's express disclosures, I conclude that the prior art both alone and taken together teaches the claimed limitation.

[1c] the organic acid is benzoic acid or lactic acid;

159. Both Sebastian and Lechuga-Ballesteros disclose either or both benzoic acid and lactic acid. Sebastian discloses lactic acid, as I explained previously. *See* §VII.A.2.[1c], *supra*. Lechuga-Ballesteros discloses both lactic and benzoic acid. Specifically, I note that Lechuga-Ballesteros provides a non-exhaustive list of "[n]umerous suitable organic acids…including…benzoic acid…[and] lactic acid[.]" EX1005, [0042].

160. Therefore, in view of Sebastian and Lechuga-Ballesteros's express disclosures, I conclude that the prior art both alone and taken together teaches the claimed limitation.

[1d] (b) the salt is present in an amount that forms a nicotine concentration of 0.5% (w/w) to 20% (w/w) in the nicotine salt liquid formulation;

161. Both Sebastian and Lechuga-Ballesteros disclose "a nicotine concentration of 0.5% (w/w) to 20% (w/w)." Sebastian discloses this limitation for the reasons I explained previously. *See* §VII.A.2.[1d], *supra*. In addition, Lechuga-Ballesteros discloses the claimed nicotine concentration range by expressly disclosing several concentrations within the claimed range. Specifically, I note that Lechuga-Ballesteros expressly discloses that "about 0.01 to about 5 weight percent of the three components is nicotine." EX1005, [0041]. This plainly overlaps with the claimed range of 0.5% to 20%. In another example, I

note that Lechuga-Ballesteros explains the "weight percent of nicotine can be varied, for example, to provide a range of MDIs that deliver difference[sic] nicotine concentrations (e.g., 0.01% w/w, 0.1% w/w, and 1% w/w)[.]" EX1005, [0060]; *see also* EX1005, [0012]-[0014]; EX1009 ¶¶ 45-47.

162. I understand from counsel that a claimed range is obvious if the range in the prior art overlaps with the claimed range. Based on this understanding, I conclude that the prior art both alone and taken together teaches the claimed limitation.

[1e] (c) the liquid carrier comprises glycerol and propylene glycol; and…

163. Both Sebastian and Lechuga-Ballesteros disclose "glycerol and propylene glycol." Sebastian expressly discloses this limitation as I explained previously. *See* §VII.A.2.[1e], *supra*. I note that Lechuga-Ballesteros also discloses "glycerol and propylene glycol" as a part of its nicotine formulation. Specifically, Lechuga-Ballesteros expressly states that co-solvents such as "propylene glycol…[and] glycerol" can be included, further noting that "[m]ixtures of two or more co-solvents may be used as well." EX1005, [0045].

164. Therefore, in view of Sebastian and Lechuga-Ballesteros's express disclosures, I conclude that the prior art both alone and taken together teaches the claimed limitation.

[1f] (d) the nicotine salt liquid formulation generates an inhalable aerosol upon heating in the electronic cigarette.

165. Both Sebastian and Lechuga-Ballesteros expressly disclose a liquid aerosol precursor composition comprised of a salt of nicotine that becomes an inhalable aerosol upon heating. Sebastian expressly discloses this limitation for the reasons I discussed previously. *See* §VII.A.2.[1f], *supra*. While Lechuga-Ballesteros describes that its liquid formulation is aerosolized through the use of a propellant, as I noted previously, the manner of aerosolization is irrelevant in my view because it would have been obvious to a POSITA to incorporate Lechuga-Ballesteros's disclosure of the benefits of incorporating a nicotine salt, such as nicotine lactate, into Sebastian's liquid aerosol precursor composition.. *See* §VII.B.2., *supra*.

166. Therefore, in view of Sebastian and Lechuga Ballesteros's express disclosures, I conclude that taken together, the prior art teaches the claimed limitation.

[2] The electronic cigarette of claim 1, wherein the liquid carrier further comprises water.

167. Both Sebastian and Lechuga-Ballesteros expressly disclose the liquid carrier further comprising water. Sebastian discloses water as part of its liquid aerosol precursor composition for the reasons I explained previously. *See* §VII.A.2.[2], *supra*. Similarly, Lechuga-Ballesteros states that a nicotine salt can

be created by combining "comparable amounts of nicotine and organic acid [] in water[.]" EX1005, [0066]. Therefore, in view of Sebastian and Lechuga-Ballesteros's express disclosures, I conclude that the prior art both alone and taken together teaches the claimed limitation.

[3] The electronic cigarette of claim 1, wherein the salt is present in an amount that forms a nicotine concentration of 1% (w/w) to 18% (w/w) in the nicotine salt liquid formulation.

168. Both Sebastian and Lechuga-Ballesteros describe the claimed range of nicotine concentrations in claim 3 for the same reasons I discussed for Element [1d]. *See* §VII.B.4.[1d], *supra*.

[4] The electronic cigarette of claim 1, wherein the salt is present in an amount that forms a nicotine concentration of 3% (w/w) to 15% (w/w) in the nicotine salt liquid formulation.

169. Both Sebastian and Lechuga-Ballesteros describe the claimed range of nicotine concentrations in claim 4 for the same reasons I discussed for Element [1d]. *See* §VII.B.4.[1d], *supra*.

[5] The electronic cigarette of claim 1, wherein the salt is present in an amount that forms a nicotine concentration of 4% (w/w) to 12% (w/w) in the nicotine salt liquid formulation.

170. Both Sebastian and Lechuga-Ballesteros describe the claimed range of nicotine concentrations in claim 5 for the same reasons I discussed for Element [1d]. *See* §VII.B.4.[1d], *supra*.

[6] The electronic cigarette of claim 1, wherein the nicotine salt liquid formulation further comprises a flavorant.

171. Sebastian discloses a flavorant for the reasons I discussed previously. *See* §VII.A.2.[6], *supra*. Therefore, in view of Sebastian's disclosures, I conclude that the combination of Sebastian and Lechuga-Ballesteros teaches the claimed limitation.

[7] The electronic cigarette of claim 1, wherein the nicotine salt liquid formulation further comprises one or more additional organic acids.

172. Both Sebastian and Lechuga-Ballesteros disclose that their respective aerosol precursor compositions can include more than one organic acid. Sebastian discloses the claimed limitation for the reasons I explained previously. *See* §VII.A.2.[7], *supra*. Likewise, Lechuga-Ballesteros expressly states that "[o]ne or more organic acids may be combined in the formulations of the present invention." EX1005, [0042].

173. Therefore, in view of Sebastian and Lechuga-Ballesteros's express disclosures, I conclude that the prior art—both alone and taken together—teaches the claimed limitation.

[8] The electronic cigarette of claim 1, wherein the cartridge is configured to serve as a mouthpiece and a reservoir, wherein the reservoir holds the nicotine salt liquid formulation.

174. Sebastian discloses this limitation for the reasons I discussed previously. *See* §VII.A.2.[8], *supra*. Therefore, in view of Sebastian's disclosures,

I conclude that the combination of Sebastian and Lechuga-Ballesteros teaches the claimed limitation.

[9] The electronic cigarette of claim 1, wherein the organic acid is benzoic acid.

175. The combination of Sebastian and Lechuga-Ballesteros discloses benzoic acid. Specifically, Lechuga-Ballesteros expressly discloses benzoic acid as one of "[n]umerous suitable organic acids," as noted in Section VII.B.4[1c] above. EX1005, [0042]. In my view, a POSITA would have understood that benzoic acid was a suitable organic acid to combine with free base nicotine to generate a nicotine salt—i.e., nicotine benzoate.

176. Therefore, I conclude that the combination of Sebastian and Lechuga-Ballesteros teaches the claimed limitation.

[10] The electronic cigarette of claim 1, wherein the organic acid is lactic acid.

177. Both Sebastian and Lechuga-Ballesteros disclose lactic acid. Sebastian expressly discloses lactic acid for the reasons I explained previously. *See* §VII.A.2.[1b]-[1c], [10], *supra*. Furthermore, as I explained above in Sections VII.B.2 and VII.B.4.[1b]-[1c], Lechuga-Ballesteros expressly discloses lactic acid as one of "[n]umerous suitable organic acids" and goes on to describe the "superior performance" of nicotine lactate over free base nicotine, which Lechuga-Ballesteros supported with empirical data. EX1005, [0042], [0084].

178. Therefore, I conclude that the prior art both alone and taken together teaches the claimed limitation.

APPENDIX A

MARTIN WENSLEY
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PRODUCT DEVELOPMENT EXPERTISE

- 30 years of experience creating products and technologies in a number of areas and markets, including medical devices, pharmaceuticals, aerospace, optical instruments, and consumer products.
- 18 years developing respiratory drug delivery products including toxicology studies, clinical trials, intellectual property, and supply chain.
- Led multidisciplinary teams in the development of novel technologies and products from early-stage research through commercialization.
- Managed regulatory requirements in highly regulated markets (FDA, MHRA, FAA).
- Led patent input and worked side-by-side with intellectual property attorneys resulting in over 50 issued patents.

BUSINESS DEVELOPMENT EXPERTISE

- Founded/co-founded five companies.
- One IPO, three company sales.
- Secured financing from multiple sources (over $100M).
- Developed management and technical/engineering teams.
- Responsible for investor and stakeholder relations.

WORK EXPERIENCE

AIRJA INC., San Francisco Ca. USA
Founder, CEO –January 2019 – Present
- Founded and managed Airja, Inc. A respiratory drug delivery company focused on the delivery of pharmaceuticals and cannabinoids, via the lung, for the treatment of acute and respiratory conditions.

FONTEM VENTURES, Amsterdam, Netherlands
Research Manager – Special Projects, February 2018 – July 2018
- Managed the development of novel products and formulations to replace combustible cigarettes.
- Head of engineering liaison with intellectual property development and monitoring.
- Led the technical assessment of business development activities.

FONTEM/BLU, Campbell, California
Director of Engineering, September 2015 – January 2018
- Technical lead for medical product for nicotine replacement therapy in the UK, under the MHRA.
- Led effort in research of novel and proprietary aerosol generation technology
- Engineered the development of proprietary aerosol generation devices for respiratory drug delivery.

E NICOTINE TECHNOLOGY, Los Gatos, California*
Co-Founder and Chief Technology Officer, October 2011 – September 2015
- Managed the development of new drug delivery devices to treat cigarette addiction.
- Responsible for the development of clinical trial materials (CTM) and the execution of pharmacokinetic study at clinical site.
- Oversaw for all aspects of technology development, including clinical trial materials, intellectual property development, and manufacturing.
- Responsible for fundraising efforts.

** E Nicotine Technology purchased by Fontem/Blu in September 2015*

CYPRESS BIOSCIENCE, La Jolla, California
Head of Device Technology, Dec 2009 – August 2011
- Lead the technical team to develop a nicotine replacement therapy (NPT) through the FDA

- Directed research into solid nicotine formulations (nicotine salts)
- Developed a small, hand held device specifically for respiratory nicotine delivery, based on a IP license from Alexza Pharmaceuticals

ALEXZA PHARMACEUTICALS, Mountain View, California
Head of Device Technology, November 2001 – May 2009
- Responsible for the development of novel respiratory drug delivery technology to treat acute conditions.
- Led research and development activities into fundamental methods to aerosolize pharmaceuticals.
- Developed clinical supplies to support phase-one clinical study of fentanyl for breakthrough pain.
- Worked closely with analytical chemists to develop analytical methods (HPLC and GCMS).
- Developed toxicology supplies for toxicology work to support clinical studies.

MOLECULAR DELIVERY CORPERATION (MDC), Pleasanton, California*
Head of Device Technology, November 2000 – May 2009
- Secured a federal and state schedule one drug research liciense (for THC)
- Developed respiratory drug delivery technology for the delivery of THC and fentanyl.
- Spearheaded research into fundamental methods to aerosolize pharmaceuticals.

** MDC merged with Alexza Pharmaceuticals in November 2000*

TECHNIQUIP, Pleasanton, California
VP of Research and Development, January 1995 – October 2000
- Responsible for the development of optical instruments, including microscopes, fiber optic illuminations, and custom lighting products for medical and industrial applications.

TDG AEROSPACE, Pleasanton, California
VP of Engineering, June 1990 – November 1995
- Responsible for the development and manufacturing of anti-icing systems for commercial aircraft.
- Created the "NoFOD" de-icing system, currently used on commercial jets.

WENSLEY AND COMPANY, Santa Cruz, California
Owner (sole proprietor) 1981-May 1990
- Architectural design of commercial and residential buildings
- Construction management including restaurants and wineries along with private residences

EDUCATION

UNIVERSITY OF CALIFORNIA AT SANTA CRUZ
Bachelor of Arts in Physics, June 1980

INTELLECTUAL PROPERTY

Over 50 patents and applications related to respiratory drug delivery:
- Methods and devices for smoking urge relief
- Electronic vaporization devices
- Devices and methods for modifying delivery devices
- Methods and devices for modulating airflow in delivery devices
- Multiple-dose condensation aerosol devices and methods of...
- Heating element connector assembly and insert molded strips
- Heating unit for use in a drug delivery device
- Method of forming an aerosol for inhalation delivery
- Delivery of aerosols containing small particles through...
- Aerosol generating method and device
- Treatment of panic disorders with alprazolam
- Delivery of nonsteroidal anti-inflammatory drugs through...
- Treatment of breakthrough pain by drug aerosol inhalation.
- Aerosol forming device for use in inhalation therapy
- Methods and devices for compound delivery

- Aerosol forming device for use in inhalation therapy
- Inhalation device for producing a drug aerosol
- Methods for treating headache with loxapine
- Thin-film drug delivery article and method of use
- Delivery of caffeine through an inhalation route
- Respiratory drug condensation aerosols and methods for making...
- Methods and devices for delivering a physiologically active compound
- Delivery of diphenhydramine through an inhalation route
- Drug condensation aerosols and kits
- Drug condensation aerosols and kits method of forming an aerosol for inhalation delivery aerosol
- Device for use in inhalation therapy inhalation device
- Producing a drug aerosol
- Aerosol generating method and device
- Rapid-heating drug delivery article

PUBLICATIONS

- Fast Onset Medications through Thermally Generated Aerosols, May 2004, *Journal of Pharmacology and Experimental Therapeutics*