

THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Clean Chemistry, Inc.,
Petitioner,

v.

Enviro Tech Chemical Services, Inc.,
Patent Owner

Review no.: IPR2025-01459

U.S. Patent No. 9,730,443

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Inventors: Michael S. Harvey and Jonathan N. Howarth

Title: Methods and Compositions for the Generation of Peracetic Acid on Site
at the Point-of-Use

Declaration of Dr. Alexander M. Klibanov for U.S. Patent No. 9,730,443

CLEAN CHEMISTRY EXH 1008
IPR2025-01459

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I. Introduction

I, Dr. Alexander Klibanov, of Del Mar, California, declare as follows:

1. I am currently a Professor Emeritus of Chemistry and Bioengineering at the Massachusetts Institute of Technology (“M.I.T.”), where I taught and conducted research for over 40 years. From 2014 to 2019 (and also from 2007 to 2012), I held the Novartis Endowed Chair Professorship in Chemistry at M.I.T. From 2012 to 2014, I held the Roger and Georges Firmenich Endowed Chair Professorship in Chemistry at M.I.T. Prior to that, I was a Professor of Chemistry and a Professor of Bioengineering at M.I.T., positions I held from 1988 and 2000, respectively. From 1979 to 1988, I was an Assistant Professor, then an Associate Professor, and thereafter a Full Professor of Applied Biochemistry in the Department of Applied Biological Sciences (formerly the Department of Nutrition and Food Science) at M.I.T.

2. I obtained my M.S. in Chemistry from Moscow University in Russia in 1971 and Ph.D. in Chemical Enzymology (a branch of Medicinal Chemistry) from the same university in 1974. Thereafter, I was a Research Chemist at Moscow University’s Department of Chemistry for three years. From 1977 to 1979, following my immigration to the United States, I was a Post-Doctoral Associate at the Department of Chemistry, University of California in San Diego.

3. Over the last 50+ years as a practicing chemist, I have extensively researched, published, and lectured in many areas of chemistry, including formulation and medicinal chemistry.

4. During my over 40 years as a M.I.T. professor, I taught numerous undergraduate and graduate courses in various areas of chemistry, including general, organic, physical, and biological chemistry.

5. I have earned numerous prestigious professional awards and honors. For example, I was elected to the U.S. National Academy of Sciences (considered among the highest honors that can be given to an American scientist) and also to the U.S. National Academy of Engineering (considered among the highest honors that can be given to an American engineer). I am also a Founding Fellow of the American Institute for Medical and Biological Engineering and a Corresponding Fellow of the Royal Society of Edinburgh (Scotland's National Academy of Science and Letters). In addition, I have received the Arthur C. Cope Scholar Award, the Marvin J. Johnson Award, the Ipatieff Prize, and the Leo Friend Award, all from the American Chemical Society (the largest professional society in the world), as well as the International Enzyme Engineering Prize.

6. I currently serve on the Editorial or Advisory Boards of over a dozen scientific publications, including "Open Access Academic Books in Chemistry," "Applied Biochemistry and Biotechnology," "Nanocarriers," "Biotechnology and

Bioengineering,” “Journal of Biological Chemistry and Molecular Pharmacology,” “Recent Patents in Biotechnology,” “Archives of Medical Biotechnology,” “Current Pharmaceutical Biotechnology,” “Open Journal of Pharmacology,” and “International Journal of Drug Design, Delivery, and Safety.”

7. I have published over 315 scientific papers in various areas of chemistry. I am also a named inventor of 33 issued United States patents and of a number of pending ones. I have given over 370 invited lectures, including many distinguished named lectureships, at scientific conferences, universities, and corporations all over the world, many of them dealing with preparation, formulation, stability, stabilization, and evaluation of biologically active compounds, such as biocides. According to a recent Stanford University-led study, the overall impact of my published work places me in the top 0.01% of all scientists in the world.

8. In addition to my research and teaching activities at M.I.T., I have consulted widely for chemical, pharmaceutical, food, and biotechnology companies. Of particular relevance to the present proceedings is my consulting experience with industrial production and applications of peracetic acid (also known as peroxyacetic acid, CH_3COOOH ; abbreviated as “PAA”).

9. I also have founded seven start-up industrial companies and have been on the scientific advisory boards and/or boards of directors of those companies and of many others.

10. As of March 24, 2011 (the priority date of the U.S. Patent No. 9,730,443 B2 (“the ‘443 Patent”)), I at least met (and indeed exceeded) the background and qualifications requirements of a person of ordinary skill in the art (“a POSA”) with respect to the ‘443 Patent, as defined below.

11. My *Curriculum vitae*, attached as Appendix 1, summarizes my education and academic experience. Among other things, it lists all my professional publications and issued U.S. patents.

II. Legal Principles

12. I am not a lawyer or patent scholar, but I have been informed of certain legal principles that are relevant to my analysis herein by Clean Chemistry’s counsel (“counsel”). My understanding of these legal principles explained by counsel is outlined below in this section of the present Declaration.

A. Priority Date

13. The ‘443 Patent has a priority date (or constructive date of invention) of March 24, 2011 (as seen in Item (62) on the cover page of the ‘443 Patent). I understand that the ‘443 Patent is a divisional application (from Appln. No. 14/019,296, now the U.S. Patent No. 9,370,180), which is itself a divisional application of another patent application (Appln. No. 13/065,553, now the U.S. Patent No. 8,546,449), and that the ‘443 Patent has the same priority date as the U.S. Patent No. 8,546,449 (i.e., March 24, 2011, as noted above).

B. Person of Ordinary Skill in the Art

14. United States patents and their prior art should be evaluated from the perspective of a hypothetical person of ordinary skill in the art at the time of the invention (“a POSA”).

15. A POSA is a competent person of ordinary creativity. He or she is presumed to be familiar with all publicly available relevant prior art at the time of the invention of the patent in question (here, the ‘443 Patent).

16. In my opinion, a POSA with respect to the subject matter of the ‘443 Patent would have had at least a bachelor’s degree in chemistry, chemical engineering, or a related discipline, plus a couple of years of practical experience in chemical syntheses, or equivalent knowledge and work experience. I consider myself at least a POSA under this definition.

17. I have considered the issues, and arrived at my conclusions described in this Declaration, from the perspective of such a POSA.

C. Claim Construction

18. Claims of a patent, and terms included in those claims, should be interpreted from the perspective of a POSA. Here, the time of the invention is March 24, 2011, because the ‘443 Patent is a divisional of a divisional, for which the earliest filing date is March 24, 2011, as explained above. Exhibit 1002.

19. A patent's claims, its specification, and the file history (collectively referred to as "intrinsic evidence") should be analyzed to arrive at the proper interpretation of a claim term.

20. Sometimes (as in the case of certain claim terms of the '443 Patent), a patentee can include a particular definition of a claim term in the patent specification. In such instances, the claim generally should be interpreted according to that definition provided in the patent specification.

21. The patent claim should be interpreted in light of the intrinsic evidence, which includes the language of the claim in question and of the other claims in the patent, the specification of the patent, and the relevant prosecution history of the patent. Other evidence, which is considered extrinsic evidence and not in the written record of the patent or its prosecution history, such as relevant technical dictionaries and learned treatises, also may be considered if it is not inconsistent with the intrinsic evidence. However, if the meaning of the claim is clear from the intrinsic evidence, then there is no reason for a POSA to look into extrinsic evidence.

D. Anticipation

22. A patent claim is considered to be anticipated by the prior art when each and every limitation of the claim is found in a single prior art reference either expressly or inherently, where inherently means that the feature is not explicitly stated but is necessarily present.

23. A prior art reference that teaches a specific value for a variable or a specific range of values within a claimed range anticipates the claimed range.

24. A prior art reference that teaches a specific range of values for a variable, which range overlaps with a claimed range for that variable, also anticipates the claimed range if there is no criticality to the claimed range (such as unexpectedly superior results).

E. Obviousness

25. Relevant factual considerations for an obviousness analysis include (1) the scope and content of the prior art; (2) differences between the prior art and the patent claims; and (3) the level of skill possessed by a hypothetical person of ordinary skill in the art at the time of the invention.

26. Obviousness of a patent claim can be based on either a single prior art reference or a combination of two or more of such references that disclose all of the features of the claim, whether expressly or inherently.

27. If a prior art reference discloses fewer than all limitations of a patent claim, the claim may still be obvious if the differences between the subject matter of the claim and the prior art reference would have been obvious to a POSA at the time of the invention.

28. Also, a patent claim that recites a specific range of values of a variable can be rendered obvious by prior art that teaches a range that encompasses, or

overlaps with, the recited range of values, unless the recited range demonstrates some criticality, such as unexpectedly superior results.

29. A patent claim that recites a combination of known elements combined according to known methods that produces predictable results is probably obvious.

30. However, an obviousness determination of a patent claim should not be based on the benefit of hindsight gained from the disclosure of the patent under consideration.

III. Summary of Conclusions

31. Based on my professional knowledge and experience, as well as on my review of the intrinsic evidence and of the prior art as of the constructive time of the invention (March 24, 2011), I have concluded that Claims 1 through 3 of the '443 Patent (i.e., all the claims of this patent) are anticipated by, and obvious over, at least the prior art cited below in this Declaration.

IV. Technology Background

A. My Experience Relevant to the Technology of the Alleged Invention of the '443 Patent

32. I am familiar with peracetic acid synthesis, in part due to having been a long-term consultant to E. I. du Pont de Nemours and Company (DuPont) starting in the early 1990s. The subject matter for which I was a consultant at DuPont dealt, among other things, with methods for synthesizing peracetic acid using perhydrolase enzymes, such as lipases.

B. Summary of the Technology

33. Peracetic acid (CH_3COOOH or $\text{CH}_3\text{-C(=O)-O-OH}$, often abbreviated as PAA) is a common name for peroxyacetic acid, which is a small organic acid known for its disinfectant (i.e., microbe-killing) properties. Interest in use of peracetic acid began increasing in the 1990s.

34. Peracetic acid is typically prepared from an acetyl source and an appropriate oxidant. Acetyl sources include acetic acid, acetaldehyde, tetraacetyl ethylene diamine (TAED), diacetin (glycerin(e)/glycerol diacetate), and triacetin (glycerin(e)/glycerol triacetate). Suitable oxidants include hydrogen peroxide (H_2O_2) or inorganic compounds that provide H_2O_2 in water, such as sodium perborate and sodium percarbonate. Hydrogen peroxide is often the preferred oxidant.

35. While initial efforts to make peracetic acid industrially centered on oxidation of acetic acid, since the early 2000s, the focus has changed to use of acetyl sources having more than one acetyl group per molecule, with TAED and especially triacetin often being preferred.

V. Overview of the ‘443 Patent (Exhibit 1001)**A. Summary of the ‘443 Patent**

36. The ‘443 Patent contains the total of three claims, of which Claim 1 is independent and Claims 2 and 3 depend directly from Claim 1. Exhibit 1001, column 35, lines 13-25. According to its Abstract, the ‘443 Patent describes methods for

generating peracetic acid (PAA) from aqueous hydrogen peroxide, triacetin, water, and an aqueous source of an alkali metal or earth alkali metal hydroxide. Exhibit 1001, Item (57).

37. The '443 Patent describes "liquid compositions and methods of using the liquid compositions for the generation of a peroxyacetic acid sanitizer." Exhibit 1001, column 1, lines 17-19. The peroxyacetic acid sanitizers are described as "non-equilibrium solutions of PAA," which "comprise PAA, unreacted hydrogen peroxide, unreacted acetyl precursor, the product of the perhydrolysis reaction of the acetyl precursor, the aqueous source of alkali metal or earth alkali metal hydroxide, and water." Exhibit 1001, column 6, lines 36-40. The '443 Patent indicates that "[a]preferable acetyl precursor is triacetin." Exhibit 1001, column 5, lines 31-32. "When the acetyl precursors is triacetin, the product of the perhydrolysis reaction is 1,2,3-propanetriol (glycerine)." Exhibit 1001, column 16, lines 11-13; also column 17, lines 65-67.

38. As part of the description of the non-equilibrium solutions of peracetic acid, the '443 Patent states that "[t]he peracetic acid solutions are alkaline, having a pH of about 11.2 to about 13.37." Exhibit 1001, column 6, lines 40-42; also column 18, lines 26-27. This pH range is also recited in Claim 2 of the '443 Patent.

39. Examples 8 through 12 and 14 of the '443 Patent describe the preparation of non-equilibrium solutions of peracetic acid. The pH values of most of

the peracetic acid solutions prepared in those six Examples correspond to, or fall within, the aforementioned pH range subsequently recited in Claim 2 of the ‘443 Patent. Exhibit 1001, column 18, line 60, to column 25, line 5; and column 26, line 38, to column 27, line 28.

40. Also as part of the description of the non-equilibrium solutions of peracetic acid, the ‘443 Patent states that “[t]he peracetic acid solutions have high levels of PAA, from about 1% to about 7.1%.” Exhibit 1001, column 18, lines 24-25. The ‘443 Patent additionally explains that “[t]he terms ‘percent’ and ‘%’ mean weight percent, except when referring to the percent converted.” Exhibit 1001, column 7, lines 62-63. Therefore, the claim term “about 1% to about 7.1%” uses weight percent (wt%) units.

41. The concentrations of peracetic acid in many of the peracetic acid solutions prepared in Examples 8 and 14 correspond to, or fall within, the range subsequently recited in Claim 3 of the ‘443 Patent. Exhibit 1001, column 18, line 60, to column 19, line 58; and column 26, line 38, to column 27, line 28.

B. Summary of the Prosecution History of the ‘443 Patent (Exhibit 1005)

42. I have reviewed the file (or prosecution) history of the ‘443 Patent.

43. The application for the ‘443 Patent was filed on March 7, 2016. The application as filed had three claims. Exhibit 1005, Page 82.

44. In an Office Action dated January 30, 2017, the Patent and Trademark Office (“PTO”) Examiner provisionally rejected Claims 1-3 for obviousness-type double patenting over Claim 5 or 6 of co-pending Application No. 15/063,293 (“the ‘293 application”; now the U.S. Patent No. 9,737,072). Exhibit 1005, Pages 120-121; Exhibit 1006.

45. The PTO rejection stated that the conflicting claims were not patentably distinct, because the rejected claims are directed to “a non-equilibrium solution of peracetic acid comprising peracetic acid, hydrogen peroxide, triacetin, 1,2,3-propanetriol and alkali metal or earth alkali metal hydroxide” and because the ‘293 application claims “a non-equilibrium solution of peracetic acid or its generation system comprising peracetic acid, hydrogen peroxide, triacetin, and alkali metal or earth alkali metal hydroxide.” Exhibit 1005, Page 121.

46. In a Response filed on March 7, 2017, the Applicants filed a Terminal Disclaimer over the ‘293 application. Exhibit 1005, Page 131.

47. On May 10, 2017, the PTO Examiner issued a Notice of Allowance, allowing Claims 1-3. Exhibit 1005, Pages 158 and 163.

48. The ‘443 Patent then issued on August 15, 2017.

VI. Claim Construction

49. From my review of the claims, specification, and file history of the ‘443 Patent, it appears that the claim terms “hydrogen peroxide,” “water,” and “pH”

would have had their plain and ordinary meanings well familiar to a POSA. The other claim terms of the '443 Patent are discussed below.

A. “A non-equilibrium solution of peracetic acid”

50. Claim 1 of the '443 Patent recites “[a] non-equilibrium solution of peracetic acid” in the preamble. This claim phrase is not expressly defined in the specification of the '443 Patent.

51. A POSA would have understood the plain and ordinary meaning of the term “an equilibrium solution” and thus would have understood that “a non-equilibrium solution” is its antonym, i.e., a solution that is *not* at equilibrium. In particular, the plain and ordinary meaning of the term “an equilibrium solution”, well familiar to a POSA, would have been a solution in which the concentration of the components is constant, i.e., does not change over time. Also well known to a POSA is that in “an equilibrium solution” the starting materials (also called reactants) continually form the product, while some of the product formed continually re-forms the starting materials at such a rate that does not change the concentrations of the components of the solution. For example, *The Condensed Chemical Dictionary* (10th edn., edited by Gessner G. Hawley, Van Nostrand Reinhold Co., New York, 1981; Exhibit 1013) defines “Chemical **equilibrium**” as “a condition in which a reaction and its opposite or reverse reaction occur at the same rate, resulting in *a constant concentration of reactants*” (Page 415, emphasis

added). Therefore, it follows that the claim term “[a] non-equilibrium solution of peracetic acid” would have meant to a POSA “a solution in which the concentration of peracetic acid is *not* constant, i.e., changes over time”. Notably, an irreversible chemical reaction is never at equilibrium (because there is no reverse reaction), and hence a solution where such a reaction occurs is necessarily “a non-equilibrium solution”.

B. “[P]eracetic acid”

52. Claim 1 of the ‘443 Patent recites the term “peracetic acid”, which is expressly defined in the patent specification: “The terms ‘PAA’ and ‘peracetic acid’ mean peroxyacetic acid or peracetic acid, and/or the conjugate base of peracetic acid (the peracetate ion).” Exhibit 1001, column 7, lines 59-61.

C. “[T]riacetin”

53. The claim term “triacetin” is not expressly defined in the specification of the ‘443 Patent, but it is a common name for glycerin(e) (also referred to as glycerol) triacetate, i.e., the triester of glycerol with acetic acid (also called glyceryl triacetate). This understanding is supported by the ‘443 Patent specification, which states that “[w]hen the acetyl precursors [*sic*] is triacetin, the product of the perhydrolysis reaction [i.e., the complete triester cleavage mediated by hydrogen peroxide] is 1,2,3-propanetriol (glycerine).” Exhibit 1001, column 16, lines 11-13.

D. “1,2,3-[P]ropanetriol”

54. Claim 1 (and hence Claims 2 and 3 that depend from it) of the ‘443 Patent recites the term “1,2,3-propanetriol”, which is a conventional chemical name for this polyhydric (specifically trihydric) alcohol and which also is expressly defined in the patent specification as “glycerine” [i.e., glycerol]. Exhibit 1001, column 16, lines 11-13; column 17, lines 65-67; column 18, lines 11-13.

E. “[A]n aqueous source of an alkali metal or earth alkali metal hydroxide”

55. The claim phrase “an aqueous source of an alkali metal or earth alkali metal hydroxide” is not expressly defined in the specification of the ‘443 Patent but, as a POSA would have understood, this phrase refers to the presence of an aqueous solution of an alkali metal hydroxide or an earth alkali metal hydroxide in the claimed peracetic acid solution. This understanding is supported by the ‘443 Patent specification, which states that “[t]he non-equilibrium solutions of PAA prepared by this method comprise PAA, ... the aqueous source of alkali metal or earth alkali metal hydroxide, and water.” Exhibit 1001, column 16, lines 7-11; also column 17, lines 61-65. The “method” referred to in this passage involves a step of adding an aqueous source of either an alkali metal hydroxide (with sodium hydroxide, NaOH, being “preferable” but potassium hydroxide also being “suitable”) or an earth alkali metal hydroxide. Exhibit 1001, column 15, lines 29-37; also column 17, lines 31-41.

F. “[A]bout 1%” and “about 7.1%”

56. Claim 3 of the ‘443 Patent recites the phrase “wherein said peracetic acid is about 1% to about 7.1%.” The ‘443 Patent specification does not expressly define this claim phrase, but it does state that “[t]he terms ‘percent’ and ‘%’ mean weight percent, except when referring to the percent converted.” Exhibit 1001, column 7, lines 62-63. The patent specification also repeatedly refers to “solutions with a high level of PAA, from about 1% to about 7.1%.” Exhibit 1001, column 6, lines 44-45; also column 18, lines 24-25. From these disclosures, the “wherein” phrase in Claim 3 would have been understood by a POSA to mean “wherein said peracetic acid concentration is from about 1 wt% to about 7.1 wt%.”

VII. Overview of Selected Prior Art References**A. U.S. 2009/0175956 A1 (also referred to herein as “Buschmann 1”; Exhibit 1014)**

57. US 2009/0175956 has a priority date of January 8, 2008, thus making this U.S. patent application publication a prior art with respect to the ‘443 Patent. Exhibit 1014, Page 1, Item (60). Buschmann 1’s Abstract indicates that the patent application publication disclosure relates to “compositions [that] comprise peracetic acid (PAA) and methods for making non-equilibrium PAA.”

58. Buschmann 1 teaches that “[t]he reaction pH can be adjusted with an appropriate base (proton acceptors such as hydroxide or amines for example).” Exhibit 1014, paragraph 0033.

59. Buschmann 1 further teaches that:

Exemplary non-equilibrium PAA reaction solution employing acetylsalicylic acid as the acetyl donor is made by combining 1.1 g/L hydrogen peroxide adjusted to pH 12.0 with sodium hydroxide with 10 g/L acetylsalicylic acid.

Exhibit 1014, paragraph 0041.

60. Buschmann 1 additionally teaches that “[e]xamples of acetyl donors include, but are not limited to, O-acetyl donors (—O—C(O)CH_3), such as acetin, diacetin, triacetin, acetylsalicylic acid.” Exhibit 1014, paragraph 0027, penultimate sentence. Triacetin is further highlighted in paragraph 0030: “For example, alkaline hydrogen peroxide can be ... mixed with triacetin or other acetyl donor to produce an alkaline mixture of non-equilibrium PAA, hydrogen peroxide, triacetin, and glycerol.”

61. In Buschmann 1, disclosures of quite “alkaline conditions (pH greater than about 10)” and “[c]austic pH ($\text{pH} > 10$)” are repeatedly made. Exhibit 1014, paragraphs 0027 and 0033. Buschmann 1 also refers to a detrimental “self-reaction decomposition process [of PAA] at alkaline pH ($7.5 \leq \text{pH} \leq 10.5$).” Exhibit 1014, paragraph 0040.

62. Buschmann 1 also discloses solutions containing “non-equilibrium PAA [“chemically produced by an irreversible, non-equilibrium reaction of

hydrogen peroxide with ... an acetyl donor”], hydrogen peroxide, triacetin, and glycerol,” as well as water as a solvent, and a[n alkaline] hydroxide as a base. Exhibit 1014, paragraphs 0030 and 0033.

B. U.S. 2009/0314652 A1 (also referred to herein as “Buschmann 2”; Exhibit 1015)

63. US 2009/0314652 has a priority date of March 19, 2008, thus making this U.S. patent application publication a prior art with respect to the ‘443 Patent. Exhibit 1015, Page 1, Item (60). Buschmann 2’s Abstract indicates that the patent application publication disclosure relates to “methods, systems and reactors for producing peroxycarboxylic acid compositions, such as non-equilibrium compositions of peracetic acid.”

64. Buschmann 2 teaches that “[t]he reaction pH can be adjusted with an appropriate base (proton acceptors such as hydroxide or amines for example).” Exhibit 1015, paragraph 0074.

65. Buschmann 2 further teaches that:

An example of a non-equilibrium reaction solution ... combin[es] 1.1 g/L hydrogen peroxide adjusted to pH 12.0 with sodium hydroxide and reacted with 10 g/L acetylsalicylic acid.

Exhibit 1015, paragraph 0077.

66. Buschmann 2 additionally teaches that “[e]xamples of acetyl donors include, but are not limited to, O-acetyl donors (—O—C(O)CH_3), such as acetin,

diacetin, triacetin, acetylsalicylic acid.” Exhibit 1015, paragraph 0058. Triacetin is further highlighted in Examples 6-10.

67. In Buschmann 2, disclosures of “a pH greater than or equal to 10 and less than or equal to 13” and “[c]austic pH ($\text{pH} > 10$)” are repeatedly made. Exhibit 1015, paragraphs 0033, 0034, and 0074. Buschmann 2 states that the term “[c]austic” refers to basic pH solutions. In an aspect the pH is greater than about 9, greater than 10, or greater than and equal to 10 and less than and equal to 13.” Exhibit 1015, paragraph 0063. Buschmann 2 also refers to a detrimental “self-reaction decomposition process at alkaline pH ($7.5 \leq \text{pH} \leq 10.5$).” Exhibit 1015, paragraphs 0079 and 0081.

68. Buschmann 2 also discloses “non-equilibrium peracetic acid solutions [that] can be chemically produced by an irreversible, non-equilibrium reaction of hydrogen peroxide with an acetyl donor in a solvent such as, but not limited to, water.” Exhibit 1015, paragraph 0074. Buschmann 2 also discloses that “[p]eracetic acid and hydrogen peroxide concentrations were determined by established titration methods. Acetic acid and glycerol concentrations were determined by HPLC.” Exhibit 1015, paragraph 0148 and Table 5.

C. U.S. Patent No. 6,221,341 B1 (also referred to herein as “Montgomery”; Exhibit 1016)

69. U.S. Patent No. 6,221,341 (“Montgomery”) has a priority date of November 19, 1997, thus making this patent a prior art with respect to the ‘443

Patent. Exhibit 1016, Cover Page, Item (60). Montgomery's Abstract indicates that the patent's invention provides "compositions includ[ing] a low molecular weight compound having a high acetyl group functionality useful in the production of a peroxy acid." Exhibit 1016, Cover Page, Item (57).

70. Montgomery states that "[a]ccording to a specific preferred embodiment of the present invention, the source of labile acetyl groups is glyceryl triacetate [i.e., triacetin], glyceryl diacetate or glyceryl acetate." Exhibit 1016, column 6, lines 13-15.

71. Montgomery further states that "[t]he use of glyceryl triacetate is advantageous due to its highly labile acetyl functionalities." Exhibit 1016, column 6, lines 31-32.

72. Montgomery also notes that "[t]he formation of peroxyacetic acid from hydrogen peroxide and glyceryl triacetate has been determined to occur most readily at pH levels in excess of about 5.2." Exhibit 1016, column 8, lines 15-17.

73. Montgomery further discloses a number of "[s]uitable buffers," such as various "alkaline buffers," whose essential components include "sodium hydroxide, potassium hydroxide, [and] ammonium hydroxide." Exhibit 1016, column 7, line 64, to column 8, line 3.

74. In Example V of Montgomery, composition B explicitly contains most of the components listed in Claim 1 of the '443 Patent: glycerin (1,2,3-propanetriol),

water, hydrogen peroxide, and glyceryl triacetate (triacetin); *see* Table 5. Exhibit 1016. Composition B is prepared from two separate (composite) components, one containing the hydrogen peroxide and the other containing the triacetin. Exhibit 1016, column 15, lines 14-49. Example V states that “The resulting mixture thus contains both the hydrogen peroxide precursor and glyceryl triacetate, and alternatively, water in a sufficient amount to allow the production of peroxyacetic acid.” Exhibit 1016, column 15, lines 64-67.

D. U.S. Patent No. 7,919,122 B2 (also referred to herein as “Okano 1”; Exhibit 1010)

75. U.S. Patent No. 7,919,122 (“Okano 1”) has a priority date of April 2, 2003, thus making this patent a prior art with respect to the ‘443 Patent. Exhibit 1010, Cover Page, Item (30). Okano 1’s Abstract indicates that the patent’s “invention provides “a composition for production of a sterilizer” in which the “sterilizer is obtained as an aqueous solution containing an organic peracid.” The Abstract also states that the “composition for production of a sterilizer” contains “(A) an ester of a polyhydric alcohol and an organic acid having a hydrocarbon group ... and (B1) hydrogen peroxide.” Exhibit 1010, Cover Page.

76. Okano 1 explains that “the component (A) is preferably an ester of glycerin [i.e., glycerol] and a C1 to C8 aliphatic monocarboxylic acid, more preferably triacetin.” Exhibit 1010, column 4, lines 14-16.

77. Okano 1 further explains that when the composition of the invention is a liquid (as are the compositions of the ‘443 Patent “for the generation of a peroxyacetic acid sanitizer” (Exhibit 1001, column 1, lines 17-19)), “hydrogen peroxide is preferable” as component (B1). Exhibit 1010, column 4, lines 18-21.

78. Regarding the pH, Okano 1 teaches alkaline pH values to generate an organic peracid sterilizer by pointing out that “the composition for production of a sterilizer being used as an aqueous solution prepared by adjustment to pH 8 to 12.” Exhibit 1010, column 2, lines 5-7.

79. For peracetic acid concentrations, Okano 1 teaches that “[t]he concentration of an organic peracid in the aqueous solution is preferably 10 to 20,000 ppm (ratio by weight; this hereinafter applies), more preferably 10 to 10,000 ppm.” Exhibit 1010, column 7, lines 15-18.

E. JP 2006-045147 A (also referred to herein as “Okano 2”; Exhibit 1018)

80. JP 2006-045147 was filed on August 6, 2004, and published on February 16, 2006, thus making this Japanese patent application publication (by the same inventor, Tetsuya Okano, as the first inventor in Okano 1 discussed above) a prior art with respect to the ‘443 Patent. Exhibit 1018, Page 1, Items (22) and (43). According to Okano 2’s Abstract, its disclosure is directed to “a sterilizing cleaner composition for hard surfaces.” The Abstract further states that the composition contains:

water and an organic peracid obtained by reacting (A) an ester of a polyhydric alcohol and an organic acid with (B1) hydrogen peroxide in a specific molar ratio in water at a pH of 8 to 12.

Exhibit 1018, Page 1.

81. Okano 2 explains that component (A) is “an ester of a polyhydric alcohol and an organic acid having a hydrocarbon group” and that “hydrogen peroxide” is “referred to as component (B1).” Exhibit 1018, paragraph 0008.

82. Okano 2 further states that “triacetin is preferable” as “the component (A).” Exhibit 1018, paragraph 0014.

83. Indeed, Example 1 of Okano 2 uses triacetin as component (A), along with hydrogen peroxide (as component (B1)), to form “the organic peroxy acid” (i.e., peracetic acid here) in water containing sodium hydroxide. Exhibit 1018, paragraph 0057.

84. Regarding the pH, Okano 2 teaches that “a[] sterilizing cleaner composition for hard surfaces, containing water and an organic peracid [was] obtained by reacting (A) an ester of a polyhydric alcohol and an organic acid having a hydrocarbon group ... (herein referred to as component (A)) and (B1) hydrogen peroxide (herein referred to as component (B1)) in water at a molar ratio of (A)/(B1) = 1/10 to 20/1 and at a pH of 8 to 12” at 25°C. Exhibit 1018, paragraph 0008.

VIII. Specific Grounds for Invalidity of the ‘443 Patent**A. Grounds 1a-1d: Claims 1-2 of the ‘443 Patent are anticipated by, and obvious over, Buschmann 1****1. Ground 1a – Claim 1 of the ‘443 Patent is anticipated by Buschmann 1**

85. Buschmann 1 discloses that alkaline hydrogen peroxide can be “mixed with triacetin or other acetyl donor to produce an alkaline mixture of non-equilibrium PAA, hydrogen peroxide, triacetin, and glycerol.” Exhibit 1014, paragraph 0030.

86. Buschmann 1 also discloses that “non-equilibrium peroxycarboxylic acid solutions, particularly those of PAA” can be produced “in a solvent such as, but not limited to, water.” Exhibit 1014, paragraph 0033.

87. Buschmann 1 states that “[t]he reaction pH can be adjusted with an appropriate base (proton acceptors such as hydroxide or amines for example).” Exhibit 1014, paragraph 0033.

88. These passages of Buschmann 1 thus disclose to a POSA all of the elements of Claim 1 of the ‘443 Patent: “[a] non-equilibrium solution of peracetic acid,” “hydrogen peroxide,” “triacetin,” “1,2,3-propanetriol” (i.e., glycerol), “an aqueous source of an alkali metal or an earth alkaline metal hydroxide,” and “water.” Therefore, Claim 1 of the ‘443 Patent is anticipated by Buschmann 1.

2. Ground 1b – Claim 1 of the ‘443 Patent is obvious over Buschmann 1

89. By its disclosures, Buschmann 1 makes it obvious to a POSA that a non-equilibrium solution of peracetic acid contains hydrogen peroxide, triacetin, 1,2,3-propanetriol (i.e., glycerol), and an alkaline hydroxide in water. A POSA would have understood that the hydroxide can be an alkali metal hydroxide because Buschmann 1 repeatedly teaches the use of sodium hydroxide (NaOH) as a “hydroxide.” Exhibit 1014, paragraphs 0034 and 0041. Thus Claim 1 of the ‘443 Patent is obvious over Buschmann 1.

3. Ground 1c – Claim 2 of the ‘443 Patent is anticipated by Buschmann 1

90. Dependent Claim 2 of the ‘443 Patent recites an additional feature beyond those of Claim 1: “a pH of about 11.2 to about 13.37” for the “non-equilibrium solution of peracetic acid” disclosed in Claim 1.

91. Buschmann 1 expressly discloses to a POSA very alkaline conditions: “in the present invention non-equilibrium peracetic acid (PAA) is produced by reacting a properly chosen acyl donor with hydrogen peroxide under alkaline conditions (pH greater than about 10).” Exhibit 1014, paragraph 0027.

92. Buschmann 1 further discloses that an “[e]xemplary non-equilibrium PAA reaction solution employing acetylsalicylic acid as the acetyl donor is made by combining 1.1 g/L hydrogen peroxide adjusted to pH 12.0 with sodium hydroxide

with 10 g/L acetylsalicylic acid.” Exhibit 1014, paragraph 0041. The same highly alkaline pH value of 12.0 is also reiterated in Buschmann 1’s paragraph 0034.

93. The pH value disclosed in Buschmann 1 (“pH 12.0”) thus falls well within the pH range recited in Claim 2 of the ‘443 Patent (i.e., “a pH of about 11.2 to about 13.37”).

94. As established above for Claim 1 of the ‘443 Patent, Buschmann 1 teaches non-equilibrium solutions of peracetic acid also containing hydrogen peroxide, triacetin, glycerol, an aqueous source of an alkaline hydroxide (such as sodium hydroxide), and water.

95. Because the pH value of 12.0 repeatedly disclosed in Buschmann 1 clearly falls within the pH range claimed in Claim 2 of the ‘443 Patent, Claim 2 is anticipated by Buschmann 1.

4. Ground 1d – Claim 2 of the ‘443 Patent is obvious over Buschmann 1

96. By its express disclosures, Buschmann 1 makes it obvious to a POSA that its non-equilibrium solution of peracetic acid also contains hydrogen peroxide, triacetin, 1,2,3-propanetriol (i.e., glycerol), and an alkaline hydroxide in water. A POSA would have understood that the said hydroxide can be an alkali metal hydroxide because Buschmann 1 specifically and repeatedly teaches the use of sodium hydroxide, a very common alkali metal hydroxide. Exhibit 1014, paragraphs 0034 and 0041. A POSA would have readily recognized that sodium hydroxide also

can be used with starting materials other than the acetylsalicylic acid exemplified in Buschmann 1 because the latter teaches that acetyl donors other than acetylsalicylic acid can be used, including specifically triacetin, which is prominently identified by name as such therein. Exhibit 1014, paragraphs 0027 and 0030.

97. As established above, Buschmann 1 teaches that an alkaline pH is “greater than about 10” and “pH > 10.” Exhibit 1014, paragraphs 0027 and 0033. Buschmann 1 also teaches a “self-reaction decomposition process at alkaline pH ($7.5 \leq \text{pH} \leq 10.5$)” for peracetic acid. Exhibit 1014, paragraphs 0039 and 0040. A POSA would have understood from these teachings that an alkaline pH of above 10.5 provides an alkaline pH while also minimizing an undesirable “self-reaction decomposition” of peracetic acid.

98. A POSA would have recognized that the pH is a result-effective reaction variable that can be optimized through routine experimentation because of the teachings in Buschmann 1 that both the formation of peracetic acid (Exhibit 1014, paragraph 0027) and the “self-reaction decomposition” of peracetic acid (Exhibit 1014, paragraphs 0039 and 0040) are pH-dependent.

99. The solutions disclosed in Buschmann 1 are “typically aqueous solutions.” Exhibit 1014, paragraph 0024. A POSA (and indeed anyone who has taken a college freshman chemistry course; and I used to teach such a course at M.I.T.) would have known that the highest conventional-scale alkaline pH in

aqueous solution is 14 (in other words, the conventional pH scale is from 0 to 14 at 25°C). From the teachings in Buschmann 1, a POSA thus would have recognized that the alkaline pH values in the solutions therein range from “greater than about 10” (or “pH > 10”) to 14. Optimizing the pH within this limited range would have been no more than routine experimentation well within the capability of a POSA.

100. The lower endpoint of the pH range in Claim 2 of the ‘443 Patent is “about 11.2”. This endpoint is quite alkaline (falling within “pH greater than about 10” and “pH > 10”) as taught in Buschmann 1 for the formation of peracetic acid. Exhibit 1014, paragraphs 0027 and 0033. The lower endpoint of the claimed pH range is also above the pH range in which the detrimental self-reaction decomposition of peracetic acid occurs, namely higher than pH 10.5. Exhibit 1014, paragraph 0040.

101. Therefore, the claimed pH range, “about 11.2 to about 13.37,” would have been readily arrived at by a POSA through routine optimization based on the disclosure of Buschmann 1. Hence the pH range claimed in Claim 2 of the ‘443 Patent would have been obvious.

B. Grounds 2a-2d – Claims 1-2 of the ‘443 Patent are anticipated by, and obvious over, Buschmann 2

1. Ground 2a – Claim 1 of the ‘443 Patent is anticipated by Buschmann 2

102. Buschmann 2 discloses “non-equilibrium peracetic acid solutions [that] can be chemically produced by an irreversible, non-equilibrium reaction of hydrogen peroxide with an acetyl donor in a solvent such as, but not limited to, water.” Exhibit 1015, paragraph 0074. Buschmann 2 also discloses that “[p]eracetic acid and hydrogen peroxide concentrations were determined by established titration methods. Acetic acid and glycerol concentrations were determined by HPLC.” Exhibit 1015, paragraph 0148 and Table 5.

103. Buschmann 2 also discloses “non-equilibrium peracetic acid solutions [that] can be chemically produced by an irreversible, non-equilibrium reaction of hydrogen peroxide with an acetyl donor in a solvent such as, but not limited to, water.” Exhibit 1015, paragraph 0074.

104. Buschmann 2 states that “[t]he reaction pH can be adjusted with an appropriate base (proton acceptors such as hydroxide or amines for example).” Exhibit 1015, paragraph 0074.

105. These passages of Buschmann 2 thus disclose to a POSA all of the elements listed in Claim 1 of the ‘443 Patent: “[a] non-equilibrium solution of peracetic acid,” “hydrogen peroxide,” “triacetin,” “1,2,3-propanetriol” (i.e.,

glycerol), “an aqueous source of an alkali metal or an earth alkali metal hydroxide,” and “water.” Therefore, Claim 1 of the ‘443 Patent is anticipated by Buschmann 2.

2. Ground 2b – Claim 1 of the ‘443 Patent is obvious over Buschmann 2

106. By its disclosures, Buschmann 2 makes it obvious to a POSA that a non-equilibrium solution of peracetic acid contains hydrogen peroxide, triacetin, 1,2,3-propanetriol (i.e., glycerol), and an alkaline hydroxide in water. A POSA would have understood that the hydroxide can be an alkali metal hydroxide because Buschmann 2 repeatedly teaches the use of sodium hydroxide (NaOH) as a “hydroxide”. Exhibit 1015, paragraphs 0075-0077, 0088, 0139, and 0145. Thus Claim 1 of the ‘443 Patent is obvious over Buschmann 2.

3. Ground 2c – Claim 2 of the ‘443 Patent is anticipated by Buschmann 2

107. Dependent Claim 2 of the ‘443 Patent recites an additional feature beyond those of Claim 1: “a pH of about 11.2 to about 13.37” for the “non-equilibrium solution of peracetic acid” disclosed in Claim 1.

108. Buschmann 2 expressly discloses very alkaline conditions: “a pH greater than or equal to 10 and less than or equal to 13” and “caustic pH (pH > 10).” Exhibit 1015, paragraphs 0033, 0034, and 0074.

109. Buschmann 2 further discloses that “[a]n example of a non-equilibrium reaction solution ... combin[es] 1.1 g/L hydrogen peroxide adjusted to pH 12.0 with

sodium hydroxide and reacted with 10 g/L acetylsalicylic acid.” Exhibit 1015, paragraph 0077.

110. The pH value disclosed in Buschmann 2 (“pH 12.0”) thus falls well within the pH range recited in Claim 2 of the ‘443 Patent (i.e., “a pH of about 11.2 to about 13.37”).

111. As established above for Claim 1 of the ‘443 Patent, Buschmann 2 teaches non-equilibrium solutions of peracetic acid also containing hydrogen peroxide, triacetin, glycerol, an aqueous source of an alkaline hydroxide (such as sodium hydroxide), and water.

112. Because the pH value of 12.0 disclosed in Buschmann 2 clearly falls within the pH range claimed in Claim 2 of the ‘443 Patent, Claim 2 is anticipated by Buschmann 2.

4. Ground 2d – Claim 2 of the ‘443 Patent is obvious over Buschmann 2

113. By its express disclosures, Buschmann 2 makes it obvious to a POSA that its non-equilibrium solution of peracetic acid also contains hydrogen peroxide, triacetin, 1,2,3-propanetriol (i.e., glycerol), and an alkaline hydroxide in water. A POSA would have understood that the said hydroxide can be an alkali metal hydroxide because Buschmann 2 specifically and repeatedly teaches the use of sodium hydroxide, a very common alkali metal hydroxide. Exhibit 1015, paragraphs 0075-0077, 0088, 0139, and 0145. A POSA would have readily recognized that

sodium hydroxide also can be used with starting materials other than the acetylsalicylic acid exemplified in Buschmann 2 because the latter teaches that acetyl donors other than acetylsalicylic acid can be used, including specifically triacetin, which is prominently identified by name as such therein. Exhibit 1015, paragraph 0058 and Examples 6-10.

114. As established above, Buschmann 2 teaches pH values “greater than about 10” and “pH > 10.” Exhibit 1015, paragraphs 0033, 0034, and 0063. Buschmann 2 also teaches a “self-reaction decomposition process at alkaline pH ($7.5 \leq \text{pH} \leq 10.5$)” for peracetic acid. Exhibit 1015, paragraphs 0079 and 0081. A POSA would have understood from these teachings that a pH of above 10.5 provides an alkaline pH while also minimizing an undesirable “self-reaction decomposition” of peracetic acid.

115. A POSA would have recognized that the pH is a result-effective reaction variable that can be optimized through routine experimentation because of the teachings in Buschmann 2 that both the formation of peracetic acid (Exhibit 1015, paragraph 0058 and Examples 6-10) and the “self-reaction decomposition” of peracetic acid (Exhibit 1015, paragraphs 0079 and 0081) are pH-dependent.

116. The solutions disclosed in Buschmann 2 are “typically aqueous solutions”. Exhibit 1015, paragraph 0074. A POSA (and indeed anyone who has taken a college freshman chemistry course) would have known that the highest

conventional-scale alkaline pH in aqueous solution is 14 (in other words, the conventional pH scale is from 0 to 14 at 25°C). From the teachings in Buschmann 2, a POSA thus would have recognized that the alkaline pH values in the solutions therein range from “greater than about 10” (or “pH > 10”) to 14. Optimizing the pH within this limited range would have been no more than routine experimentation well within the capability of a POSA.

117. The lower endpoint of the pH range in Claim 2 of the ‘443 Patent is “about 11.2.” This endpoint is quite alkaline (falling within “pH greater than about 10” and “pH > 10”) as taught in Buschmann 2 for the formation of peracetic acid. Exhibit 1015, paragraphs 0033, 0034, and 0063. The lower endpoint of the claimed pH range is also above the pH range in which the undesirable self-reaction decomposition of peracetic acid occurs, namely higher than 10.5. Exhibit 1015, paragraphs 0079 and 0081.

118. Therefore, the claimed pH range, “about 11.2 to about 13.37,” would have been arrived at by a POSA through routine optimization based on the disclosure of Buschmann 2. Hence the pH range claimed in Claim 2 of the ‘443 Patent would have been obvious.

C. Ground 3: Claim 1 of the ‘443 Patent is obvious over U.S. Patent No. 6,221,341 B1 (“Montgomery”)

119. According to Montgomery, “[t]he acyl group source and the peroxide precursor, upon contact with an aqueous solution, generate a peroxyacid.” Exhibit 1016, column 4, lines 6-8.

120. In Example V of Montgomery, composition B explicitly contains most of the components listed in Claim 1 of the ‘443 Patent: “the hydrogen peroxide [] and glyceryl triacetate, and alternatively, water in a sufficient amount to allow the production of peroxyacetic acid.” Exhibit 1016, column 15, lines 64-67. The mixture also contains glycerol and ammonium hydroxide as ingredients. Exhibit 1016, Table 5.

121. Montgomery discloses that “the peroxide source is hydrogen peroxide or a hydrogen peroxide precursor [*sic*] and the source of acetyl or functionally similar groups is a C₁–C₅ molecule having between 1 to 5 labile C₁–C₅ acyl containing groups.” Exhibit 1016, column 5, lines 4-7.

122. Montgomery states that “[a]ccording to a specific preferred embodiment of the present invention, the source of labile acetyl groups is glyceryl triacetate, glyceryl diacetate or glyceryl acetate.” Exhibit 1016, column 6, lines 13-15. As noted above, “glyceryl triacetate” is a synonym for triacetin.

123. Montgomery further states that “[t]he use of glyceryl triacetate is advantageous due to its highly labile acetyl functionalities.” Exhibit 1016, column 6, lines 31-32.

124. A POSA would have recognized that when the three ester groups of triacetin in the aforementioned composition react with hydrogen peroxide to form peracetic acid, some 1,2,3-propanetriol (glycerin(e)) is also formed as another product. Therefore, 1,2,3-propanetriol, the perhydrolysis product of triacetin during the reaction to form peracetic acid, is necessarily present in the compositions of Montgomery.

125. While glycerin (glycerol) is formed inherently as the perhydrolysis by-product of the peracetic acid formation, glycerin is also one of the listed ingredients of composition B in Example V in Montgomery. Exhibit 1016, Table 5.

126. Montgomery also notes that “[t]he formation of peroxyacetic acid from hydrogen peroxide and glyceryl triacetate has been determined to occur most readily at pH levels in excess of about 5.2,” and that “[t]he compositions of the present invention may also contain a buffer to provide a specific pH ... for optimal generation of peroxyacetic acid from the hydrogen peroxide precursor and glyceryl triacetate.” Exhibit 1016, column 8, lines 15-17; column 7, lines 60-64.

127. Montgomery further discloses that “[s]uitable buffers include” various “alkaline buffers” that contain sodium hydroxide, potassium hydroxide, [and]

ammonium hydroxide” as their essential components. Exhibit 1016, column 7, line 64, to column 8, line 3.

128. Composition B of Montgomery’s Example V is prepared from two separate (composite) components, one component containing the hydrogen peroxide and the other component containing the triacetin. Exhibit 1016, column 15, lines 14-17. Example V states that “[t]he resulting mixture thus contains both the hydrogen peroxide precursor and glyceryl triacetate, and alternatively, water in a sufficient amount to allow the production of peroxyacetic acid.” Exhibit 1016, column 15, lines 64-67.

129. While composition B of Example V uses ammonium hydroxide rather than an alkali metal hydroxide or an earth alkali metal hydroxide, it would have been obvious to a POSA to substitute an alkali metal hydroxide for the ammonium hydroxide (which is also an alkaline hydroxide) because Montgomery discloses that sodium hydroxide and potassium hydroxide, which are both alkali metal hydroxides, can be used in these solutions as noted above.

130. The resulting mixture which is composition B in Example V explicitly contains most (indeed all but one) of the components listed in Claim 1 of the ‘443 Patent: peracetic acid, hydrogen peroxide, triacetin, water, and glycerin (1,2,3-propanetriol).

131. Further, Montgomery renders obvious the presence of (an aqueous source of) an alkali metal hydroxide in a solution containing glycerin (1,2,3-propanetriol), water, hydrogen peroxide, glyceryl triacetate (triacetin), and peracetic acid. A POSA would have both understood that an alkali metal hydroxide can be used instead of ammonium hydroxide (which is also an alkaline hydroxide) in composition B in Example V and been motivated to do so because Montgomery teaches that sodium hydroxide and potassium hydroxide are equivalent to ammonium hydroxide by listing all three of them side by side as alkaline buffer essential components. Exhibit 1016, column 7, line 64, to column 8, line 3. Therefore, Claim 1 of the '443 Patent is obvious to a POSA in view of the disclosures of Montgomery.

D. Grounds 4a-4f: Claims 1-3 of the '443 Patent are anticipated by, and obvious over, U.S. Patent No. 7,919,122 B2 ("Okano 1")

1. Ground 4a – Claim 1 of the '443 Patent is anticipated by Okano 1

132. In Example 3 of Okano 1, several ingredients are combined to form a mixture: (deionized) water, "components (A) and (B), organic phosphonic acid (trade name: Dequest 2010," which is a peroxide stabilizer), "and an alkaline pH adjusting agent in the amounts shown in Table 10," so that "[t]he pH in this step was 8 to 12." Exhibit 1010, column 29, lines 30-36. The amounts of the ingredients were selected such that the total weight of the mixture was 100 g; "the mixture was mixed

with stirring for about 10 minutes.” Exhibit 1010, column 29, lines 33-35. In Runs 3-3 and 3-6, component (A) was triacetin, component (B) was aqueous hydrogen peroxide, and the “[a]lkaline pH adjusting agent” was sodium hydroxide. Exhibit 1010, Table 10. A POSA would have further recognized that when the three ester groups of triacetin in the aforementioned alkaline aqueous solution react with hydrogen peroxide to form peracetic acid, some 1,2,3-propanetriol is also formed as another product. Therefore, 1,2,3-propanetriol, the perhydrolysis product of triacetin during the reaction to form the peracetic acid, is necessarily present in the solutions of Runs 3-3 and 3-6.

133. Example 6 of Okano 1 was performed using the same ingredients and procedure as in its Example 3. Exhibit 1010, column 47, lines 43-48. In Runs 6-3 and 6-6, component (A) was triacetin, component (B) was aqueous hydrogen peroxide, and the “[a]lkaline pH adjusting agent” was sodium hydroxide. Exhibit 1010, Table 23. Thus the product of perhydrolysis of triacetin, 1,2,3-propanetriol, necessarily forms in the solutions of Runs 6-3 and 6-6, which presence would have been recognized by a POSA.

134. Therefore, at least Runs 3-3, 3-6, 6-3, and 6-6 in Okano 1 disclose to a POSA aqueous solutions containing peracetic acid, triacetin, hydrogen peroxide, water, 1,2,3-propanetriol, and an aqueous source of an alkali metal hydroxide. Exhibit 1010, column 29, lines 30-34; Table 10; column 47, lines 43-48; Table 23.

135. Okano 1 also discloses that “since the reaction between the component (A) and the component (B1) is an *irreversible reaction*, an *aqueous solution* containing an organic peracid at desired concentration is produced without accumulation of hydrogen peroxide in the system.” Exhibit 1010, column 11, lines 16-23 (emphases added). A POSA would have recognized that an irreversible reaction necessarily results in a non-equilibrium solution. Therefore, the corresponding solutions taught in Okano 1 are not at equilibrium.

136. Because the solutions in Okano 1’s Runs 3-3 and 3-6 were made in the same manner as those in Runs 6-3 and 6-6, the solutions in Runs 3-3 and 3-6 are also not at equilibrium, i.e., are non-equilibrium solutions.

137. The solutions in Runs 3-3, 3-6, 6-3, and 6-6 of Okano 1 thus contain all of the components required by Claim 1 of the ‘443 Patent: “peracetic acid,” “triacetin,” “hydrogen peroxide,” “water,” “1,2,3-propanetriol,” and “an aqueous source of an alkali metal hydroxide.” Furthermore, these claimed components constitute “[a] non-equilibrium solution of peracetic acid” (assuming that the claim phrase in the preamble of Claim 1 has its plain and ordinary meaning described above). Therefore, Okano 1 anticipates Claim 1 of the ‘443 Patent.

2. Ground 4b – Claim 1 of the ‘443 Patent is obvious over Okano 1

138. By its above-described disclosures in Runs 3-3, 3-6, 6-3, and 6-6, Okano 1 makes it obvious to a POSA that 1,2,3-propanetriol is present in a solution

comprising peracetic acid, triacetin, hydrogen peroxide, an aqueous source of an alkali metal hydroxide, and water. In particular, a POSA would have understood that 1,2,3-propanetriol is the perhydrolysis product of the complete reaction of triacetin and hydrogen peroxide to form peracetic acid as another product. Okano 1 also makes it clear that the solutions of peracetic acid are non-equilibrium solutions from the teachings that the reaction of PAA formation is irreversible, as described above. Exhibit 1010, column 11, lines 16-23; column 29, lines 30-34; Table 10; column 47, lines 43-48; Table 23. Therefore, Claim 1 of the '443 Patent is obvious in view of Okano 1.

3. Ground 4c – Claim 2 of the '443 Patent is anticipated by Okano 1

139. As noted above, Claim 2 of the '443 Patent recites a pH range “of about 11.2 to about 13.37” for the solution of Claim 1. Okano 1 teaches in Examples 3 and 6 that when water, components (A) and (B), organic phosphonic acid (peroxide stabilizer), and an alkaline pH adjusting agent have been added, then “[t]he pH of this mixture was 8 to 12.”

140. The pH range in Examples 3 and 6 of Okano 1 thus significantly overlaps with that recited in Claim 2.

141. As established above for Claim 1 of the '443 Patent, Okano 1 teaches non-equilibrium peracetic acid solutions also containing hydrogen peroxide, triacetin, glycerol, an alkali metal hydroxide, and water.

142. Because the pH range disclosed in Okano 1 overlaps with that recited in Claim 2 of the ‘443 Patent, Claim 2 is anticipated by Okano 1.

4. Ground 4d – Claim 2 of the ‘443 Patent is obvious over Okano 1

143. By its above-referenced disclosures, Okano 1 makes it obvious to a POSA that its non-equilibrium solution of peracetic acid also contains hydrogen peroxide, triacetin, 1,2,3-propanetriol, water, and an alkali metal hydroxide.

144. In addition, the alkaline pH range for the non-equilibrium peracetic acid solutions overlaps with that disclosed in Claim 2 of the ‘443 Patent, thereby making Claim 2 obvious in view of Okano 1. I see nothing surprisingly beneficial or extraordinary about the particular pH range limitation in Claim 2 (“about 11.2 to about 13.37”) outside of that taught by Okano 1 (pH “8 to 12”), and no particular benefits of this pH range differential (i.e., from pH “12” to pH of “about 13.37”) are suggested, much less disclosed, in the specification of the ‘443 Patent.

5. Ground 4e – Claim 3 of the ‘443 Patent is anticipated by Okano 1

145. Claim 3 of the ‘443 Patent recites a peracetic acid concentration of “about 1% to about 7.1%” for the solution of Claim 1, where the “%” is defined in the patent specification as a weight percent (wt%). Exhibit 1001, column 7, lines 62-63. Okano 1 discloses that the peracetic acid concentration “[j]ust after preparation”

in Runs 3-3, 3-6, 6-3, and 6-6 was 27,000 ppm (i.e., parts per million), which is equivalent to 2.7 wt% ($100\% \times 27,000/1,000,000$). Exhibit 1010, Tables 10 and 23.

146. The peracetic acid concentrations in Okano 1's Runs 3-3, 3-6, 6-3, and 6-6 hence fall within the range recited in Claim 3 (i.e., "about 1% to about 7.1%"). Therefore, since Okano 1 discloses all of the limitations of Claim 3 of the '443 Patent, Claim 3 is anticipated by Okano 1.

6. Ground 4f – Claim 3 of the '443 Patent is obvious over Okano 1

147. By its above-discussed disclosures, Okano 1 makes it obvious to a POSA that a non-equilibrium solution of peracetic acid also contains hydrogen peroxide, triacetin, 1,2,3-propanetriol, water, and an alkali metal hydroxide.

148. In addition, as shown above, the concentrations of peracetic acid in Okano 1's non-equilibrium peracetic acid solutions fall within the wt% range claimed in Claim 3 of the '443 Patent, thereby making Claim 3 obvious in view of Okano 1.

E. Grounds 5a-5f: Claims 1-2 of the '443 Patent are anticipated by, and obvious over, JP 2006-045147 A ("Okano 2")

1. Ground 5a – Claim 1 of the '443 Patent is anticipated by Okano 2

149. In its Example 1, Okano 2 discloses combining triacetin, hydrogen peroxide, water, an alkaline aqueous solution containing 27% sodium hydroxide

(i.e., an alkali metal hydroxide), and 1.3% of organic phosphonic acid (a peroxide stabilizer). Exhibit 1018, paragraph 0057 (Page 19).

150. Paragraph 0059 of Okano 2 is directed to “Measurement of Organic Peroxy Acid Concentration” for sterilizing cleaner compositions (I) and (II), and it states that “an organic peroxy acid concentration (as peracetic acid concentration) was found using the following formula.” That the organic peroxy acid is indeed peracetic acid is further confirmed within that formula: “organic peroxy acid (*peracetic acid*) concentration (%) = ...” Exhibit 1018, Page 20 (emphasis added). Paragraph 0057 within Example 1 is entitled “Preparation of Sterilizing Cleaner Composition (I).”

151. Five of the six components recited in Claim 1 of the ‘443 Patent are thus expressly present in Composition (I) of Example 1 of Okano 2: peracetic acid, triacetin, hydrogen peroxide, an aqueous source of an alkali metal hydroxide, and water. Furthermore, according to Okano 2, such a “sterilizing cleaner composition for hard surfaces of the present invention is an aqueous solution.” Exhibit 1018, Page 9 (lines 4-5).

152. The only component of Claim 1 of the ‘443 Patent that is not explicitly disclosed in Okano 2 is 1,2,3-propanetriol (i.e., glycerin(e)/glycerol). A POSA would have recognized, however, that when the three ester groups of triacetin in the aforementioned alkaline aqueous solution react with hydrogen peroxide to form

peracetic acid, some 1,2,3-propanetriol is also formed as another product. Therefore, 1,2,3-propanetriol, the perhydrolysis product of triacetin formed during the reaction to form the peracetic acid, is necessarily present in the solution.

153. Under the foregoing interpretation of the claim phrase “[a] non-equilibrium solution of peracetic acid” as having its plain and ordinary meaning of a solution of peracetic acid that is not at equilibrium under a given set of conditions, Okano 2 hence discloses to a POSA forming non-equilibrium solutions of peracetic acid when water, components (A) and (B1), and aqueous sodium hydroxide are brought together, at least in Example 1, where component (A) is triacetin and component (B1) is hydrogen peroxide. A POSA would have understood that the reaction of triacetin with hydrogen peroxide to form peracetic acid in alkaline media is essentially irreversible because there is no evidence for a back-reaction (esterification) of the 1,2,3-propanetriol to re-form triacetin, which would have required at least an undissociated acetic acid.

154. Therefore, Claim 1 of the ‘443 Patent is anticipated by Okano 2.

2. Ground 5b – Claim 1 of the ‘443 Patent is obvious over Okano 2

155. By its disclosures, especially in Example 1 as described in the preceding paragraphs, Okano 2 makes it obvious to a POSA that peracetic acid and 1,2,3-propanetriol would have been present in an alkaline solution comprising

triacetin, hydrogen peroxide, an aqueous source of an alkali metal hydroxide, and water.

156. In particular, a POSA would have recognized the presence of peracetic acid and 1,2,3-propanetriol in such a solution because Okano 2 shows that peracetic acid is formed in aqueous solutions containing triacetin, hydrogen peroxide, and an aqueous source of an alkali metal hydroxide. Exhibit 1018, paragraphs 0057 and 0059 (Pages 19-20). Therefore, Claim 1 of the '443 Patent is obvious in view of Okano 2.

3. Ground 5c – Claim 2 of the '443 Patent is anticipated by Okano 2

157. Dependent Claim 2 of the '443 Patent recites the following feature beyond those taught in Claim 1: “a pH of about 11.2 to about 13.37” for the solution of Claim 1. Okano 2 repeatedly discloses that the reaction is conducted at “a pH of 8 to 12”. Exhibit 1018, paragraphs 0008, 0009, 0015, and 0029.

158. This “8 to 12” pH range disclosed in Okano 2 clearly overlaps the pH range recited in Claim 2 (“about 11.2 to about 13.37”).

159. As established above for Claim 1 of the '443 Patent, Okano 2 teaches a POSA solutions containing peracetic acid, hydrogen peroxide, triacetin, 1,2,3-propanetriol, an alkali metal hydroxide, and water.

160. It would also have been evident to a POSA that the alkaline solution disclosed in Okano 2 is a non-equilibrium solution because, as noted above, once

formed, 1,2,3-propanetriol does not react to re-form triacetin, i.e., this reaction is essentially irreversible.

161. Because the pH range disclosed in Okano 2 overlaps with that taught in Claim 2, all of the limitations of Claim 2 are disclosed in Okano 2. Claim 2 of the ‘443 Patent, therefore, is anticipated by Okano 2.

4. Ground 5d – Claim 2 of the ‘443 Patent is obvious over Okano 2

162. By its disclosures, as explained above, Okano 2 makes it obvious to a POSA that a non-equilibrium solution of peracetic acid also contains hydrogen peroxide, triacetin, 1,2,3-propanetriol, and an alkali metal hydroxide in water.

163. In addition, the pH range for the non-equilibrium peracetic acid solutions overlaps with that recited in Claim 2 of the ‘443 Patent, thereby making Claim 2 obvious in view of Okano 2.

5. Ground 5e – Claim 3 of the ‘443 Patent is anticipated by Okano 2

164. Claim 3 of the ‘443 Patent recites a peracetic acid concentration of “about 1% to about 7.1%” for the solution of Claim 1, where the “%” is defined in the patent specification as a weight percent (wt%). Exhibit 1001, column 7, lines 62-63.

165. In Okano 2, the sterilizing cleanser “is an aqueous solution containing an organic peracid, and the concentration of the organic peracid in the composition

is preferably 10 to 20,000 ppm, more preferably 10 to 10,000 ppm.” Exhibit 1018, paragraph 0023. Okano 2 reiterates this concentration range for the second composition for producing a sterilizing cleaner: “The organic peroxy acid concentration in the aqueous solution is preferably 10 to 20,000 ppm (weight ratio, same as below) and more so 10 to 10,000 ppm.” Exhibit 1018, paragraph 0044.

166. The 10 to 20,000 ppm range is equivalent to 0.001 wt% to 2 wt%, and the 10 to 10,000 ppm range is equivalent to 0.001 wt% to 1 wt%. At least the broader peracetic acid concentration range (and arguably even the narrower one) clearly overlaps with that recited in Claim 3 of the ‘443 Patent (i.e., “about 1% to about 7.1%”).

167. In its Example 1, Okano 2 discloses a preparation of peracetic acid from triacetin, hydrogen peroxide, water, and sodium hydroxide, in which 50 grams of triacetin and 25 grams of a 60% aqueous solution of hydrogen peroxide were used. Exhibit 1018, paragraph 0057. The 50 grams of triacetin is 0.23 moles of triacetin. The 60% aqueous solution of hydrogen peroxide contains 15 grams of pure hydrogen peroxide, or 0.44 moles of hydrogen peroxide.

168. Three moles of hydrogen peroxide are needed for a complete perhydrolysis reaction with each mole of triacetin, so the hydrogen peroxide present can only convert $0.44 \div 3 = 0.15$ moles of triacetin. Since there are more than 0.15 moles of triacetin present (namely, 0.23 moles; see the preceding paragraph),

hydrogen peroxide is the limiting reagent in this case. Assuming a complete reaction, 0.44 moles of peracetic acid, or 33 grams of peracetic acid, were formed. The total weight of the preparation solution was 1000 grams (= 50 g of triacetin + 25 g of 60% H_2O_2 + 850 g of water + 75 g of aqueous NaOH), and the 33 g of peracetic acid therein is 3.3 wt%, which falls well within the range in Claim 3 of the '443 Patent (i.e., "about 1% to about 7.1%").

169. Because the concentration range and concentration value disclosed in Okano 2 overlap with the aforementioned range recited in Claim 3, all of the limitations of Claim 3 are disclosed in Okano 2. Claim 3 of the '443 Patent, therefore, is anticipated by Okano 2.

6. Ground 5f – Claim 3 of the '443 Patent is obvious over Okano 2

170. By its disclosures, as explained above, Okano 2 makes it obvious to a POSA that its non-equilibrium solution of peracetic acid also contains hydrogen peroxide, triacetin, 1,2,3-propanetriol, and an alkali metal hydroxide in water.

171. In addition, the concentration range and concentration value for peracetic acid in the solutions of Okano 2 overlap with the aforementioned range recited in Claim 3 of the '443 Patent, thereby making Claim 3 obvious in view of Okano 2.

F. Grounds 6a-6c: Claims 1-3 of the ‘443 patent are obvious over the combination of U.S. Patent No. 7,919,122 B2 (“Okano 1”) and JP 2006-045147 A (“Okano 2”)

172. As noted above, Okano 1’s Abstract indicates that the patent’s “invention provides a composition for production of a sterilizer” in which the “sterilizer is obtained as an aqueous solution containing an organic peracid.” The Abstract also states that the “composition for production of a sterilizer” contains: “(A) an ester of a polyhydric alcohol and an organic acid having a hydrocarbon group ... and (B1) hydrogen peroxide.” Exhibit 1010, Cover Page.

173. As also noted above, Okano 2’s Abstract indicates that the disclosure is directed to “[a] sterilizing cleaner composition for hard surfaces.” The Abstract further states that the composition contains:

water and an organic peracid obtained by reacting (A) an ester of a polyhydric alcohol and an organic acid with (B1) hydrogen peroxide in a specific molar ratio in water at a pH of 8 to 12.

Exhibit 1018, Page 1.

174. A POSA would have been motivated to find a sterilizer or sterilizing cleanser that is not chlorine-based, due to the known problems with such sterilizers, including their “low sterilizing effect on [bacterial] spores and molds,” as well as “corrosion of metal [] and generation of chlorine gas by misuse.” Exhibit 1018, paragraph 0005; Exhibit 1010, column 1, lines 22-23. A POSA hence would have been motivated to combine Okano 1 and Okano 2 because both references address

this problem, and the solution to the problem in both references involves preparation of a chlorine-free sterilizer or sterilizer composition from an ester, which is preferably triacetin, and hydrogen peroxide. Okano 1 and Okano 2 use the same components, so there would have been a reasonable expectation of success for their combination by a POSA.

1. Ground 6a – Claim 1 of the ‘443 Patent is obvious over the combination of Okano 1 and Okano 2

175. As described above, in Example 3 of Okano 1 several ingredients are combined to form a mixture: (deionized) water, components (A) and (B), organic phosphonic acid (a peroxide stabilizer), and an alkaline pH adjusting agent in the amounts shown in Table 10. Exhibit 1010, column 29, lines 30-36. In Runs 3-3 and 3-6, component (A) was triacetin, component (B) was aqueous hydrogen peroxide, and the alkaline pH adjusting agent was sodium hydroxide. Exhibit 1010, Table 10.

176. Example 6 of Okano 1 was performed using the same ingredients and procedure as in its Example 3. Exhibit 1010, column 47, lines 43-48. In Runs 6-3 and 6-6, component (A) was triacetin, component (B) was aqueous hydrogen peroxide, and the alkaline pH adjusting agent was sodium hydroxide. Exhibit 1010, Table 23.

177. Therefore, at least Runs 3-3, 3-6, 6-3, and 6-6 in Okano 1 disclose to a POSA aqueous solutions containing peracetic acid, triacetin, hydrogen peroxide,

water, and an aqueous source of an alkali metal hydroxide. Exhibit 1010, column 29, lines 30-34; Table 10; column 47, lines 43-48; and Table 23.

178. In its Example 1, Okano 2 discloses combining triacetin, hydrogen peroxide, water, an alkaline aqueous solution containing 27% sodium hydroxide (i.e., an alkali metal hydroxide), and 1.3% of organic phosphonic acid (a peroxide stabilizer). Exhibit 1018, paragraph 0057 (Page 19).

179. Five of the six components recited in Claim 1 of the '443 Patent are thus expressly present in Composition (I) of Okano 2's Example 1: peracetic acid, triacetin, hydrogen peroxide, an aqueous source of an alkali metal hydroxide, and water. Furthermore, according to Okano 2, such a "sterilizing cleaner composition for hard surfaces of the present invention is an aqueous solution." Exhibit 1018, Page 9 (lines 4-5).

180. The only component of Claim 1 of the '443 Patent that is not explicitly disclosed in Okano 1 or Okano 2 is 1,2,3-propanetriol (i.e., glycerin(e)/glycerol). A POSA would have recognized, however, that when the three ester groups of triacetin in the aforementioned alkaline aqueous solutions react with hydrogen peroxide to form peracetic acid, some 1,2,3-propanetriol is also formed as another product. Therefore, 1,2,3-propanetriol, the perhydrolysis product of triacetin, formed during the reaction to form the peracetic acid, is necessarily present in these solutions.

181. Okano 1 also discloses that “since the reaction between the component (A) and the component (B1) is an *irreversible reaction*, an *aqueous solution* containing an organic peracid at desired concentration is produced without accumulation of hydrogen peroxide in the system.” Exhibit 1010, column 11, lines 16-23 (emphases added).

182. A POSA would have recognized that such an irreversible reaction necessarily results in a non-equilibrium solution. Therefore, the corresponding solutions taught in Okano 1 and Okano 2 are not at equilibrium.

183. The solutions in Runs 3-3, 3-6, 6-3, and 6-6 of Okano 1 and the solution in Example 1 of Okano 2 thus contain all of the components disclosed in Claim 1 of the ‘443 Patent: “peracetic acid,” “triacetin,” “hydrogen peroxide,” “water,” “1,2,3-propanetriol,” and “an aqueous source of an alkali metal hydroxide.” Furthermore, these claimed components constitute “[a] non-equilibrium solution of peracetic acid” (assuming that the claim phrase in the preamble of Claim 1 has its plain and ordinary meaning, as described above).

184. Therefore, Claim 1 of the ‘443 Patent is obvious over the combination of Okano 1 and Okano 2.

2. Ground 6b – Claim 2 of the ‘443 Patent is obvious over the combination of Okano 1 and Okano 2

185. As established above for Claim 1 of the ‘443 Patent, Okano 1 and Okano 2 disclose non-equilibrium peracetic acid solutions also containing hydrogen peroxide, triacetin, glycerol, an alkali metal hydroxide, and water.

186. As noted above, Claim 2 of the ‘443 Patent recites “a pH of about 11.2 to about 13.37” for the solution of Claim 1.

187. Okano 1 teaches in Examples 3 and 6 that when water, components (A) and (B), organic phosphonic acid (peroxide stabilizer), and an alkaline pH adjusting agent have been added, “[t]he pH of this mixture was 8 to 12.” The pH range in Examples 3 and 6 of Okano 1 thus significantly overlaps with that recited in Claim 2 (“about 11.2 to about 13.37”).

188. Okano 2 repeatedly discloses that the reaction is conducted at “a pH of 8 to 12”. Exhibit 1018, paragraphs 0008, 0009, 0015, and 0029. This pH range disclosed in Okano 2 clearly overlaps with that recited in Claim 2 (“about 11.2 to about 13.37”).

189. Because the pH ranges disclosed in Okano 1 and Okano 2 overlap with the pH range recited in Claim 2 of the ‘443 Patent, Claim 2 is obvious over the combination of Okano 1 and Okano 2.

3. Ground 6c – Claim 3 of the ‘443 Patent is obvious over the combination of Okano 1 and Okano 2

190. Claim 3 of the ‘443 Patent recites a peracetic acid concentration of “about 1% to about 7.1%” for the solution of Claim 1, where the “%” is defined in the patent specification as a weight percent (wt%). Exhibit 1001, column 7, lines 62-63.

191. Okano 1 discloses that the peracetic acid concentration “[j]ust after preparation” in Runs 3-3, 3-6, 6-3, and 6-6 was 27,000 ppm (i.e., parts per million), which is equivalent to 2.7 wt% ($100\% \times 27,000/1,000,000$). Exhibit 1010, Tables 10 and 23.

192. The peracetic acid concentrations in Okano 1’s Runs 3-3, 3-6, 6-3, and 6-6 hence fall well within the range recited in Claim 3 (i.e., “about 1% to about 7.1%”).

193. In Okano 2, the sterilizing cleanser “is an aqueous solution containing an organic peracid, and the concentration of the organic peracid in the composition is preferably 10 to 20,000 ppm, more preferably 10 to 10,000 ppm.” Exhibit 1018, paragraph 0023. Okano 2 reiterates this concentration range for the second composition for producing a sterilizing cleaner: “The organic peroxy acid concentration in the aqueous solution is preferably 10 to 20,000 ppm (weight ratio, same as below) and more so 10 to 10,000 ppm.” Exhibit 1018, paragraph 0044. The

10 to 20,000 ppm range is equivalent to 0.001 wt% to 2 wt%, and the 10 to 10,000 ppm range is equivalent to 0.001 wt% to 1 wt%.

194. At least the broader of these peracetic acid concentration ranges (and arguably even the narrower one) of Okano 2 clearly overlaps with that recited in Claim 3 of the '443 Patent (i.e., “about 1% to about 7.1%”).

195. In Example 1 of Okano 2, the preparation of peracetic acid used 50 grams of triacetin and 25 grams of a 60% aqueous solution of hydrogen peroxide. Exhibit 1018, paragraph 0057. The 50 grams of triacetin is 0.23 moles of triacetin. The 60% aqueous solution of hydrogen peroxide contained 15 grams of pure hydrogen peroxide, or 0.44 moles of hydrogen peroxide. Three moles of hydrogen peroxide are needed for a complete perhydrolysis reaction with each mole of triacetin, so the hydrogen peroxide present can only convert $0.44 \div 3 = 0.15$ moles of triacetin. Since there are more than 0.15 moles of triacetin present (namely, 0.23 moles), hydrogen peroxide is the limiting reagent in this case. Assuming a complete reaction, 0.44 moles of peracetic acid, or 33 grams of peracetic acid, were formed. The total weight of the preparation solution was 1000 grams (= 50 g of triacetin + 25 g of 60% H_2O_2 + 850 g of water + 75 g of aqueous NaOH), and the 33 g of peracetic acid therein is 3.3 wt%.

196. The peracetic acid concentration in Example 1 of Okano 2 hence falls well within the range in Claim 3.

197. Because the peracetic acid concentration value disclosed in Okano 2 falls within the range recited in Claim 3 and the peracetic acid concentration ranges disclosed in Okano 1 and Okano 2 overlap with the range recited in Claim 3 of the '443 Patent (i.e., "about 1% to about 7.1%"), Claim 3 is obvious over the combination of Okano 1 and Okano 2.

IX. Reservation of Rights

I reserve the right to supplement my opinions expressed herein in the future to respond to any arguments that the Patent Owner and/or its expert(s) may raise and to consider new information as it becomes available to me.

X. Attestation

I declare that all statements made herein of my own knowledge are true to the best of my knowledge and that all statements made on information and belief are believed by me 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: 08/25/2025



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Honors:

2015	Tau Beta Pi's Leonardo Da Vinci Lecturer, MIT
2007-11 and 2014	Novartis Chair Endowed Professorship, MIT
2012-13	Roger and Georges Firmenich Endowed Professorship, MIT
2011	MIT Biological Engineering Senior Class Faculty Award
2006	Distinguished GRUM Lecturer in Drug Discovery & Development, University of Montreal (Canada)
2004	UNAM Distinguished Lecturer, National University of Mexico (Mexico City)
2001	Walter Enz Lecturer in Pharmaceutical Chemistry, University of Kansas
2001	Elected a Corresponding Fellow of the Royal Society of Edinburgh (Scotland's National Academy of Science and Letters)
2000	Merck Distinguished Lecturer, Rutgers University
2000	Top 20 Biotechnology & Bioengineering Papers of the Last Forty Years
1998	Robert Lutz Lecturer, University of Virginia
1996	Perkin-Elmer Distinguished Lecturer, University of Pittsburgh
1995	Elected to the National Academy of Sciences of the U.S.A.

1995	Nathan O. Kaplan Memorial Lecturer in Biological Chemistry, University of California at San Diego
1994	R.W. Johnson PRI Lecturer, Pharmaceutical Research Institute
1994	Warren McCabe Lecturer, North Carolina State University
1993	Elected to the National Academy of Engineering of the U.S.A.
1993	Arthur C. Cope Scholar Award of the American Chemical Society
1993	Biotechnology Divisional Lectureship Award of the Institute of Food Technologists
1992	Charles Sabat Lecturer, Rutgers University
1992	Elected a Founding Fellow of the American Institute for Medical and Biological Engineering
1992	Louis C. Jordy Research Scholar Lecturer, Drew University
1991	International Enzyme Engineering Award
1991	Marvin J. Johnson Award of the American Chemical Society
1990	Monsanto Lecturer, Ohio State University
1990	NRC Distinguished Lecturer, Academia Sinica (Taiwan)
1989	Ipatieff Prize of the American Chemical Society
1989	Backer Lecturer, Groningen University (Holland)
1988	Dow Lecturer, University of Ottawa (Canada)
1987	Distinguished Scholar Lecturer, Hope College
1986	Leo Friend Award of the American Chemical Society

1984	Who's Who in Frontier Science and Technology
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1982	American Men and Women of Science
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Professional Experience:

2019-present	Novartis Chair Professor Emeritus of Chemistry and Bioengineering, MIT
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Professional Societies:

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Current Research Interests:

Drug synthesis and modification	Medicinal and formulation chemistry
Protein and nucleic acid delivery	Antimicrobial polymers
Enzymes as catalysts in organic syntheses	
Stabilization and formulation of macromolecular pharmaceuticals	

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301. Larson, A.M., Oh, H.S., Knipe, D.M., Klibanov, A.M. 2013. Decreasing herpes simplex viral infectivity in solution by surface-immobilized and suspended *N,N*-dodecyl,methyl-polyethylenimine. Pharm. Res. 30: 25-31.
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303. Srinivasan, C., Weight, A.K., Bussemer, T., Klibanov, A.M. 2013. Non-aqueous suspensions of antibodies are much less viscous than equally concentrated aqueous solutions. Pharm. Res. 30: 1749-1757.
304. Larson, A.M., Klibanov, A.M. 2013. Biocidal packaging of pharmaceuticals, foods, and other perishables. Ann. Rev. Chem. Biomolec. Eng. 4: 171-186.

305. Gerrard, S.E., Larson, A.M., Klivanov, A.M., Slater, N.K.H., Hanson, C.V., Abrams, B.F., Morris, M.K. 2013. Reducing infectivity of HIV upon exposure to surfaces coated with *N,N*-dodecyl,methyl-polyethylenimine. Biotechnol. Bioeng. 110: 2058-2062.
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307. Weight, A.K., Belser, J.A., Tumpey, T.M., Chen, J., Klivanov, A.M. 2013. Zanamivir conjugated to poly-L-glutamine is much more active against influenza viruses in mice and ferrets than the drug itself. Pharm. Res. 31: 466-474.
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310. Zhu, A., Liu, H.K., Long, F., Su, E., Klivanov, A.M. 2015. Biocidal action of electric current applied to composite membranes containing carbon nanotubes. Appl. Biochem. Biotechnol. 175: 666-676.
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315. Larson, A.M., Weight, A.K., Love, K., Bonificio, A., Wescott, C.R., Klibanov, A.M. 2017. Bulky polar additives that greatly reduce the viscosity of concentrated solutions of therapeutic monoclonal antibodies. J. Pharm. Sci. **106**: 1211-1217.
316. Kumar, A., Klibanov, A.M. 2017. Viscosity-lowering bulky-salt excipients prevent gelation of protein, but not carbohydrate, solutions. Appl. Biochem. Biotechnol. **182**: 1491-1496.
317. Weight, A.K., Sule, S.V., Bonificio, A.S., Gupta, K., Wescott, C.R., Klibanov, A.M. 2019. Excipients that lower viscosity of concentrated protein solutions by reducing intermolecular interactions. Pharm. Res., submitted.
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Patents:

1. Klibanov, A.M., Langer, R.S. Methods of decreasing the hydrophobicity of fibroblast and other interferons. U.S. Patent No. 4,414,147 A; November 8, 1983.
2. Klibanov, A.M., Kirchner, G. Enzymatic production of optical isomers of 2-halopropionic acids. U.S. Patent No. 4,601,987; July 22, 1986.
3. Klibanov, A.M. Removal of combined organic substances from aqueous solutions. U.S. Patent No. 4,623,465; November 18, 1986.
4. Klibanov, A.M. Enzymatic resolution of racemic mixtures of hydroxy compounds. U.S. Patent No. 4,659,671; 1987.
5. Klibanov, A.M., Dordick, J.S. Enzymatic temperature change indicator. U.S. Patent No. 4,826,762; May 2, 1989.
6. Dorval, B.L., Denham, L., Klibanov, A.M. Radial flow assay, delivering membrane, test kit, and methods. U.S. Patent No. 5,547,833; August 20, 1996.
7. Dorval, B.L., Denham, L., Klibanov, A.M. Detection reagent, particle, and immunoassay method. U.S. Patent No. 5,561,045; October 1, 1996.
8. Dorval, B.L., Chow, M., Klibanov, A.M. Stabilized vaccine compositions. U.S. Patent No. 5,618,539; April 8, 1997. European Patent No. 0 487 632; March 4, 1998.
9. Klibanov, A.M., Lewis, K., Ferrante, A.A., Coyle, C.L., Zylstra, G., Logan, M.S.P., Grossman, M.J. Solvent-resistant microorganisms. U.S. Patent No. 5,807,735; September 15, 1998.
10. Gresser, J.D., Trantolo, D.J., Langer, R., Klibanov, A.M., Wise, D.L. Material for buffered resorbable internal fixation devices and method for making the same. U.S. Patent No. 5,817,328; October 6, 1998.
11. Hekal, I.M., Langer, R.S., Klibanov, A.M., Mathiowitz, E. Monolithic polymer composition having a water absorption material. U.S. Patent No. 6,174,952; January 16, 2001.
12. Gresser, J.D., Trantolo, D.J., Langer, R., Lewandrowski, K.-U., Klibanov, A.M., Wise, D.L. Resorbable interbody spinal fusion devices. U.S. Patent No.

6,241,771; June 5, 2001.

13. Trantolo, D.J., Langer, R., Klibanov, A.M., Wise, D.L. Buffered resorbable internal fixation devices and methods for making material therefor. U.S. Patent No. 6,419,945; July 16, 2002.
14. Gresser, J.D., Trantolo, D.J., Langer, R., Lewandrowski, K.-U., Klibanov, A.M., Wise, D.L. Method of making biodegradable interbody spinal fusion devices. U.S. Patent No. 6,548,002; April 15, 2003.
15. Klibanov, A.M. Nonaqueous solutions and suspensions of macromolecules for pulmonary delivery. U.S. Patent No. 6,660,715; December 9, 2003.
16. Tiller, J.C., Lewis, K., Liao, C.-J., Klibanov, A.M. Antimicrobial polymeric surfaces. U.S. Patent No. 7,151,139; December 19, 2006.
17. Hirsh, J.C., Fleming, A.B., Rariy, R.V., Klibanov, A.M. Abuse-deterrent drug formulations. U.S. Patent No. 7,771,707; August 10, 2010.
18. Hirsh, J.C., Fleming, A.B., Rariy, R.V., Klibanov, A.M. Abuse-deterrent drug formulations. U.S. Patent No. 8,449,909; May 28, 2013.
19. Rariy, R.V., Fleming, A.B., Hirsh, J.C., Klibanov, A.M. Abuse-deterrent pharmaceutical compositions of opioids and other drugs. U.S. Patent No. 8,557,291; October 15, 2013.
20. Hirsh, J., Fleming, A.B., Rariy, R.V., Klibanov, A.M. Abuse-deterrent drug formulations. U.S. Patent No. 8,758,813; June 24, 2014.
21. Hirsh, J.C., Klibanov, A.M., Swager, T.M., Buchwald, S.L., Lo, W.Y., Fleming, A.B., Rariy, R.V. Abuse-deterrent pharmaceutical compositions of opioids and other drugs. U.S. Patent No. 9,044,398; June 2, 2015.
22. Schaer, T.P., Stewart, S., Klibanov, A.M. Antibacterial coatings that inhibit biofilm formation on implants. U.S. Patent No. 9,089,407; July 28, 2015.
23. Rariy, R.V., Fleming, A.B., Hirsh, J.C., Klibanov, A.M. Abuse-deterrent pharmaceutical compositions of opioids and other drugs. U.S. Patent No. 9,248,195; February 2, 2016.
24. Rariy, R.V., Fleming, A.B., Hirsh, J., Klibanov, A.M. Abuse-deterrent pharmaceutical compositions of opioids and other drugs. U.S. Patent No. 9,592,200; March 14, 2017.

25. Haldar, J., An, D., Álvarez de Cienfuegos, L., Chen, J., Klibanov, A.M. Polymeric coatings that inactivate viruses and bacteria. U.S. Patent Appl. Publ. No. 2010/0136072; June 3, 2010.
26. Pedersen, M., Stanley, M., Gouin, S., Klibanov, A.M, Hsu, B.B. Antimicrobial quat coating on fabrics. PCT Intl. Appl. W O 2012/06561, 2012.
27. Haldar, J., Alvarez de Cienfuegos, L., Klibanov, A.M., Chen, J. Bi-functional polymer-attached inhibitors of influenza virus. PCT Intl. Appl.WO 2009/032605, 2012.
28. Klibanov, A.M., Su, E. Neat liquid pharmaceutical formulations. U.S. Patent No. 9,731,026; August 15, 2017.
29. Hirsh, J.C., Fleming, A.B., Rariy, R.V., Klibanov, A.M. Abuse-deterrent pharmaceutical compositions. U.S. Patent No. 9,763,883; September 19, 2017.
30. Larson, A.M., Weight, A.K., Love, K., Crane, A., Langer, R.S., Klibanov, A.M. Liquid pharmaceutical formulations for injection comprising thiamine pyrophosphate 1-(3-aminopropyl)-2-methyl-1H-imidazole and uses thereof. U.S. Patent No. 9,913,905; March 13, 2018.
31. Larson, A.M., Love, K., Weight, A.K., Crane, A., Langer, R.S., Klibanov, A.M. Liquid pharmaceutical formulations for injection comprising procaine and uses thereof. U.S. Patent No. 9,925,263; March 27, 2018.
32. Larson, A.M., Love, K., Weight, A.K., Crane, A., Langer, R.S., Klibanov, A.M. Liquid pharmaceutical formulations for injection comprising Yellow 5 Orange G and uses thereof. U.S. Patent No. 10,179,172; March 27, 2018.
33. Schaer, T.P., Stewart, S., Klibanov, A.M. Antibacterial coatings that inhibit biofilm formation on implants. U.S. Patent No. 10,500,317; December 10, 2019.
34. Hirsh, J.C., Fleming, A.B., Rariy, R.V., Klibanov, A.M. Abuse-deterrent drug formulations. U.S. Patent No. 10,525,052; January 7, 2020.
35. Abrams, R., Klibanov, A.M., Langer, R., Fredrickson, G. Pharmaceutical container with pH protective layer deposited by atomic layer deposition. U.S. Patent No. 12,109,173; October 8, 2024.

Invited Lectures:

1. Gordon Conference on Immobilized Enzymes, Complexes, and Cells (Plymouth, NH). August 1978.
2. 5th International Conference on Enzyme Engineering (Henniker, NH). August 1978.
3. Miles Laboratories (Elkhart, IN). February 1980.
4. Gordon Conference on Immobilized Species (Henniker, NH). August 1980.
5. Novo Laboratories (Wilton, CT). October 1980.
6. Corning Glass Works Co. (Corning, NY). October 1980.
7. Stauffer Chemical Co. (Dobbs Ferry, NY). December 1980.
8. DuPont Experimental Station (Wilmington, DE). January 1981.
9. Dow Chemical Co. (Wayland, MA). April 1981.
10. Cetus Corp. (Berkeley, CA). April 1981.
11. Exxon Research & Engineering Co. (Linden, NJ). April 1981.
12. Meeting of the American Solar Energy Society (Philadelphia, PA). May 1981.
13. 6th International Conference on Enzyme Engineering (Kashikojima, Japan). September 1981.
14. Genex Corp. (Rockville, MD). October 1981.
15. ILP Symposium for Senior Executives (London, England). November 1981.
16. California Institute of Technology (Pasadena, CA). December 1981.
17. Symposium of the American Society for Microbiology (Atlanta, GA). March 1982.
18. Kodak Research Center (Rochester, NY). March 1982.
19. Repligen Corp. (Cambridge, MA). April 1982.

20. Symposium on the Biological Basis of New Developments in Biotechnology (Minneapolis, MN). May 1982.
21. Meeting of the Biochemical Society (Oxford, England). July 1982.
22. Meeting of the American Chemical Society (Kansas City, MO). September 1982.
23. Rotenburger Symposium on Enzyme Technology (Kassel, Germany). September 1982.
24. Genetics Institute (Boston, MA). September 1982.
25. Meeting of the American Institute of Chemical Engineers (Los Angeles, CA). November 1982.
26. G.D. Searle Co. (Chicago, IL). October 1982.
27. Halcon International Research Center (Montvale, NJ). October 1982.
28. International Workshop on Immobilized Enzymes and Cells (Bangkok, Thailand). December 1982.
29. Amoco Research Center (Naperville, IL). January 1983.
30. University College London (London, England). May 1983.
31. International Conference on Biotechnology Biotech '83 (London, England). May 1983.
32. Tufts University Workshop on Immobilized Enzymes and Proteins (Medford, MA). June 1983.
33. Gordon Conference on Organic Reactions and Processes (New Hampton, NH). July 1983.
34. Symposium "Biocatalysis: New Discoveries and Uses", Meeting of the American Society for
35. Industrial Microbiology (Sarasota, FL). August 1983.
36. Monsanto Co. (St. Louis, MO). September 1983.
37. Pasteur Biosciences '83 Conference (Paris, France). September 1983.

38. 7th International Conference on Enzyme Engineering (White Haven, PA). September 1983.
39. University of Iowa (Iowa City, IA). October 1983.
40. CPC Moffett Technical Center (Summitt-Argo, IL). December 1983.
41. General Foods Co. (Dobbs Ferry, NY). December 1983.
42. U.S. National Bureau of Standards (Gaithersburg, MD). April 1984.
43. Millipore Corp. (Bedford, MA). April 1984.
44. Technical University of Munich (Munich, F.R.G.). May 1984.
45. Danish Academy of Technical Sciences (Copenhagen, Denmark). May 1984.
46. Novo International Biotechnology Symposium (Copenhagen, Denmark). May 1984.
47. CRA Scientific Conference (St. Charles, IL). June 1984.
48. Gordon Conference on Immobilized Species in Biotechnology (Plymouth, NH). August 1984.
49. Meeting of the American Chemical Society (Philadelphia, PA). August 1984.
50. International Biotechnology Conference Biotech '84 (Washington, DC). September 1984.
51. Staley Manufacturing Co. (Decatur, IL). October 1984.
52. Case Western Reserve University (Cleveland, OH). October 1984.
53. IMC Corp. (Terre Haute, IN). October 1984.
54. Syracuse University (Syracuse, NY). November 1984.
55. National University of Mexico (Mexico City, Mexico). November 1984.
56. National Starch & Chemical Corp. (Bridgewater, NJ). November 1984.
57. Mead Corp. (Chillicothe, OH). November 1984.
58. Hebrew University of Jerusalem (Jerusalem, Israel). November 1984.

59. U.S. Army Chemical R&D Center (Aberdeen Proving Ground, MD). December 1984.
60. Allied Corp. (Morristown, NJ). December 1984.
61. Bristol Laboratories (Syracuse, NY). January 1985.
62. University of Rochester (Rochester, NY). January 1985.
63. G.D. Searle Co. (Chicago, IL). February 1985.
64. Welcome Research Laboratories (Research Triangle Park, NC). February 1985.
65. UCLA Symposium on Protein Structure, Folding and Design (Keystone, CO). April 1985.
66. International Conference on Application of Biocatalysts in Organic Synthesis (Noordwijkerhout, Holland). April 1985.
67. Guido Donegani Research Institute (Novara, Italy). April 1985.
68. Hoffmann-LaRoche Co. (Basel, Switzerland). April 1985.
69. Pittsburgh-Cleveland Catalysis Society Meeting (Pittsburgh, PA). May 1985.
70. Ethyl Corp. (Baton Rouge, LA). May 1985.
71. Stony Brook Symposium on Protein Engineering (Stony Brook, NY). May 1985.
72. Amgen Corp. (Thousand Oaks, CA). June 1985.
73. Gordon Conference on Applied Microbiology (New London, NH). August 1985.
74. International Congress of Biochemistry (Amsterdam, Holland). August 1985.
75. IUPAC Congress (Manchester, England). September 1985.
76. International Enzyme Engineering Conference (Helsingor, Denmark). September 1985.

77. Biotechnica '85 (Hannover, West Germany). October 1985.
78. Biotec 85 (Dusseldorf, West Germany). October 1985.
79. Smith Kline & French Co. (Philadelphia, PA). November 1985.
80. Exxon Corporate Research (Anandale, NJ). December 1985.
81. Pennsylvania State University (University Park, PA). December 1985.
82. Georgetown University (Washington, DC). February 1986.
83. Columbia University (New York, NY). February 1986.
84. Upjohn Co. (Kalamazoo, MI). February 1986.
85. UNIDO Workshop on Biotechnology (Trieste, Italy). March 1986.
86. Eniricerca (Monterotondo, Italy). March 1986.
87. EEC Biomolecular Engineering Meeting (Compiègne, France). April 1986.
88. ACS Conference on Chemical Aspects of Biotechnology (Gaithersburg, MD). May 1986.
89. Biotech '86 Europe International Conference (London, England). May 1986.
90. IUPAC International Symposium on Organic Chemistry in Technological Perspective (Jerusalem, Israel). June 1986.
91. University of Tel-Aviv (Ramat-Aviv, Israel). June 1986.
92. Annual Meeting of the Canadian Biochemical Society (Guelph, Canada). June 1986.
93. International Symposium on Biologically Engineered Polymers (Cambridge, England). July 1986.
94. TNO Institute of Applied Chemistry (Zeist, The Netherlands). August 1986.
95. IUPAC International Symposium on the Chemistry of Natural Products (The Hague, The Netherlands). August 1986.
96. American Chemical Society National Meeting (Anaheim, CA). September 1986.

97. Catalytica Annual Science and Technology Symposium (San Jose, CA). September 1986.
98. International Conference on Enzyme Engineering (Cambridge, England). September 1986.
99. Ohio State University (Columbus, OH). October 1986.
100. Michigan State University (Lansing, MI). October 1986.
101. Biotechnology Process Engineering Symposium (Cambridge, MA). October 1986.
102. University of Delaware (Newark, DE). November 1986.
103. American Red Cross Blood Research Institute (Bethesda, MD). November 1986.
104. International Symposium on Biocatalysis in Non-Aqueous Solvents (Wageningen, The Netherlands). December 1986.
105. University of Trondheim (Trondheim, Norway). December 1986.
106. Colgate-Palmolive Research Center (Piscataway, NJ). January 1987.
107. International Paper Co. (Tuxedo Park, NY). January 1987.
108. University of Massachusetts (Amherst, MA). February 1987.
109. American Society for Microbiology Biocatalysis Symposium (Atlanta, GA). March 1987.
110. Hope College (Holland, MI). March 1987.
111. Pfizer Corporate Research Center (Groton, CT). April 1987.
112. OBBS Symposium on Protein Engineering (Ottawa, Canada). April 1987.
113. University of Texas (Austin, TX). April 1987.
114. Florida Catalysis Conference (Palm Coast, FL). May 1987.
115. PPG Industries (Barberton, OH). May 1987.
116. Abbott Laboratories (North Chicago, IL). May 1987.

117. American Oil Chemists Society Symposium on Lipases (New Orleans, LA). May 1987.
118. Argonne National Laboratory (Argonne, IL). June 1987.
119. Canadian Chemical Conference (Quebec City, Canada). June 1987.
120. Squibb Co. (New Brunswick, NJ). June 1987.
121. FEBS Annual Meeting (Ljubljana, Yugoslavia). July 1987.
122. L'Oreal Research Institute (Paris, France). July 1987.
123. International Symposium on Biointeractions (Cambridge, England). July 1987.
124. Eli Lilly Co. (Indianapolis, IN). August 1987.
125. Upjohn Co. (Kalamazoo, MI). September 1987.
126. International Enzyme Engineering Conference (Santa Barbara, CA). October 1987.
127. Shell Development Co. (Houston, TX). October 1987.
128. DuPont Experimental Station (Wilmington, DE). October 1987.
129. University of Helsinki (Helsinki, Finland). November 1987.
130. International Conference on Bioreactors and Biotransformations (Gleneagles, Scotland). November 1987.
131. Sandoz Co. (Basel, Switzerland). November 1987.
132. University of Waterloo (Waterloo, Canada). December 1987.
133. Norwegian Biochemical Society Annual Meeting (Bejito, Norway). January 1987.
134. Rutgers University (New Brunswick, NJ). February 1988.
135. University of Ottawa (Ottawa, Canada). February 1988.
136. Boston Biomedical Research Institute (Boston, MA). March 1988.

137. Princeton University (Princeton, NJ). March 1988.
138. Royal Society of Chemistry Meeting (Kent, England). April 1988.
139. Stanford University (Stanford, CA). May 1988.
140. University of Graz (Graz, Austria). May 1988.
141. Belgian Organic Chemistry Symposium (Ghent, Belgium). May 1988.
142. Dow Chemical Co. (Midland, MI). May 1988.
143. Michigan State University (Lansing, MI). May 1988.
144. American Chemical Society Meeting (Toronto, Canada). June 1988.
145. Proctor & Gamble Co. (Cincinnati, OH). June 1988.
146. International Congress of Biochemistry (Prague, Czechoslovakia). July 1988.
147. International Biotechnology Symposium (Paris, France). July 1988.
148. Gordon Conference on Catalysis (Newport, RI). August 1988.
149. Conference on Biocatalytic Synthesis of Organic Compounds (Saratoga, NY). August 1988.
150. International Symposium on Thermodynamics Applied to Biological Systems (Santa Margherita, Italy). September 1988.
151. Cornell University (Ithaca, NY). September 1988.
152. Eastman Kodak Co. (Kingsman, TN). September 1988.
153. Symposium on Biotechnology Challenges in the Food Industry (Williamsburg, VA). October 1988.
154. University of California at Irvine (Irvine, CA). October 1988.
155. UCSF Symposium on Protein and Drug Design (San Francisco, CA). October 1988.
156. Boston University (Boston, MA). October 1988.
157. Wayne State University (Detroit, MI). November 1988.

158. Kyoto Symposium on Frontiers in Biocatalysis (Kyoto, Japan). November 1988.
159. Rohm & Haas Co. (Spring House, PA). January 1989.
160. Block Drug Co. (Jersey City, NJ). January 1989.
161. State University of New York (Albany, NY). March 1989.
162. Scripps Clinic and Research Foundation (La Jolla, CA). April 1989.
163. Texas A&M University (College Station, TX). May 1989.
164. University of Texas (Austin, TX). May 1989.
165. International Congress of Food Engineering (Cologne, F.R.G.). May 1989.
166. University of Groningen (Groningen, The Netherlands). June 1989.
167. Gordon Conference on Enzymes, Coenzymes, and Metabolic Pathways (Meridan, NH). July 1989.
168. American Peptide Symposium (La Jolla, CA). July 1989.
169. International Symposium on Prospects in Protein Engineering (Haren, The Netherlands). August 1989.
170. Connaught Laboratories (Toronto, Canada). September 1989.
171. University of Georgia (Athens, GA). October 1989.
172. Spanish National Congress of Biochemistry (Alicante, Spain). October 1989.
173. Symposium on Receptor- and Enzyme- Based Drug Design (Chapel Hill, NC). October 1989.
174. Wesleyan University (Middletown, CT). November 1989.
175. University of Wisconsin (Madison, WI). February 1990.
176. Merck Sharp & Dohme Research Laboratories (Rahway, NJ). February 1990.
177. International Symposium on Biochemical Engineering (Stuttgart, F.R.G.). March 1990.

178. University of Geneva (Geneva, Switzerland). March 1990.
179. University of Lausanne (Lausanne, Switzerland). March 1990.
180. University of Bern (Bern, Switzerland). March 1990.
181. University of Fribourg (Fribourg, Switzerland). March 1990.
182. International Conference on Protein Stability (Cambridge, England). March 1990.
183. AFRC Institute of Food Research (Reading, England). March 1990.
184. Lehigh University (Bethlehem, PA). April 1990.
185. Biotechnology Research Institute (Montreal, Canada). April 1990.
186. Ohio State University (Columbus, OH). April 1990.
187. Pharmaceutical Manufacturers Association Annual Meeting (St. Louis, MO). April 1990.
188. International Conference on Industrial Use of Enzymes (Chicago, IL). May 1990.
189. Korea Advanced Institute of Science and Technology (Seoul, Korea). June 1990.
190. Academia Sinica and National Taiwan University (Taipei, Taiwan). June 1990.
191. Gordon Conference on Biocatalysis (Plymouth, NH). June 1990.
192. IUPAC Conference on Organic Synthesis (Helsinki, Finland). July 1990.
193. International Conference on Solution Chemistry (Ottawa, Canada). August 1990.
194. Gordon Conference on Biomolecular Recognition (Plymouth, NH). August 1990.
195. University of Naples (Naples, Italy). September 1990.

196. International Conference on Water and Life (Crans-sur-Sierre, Switzerland). September 1990.
197. International Symposium on Thermodynamic Basis of Protein Structure and Function (Kansas City, MO). October 1990.
198. Johns Hopkins University (Baltimore, MD). October 1990.
199. Institute of Medicine Workshop on Microheterogeneity of Biological Macromolecules (Arlington, VA). November 1990.
200. U.S.-Japan Biotechnology Conference (Honolulu, HI). January 1991.
201. Ciba-Geigy Corp. (Summit, NJ). February 1991.
202. City University of New York (New York, NY). March 1991.
203. Rensselaer Polytechnic Institute (Troy, NY). March 1991.
204. Bristol-Myers Squibb Co. (Wallingford, CT). April 1991.
205. British Biochemical Society Meeting (Reading, England). April 1991.
206. University of California at Berkeley (Berkeley, CA). April 1991.
207. California Institute of Technology (Pasadena, CA). April 1991.
208. Merck, Sharp & Dohme Research Laboratories (West Point, PA). May 1991.
209. Bristol-Myers Squibb Research Institute (Princeton, NJ). May 1991.
210. International Conference on Biocatalysis (Orlando, FL). June 1991.
211. U.S. Army Research, Development and Engineering Center (Natick, MA). July 1991.
212. Gordon Conference on Natural Products (Plymouth, NH). July 1991.
213. Lederle-Praxis Biologicals Co. (Sanford, NC). July 1991.
214. International Biochemistry Congress (Jerusalem, Israel). August 1991.
215. American Chemical Society Meeting (New York, NY). August 1991.
216. International Enzyme Engineering Conference (Kona, HI). September 1991.

217. University of Lowell (Lowell, MA). October 1991.
218. Rutgers University (Piscataway, NJ). November 1991.
219. International Symposium on Enzymes in Organic Synthesis (New Delhi, India). January 1992.
220. International BioSymposium Nagoya '92 (Nagoya, Japan). January 1992.
221. International Symposium on Biomolecules in Organic Solvents (Taxco, Mexico). February 1992.
222. Rockefeller University (New York, NY). March 1992.
223. Symposium on Molecular Chirality of the Pharmaceutical Society of Japan (Tokyo, Japan). April 1992.
224. Conference on Enzymes in Organic Chemistry of the Dutch Chemical Society (Wageningen, The Netherlands). April 1992.
225. International Symposium on Bioprocessing of Coal (Clearwater Beach, FL). May 1992.
226. Exxon Workshop on New Leads in Coal Depolymerization (Montgomery, TX). May 1992.
227. Italian Symposium on Biochemical Biotechnology (Capri, Italy). June 1992.
228. Gordon Conference on Biocatalysis (Meriden, NH). July 1992.
229. FEBS Meeting (Dublin, Ireland). August 1992.
230. International Biotechnology Symposium (Washington, DC). August 1992.
231. International Symposium Bio Japan '92 (Yokohama, Japan). August 1992.
232. Texas College of Osteopathic Medicine (Fort Worth, TX). October 1992.
233. Rutgers University (Newark, NJ). October 1992.
234. Schering-Plough Co. (Bloomfield, NJ). November 1992.
235. International Symposium ISOPOW -V: *Properties of Water in Foods* (Peniscola, Spain). November 1992.

236. Carlsberg Laboratory (Copenhagen, Denmark). November 1992.
237. International Food Technology Conference (The Hague, The Netherlands). November 1992.
238. Singapore Institute of Standards and Industrial Research (Singapore). November 1992.
239. Drew University (Madison, NJ). December 1992.
240. Northeastern University (Boston, MA). January 1993.
241. Ciba Corning Diagnostics Corp. (Irvine, CA). January 1993.
242. University of Kansas (Lawrence, KS). January 1993.
243. 6th International Symposium on Recent Advances in Drug Delivery Systems (Salt Lake City, UT). February 1993.
244. Pennsylvania State University (University Park, PA). March 1993.
245. Northwestern University (Evanston, IL). March 1993.
246. International Symposium on Technologies for the Production of Enantiomerically Pure Chemicals (Amelia Island, FL). March 1993.
247. Gordon Conference on Bioanalytical Sensors (Ventura, CA). March 1993.
248. Pharmaceutical Manufacturers Association Analytical R&D/Pharmaceutical Development Subsections Joint Annual Meeting (Lake Buena Vista, FL). April 1993.
249. University of Massachusetts Symposium on Breakthrough Technologies: *Paradigms for a New Century* (Amherst, MA). May 1993.
250. Parke-Davis Corp. (Ann Arbor, MI). May 1993.
251. NutraSweet Co. (Mt. Prospect, IL). June 1993.
252. IGT/GRI Workshop on Novel Concepts for the Production of Regio- and Stereospecific Compounds (Chicago, IL). June 1993.
253. Northeast Regional Meeting of the American Chemical Society (Boston, MA). June 1993.

254. Institute of Food Technologists' Biotechnology Meeting (Chicago, IL). July 1993.
255. Annual Meeting of Department of Energy's Biological and Chemical Technology Research Program Principal Investigators (Tiburon, CA). July 1993.
256. Allied-Signal Corp. (Des Plains, IL). July 1993.
257. American Chemical Society Meeting (Chicago, IL). August 1993.
258. University of Illinois at Urbana-Champaign (Urbana, IL). September 1993.
259. International Enzyme Engineering Conference (Deauville, France). September 1993.
260. Queens College (Flushing, NY). November 1993.
261. Exxon Chemical Research Meeting (Galveston, TX). November 1993.
262. Hoffmann-LaRoche Co. (Nutley, NJ). December 1993.
263. U.S.-Japan Symposium on Drug Delivery (Maui, HI). December 1993.
264. North Dakota State University (Fargo, ND). February 1994.
265. Annual Meeting of the American Institute for Medical and Biological Engineering (Washington, DC). March 1994.
266. Rhone-Poulenc Rorer Symposium on Visions in Chemistry (Collegeville, PA). May 1994.
267. International Flavors & Fragrances R&D (Union Beach, NJ). May 1994.
268. Istituto degli Ormoni (Milan, Italy). June 1994.
269. Gordon Conference on Enzymes, Coenzymes, and Metabolic Pathways (Meriden, NH). July 1994.
270. Annual Meeting of Department of Energy's Biological and Chemical Technology Research Program Principal Investigators (Denver, CO). July 1994.

271. William S. Johnson Symposium in Organic Chemistry (Stanford, CA). October 1994.
272. R.W. Johnson Pharmaceutical Research Institute (Spring House, PA). October 1994.
273. International Congress of Biochemical Engineering (Mexico City, Mexico). October 1994.
274. National University of Mexico (Mexico City, Mexico). October 1994.
275. DuPont Merck Pharmaceutical Co. (Deepwater, NJ). December 1994.
276. Symposium on Therapeutic Protein Production and Processing (Cambridge, MA). January 1995.
277. International Symposium on Biocatalysts for Flavor Production, BioFlavour '95 (Dijon, France). February 1995.
278. Institut Pasteur (Paris, France). February 1995.
279. Florida State University (Tallahassee, FL). March 1995.
280. Abbott Laboratories (North Chicago, IL). March 1995.
281. University of Maryland, Baltimore County (Baltimore, MD). March 1995.
282. University of California at San Diego (La Jolla, CA). April 1995.
283. Great Lakes Regional Meeting of the American Chemical Society (LaCrosse, WI). June 1995.
284. Gordon Conference on Bioorganic Chemistry (Andover, NH). June 1995.
285. Annual Meeting of Department of Energy's Biochemical and Chemical Technology Research Principal Investigators (Albuquerque, NM). July 1995.
286. International Symposium "Biocatalysis-95" (Suzdal, Russia). August 1995.
287. International Enzyme Engineering Conference (San Diego, CA). October 1995.

288. Symposium on Biomacromolecules: *From 3-D Structure to Applications* (Pasco, W A). October 1995.
289. Enzymol International Inc. (Columbus, OH). December 1995.
290. International Symposium PacifiChem '95 (Honolulu, HI). December 1995.
291. 3rd U.S.-Japan Symposium on Drug Delivery (Maui, HI). December 1995.
292. New England Section of the Society for Industrial Microbiology (Cambridge, MA). February 1996.
293. Brown University (Providence, RI). February 1996.
294. University of Pittsburgh (Pittsburgh, PA). February 1996.
295. Food Research Institute (Reading, England). March 1996.
296. International Symposium Chiral USA '96 (Boston, MA). May 1996.
297. BP Catalyst Colloquium (Uxbridge, England). June 1996.
298. International Symposium on Homogeneous Catalysis (Princeton, NJ). August 1996.
299. Juan March Foundation's International Workshop on Novel Biocatalysts (Madrid, Spain). March 1997.
300. University of Kentucky (Lexington, KY). April 1997.
301. Gordon Conference on Organic Reactions and Processes (Henniker, NH). August 1997.
302. Novo Nordisk Symposium on Protein Stability (Klampenborg, Denmark). August 1997.
303. International Enzyme Engineering Conference (Beijing, China). October 1997.
304. Biogen Inc. (Cambridge, MA). December 1997.
305. INBIO Europe'98 Conference on Advances in Industrial Biocatalysis (Amsterdam, The Netherlands). February 1998.

306. International Symposium on Stability and Stabilization of Biocatalysts (Córdoba, Spain). April 1998.
307. International Symposium on Protein Structure, Stability and Folding: *Fundamental and Medical Aspects* (Moscow, Russia). June 1998.
308. International Conference on Protein Stabilization (Leeds, England). June 1998.
309. University of Virginia (Charlottesville, VA). September 1998.
310. Danish Biotechnology Conference (Vejle, Denmark). May 1999.
311. International Conference on Biocatalysis and Biotransformation Biotrans '99 (Giardini Naxos, Italy). September 1999.
312. Annual Meeting of the American Association of Pharmaceutical Scientists (New Orleans, LA). November 1999.
313. Brandeis University (Waltham, MA). November 1999.
314. Rutgers University (Piscataway, NJ). March 2000.
315. Chiral USA 2000 Conference (Boston, MA). May 2000.
316. Land O'Lakes Conference on Solid-State Reactivity in Pharmaceutical Systems (Merrimac, WI). June 2000.
317. Agouron Pharmaceuticals Inc. (San Diego, CA). July 2000.
318. U.S. Patent and Trademark Office Technology Fair (Arlington, VA). July 2000.
319. 23rd Gulf Coast Chemistry Conference (Pensacola, FL). September 2000.
320. Avon Products (Suffern, NY). November 2000.
321. Procter & Gamble Co. (Cincinnati, OH). November 2000.
322. Flamel Technologies (Venissieux, France). December 2000.
323. BioVision 2001 International Conference (Lyon, France). February 2001.
324. 9th Baxter Science and Technology Symposium (Hyland, IL). May 2001.

325. International Symposium on Applications of Enzymes in Chemical and Biological Defense (Orlando, FL). May 2001.
326. International Conference on Applied Biocatalysis (Trondheim, Norway). June 2001.
327. PPG Industries (Allison Park, PA). August 2001.
328. University of Kansas (Lawrence, KS). August 2001.
329. Alkermes Inc. (Cambridge, MA). October 2001.
330. 6th U.S.-Japan Symposium on Drug Delivery Systems (Maui, HI). December 2001.
331. Acambis Inc. (Cambridge, MA). January 2002.
332. Baxter BioScience Co. (Duarte, CA). January 2002.
333. International Symposium on Challenges in Drug Discovery and Development in the 21st Century (Kolkata, India). March 2002.
334. National Institute of Standards and Technology (Gaithersburg, MD). April 2002.
335. Albany Molecular Research, Inc. (Mt. Prospect, IL). April 2002.
336. Institute for International Research Conference on Protein and Peptide Formulation Strategies for Drug Development and Delivery (San Francisco, CA). August 2002.
337. R&D Management Council Meeting of the Technical Association of the Pulp and Paper Industry (Cambridge, MA). November 2002.
338. DuPont Central R&D Center (Wilmington, DE). December 2002.
339. *ACTIVE*Pack 2003 Conference (Ponte Verde Beach, FL). February 2003.
340. International Symposium on Industrial Applications of Biocatalysis: *Chemical Development Issues* (Boston, MA). September 2003.
341. U.S. Army Workshop on Self-Decontaminating Materials and Multifunctional Coatings (Arlington, VA). October 2003.

- 342. British Royal Society Meeting on Biocatalysis in Alternative Media (London, England). December 2003.
- 343. National Autonomous University of Mexico (Mexico City, Mexico). March 2004.
- 344. Healthcare Research Initiative Workshop on the Effect of Radiofrequency Radiation on Pharmaceutical Product Quality (Cambridge, MA). June 2004.
- 345. Rensselaer Biotechnology Symposium on Biological Discoveries That Will Change the World (Troy, NY). September 2004.
- 346. Barnett International Conference: *The Consequences of Aggregation in Drug Development, Immunology, Quality Control, and Disease Genesis* (Philadelphia, PA). September 2004.
- 347. 4th Annual IBC Conference on Formulation Strategies for Protein Therapeutics (Boston, MA). October 2004.
- 348. U.S. Army Edgewood Chemical Biological Center (Aberdeen Proving Ground, MD). August 2005.
- 349. World Congress on Synthetic Receptors (Salzburg, Austria). September 2005.
- 350. International Conference “Celebrating 30 Years of Robert Langer’s Science” (Cambridge, MA). July 2006.
- 351. University of Montreal (Montréal, Québec, Canada). October 2006.
- 352. The Boeing Company Research Center (Everett, W A). December 2006.
- 353. Instrumentation Laboratory (Lexington, MA). December 2006.
- 354. Acambis Inc. (Cambridge, MA). January 2007.
- 355. 6th International Symposium on Industrial Microbiology and Biotechnology (Cambridge, MA). August 2007.
- 356. Scientific Conference on Chemical & Biological Defense Research (Timonium, MD). November 2007.
- 357. MIT Research and Development Conference (Cambridge, MA). November 2007.

358. Nanotech '2008 International Conference (Boston, MA). June 2008.
359. Materials Research Society Symposium (Boston, MA). December 2008.
360. Johnson & Johnson Research Briefing at MIT (Cambridge, MA). January 2009.
361. 3rd Annual Lyophilization Conference: *Ensuring Optimum Formulations for Pharmaceuticals and Biologics* (Boston, MA). February 2010.
362. DSM Corporate Research Center (Geleen, The Netherlands). June 2010.
363. Merck Serono Pharmaceutical Co. (Darmstadt, Germany). June 2010.
364. NanoFormulations '2010 International Conference (Stockholm, Sweden). June 2010.
365. Covidien Surgical Devices and Vascular Therapies Divisions (Cambridge, MA). October 2010.
366. World Lyophilization Summit (Cambridge, MA). May 2011.
367. Alvogen (Cambridge, MA). March 2012.
368. Colgate-Palmolive Co. (Cambridge, MA). April 2012.
369. FDA Parenteral Drug Association Glass Quality Conference (Washington, DC). June 2012.
370. University of Puerto Rico (Humacao, Puerto Rico). January 2013.
371. International Conference on Creating and Leveraging Intellectual Property in Developing Countries (Durban, South Africa – *via teleconference*). November 2013.
372. Northwestern University (Evanston, IL). April 2015.
373. FDA and Parenteral Drug Association Joint Regulatory Conference (Washington, DC). September 2016.
374. Annual Partnership Opportunities in Drug Delivery (PODD) Conference (Boston, MA). October 2017.