

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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INTAS PHARMACEUTICALS LTD.,

Petitioner

v.

ATOSSA THERAPEUTICS, INC.,

Patent Owner

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Case PGR2025-00043

Patent No. 12,071,391

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**EXPERT DECLARATION OF JASON McCONVILLE, Ph.D.**

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A. Claim 30 .....75

I, Jason McConville, Ph.D., do hereby declare:

## **I. Introduction**

1. I have been retained to provide my expert opinions on behalf of Intas Pharmaceuticals, Limited in support of a petition for post grant review of claims 1-44 of U.S. Patent No. 12,071,391 (“the 391 patent”; Ex. 1001), which challenges the validity of the 391 patent.

2. The opinions set out by this declaration are based on my education, knowledge and experience. I have considered the materials and items identified by this declaration.

## **II. Education and Professional Background**

3. My qualifications and credentials to testify as an expert in this case are set forth in my curriculum vitae (attached as Appendix A).

4. I am an Associate Professor of Pharmaceutics at the University of New Mexico College of Pharmacy and an Adjunct Professor at the University of Bonn, in the Department of Pharmaceutical Technology, in Bonn, Germany.

5. I received my Bachelor of Science, with Honours, in Applied Chemistry from Coventry University, in Coventry, United Kingdom in 1994. From 1994 to 1999, I was a Research Technician in Pharmaceutics at the Centre for Drug Formulation Studies at the University of Bath, in Bath, United Kingdom. My main

research project pertained to controlled-release drug delivery, and specifically hydrophilic gel formation and drug release.

6. I subsequently earned my Ph.D. in Pharmaceutics from the University of Strathclyde, in Glasgow, United Kingdom in 2002. My Ph.D. dissertation was titled “Pulsed-Release Drug Delivery and Development of the Time-Delayed Capsule.”

7. After earning my Ph.D., I was a Post-Doctoral Fellow at the University of Texas at Austin College of Pharmacy from 2002 to 2006.

8. In 2006, I joined the faculty at the University of Texas at Austin as an Assistant Professor of Pharmaceutics in the College of Pharmacy. I assumed my present positions at the University of New Mexico and the University of Bonn in 2012.

9. I am a member of several professional societies, including the American Association of Colleges of Pharmacy, the American Association of Pharmaceutical Scientists, and the International Pharmaceutical Excipients Council (IPEC) of the Americas. Additionally, I have served as a scientific advisor to the Respiratory Drug Delivery Conference in Arizona, 2012, as a scientific advisor to the IPEC Americas excipient conference from 2017-2019. Furthermore, in 2017 I also served as a reviewer for the conference proceedings at the 2017 Annual Meeting of the International Pharmaceutical Excipient Council, which included publications

on the use and functionality of a wide range of pharmaceutical excipients. Additionally, I have had a recurring role as scientific advisor to the Drug Delivery to the Lungs conference since 2016.

10. I have taught many courses related to pharmaceutical dosage form, design, and development. For example, I have taught biopharmaceutics and pharmacokinetics to pharmacy students since 2007, in a variety of different core pharmacy courses. As an overview, the course material includes instruction on all main routes of drug delivery and formulation, and includes oral delivery systems such as tablets, capsules formed of film compositions, and oral suspensions. I have also been an advisor to 28 graduate and Pharm.D. students and have been on the dissertation committee for 14 students.

11. I have performed practical-design, development and manufacturing work related to a wide variety of solid oral dosage forms over the last 25-plus years. Further, during my doctoral studies, I worked extensively with delayed drug-release formulations, which included coated capsule formulation designs to delay drug release for targeting to specific parts of the GI tract, such as the distal small intestine or colon. During the course of these studies, I looked extensively at the process of capsule coating, different excipients for capsule filling, and particularly the dissolution performance of delayed release capsules using standardized testing.

12. I have co-authored more than 60 articles, more than 130 abstracts, and many book chapters, including on the topics of oral-dosage design, formulation, and delivery. I have also been a session chair, an invited speaker, or workshop participant on more than 40 occasions, and have served as a Review Panel Member at the National Institutes of Health in 2011, 2017, and 2020.

13. I have acted as the editor of at least four special themed editions for journals, and serve on the editorial boards for journals *Inhalation*, and *Pharmaceutics*, and as an Associate Editor for *Drug Development and Industrial Pharmacy* I have also served, and currently serve, as a reviewer for several leading scientific journals, including *Drug Development and Industrial Pharmacy*, *European Journal of Pharmaceutical Sciences*, *European Journal of Pharmaceutics and Biopharmaceutics*, *International Journal of Pharmaceutics*, *Journal of Controlled Release*, *Journal of Pharmaceutical Sciences*, *Pharmaceutical Research*, and *Molecular Pharmaceutics*.

14. I have received various awards and recognition for my research, including an Annual Research Day Award for a presentation titled “Design and Evaluation of Pulsatile Drug Delivery Capsule” (University of Strathclyde, Glasgow, May 2001), an Outstanding Presentation Award for “Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets” (British Pharmaceutical Conference, Glasgow, United Kingdom, September 2001), a

Graduate/Post-Doc Award in Innovative Aspects of Oral Drug Delivery and Absorption for “Improved Dissolution Rate and Bioavailability through the Formation of a Highly Miscible Binary Mixture” (International Symposium on Controlled Release of Bioactive Materials, Miami, FL, June 2005), and a Best Resident and Research Presentation Award for “Aerosolized Itraconazole (ITZ) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*” (American College of Clinical Pharmacy Annual Meeting, 2006). Additionally, I have received three Research Presentation Awards for novel excipient use presentations from the International Pharmaceutical Excipients Council of the Americas (2009, 2012, and 2014). I have been invited to submit original papers to renowned pharmaceutical science peer-reviewed journals at least 18 times and have been invited to judge research at international conferences at least six times. Furthermore, I was selected as a Member of the Society for Teaching Excellence at the University of Texas at Austin in 2011, nominated for the University of Texas System Regents’ Outstanding Teaching Award in 2012, and received an Innovation Award for my work on controlled release thermally gelling polymeric systems.

15. I am a named inventor on thirteen patents or patent applications.

### III. Compensation

16. I am being compensated for the time I spend on this matter at my ordinary rate of \$700 per hour for expert consulting and \$900 per hour for expert testimony. I am reimbursed for my reasonable expenses incurred in connection with my work on this matter. My compensation does not depend on the opinions I offer or on the outcome of this proceeding or any other proceeding.

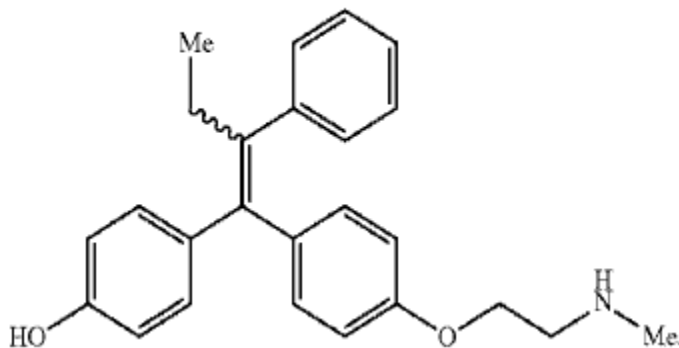
### IV. Background

17. The claims of the 391 patent are directed to compositions comprising a endoxifen (or a salt thereof) and an enteric material, where the composition is at least 90% by weight (Z)-endoxifen.

18. Endoxifen (4-hydroxy-N-desmethyltamoxifen) is a nonsteroidal selective estrogen receptor modulator. I understand that Intas sells endoxifen in India under the brand name Zonalta for the treatment of manic depressive disorder.

19. Endoxifen can be depicted as the below chemical structure, which is referred to as Formula (III) in the 391 patent:

Formula (III)



*See, e.g.*, Ex. 1001 at 3:6-22.

20. It was well-known in the art that “[e]ndoxifen exists as two forms, E and Z.” Ex. 1004 at [0004]. It was known in the art that (Z)-endoxifen is more active than (E)-Endoxifen at the estrogen receptor. *Id.* (Z)-endoxifen has been used in the treatment of breast cancer. *Id.* at [0003]. Methods of synthesizing highly pure (Z)-endoxifen were also well-known in the prior art. *See, e.g., id.* at [0076] (“The solid was dried in vacuo at 35 °C to a constant weight to give 1698 g (34%) of (Z)-endoxifen, with an isomeric purity of 99% (HPLC analysis).”)

21. Oral dosages of (Z)-endoxifen, salts of endoxifen, and the use of enteric materials were well-known in the art. For example, some drugs, including endoxifen, are subject to acid-catalyzed degradation under the acidic conditions of the stomach. Ex. 1003, 18:19-21. To prevent such degradation, enteric materials, such as coatings, capsules, or tablets, may be used to prevent release of the active ingredient in the stomach and instead delay release of the active substance until it reaches the intestines. Ex. 1003, 18:19-21; Ex. 1008, 83; Ex 1010, 34. Intas’s Zonalta endoxifen product is sold as Enteric coated tablets. Likewise, fillers, carriers, diluents, and other commonly used pharmaceutical substances were well known in the art.

## V. The 391 Patent

22. The 391 patent is entitled “Methods for Making and Using Endoxifen.” Ex. 1001 at Cover. I understand that the 391 patent was filed on March 30, 2023 and is a continuation of Application No. 18/090,757 (now USPN 11,680,036), which is a continuation of Application No. 17/580,428 (now USPN 11,572,334), which is a continuation of Application No. 16/641,985 (now USPN 11,261,151), and claims priority to Provisional Application No. 62/556,799, dated September 11, 2017. *Id.* I have been instructed to use September 11, 2017 as the time of invention, and to consider my opinions from the perspective of a person of skill at that time.

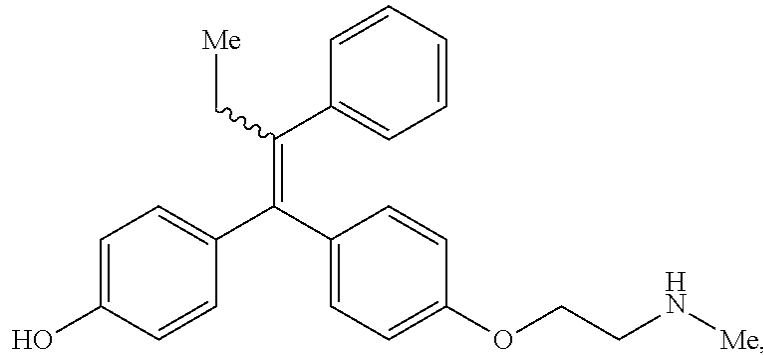
23. The 391 patent is directed to compositions of (Z)-endoxifen or (Z)-endoxifen salts and an enteric material and methods of administering such formulations.

24. I understand that the 391 patent contains the following 44 claims:

### **Independent claim 1 and dependent claims 2-31**

1. A composition comprising an endoxifen and an enteric material, wherein:  
the endoxifen comprises a compound of Formula (III):

Formula (III)



or a pharmaceutically acceptable salt thereof, and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.

2. The composition of claim 1, wherein the pharmaceutically acceptable salt is selected from the group consisting of an: arecoline, besylate, bicarbonate, bitartrate, butylbromide, citrate, camysylate, gluconate, glutamate, glycolylarsanilate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthanoate, isethionate, malate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, pamaoate (Embonate), pantothenate, phosphate/diphosphate, polygalacuronate, salicylate, stearate, sulfate, tannate, Teoate, triethiodide, benzathine, clemizole, chlorprocaine, choline, diethylamine, diethanolamine, ethylenediamine, meglumine, piperazine, procaine, aluminum, barium, bismuth, lithium, magnesium, potassium, and zinc salt.

3. The composition of claim 1, wherein the pharmaceutically acceptable salt of the compound of Formula (III) is endoxifen gluconate.

4. The composition of claim 1, wherein the composition is a delayed-release formulation.

5. The composition of claim 1, wherein the composition is a tablet.

6. The composition of claim 1, wherein the composition is a capsule.

7. The composition of claim 1, wherein the composition is uncoated.

8. The composition of claim 1, wherein the composition comprises an enteric coating.

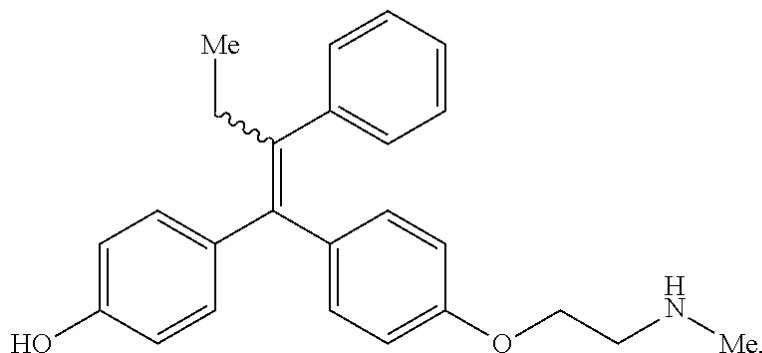
9. The composition of claim 1, wherein the composition is formulated as a suspension.
10. The composition of claim 9, wherein the suspension comprises a syrup or an elixir.
11. The composition of claim 9, wherein the suspension comprises a fluid.
12. The composition of claim 11, wherein the fluid comprises an alcohol.
13. The composition of claim 12, wherein the alcohol comprises ethanol.
14. The composition of claim 9, wherein the suspension comprises an alcohol, a plant oil, a mineral oil, a glycol, an agar, or a mixture thereof.
15. The composition of claim 9, wherein the suspension comprises ethanol, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.
16. The composition of claim 1, wherein the compound of Formula (III) is stable in the composition for at least 10 days at about 25° C.
17. The composition of claim 1, formulated such that the composition is resistant to dissolution in an acidic environment for at least 2 hours, as measured in a dissolution test performed according to a method of USP 711.
18. The composition of claim 1, formulated such that the composition releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.
19. The composition of claim 1, formulated such that the composition releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.
20. The composition of claim 1, wherein the composition further comprises hydroxypropylmethyl cellulose.

21. The composition of claim 1, wherein the composition further comprises a filler.
22. The composition of claim 21, wherein the filler comprises a sugar, salt, talc, calcium carbonate, microcrystalline cellulose, methyl cellulose, carboxymethyl cellulose, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinized starch, or combinations thereof.
23. The composition of claim 1, wherein the composition further comprises a disintegrant.
24. The composition of claim 1, wherein the composition further comprises a lubricant.
25. The composition of claim 24, wherein the lubricant comprises calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, ethyl oleate, ethyl laureate, agar, or combinations thereof.
26. The composition of claim 1, wherein the composition comprises from 0.01 mg to 200 mg (Z)-endoxifen.
27. The composition of claim 1, wherein the composition comprises from 1 mg to 20 mg of (Z)-endoxifen.
28. The composition of claim 1, wherein the composition comprises from 1 mg to 4 mg of (Z)-endoxifen.
29. The composition of claim 1, wherein the composition comprises 8 mg of (Z)-endoxifen.
30. A method of making the composition of claim 9, the method comprising suspending the endoxifen and the enteric material in a fluid.
31. The method of claim 30, wherein the fluid comprises an alcohol, ethanol, a plant oil, a mineral oil, a glycol, an agar, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.

**Independent claim 32 and dependent claims 33-44**

32. A method comprising administering to a subject a composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):

Formula (III)



or a pharmaceutically acceptable salt thereof; and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.

33. The method of claim 32, comprising administering 1 mg to 20 mg of (Z)-endoxifen.

34. The method of claim 32, comprising administering 1 mg to 4 mg of (Z)-endoxifen.

35. The method of claim 32, comprising administering 8 mg of (Z)-endoxifen.

36. The method of claim 32, wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level above 30 nM.

37. The method of claim 32, wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level from 30 nM to 300 nM.

38. The method of claim 32, further comprising releasing no more than 10% of the (Z)-endoxifen in a stomach of the subject within 2 hours following the administering of the composition.

39. The method of claim 32, further comprising releasing at least 50% of the (Z)-endoxifen in a small intestine of the subject within 8 hours following the administering of the composition.

40. The method of claim 32, further comprising producing an area under curve ( $AUC_{0-inf}$ ) of (Z)-endoxifen in the subject of from 200 hr\*ng/mL to 10,000 hr\*ng/ml per 4 mg of (Z)-endoxifen administered.

41. The method of claim 32, further comprising producing a maximum blood plasma concentration ( $C_{max}$ ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/ml per 4 mg of (Z)-endoxifen administered.

42. The method of claim 32, further comprising treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in the subject in need thereof.

43. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is a benign breast disorder, hyperplasia, atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, increased breast density, gynecomastia, ductal carcinoma in situ, lobular carcinoma in situ, breast cancer, precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.

44. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is tamoxifen-refractory or tamoxifen resistant.

## **VI. Person of Ordinary Skill in the Art**

25. I understand that the content of a patent (including its claims) and prior art should be interpreted the way a person of ordinary skill in the art (or “POSA”) would have interpreted the material at the time of the alleged invention. In my opinion, a POSA for purposes of the 391 patent is a person with a graduate degree in organic chemistry, medicinal chemistry, pharmaceutical chemistry, or a related

field, and four to six years of experience in the synthesis, purification, design, and/or formulation of pharmaceutical compounds and derivatives. A POSA would have worked with a team of professionals with training in related disciplines, such as pharmacology, pharmacokinetics, formulation, drug discovery and/or drug development as of the date of the claimed inventions.

26. I base my opinion on my review of the 391 patent, the problems the 391 patent was attempting to solve, the prior art discussed below, and my general experience with pharmaceutical synthesis and the people working in the field. I meet and/or exceed the definition of a POSA. I also note that my opinions would not change if the level of skill in the art were found to be lower.

## **VII. Claim Construction**

27. I understand that terms should be given their plain and ordinary meaning to a person of skill at the time of invention. I have applied this principle to all terms in the 391 patent.

## **VIII. Summary of the Prior Art**

### **A. US 9,333,190 (“Ahmad”)**

28. Ahmad “provides compositions containing endoxifen, formulations and liposomes of endoxifen, methods of preparation of such agents and formulations, and use of such agents and formulations for the treatment of breast cancer and other breast diseases and diseases susceptible to endoxifen.” Ex. 1003, Abstract. Ahmad teaches that “[o]ne object of the present invention is to provide E-

endoxifen or (Z)-endoxifen with at least 80% purity, such as at least 90% pure....”  
*Id.* at 12:14-17; *see also id.* at 2:24-40, 3:55-61. Ahmad teaches that such purity levels can be accomplished using crystallization or chromatography. *Id.* at 11:17-23. Ahmad further teaches that its compositions can be in the form of a pharmaceutically acceptable salt, and lists many examples of such salts. *Id.* at 2:24-30 (“In some embodiments, the endoxifen...is in the form of a salt.”), 8:47-63 (listing salts), 9:1-20 (same).

29. Ahmad also teaches that its compositions can include enteric materials. For example, Ahmad teaches that “[i]n some embodiments, the composition comprises a tablet or a filled capsule, wherein said tablet or filled capsule optionally comprises an enteric coating material.” *Id.* at 4:41-44. Ahmad explains that the “term ‘enteric’ refers to the small intestine, and enteric coatings prevent release of medication before it reaches the small intestine.” *Id.* at 18:19-26. As such, Ahmad teaches that the “composition containing endoxifen or endoxifen-lipid complex can be encapsulated in enteric-coated capsules to protect it from acids in the stomach.” *Id.* Ahmad further teaches that “[m]ost enteric coatings work by presenting a surface that is stable at acidic pH but breaks down rapidly at higher pH.” *Id.*

30. Thus, Ahmad teaches formulations of highly pure (Z)-endoxifen and an enteric material, for the treatment of breast cancer and other breast diseases.

**B. WO 2017/070651 (“Liu”)**

31. Liu describes that “[e]ndoxifen is frequently synthesized as a mixture of E and Z, with a difficult separation of isomers required to obtain pure Z isomer” and that “[s]ome procedures in the art separate the E and Z isomers via methods which are expensive and difficult to perform on larger scale, such as preparative HPLC.” Ex. 1004 at [0004]. “[T]here is a need in the art for a practical, scalable synthesis that gives access to highly pure (Z)-endoxifen.” *Id.*

32. Liu teaches methods for synthesizing and purifying (Z)-endoxifen with a 99% isomeric purity. *See, e.g., id.* at [0076]. In particular, Liu teaches: (i) synthesis followed by sequential recrystallizations, *id.* at [0021]-[0045], and (ii) synthesis followed by isomerization and sequential recrystallizations. *Id.* at [0046]-[0055]. In addition to detailed disclosure of the synthesis and purification approach, *see id.* at [0017]-[0059], Liu also provides specific examples, including experimental protocols, of the preparation of (Z)-endoxifen having 99% isomeric purity. *See id.* at [0062]-[0077]. Liu teaches that its “procedure provides a very attractive approach for obtaining the compound as it proceeds efficiently from commercially available starting materials and without the need of protection and de-protection steps.” *Id.* at [0005]. Liu’s procedure “avoids the use of chromatography in the separation of the Z- and E-isomers and enables facile scale-up operations in multi-kilogram quantities.” *Id.*

33. Liu also teaches that “[e]ndoxifen exists as two forms, E and Z, with the Z form more active at the estrogen receptor.” *Id.* at [0004].

**C. HANDBOOK OF PHARMACEUTICAL SALTS: PROPERTIES, SELECTION, & USE (P. Heinrich Stahl & Camille G. Wermuth eds., 1st ed., 2002) (“Stahl”)**

34. Stahl discloses commonly used pharmaceutical salts. Ex. 1005 at 334-45. Stahl provides a table including pharmaceutically acceptable salt-forming acids and bases. *Id.* at 331. Stahl also provides a ranking of “first, second, and third choice” for each acid and base listed. *Id.* Stahl describes that “first class salt-formers are those of unrestricted use...because they form physiologically ubiquitous ions, or because they occur as intermediate metabolites in biochemical pathways.” *Id.*

**D. Benameur, H., Capsule Technology, Enteric Capsule Drug Delivery Technology – Achieving Protection Without Coating, 15(5) DRUG DEV. & DELIVERY 34-37 (2015) (“Benameur”)**

35. Benameur teaches intrinsically enteric capsules that do not require a coating. Benameur teaches that the “major hurdle in oral delivery of many sensitive molecules, such as nucleotides, peptides, live biopharmaceutical products, and vaccines, is protecting the active entity from acidic and enzymatic degradation in the GI tract.” Ex. 1006 at 35. It further teaches that “[e]nteric capsule drug delivery technology (ECDDT) was developed to provide oral delivery with full enteric protection and rapid release in the upper gastrointestinal (GI) tract without the use of coatings.” *Id.* at 34. “ECDDT’s intrinsically enteric properties are attained by

incorporating pharmaceutically approved enteric polymers in the capsule shell using conventional pin-dipping capsule manufacturing processes.” *Id.* “The enteric properties and rapid release of specialized ECDDT capsule shells have been demonstrated to meet pharmacopeia standards for both in vitro and in vivo performance using esomeprazole magnesium trihydrate (EMT) as a model compound.” *Id.*

36. Benameur describes that “[i]n vivo results (Figure 2) showed that no pellets were released from ECDDT capsules in the stomach and that the capsule quickly opened in the small intestine 30 minutes from gastric emptying to the onset of drug release from the pellet dissolution.” *Id.* at 36.<sup>1</sup>

**E. Melgardt de Villiers, *Pharmaceutical Solvents & Solubilizing Agents*, in A PRACTICAL GUIDE TO CONTEMPORARY PHARMACY PRACTICE (3d ed., 2009) (“de Villiers”)**

37. De Villiers discloses various pharmaceutical excipients, including common solvents and liquid vehicles. Ex. 1007 at 190-91. De Villiers discusses different properties and uses for well-known excipients. *Id.* 191-202.

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<sup>1</sup> Such capsules are sold as Vcaps Enteric. <https://www.capsugel.com/biopharmaceutical-products/vcaps-enteric-capsules>. These capsules were released October 7, 2016. <https://www.capsugel.com/news/capsugel-launches-vcaps-enteric-capsules-for-enteric-protection-and-delayed>.

**F. Stegemann, S., *Hard gelatin capsules today–and tomorrow*, CAPSUGEL LIBRARY (2002) (“Stegemann”)**

38. Stegemann teaches that the “capsule is one of the oldest dosage forms in pharmaceutical history, known to the ancient Egyptians.” Ex. 1008 at 3. Stegemann further teaches both “[t]he production process” and the “[u]se of [e]xcipients” for capsules. Table 4 displays “Excipients used in formulations of immediate release hard gelatin capsules”:<sup>2</sup>

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<sup>2</sup> While this table is for immediate-release hard gelatin capsules, a POSA would understand that the same excipients are used for a delayed-release capsule where the delay is produced by a coating or the capsule material itself, rather than the excipients internal to the capsule. McConville, ¶¶ 48-49.

#### Diluents

---

→ Improved plug formation and compression

- Mannitol
- Lactose
- Corn starch
- Microcrystalline cellulose
- Starch 1500

#### Lubricants

---

→ Improved flow properties and reduced powder adhesion to metal parts

- Magnesium stearate
- Stearic acid
- Glyceryl monostearate

#### Glidants

---

→ Improved powder flow properties

- Aerosil
- Talcum

#### Disintegrants

---

→ To ensure disintegration of powder mixture

- Croscarmellose
- Crospovidone
- Sodium glycol starch
- Corn starch
- Starch 1500
- Alginic acid

#### Wetting agents

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→ Improved water penetration into powder mixture

- Sodium lauryl sulphate
- Tween 80

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Table 4: Excipients used in formulations of immediate-release hard gelatin capsules.

*Id.* at 8.

**G. HANDBOOK OF PHARMACEUTICAL EXCIPIENTS (Rowe, R., Sheskey, J. & Owen, S., eds., 5th ed., 2006) (the “HPE”)**

39. “The *Handbook of Pharmaceutical Excipients* is an internationally acclaimed reference work recognized as one of the most authoritative and comprehensive sources of information on excipients used in pharmaceutical formulation” which is “[j]ointly published by the American Pharmacists Association and the Pharmaceutical Press, the publications department of the Royal

Pharmaceutical Society of Great Britain.” Ex. 1009 at Back Cover. The HPE teaches the use of various pharmaceutical excipients.

**H. Cole, E., et al., *Enteric coated HPMC capsules designed to achieve intestinal targeting*, 231 INTL J. PHARMACEUTICS 83-95 (2002) (“Cole”)**

40. Cole teaches the use of enteric coated capsules. Cole teaches that “[e]nteric coated products are designed to remain intact in the stomach and then to release the active substance in the upper intestine” and that “the reasons for using enteric coated preparations are well documented.” Ex. 1010 at 83. Cole explains that “[t]he polymers commonly used to achieve enteric properties are anionic polymethacrylates (copolymerisate of methacrylic acid and either methylmethacrylate or ethyl acrylate (Eudragit®), cellulose based polymers, e.g. cellulose acetate phthalate (Aquatec®) or polyvinyl derivatives, e.g. polyvinyl acetate phthalate (Coateric®).” *Id.* Cole notes that “site specific delivery into the upper intestine has been achieved for many years by the use of pH-sensitive coatings...” *Id.* at 84. While capsules were traditionally made from gelatin, Cole notes that “HPMC capsules have been available commercially...for approximately 10 years.” *Id.*

41. Cole “describe[d] the manufacture of two different Eudragit® coated HPMC capsules and their in vitro/in vivo performance.” *Id.* at 84. Cole found that no drug “was released over 2 h at pH 1.2 from the capsules coated with 6 and 8 mg

cm<sup>-2</sup> Eudragit® L 30 D-55” while at “pH 6.8 release of paracetamol was rapid....”

*Id.* at 89.

**I. ALLEN & ANSEL, ANSEL’S PHARMACEUTICAL DOSAGE FORMS & DRUG DELIVERY SYSTEMS (10th ed. 2013) (“Ansel”)**

42. I understand that the Tenth Edition of Ansel was published in 2013 and is therefore prior art to the 391 patent. Ex. 1030.

43. Ansel is well known to those of skill in the art as a go-to guide to learn about various pharmaceutical dosage forms and drug delivery systems. Ansel includes a chapter on dosage form design, which provides advantages and disadvantages of different dosage forms, describes mechanisms of drug degradation, and summarizes approaches to stabilize drugs in pharmaceutical dosage forms. *Id.*

**J. SHARGEL, LEON & YU, ANDREW, APPLIED BIOPHARMACEUTICS & PHARMACOKINETICS (7th ed. 2016) (“Shargel”)**

44. Shargel was published and publicly available in 2016 and thus is prior art to the 391 patent. Ex. 1029 at iv.

45. Shargel explains that “pharmacokinetics is the science of the kinetics of drug absorption, distribution, and elimination (ie, metabolism and excretion).” *Id.* at 4. Shargel further explains that “pharmacokinetics involves the development of pharmacokinetic models that predict drug disposition after drug administration” and is used to “design[] and predict[] optimal dosing regimens for individuals or groups of patients.” *Id.* Shargel states that “recommended dosage regimens produce the

desired pharmacologic response in the majority of the anticipated patient population.” *Id.* at 5.

**K. WO 2011/107855 (“Gandhi”)**

46. Gandhi teaches a “stable, sustained release oral liquid suspension dosage form of pharmaceutical active ingredients...” Ex. 1022 at Abstract. In particular, Gandhi teaches an active ingredient and an enteric material (*e.g.*, a “rate controlling polymer”) suspended in an aqueous or non-aqueous media, and a process of preparing such a suspension. *See id.* at 13:16-14:5.

**L. Ahmad, A. et al., *Endoxifen, a New Cornerstone of Breast Cancer Therapy: Demonstration of Safety, Tolerability and Systemic Bioavailability in Healthy Human Subjects*, 88(6) CLIN. PHARMACOLOGY & THERAPEUTICS 814-817 (2010) (“Ahmad 2010”)**

47. Ahmad 2010 discloses pre-clinical trials of endoxifen showing that it is likely to be a safe and effective treatment for breast cancers. Ahmad 2010 reports on a study “demonstrating that single oral doses of endoxifen are safe and well tolerated and have sufficient bioavailability to reach systemically effective levels in human subjects” for treatment of breast cancer. *Id.* Ahmad 2010 concluded that “multiple daily endoxifen doses of 2.0-4.0 mg will result in endoxifen exposures that would be similar to those found in patients with normal CYP2D6 function who are administered tamoxifen at 20 mg/day,” or, in other words, “a dose of 4 mg of endoxifen should be appropriate for breast cancer prevention and therapy.” *Id.* at 816. In summary, the authors “propose that substitution of endoxifen for tamoxifen

will provide an improved approach toward treating patients with breast cancer because it bypasses the CYP2D6 enzyme that is required for metabolic activation of tamoxifen” and “[c]onsequently, its activity is not likely to be affected by either CYP2D6 genetic polymorphisms or drug-drug interactions that inhibit CYP2D6 activity.” *Id.*

M. Ahmad, A. et al., *Endoxifen for breast cancer: Multiple-dose, dose-escalation study characterizing pharmacokinetics and safety in metastatic breast cancer patients*, ASCO MEETING LIBRARY, presented June 4, 2012 (“Ahmad 2012”)

48. Ahmad 2012 discloses pre-clinical trials of endoxifen showing that it is likely to be a safe and effective treatment for breast cancers. Ahmad 2012 was presented by the first named inventor on the Ahmad patent. *Compare Ex. 1012 with Ex. 1003.* Ahmad 2012 disclosed that the group’s “preclinical studies (Breast Cancer Treat 122, 579-584, 2010) have validated the concept of using endoxifen for the treatment of breast cancer.” Ex. 1012 at 1. Ahmad 2012 disclosed test results showing that “the single oral doses tested up to 4 mg of endoxifen were safe, well tolerated and bioavailable” *Id.* Ahmad 2012 concludes that “[m]ultiple daily endoxifen doses of 4.0-8.0 mg resulted in endoxifen exposures that would be sufficient for effective therapy.” *Id.* at 2.

## **IX. Motivation to Combine the References**

49. I have been informed that a claim is not novel or non-obvious if the elements of the claim were known in one or more prior art references and a POSA

would have had a motivation to combine these references and a reasonable expectation of success at arriving at the claimed invention. I have also been informed that the motivation to combine can be found in the knowledge of a POSA and the state of the art. At least for the reasons set forth below, it is my opinion that a POSA would have been motivated to independently arrive at the claimed invention. Further, a POSA would have had a reasonable expectation of success at least because (i) the therapeutic advantages of Z-endoxifen over tamoxifen were well-known; (ii) the use of enteric materials, fillers, lubricants, disintegrants, and other pharmaceutical excipients was well known; and (iii) known synthesis methods at the time of the invention resulted in the claimed, inherent properties of Z-endoxifen. The claims do nothing to improve upon the then state of the art.

50. Indeed, at least as early as December 2010, tamoxifen was a crucial element of the treatment regimen for patients with hormone receptor–positive breast cancer. Ex. 1011 at 814; *see also* Ex. 1004 at [0003]. Tamoxifen, when orally administered, was extensively metabolized by cytochrome P450 (CYP) enzymes into active metabolites, including afimoxifene (4-hydroxy tamoxifen) and endoxifen (4-hydroxy N-desmethyl tamoxifen). Ex. 1011 at 814; *see also* Ex. 1004 at [0003]. Some patients did not respond to tamoxifen treatment because they did not produce adequate amounts of afimoxifen and endoxifen, sometimes due to low levels of the metabolizing enzymes. Ex. 1011 at 814; Ex. 1004 at [0003]. Separately,

coadministration of antidepressants significantly affected survival in women receiving tamoxifen for breast cancer because of drug-drug interactions. Ex. 1011 at 814 (“CYP2D6 is inhibited by specific selective serotonin reuptake inhibitors that are frequently used to prevent the hot flushes experienced by up to 45% of patients taking tamoxifen.”).

51. Studies revealed that after a single dose of 4 mg, a  $C_{max}$  of 15.1 ng/ml was observed. *Id.* at 816. Based on the results of this study, there was a reasonable expectation of success that multiple daily endoxifen doses of 2.0-4.0 mg would result in endoxifen exposures that would be similar to those found in patients with normal CYP2D6 function who were administered tamoxifen at 20 mg/day. *Id.* That is, a dose of 4 mg of endoxifen would be appropriate for breast cancer prevention and therapy. *Id.* A single daily dose is a most preferred dosing regimen because it improves patient compliance.

52. Z-endoxifen was known to be more active at the estrogen receptor. Ex. 1004 at [0004]. Accordingly, a POSA would be motivated to create a dosage form comprising a high percentage of Z-endoxifen (*e.g.*, a formulation with a high isomeric purity of Z-endoxifen). Prior art reference Ahmad discloses compositions and formulations comprising endoxifen where over 90% by weight is Z-endoxifen, *see* Ex. 1003 at 12:14-17, and prior art reference Liu describes methods of formulating pure forms of Z-endoxifen. Ex. 1004 at [0076]. Other prior art

references, such as Benameur, de Villiers, and Cole, teach the use of common pharmaceutical additives like enteric materials and excipients. *See, e.g.*, Ex. 1006; Ex. 1007; Ex. 1010.

**X. Claims 1, 2, 4-6, 8, 9, 11-15, 20, 23, 26-37, and 40-44 Over Ahmad**

**A. Claim 1**

53. Claim 1 presents identical issues of patentability to claim 1 of the 334 patent that was found unpatentable by the Board in IPR2023-00043. For example, both claims recite endoxifen in the form of Formula (III), an enteric material, and that at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen. *Compare* Ex. 1001, Claim 1, *with* Ex. 1023, Claim 1. An annotated comparison chart highlighting the similarities of the two claims is below.

391 Patent	334 Patent (Unpatentable)
<p>1. A composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <div data-bbox="326 1402 704 1593" style="text-align: center;"> <p>Formula (III)</p> </div> <p>or a pharmaceutically acceptable salt thereof, and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>	<p>1. An oral formulation comprising an endoxifen composition encapsulated in an enteric capsule, wherein the endoxifen composition comprises a compound of Formula (III):</p> <div data-bbox="943 1402 1321 1593" style="text-align: center;"> <p>Formula (III)</p> </div> <p>wherein at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>

*A composition comprising an endoxifen and an enteric material,*

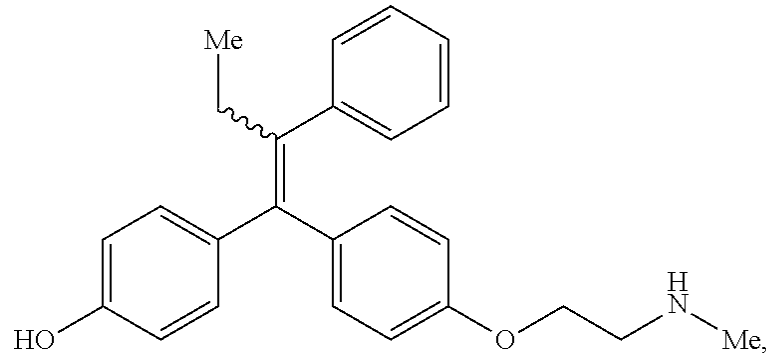
54. Ahmad is titled “Endoxifen compositions and methods” and “provides compositions containing endoxifen.” Ex. 1003 at Title, Abstract. Ahmad further teaches that “[w]hen desired, [the] composition containing endoxifen or endoxifen-lipid complex can be encapsulated in enteric-coated capsules to protect it from acids in the stomach.” *Id.*, 18:19-21. Ahmad explains that the “enteric coatings prevent release of medication before it reaches the small intestine.” *Id.* at 18:22-24. It further teaches that “[m]ost enteric coatings work by presenting a surface that is stable at acidic pH but breaks down rapidly at higher pH.” *Id.* at 18:24-26. It finally notes that “[e]nteric coating of capsules filled with compositions containing endoxifen can be done as methods known in the art.” *Id.* at 18:27-29. Thus, Ahmad teaches compositions comprising endoxifen and an “enteric material.”

55. A POSA would have known how to formulate the compositions of Ahmad with an enteric material, as the use of enteric materials was well known in the art. For example, Cole explains that “site specific delivery into the upper intestine has been achieved for many years by the use of pH-sensitive coatings...” Ex. 1010 at 84. Cole teaches that “[e]nteric coated products are designed to remain intact in the stomach and then to release the active substance in the upper intestine” and that “the reasons for using enteric coated preparations are well documented.” *Id.* at 83. Cole describes numerous polymers used to achieve this delayed-release effect: “[t]he

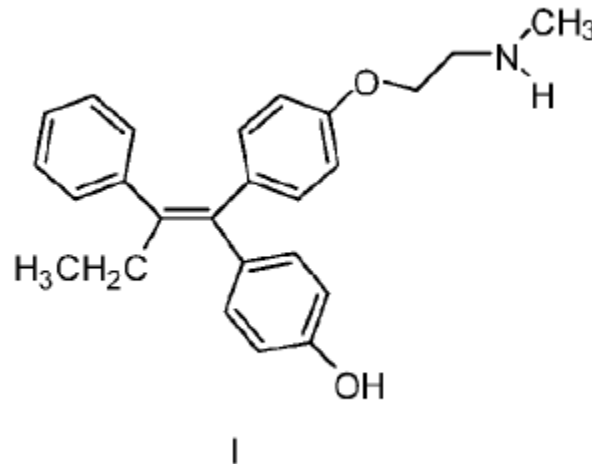
polymers commonly used to achieve enteric properties are anionic polymethacrylates (copolymerisate of methacrylic acid and either methylmethacrylate or ethyl acrylate (Eudragit®), cellulose based polymers, e.g. cellulose acetate phthalate (Aquateric®) or polyvinyl derivatives, e.g. polyvinyl acetate phthalate (Coateric®).” *Id.* at 83. The 391 patent also describes the use of these same, well-known polymers for this purpose. *See* Ex. 1001 at 39:22-51 (describing EUDRAGIT L and S copolymers as “pH dependent polymers” that “target upper small intestines and colon”); *see also* Ex. 1001 at 84:61-67, 85:45-49 (examples using Eudragit FS D30 and Eudragit L30 D55 as enteric materials). Other enteric capsules were also well known. *See, e.g.* Ex. 1009 at 899 (HPE listing numerous “Enteric formulations/coating agents”).

*wherein: the endoxifen comprises a compound of Formula (III):*

Formula (III)



56. As discussed, Ahmad's compositions comprise endoxifen. Endoxifen is the compound depicted in Formula III of the 391 patent. Ahmad depicts the same chemical structure for endoxifen (though depicted slightly differently):



Ex. 1003 at Cover, Figure 1.

*or a pharmaceutically acceptable salt thereof,*

57. Ahmad teaches that its formulations of (Z)-endoxifen can include a salt of (Z)-endoxifen. Ahmad discloses that “[i]n some embodiments, the endoxifen . . . is in the form of a salt.” Ex. 1003 at 2:24-26; *see also id.* at Claim 1. Ahmad

provides examples of such pharmaceutically acceptable salts, such as, “acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, flucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, chloride, bromide, iodide, 2-hydroxyethanesulfonate, lactate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, palmoate, pectinate, persulfate, phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, undecanoate, and the like” as examples of salts. *Id.* at 8:47-63, 9:1-20.

***and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen***

58. Ahmad teaches that “[o]ne object of the present invention is to provide E-endoxifen or Z-endoxifen with at least 80% purity, such as at least 90% pure or at least 95% pure or at least 98% pure or at least 99% pure or at least 100% pure.” *Id.* at 12:14-17; *see also id.* at 2:24-40, 3:55-61. Ahmad teaches that this can be accomplished using crystallization or chromatography. *Id.* at 11:17-23. Thus, Ahmad teaches “wherein at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.”

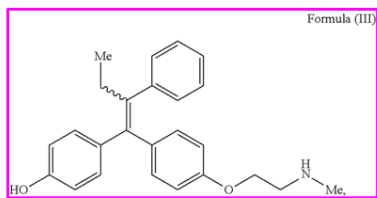
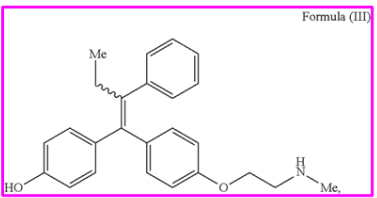
59. Ahmad also provides significant teachings relevant to obtaining 90% (Z)-endoxifen and forming pure (Z)-endoxifen was known in the art as taught by, for example, Liu and Fauq. *See, e.g.,* Ex. 1004 at [0076]; Ex. 1013 at [92]-[94], [97]-

[98]. For example, Liu teaches how to take a 50/50 E/Z mixture and achieve 90% (Z)-isomer by crystallization and/or isomerization. Ex. 1004 at [0072]-[0075]. Fauq teaches how to make highly pure (Z)-endoxifen by chromatography (as does Milroy). Ex. 1013; Ex. 1014. A POSA would have followed these teachings before the date of the 391 patent without undue experimentation. In fact, Dr. Bihovsky carried out the synthesis and purification of Liu and readily obtained purities in excess of 90%. Bihovsky, ¶¶X (explaining how he carried out Liu's teachings to form (Z)-endoxifen with 100% (recrystallization) and 93% (isomerization followed by recrystallization) isomeric purity, respectively). Thus, a POSA would have been able to make Ahmad's invention prior to the 391 patent.

60. As detailed above, Ahmad discloses all of the elements of claim 1.

## B. Claim 32

61. Claim 32 presents identical issues of patentability to claim 15 of the 334 patent that was found unpatentable by the Board. Both claims recite endoxifen in the form of Formula (III), an enteric material, and that at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen. Compare Ex. 1001, Claim 32, with Ex. 1023, Claim 15. An annotated comparison chart highlighting the similarities of the two claims is below.

391 Patent	334 Patent (Unpatentable)
<p>32. A method comprising administering to a subject a composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <div data-bbox="321 1108 695 1304" style="text-align: center;"><p>Formula (III)</p></div> <p>or a pharmaceutically acceptable salt thereof; and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>	<p>15. A method of delivering (Z)-endoxifen to a subject, the method comprising administering to the subject an oral formulation comprising an endoxifen composition encapsulated in an enteric capsule, wherein the endoxifen composition comprises a compound of Formula (III):</p> <div data-bbox="938 1192 1312 1388" style="text-align: center;"><p>Formula (III)</p></div> <p>wherein at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>

***32. A method comprising administering to a subject a composition comprising an endoxifen and an enteric material, wherein:***

***the endoxifen comprises a compound of Formula (III) or a pharmaceutically acceptable salt thereof;***

62. and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen. As discussed above with respect to claim 1, Ahmad discloses a composition comprising an endoxifen and an enteric material, wherein the endoxifen comprises a compound of Formula (III) or a pharmaceutically acceptable salt thereof, and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen. Claim 32 recites a “method comprising administering to a subject” a composition that is identical to the composition recited in claim 1.

63. Ahmad teaches administering such a composition to a subject. For example, Ahmad discloses “methods for treating and preventing breast cancer and other breast related diseases by administering novel formulations or compositions comprising a therapeutically effective amount of endoxifen.” Ex. 1003 at Abstract; *see also id.*, 19:27-30 (“[C]ompositions of the present invention may be administered in any dosage form and via any system that delivers the active compound endoxifen to breast estrogen receptors in vivo.”).

### C. Claim 2

**2. The composition of claim 1, wherein the pharmaceutically acceptable salt is selected from the group consisting of an: arecoline, besylate, bicarbonate, bitartrate, butylbromide, citrate, camysylate, gluconate, glutamate, glycolylarsanilate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthanoate, isethionate, malate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, pamaoate (Embonate), pantothenate, phosphate/diphosphate, polygalacuronate, salicylate, stearate, sulfate, tannate, Teoclate, triethiodide, benzathine, clemizole, chlorprocaine, choline, diethylamine, diethanolamine, ethylenediamine, meglumine, piperazine, procaine, aluminum, barium, bismuth, lithium, magnesium, potassium, and zinc salt.**

64. Ahmad discloses that its composition of highly pure (Z)-endoxifen can be in the form of a salt. As such, Ahmad teaches various pharmaceutically acceptable salts, including, for example, citrate, phosphate, sulfate, and digluconate. Ex. 1003, 9:1-16. Ahmad further teaches that pharmaceutically acceptable salts may be derived from acids including “hydrochloric, hydrobromic, sulfuric, nitric, perchloric, fumaric, maleic, phosphoric, glycolic, lactic, salicylic, succinic, toluene-psulfonic, tartaric, acetic, citric, methanesulfonic, ethanesulfonic, formic, benzoic, malonic, sulfonic, naphthalene-2-sulfonic, benzenesulfonic acid, and the like.” *Id.*, 8:52-59.

### D. Claims 4 and 8

65. Claims 4 and 8 present identical issues of patentability to claims 2 and 4 of the 334 patent that were found unpatentable by the Board. A comparison chart showing the similarities of the claims is below.

391 Patent	334 Patent (Unpatentable)
4. The composition of claim 1, wherein the composition is a delayed-release formulation.	2. The oral formulation of claim 1, wherein the oral formulation is a delayed-release formulation.
8. The composition of claim 1, wherein the composition comprises an enteric coating.	4. The oral formulation of claim 1, wherein the enteric capsule further comprises an enteric coating.

***4. The composition of claim 1, wherein the composition is a delayed-release formulation.***

66. As described above, Ahmad discloses an enteric coated capsule. Ahmad explains that the described enteric capsule is designed to prevent release of the drug throughout its time in the stomach until it reaches the intestine. Ex. 1003 at 18:22-24. A POSA would understand this description of Ahmad to teach a delayed-release formulation.

***8. The composition of claim 1, wherein the composition comprises an enteric coating.***

67. As described above, Ahmad discloses an enteric coated capsule such that the capsule does not release drug throughout its time in the stomach. Thus, Ahmad teaches the use of an enteric coating.

**E. Claims 5 and 6**

***5. The composition of claim 1, wherein the composition is a tablet.***

68. Ahmad teaches that “[e]xemplary routes of administration...can be through the...mouth (oral)...” Ex. 1003, 7:43-45. Ahmad further discloses “[p]harmaceutical preparations that find use with the compositions of the present

invention include but are not limited to tablets, capsules, pills” and that “[f]or the oral mode of administration, preferred forms of endoxifen...include tablets, capsules....” Ex. 1004, 18:1-6. Thus, Ahmad teaches oral administration of highly pure (Z)-endoxifen.

***6. The composition of claim 1, wherein the composition is a capsule.***

69. As discussed, Ahmad teaches oral administration of highly pure (Z)-endoxifen, including as “tablets, capsules, [and] pills.” Ex. 1004, 18:1-6.

**F. Claims 9, 11-15, 30, and 31**

***9. The composition of claim 1, wherein the composition is formulated as a suspension.***

70. Ahmad discloses that “[p]harmaceutical preparations that find use with the compositions of the present invention include...suspensions....” Ex. 1003, 18:1-4. Thus, Ahmad teaches a composition of highly pure (Z)-endoxifen formulated as a suspension.

***11. The composition of claim 9, wherein the suspension comprises a fluid.***

71. As discussed, Ahmad teaches that (Z)-endoxifen can be administered as a suspension. Ahmad describes that its suspension includes a fluid. For example, Ahmad describes “suspending endoxifen and lipids together in an aqueous solution, e.g., water.” Ex. 1003, 16:53-55. An “aqueous solution” is a fluid.

72. Plus, a suspension necessarily includes a fluid. *See, e.g., Oral Suspension*, MERRIAM-WEBSTER, available from <https://www.merriam->

webster.com/medical/oral%20suspension#:~:text=noun,liquid%20vehicle%20for%20oral%20administration (last accessed January 3, 2025) (“[U]ndissolved particles of one or more medicinal agents mixed with a liquid vehicle for oral administration”).

***12. The composition of claim 11, wherein the fluid comprises an alcohol.***

***14. The composition of claim 9, wherein the suspension comprises an alcohol, a plant oil, a mineral oil, a glycol, an agar, or a mixture thereof.***

73. Ahmad teaches that “the composition of [the] invention containing endoxifen may also contain one or more nonaqueous vehicles, such as alcoholic vehicles.” Ex. 1003, 20:63-65. The “alcoholic vehicle” described by Ahmad would be used as a fluid for the suspension containing (Z)-endoxifen taught by Ahmad. Thus, Ahmad teaches that its composition of (Z)-endoxifen can include an alcoholic vehicle.

***13. The composition of claim 12, wherein the alcohol comprises ethanol.***

***15. The composition of claim 9, wherein the suspension comprises ethanol, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.***

***31. The method of claim 30, wherein the fluid comprises an alcohol, ethanol, a plant oil, a mineral oil, a glycol, an agar, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.***

74. Ahmad teaches that its composition of (Z)-endoxifen can include an alcoholic vehicle such as ethanol. Ex. 1003, 20:65-67 (“Examples of nonaqueous vehicles include ethyl acetate, ethanol, and isopropanol, preferably ethanol and

isopropanol.”). The “alcoholic vehicle” of ethanol described by Ahmad would be used as a fluid for the suspension containing (Z)-endoxifen taught by Ahmad.

75. Ahmad also discloses the use of “sodium lauryl sulfate” as a “pharmaceutically acceptable carrier.” *Id.* at 8:31-40. A POSA would understand that a “pharmaceutically acceptable carrier” taught by Ahmad would be used as a fluid for the suspension containing (Z)-endoxifen.

**G. Claims 20 and 23**

***20. The composition of claim 1, wherein the composition further comprises hydroxypropylmethyl cellulose.***

76. Ahmad teaches that a capsule of its (Z)-endoxifen composition can include a gelling agent such as “hydroxypropyl methyl cellulose (HPMC).” Ex. 1003, 21:31-36. Thus, Ahmad teaches that its compositions can include hydroxypropylmethyl cellulose.

***23. The composition of claim 1, wherein the composition further comprises a disintegrant.***

77. Ahmad teaches that its disclosure of a “pharmaceutical composition” refers to the combination of an active agent with a carrier. Ex. 1003, 8:15-20. Ahmad further teaches that a “pharmaceutically acceptable carrier” “refers to any of the standard pharmaceutical carriers including...disintegrants [sic] (e.g., potato starch or sodium starch glycolate)....” Ex. 1003, 8:31-38.

**H. Claims 26-29 and 33-35**

**26. The composition of claim 1, wherein the composition comprises from 0.01 mg to 200 mg (Z)-endoxifen.**

**27. The composition of claim 1, wherein the composition comprises from 1 mg to 20 mg of (Z)-endoxifen.**

**33. The method of claim 32, comprising administering 1 mg to 20 mg of (Z)-endoxifen.**

78. Ahmad discloses doses of 1 to 10 mg/day of endoxifen. Ex. 1004, 29:20-31 (“[O]ral doses of endoxifen (1 mg-10 mg/day) with biculatamide [sic] are expected to prevent development of biclutamide-induced [sic] gynecomastia and breast pain.”). Thus, Ahmad discloses doses of highly pure (Z)-endoxifen within the claimed ranges.

**28. The composition of claim 1, wherein the composition comprises from 1 mg to 4 mg of (Z)-endoxifen.**

**29. The composition of claim 1, wherein the composition comprises 8 mg of (Z)-endoxifen.**

**34. The method of claim 32, comprising administering 1 mg to 4 mg of (Z)-endoxifen.**

**35. The method of claim 32, comprising administering 8 mg of (Z)-endoxifen.**

79. The claimed dosages overlap with Ahmad’s disclosed range. A POSA would not understand a reasonable difference in how (Z)-endoxifen operates over the claimed ranges. Indeed, Ahmad 2010 and Ahmad 2012 performed experimental studies using the claimed dosages of endoxifen, and found that dosages from 2 to 8 mg will likely be efficacious. Ex. 1011, 816 (“On the basis of these results, we

expect that multiple daily endoxifen doses of 2.0–4.0 mg will result in endoxifen exposures that would be similar to those found in patients with normal CYP2D6 function who are administered tamoxifen at 20 mg/day. That is, a dose of 4 mg of endoxifen should be appropriate for breast cancer prevention and therapy.”); Ex. 1012, 2 (“Multiple daily endoxifen doses of 4.0-8.0 mg resulted in endoxifen exposures that would be sufficient for effective therapy.”).

**I. Claims 36, 37, 40, and 41**

***36. The method of claim 32, wherein the administering of the composition maintains the subject’s plasma endoxifen at a steady state level above 30 nM.***

***37. The method of claim 32, wherein the administering of the composition maintains the subject’s plasma endoxifen at a steady state level from 30 nM to 300 nM.***

***40. The method of claim 32, further comprising producing an area under curve ( $AUC_{0-inf}$ ) of (Z)-endoxifen in the subject of from 200 hr\*ng/mL to 10,000 hr\*ng/ml per 4 mg of (Z)-endoxifen administered.***

***41. The method of claim 32, further comprising producing a maximum blood plasma concentration ( $C_{max}$ ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/ml per 4 mg of (Z)-endoxifen administered.***

80. Pharmacokinetics reflect the absorption, distribution, metabolism, and excretion of a particular drug at a certain dosage. See Ex. 1029 at 4 (explaining pharmacokinetics are used to “design[] and predict[] optimal dosing regimens for individuals or groups of patients.”); Ex. 1017 at Abstract (“Pharmacokinetics (PK) is the study of the time course of the absorption, distribution, metabolism and excretion (ADME) of a drug, compound or new chemical entity (NCE) after its

administration to the body.”). In this way, the pharmacokinetics are inherent properties of a particular drug. Indeed, “[a] single kinetic profile may be well summarized by  $C_{\max}$ ,  $T_{\max}$ ,  $t_{1/2}$  and AUC,” and that “the mean and standard deviation of these parameters, may well summarize the drug kinetics in the whole population.” Ex. 1018 at Abstract. As such, “recommended dosage regimens produce the desired pharmacologic response in the majority of the anticipated patient population.” Ex. 1029 at 5. Therefore, because Ahmad teaches the claimed composition of claim 32, Ahmad inherently teaches the pharmacokinetics recited in claims 36, 37, 40, and 41.

**J. Claims 42-44**

81. Claims 42-44 present identical issues of patentability to claims 20-22 of the 334 patent that were found unpatentable by the Board. A comparison chart showing the similarities of the claims is below.

<b>391 Patent</b>	<b>334 Patent (Unpatentable)</b>
42. The method of claim 32, further comprising treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in the subject in need thereof.	20. The method of claim 15, further comprising treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in the subject.
43. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is a benign breast disorder, hyperplasia, atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, increased breast density, gynecomastia, ductal carcinoma in situ, lobular carcinoma in situ, breast cancer, precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.	21. The method of claim 20, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is a benign breast disorder, hyperplasia, atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, increased breast density, gynecomastia, ductal carcinoma in situ, lobular carcinoma in situ, breast cancer, precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.
44. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is tamoxifen-refractory or tamoxifen resistant.	22. The method of claim 20, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is tamoxifen-refractory or tamoxifen resistant.

**42. The method of claim 32, further comprising treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in the subject in need thereof.**

82. Ahmad states that the “present invention also provides methods of inhibiting hormone-dependent breast carcinoma in a mammal...” Ex. 1003 at 5:33-36; *see also id.* at 18:47-52, 28:37-38 (teaching treatment of breast cancer and “other estrogen-sensitive conditions” such as benign breast disease). As such, Ahmad teaches that its formulations may be used to treat hormone-dependent breast disorders, and a method of treating a patient with “a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder.”

**43. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is a benign breast disorder, hyperplasia, atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, increased breast density, gynecomastia, ductal carcinoma in situ, lobular carcinoma in situ, breast cancer, precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.**

83. As described above, Ahmad teaches the use of its formulations for benign breast disorder, hyperplasia, gynecomastia, and breast cancer (among others). *See* Ex. 1003, Abstract (breast cancer), 18:54-60 (benign breast disorders, hyperplasia), 29:21-31 (gynecomastia). Thus, Ahmad teaches a method of treating a patient with the (Z)-endoxifen formulation, “wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is a benign breast disorder [or] hyperplasia....”

**44. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is tamoxifen-refractory or tamoxifen resistant.**

84. Tamoxifen had long been used to treat breast cancer. Ex. 1001 at Fig 1, 1:63-2:6; Ex. 1003 at Fig. 3, 1:35-56; Ex. 1004 at [0003]. It was also well-known in the art that endoxifen is a metabolite of tamoxifen. For example, Ahmad teaches that “[e]ndoxifen is generated via CYP3A4-mediated N-demethylation and CYP2D6 mediated hydroxylation of Tamoxifen.” Ex. 1003 at 1:57-59. It was also known that endoxifen could be used on patients who could not metabolize or had difficulty metabolizing tamoxifen. Such patients could be tamoxifen-refractory or tamoxifen-resistant. As Ahmad notes, “[u]se of endoxifen, e.g., in place of Tamoxifen, avoids several metabolic steps that rely on CYP2D6.” *Id.* at 2:2-5; *see also id.* at 1:64-2:20. Therefore, a POSA would understand that endoxifen would be expected to be efficacious in patients who were tamoxifen-resistant or tamoxifen-refractory due to metabolic deficiencies as discussed in Ahmad. As such, a POSA would understand Ahmad to teach a method of using its formulation for tamoxifen-refractory or resistant conditions.

**XI. Claims 1-6, 8, 9, 11-15, 20, 23, 26-37, and 40-44 Over Ahmad in View of the Knowledge of a POSA**

**A. Claims 1, 2, 4-6, 8, 9, 11-15, 20, 23, 30-32, and 42-44**

85. Although Ahmad discloses every element of claims 1-6, 8, 9, 11-15, 20, 23, 26-37, and 40-44 of the 391 patent, each of the elements of these claims were

also separately known and obvious in view of the knowledge of a POSA. For example, as discussed, it was well-known that that endoxifen is an active metabolite of tamoxifen, which has been used in the treatment of breast cancer. Ex. 1001 at Fig 1, 1:63-2:6; Ex. 1003 at Fig. 3, 1:35-56; Ex. 1004 at [0003]. It was also well-known that the (Z)-form of endoxifen is more active at the estrogen receptor. Ex. 1004 at [0004]. Thus, it was known to use endoxifen and/or endoxifen salts in the treatment of breast cancer. Ex. 1003 at 1:64-2:4; Ex. 1004 at [0003]; Ex. 1011; Ex. 1012. The use of enteric materials, suspensions, oral delivery, and excipients/additives was also well-known in the art. Ex. 1006; Ex. 1007; Ex. 1008; Ex. 1009; Ex. 1010.

86. In formulating compositions of (Z)-endoxifen, a POSA would have used target pharmacokinetics (such as those of tamoxifen and endoxifen as described by Ahamd 2010 and Ahmad 2012) to develop the claimed compositions before the date of the invention of the 391 patent. Creating such formulations would have been routine and within the skill of a POSA, and a POSA would have a reasonable expectation of success in doing so. Indeed, creating the claimed invention would have involved simply utilizing known, conventional, and predictable processes.

## **B. Claim 3**

***3. The composition of claim 1, wherein the pharmaceutically acceptable salt of the compound of Formula (III) is endoxifen gluconate.***

87. Ahmad teaches a composition of highly pure (Z)-endoxifen as a digluconate salt. Ex. 1003, 9:1-4. It would have been routine for a POSA to

formulate the highly pure (Z)-endoxifen composition of Ahmad as a gluconate salt (e.g., to form endoxifen gluconate) rather than a digluconate salt because it would have been easier to synthesize a gluconate salt of endoxifen than a digluconate salt of endoxifen. For example, because (Z)-endoxifen contains a basic amine group and typically forms a monocation (+1) under acidic conditions, it would have been more favorable to form a cation of endoxifen with a charge of +1 to form a monogluconate salt rather than a cation with a charge of +2 to form a digluconate salt, under such conditions. This is because forming a digluconate salt would require the protonation of two basic sites to achieve a +2 charge, which may not be feasible under standard conditions if (Z)-endoxifen has only one strongly basic site.

88. Additionally, a POSA would have been motivated to formulate endoxifen gluconate given Ahmad's description of endoxifen digluconate. Indeed, a gluconate salt is simply a salt containing two gluconate anions rather than a single gluconate anion.

89. Moreover, even without Ahmad's disclosure of a digluconate salt, the use of a gluconate salt in pharmaceutical compounds was well-known and a POSA would have been motivated to formulate endoxifen gluconate because gluconate salts were common, effective, and safe pharmaceutical salts. *See, e.g.*, Ex. 1005 at 334 (listing D-gluconic acid as a "class 1" preferred acid to form pharmaceutical salts).

90. Single anion salts of endoxifen were also well known in the art. For example, the prior art teaches the use of endoxifen citrate and endoxifen hydrochloride for the treatment of breast cancer and other disorders. *See, e.g.*, Ex. 1003 at 29:3-6 (experimental examples using endoxifen citrate); Ex. 1011 at 816 (same); Ex. 1028 (evaluating pharmacokinetics of endoxifen hydrochloride in mice for breast cancer treatment); Ex. 1023 (endoxifen citrate for bipolar disorder treatment).

91. Therefore, it would have been routine and conventional for a POSA to formulate Ahmad’s highly pure (Z)-endoxifen as a gluconate salt, and a POSA would have had a reasonable expectation of success in doing so.

**XII. Claim 3 Is Over Ahmad and Ahmad 2010/2012 in View of the Knowledge of a POSA**

**A. Claims 26-29 and 33-35**

92. Claim 26 presents identical issues of patentability to claim 14 of the 334 patent that were found unpatentable by the Board. A comparison chart showing the similarities of the claims is below.

391 Patent	334 Patent (Unpatentable)
26. The composition of claim 1, wherein the composition comprises from 0.01 mg to 200 mg (Z)-endoxifen.	14. The oral formulation of claim 1, wherein the endoxifen composition comprises from 0.01 mg to 200 mg (Z)-endoxifen per enteric capsule.

**26. The composition of claim 1, wherein the composition comprises from 0.01 mg to 200 mg (Z)-endoxifen.**

**27. The composition of claim 1, wherein the composition comprises from 1 mg to 20 mg of (Z)-endoxifen.**

**28. The composition of claim 1, wherein the composition comprises from 1 mg to 4 mg of (Z)-endoxifen.**

**29. The composition of claim 1, wherein the composition comprises 8 mg of (Z)-endoxifen.**

**33. The method of claim 32, comprising administering 1 mg to 20 mg of (Z)-endoxifen.**

**34. The method of claim 32, comprising administering 1 mg to 4 mg of (Z)-endoxifen.**

**35. The method of claim 32, comprising administering 8 mg of (Z)-endoxifen.**

93. As discussed, Ahmad discloses doses of 1 to 10 mg/day of endoxifen.

Ex. 1004, 29:20-31 (“[O]ral doses of endoxifen (1 mg-10 mg/day) with biclutamide [sic] are expected to prevent development of bicultamide-induced [sic] gynecomastia and breast pain.”). In addition, the dosages claimed cover a wide range of dosages. A POSA would expect a dose within the claimed ranges to be efficacious and would have been motivated to try such dosages while formulating a (Z)-endoxifen composition. For example, both Ahmad 2010 and Ahmad 2012 experimented with dosages the same or similar to those claimed. *See* Ex. 1011, 816 (“On the basis of these results, we expect that multiple daily endoxifen doses of 2.0–4.0 mg will result in endoxifen exposures that would be similar to those found in patients with normal CYP2D6 function who are administered tamoxifen at 20

mg/day. That is, a dose of 4 mg of endoxifen should be appropriate for breast cancer prevention and therapy.”); Ex. 1012, 2 (“Multiple daily endoxifen doses of 4.0-8.0 mg resulted in endoxifen exposures that would be sufficient for effective therapy.”).

**B. Claims 36, 37, 40, and 41**

94. Claims 40 and 41 present “identical issues of patentability” to claims 18 and 19 of the 334 patent that were found unpatentable by the Board. McConville, ¶94; 334 FWD, \*48-49. A comparison chart showing the similarities of the claims is below.

391 Patent	334 Patent (Unpatentable)
40. The method of claim 32, further comprising producing an area under curve (AUC <sub>0-inf</sub> ) of (Z)-endoxifen in the subject of from 200 hr*ng/mL to 10,000 hr*ng/ml per 4 mg of (Z)-endoxifen administered.	18. The method of claim 15, further comprising producing an area under curve (AUC <sub>0-inf</sub> ) of (Z)-endoxifen in the subject of from 200 hr*ng/mL to 10,000 hr*ng/mL per 4 mg of (Z)-endoxifen administered.
41. The method of claim 32, further comprising producing a maximum blood plasma concentration (C <sub>max</sub> ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/ml per 4 mg of (Z)-endoxifen administered.	19. The method of claim 15, further comprising producing a maximum blood plasma concentration (C <sub>max</sub> ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/mL per 4 mg of (Z)-endoxifen administered.

95. The claimed pharmacokinetic properties are merely inherent properties that arise from dosing a patient with 1 to 200 mg of Ahmad’s (Z)-endoxifen formulation. In addition, like Ahmad, Ahmad 2010 and Ahmad 2012 recognize that (Z)-endoxifen may be used to treat breast cancer. Ex. 1011, 814; Ex. 1012, 1. Ahmad 2010 and Ahmad 2012 tested the safety, tolerability, and pharmacokinetics

of endoxifen in human subjects. Ex. 1011, 814; Ex. 1012, 1. Ahmad 2010 and 2012 describe the pharmacokinetics of an endoxifen citrate tablet and indicate the endoxifen pharmacokinetics expected to be efficacious by comparing the pharmacokinetics of endoxifen citrate to the pharmacokinetics of the known anti-cancer drug, tamoxifen. Ex. 1011, 816 (“On the basis of these results, we expect that multiple daily endoxifen doses of 2.0–4.0 mg will result in endoxifen exposures that would be similar to those found in patients with normal CYP2D6 function who are administered tamoxifen at 20 mg/day. That is, a dose of 4 mg of endoxifen should be appropriate for breast cancer prevention and therapy.”); Ex. 1012, 2 (“Multiple daily endoxifen doses of 4.0-8.0 mg resulted in endoxifen exposures that would be sufficient for effective therapy.”). Ahmad 2010 and Ahmad 2012 indicate that the claimed pharmacokinetic properties are not surprising or unexpected.

96. Moreover, to the extent the claimed pharmacokinetics were not inherently achieved following Ahmad, a POSA would have been aware of the target pharmacokinetics expected to be efficacious and would have optimized a formulation to achieve them (*e.g.*, as indicated by Ahmad 2010 and Ahmad 2012). For example, a POSA would have used the known pharmacokinetics associated with the long-used anti-cancer drug tamoxifen as a baseline or starting point to modify a formulation of highly pure (Z)-endoxifen as taught by Ahmad and would have arrived at the claimed pharmacokinetics. For example, a POSA would have

increased or decreased the amount of (Z)-endoxifen in the formulation to adjust  $C_{\max}$ , added an absorption enhancer to the formulation, changed the particle size of the (Z)-endoxifen, and/or added a surfactant to increase solubilization.

**36. The method of claim 32, wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level above 30 nM.**

97. The pharmacokinetics described in Ahmad 2010 and Ahmad 2012 for an endoxifen salt (*e.g.*, endoxifen citrate) fall within the scope of claim 36. For example, Ahmad 2010 teaches that “the estimated steady-state plasma concentration ( $C_{\max}^{\text{SS}}$ ) of endoxifen is 55.1 ng/ml when the drug is administered in multiple doses of 4 mg at dose intervals of 24 h...” Ex. 1011 at 816. Converting the  $C_{\max}^{\text{SS}}$  from ng/ml to nM yields a  $C_{\max}^{\text{SS}}$  of 147.5 nM.<sup>3</sup> The steady state plasma level of the endoxifen disclosed by Ahmad 2010 is greater than 30 nM. Ahmad 2012 also provides steady state plasma levels ranging from 65.5 to 359 nM<sup>4</sup>. Ex. 1012 at 2.

98. To the extent the claimed pharmacokinetics were not inherently achieved following Ahmad, a POSA would have been aware of the target

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<sup>3</sup> (55.1 ng/ml \* 373.5 g/mol) / 1000 = 147.5 nM. See Ex. 1019 (providing molecular weight of endoxifen).

<sup>4</sup> After converting from ng/ml to nM.

pharmacokinetics expected to be efficacious and would have optimized a formulation to achieve them (*e.g.*, as indicated by Ahmad 2010 and Ahmad 2012) with a reasonable expectation of success.

***37. The method of claim 32, wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level from 30 nM to 300 nM.***

99. The pharmacokinetics described in Ahmad 2010 and Ahmad 2012 for endoxifen citrate fall within the scope of claim 37. Ahmad 2010 teaches that a  $C_{\max}^{SS}$  of 147.5 nM<sup>5</sup> and Ahmad 2012 teaches steady state plasma levels ranging from 65.5 to 359 nM<sup>6</sup>. Ex. 1011, 816; Ex. 1012 at 2.

100. To the extent the claimed pharmacokinetics were not inherently achieved following Ahmad, a POSA would have been aware of the target pharmacokinetics expected to be efficacious and would have optimized a formulation to achieve them (*e.g.*, as indicated by Ahmad 2010 and Ahmad 2012) with a reasonable expectation of success.

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<sup>5</sup> (55.1 ng/ml \* 373.5 g/mol) / 1000 = 147.5 nM. See Ex. 1019 (providing molecular weight of endoxifen).

<sup>6</sup> After converting from ng/ml to nM.

**40. The method of claim 32, further comprising producing an area under curve ( $AUC_{0-inf}$ ) of (Z)-endoxifen in the subject of from 200 hr\*ng/mL to 10,000 hr\*ng/ml per 4 mg of (Z)-endoxifen administered.**

101. Similar to the claims discussed above, Ahmad 2010 suggests that the inherent pharmacokinetics of the composition of Ahmad are within the range recited in claim 40. Ahmad 2010 produced data demonstrating the AUC in subjects treated with from 0.5 to 4.0 mg of endoxifen:

**Table 1 Endoxifen doses and pharmacokinetic parameters**

Dose	$C_{max}$ (ng/ml)	$AUC_{0-\infty}$ (ng-h/ml)	$t_{1/2}$ (h (CV%))	$V_z$ (l)	CI (l/h)
Endoxifen 0.5 mg	1.38 ± 0.25	99.9 ± 13.6	58.11 (18.0)	427 ± 101	5.1 ± 0.7
Endoxifen 1.0 mg	3.98 ± 1.7	239 ± 70	54.1 (10.6)	346 ± 88	4.5 ± 1.1
Endoxifen 2.0 mg	6.79 ± 1.85	401 ± 113	55.4 (16.3)	428 ± 133	5.4 ± 1.8
Endoxifen 4.0 mg	15.1 ± 4.24	801 ± 262	52.1 (12.9)	406 ± 119	5.5 ± 1.9
Tamoxifen 20 mg	0.417 ± 0.013	381 ± 47.6	1,051 (16.4) <sup>a</sup>	Fixed	Fixed

Data are given as mean values ± SD except for  $t_{1/2}$  (coefficient of variation percentage);  $n = 8$  subjects/treatment group. Fixed—could not be estimated from data for tamoxifen, and therefore, values fixed at  $V_z = 400$  l and  $CI = 5.0$  l/h.

$AUC_{0-\infty}$ , area under the concentration–time curve extrapolated from 0 to  $\infty$ ;  $C_{max}$ , peak drug concentrations in plasma; CI, confidence interval; CV, coefficient of variation;  $t_{1/2}$ , half-life.

<sup>a</sup>Apparent  $t_{1/2}$  estimated from terminal exponential phase of the concentration-vs.-time curve.

Ex. 1006 at 815. The AUC reported by Ahmad 2010 for 4 mg is well within the claimed range. *Id.*

102. To the extent the claimed pharmacokinetics were not inherently achieved following Ahmad, a POSA would have been aware of the target pharmacokinetics expected to be efficacious and would have optimized a formulation to achieve them (*e.g.*, as indicated by Ahmad 2010 and Ahmad 2012) with a reasonable expectation of success.

**41. The method of claim 32, further comprising producing a maximum blood plasma concentration ( $C_{max}$ ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/ml per 4 mg of (Z)-endoxifen administered.**

103. Ahmad 2010 teaches that “the estimated steady-state plasma concentration ( $C_{max}^{SS}$ ) of endoxifen is 55.1 ng/ml when the drug is administered in multiple doses of 4 mg at dose intervals of 24 h...” Ex. 1006 at 816.

104. To the extent the claimed pharmacokinetics were not inherently achieved following Ahmad, a POSA would have been aware of the target pharmacokinetics expected to be efficacious and would have optimized a formulation to achieve them (*e.g.*, as indicated by Ahmad 2010 and Ahmad 2012) with a reasonable expectation of success.

### **XIII. Claim 3 Over Ahmad and Stahl in View of the Knowledge of a POSA**

#### **A. Claim 3**

**3. The composition of claim 1, wherein the pharmaceutically acceptable salt of the compound of Formula (III) is endoxifen gluconate.**

105. As discussed above, Ahmad teaches a composition of highly pure (Z)-endoxifen as a digluconate salt. Ex. 1003, 9:1-4. Stahl teaches a variety of common, well-known salts for use in pharmaceutical compositions. Ex. 1005 at 334-45. Stahl lists gluconate as a common pharmaceutical salt. *Id.* at 334 (D-gluconic acid). Stahl further classifies gluconate as “class 1,” that is “of unrestricted use...because they form physiologically ubiquitous ions, or because they occur as intermediate metabolites in biochemical pathways.” *Id.* at 331.

106. A POSA would have been motivated to formulate endoxifen gluconate in view of Ahmad’s discussion of endoxifen digluconate and the well-known, routine use of gluconate salts in pharmaceutical compositions. A POSA would have had a reasonable expectation of success in formulating a highly pure (Z)-endoxifen composition as an endoxifen gluconate salt because a POSA would have had experience formulating pharmaceutical salts, such as gluconate salts, with various active ingredients. Indeed, the use of salts for pharmaceutical applications was very common. The use of single anion salts with endoxifen was also well known, as discussed above. *See, e.g.*, Ex. 1023 (endoxifen citrate); Ex. 1003 at 29:3-6 (experimental examples using endoxifen citrate); Ex. 1011 at 816 (same); Ex. 1028 (evaluating pharmacokinetics of endoxifen hydrochloride in mice for breast cancer treatment).

**XIV. Claim 7 Over Ahmad and Benameur in View of the Knowledge of a POSA**

**A. Claim 7**

107. Claim 7 presents identical issues of patentability to claim 3 of the 334 patent that were found unpatentable by the Board. A comparison chart showing the similarities of the claims is below.

391 Patent	334 Patent (Unpatentable)
7. The composition of claim 1, wherein the composition is uncoated.	3. The oral formulation of claim 1, wherein the enteric capsule is uncoated.

***7. The composition of claim 1, wherein the composition is uncoated.***

108. As discussed above, Ahmad teaches the use of an enteric coated capsule for its endoxifen formulations. It would have been a routine and obvious modification of Ahmad to instead use an uncoated enteric capsule, as had been developed in the art (*e.g.*, Capsugel).

109. Benameur teaches an intrinsically enteric capsule. For example, Benameur teaches that “[e]nteric capsule drug delivery technology (ECDDT) was developed to provide oral delivery with full enteric protection and rapid release in the upper gastrointestinal (GI) tract without the use of coatings.” Ex. 1006 at 34. Benameur further explains that “ECDDT’s intrinsically enteric properties are attained by incorporating pharmaceutically approved enteric polymers in the capsule shell using conventional pin-dipping capsule manufacturing processes.” *Id.* “The enteric properties and rapid release of specialized ECDDT capsule shells have been demonstrate to meet pharmacopeia standards for both in vitro and in vivo performance using esomeprazole magnesium trihydrate (EMT) as a model compound.” *Id.* Further, such capsules were commercially available by October 7, 2016.<sup>7</sup>

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<sup>7</sup> Such capsules are sold as Vcaps Enteric. <https://www.capsugel.com/biopharmaceutical-products/vcaps-enteric-capsules>. These capsules were released October 7, 2016.

110. A POSA would understand Benameur to teach the alternative use of an uncoated enteric capsule rather than an enteric coated capsule as taught by Ahmad. A POSA would have been motivated to use an uncoated enteric capsule to produce a drug without exposing it to the heating necessary for a coating process and/or to eliminate the need for process development of an enteric coating step. Ex. 1006 at 34. Doing so would have been a routine design choice and would have been obvious to try.

**XV. Claims 10, 12-15, and 31 Over Ahmad and de Villiers in View of the Knowledge of a POSA**

**A. Claim 10**

*10. The composition of claim 9, wherein the suspension comprises a syrup or an elixir.*

111. Ahmad discloses that its endoxifen compositions can be in the form of a syrup or a suspension. Ex. 1003, 18:4-7. A POSA would understand that a syrup (or an elixir) would be used in the formulation of a suspension as described by Ahmad.

112. de Villiers lists common liquid vehicles that could be used for a suspension. Ex. 1007 at 191, Table 15.1 (listing common liquid vehicles). As shown below, de Villiers specifically lists syrups and elixirs as common vehicles.

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<https://www.capsugel.com/news/capsugel-launches-vcaps-enteric-capsules-for-enteric-protection-and-delayed>

*Id.* Therefore, it would have been routine and within the skill of a POSA to formulate a suspension of highly-pure (Z)-endoxifen as taught by Ahmad with a syrup or elixir vehicle as taught by de Villiers. Formulating a suspension of highly-pure (Z)-endoxifen as taught by Ahmad with a syrup or elixir vehicle as taught by de Villiers would have been nothing more than a routine design choice for a POSA.

**Table 15.1**

**USP AND NF EXCIPIENTS CATEGORIZED AS SOLVENTS AND VEHICLES**

SOLVENT	VEHICLE
Acetone	FLAVORED AND/OR SWEETENED
Alcohol	Aromatic Elixir
Alcohol, Diluted	Benzaldehyde Elixir, Compound
Amylene Hydrate	Dextrose
Benzyl Benzoate	Peppermint Water
Butyl Alcohol	Sorbitol Solution
Canola Oil	Syrup
Caprylocaproyl Polyoxylglycerides	OLEAGINOUS
Corn Oil	Alkyl (C12-15) Benzoate
Cottonseed Oil	Almond Oil
Diethylene Glycol Monoethyl Ether	Canola Oil
Ethyl Acetate	Corn Oil
Glycerin	Cottonseed Oil
Hexylene Glycol	Ethyl Oleate
Isopropyl Alcohol	Isopropyl Myristate
Lauroyl Polyoxylglycerides	Isopropyl Palmitate
Linoleoyl Polyoxylglycerides	Mineral Oil
Methyl Alcohol	Mineral Oil, Light
Methylene Chloride	Octyldodecanol
Methyl Isobutyl Ketone	Olive Oil
Mineral Oil	Peanut Oil
Oleoyl Polyoxylglycerides	Safflower Oil
Peanut Oil	Sesame Oil
Polyethylene Glycol	Soybean Oil
Polyethylene Glycol Monomethyl Ether	Squalane
Propylene Glycol	STERILE
Sesame Oil	Sodium Chloride Injection, Bacteriostatic
Stearoyl Polyoxylglycerides	Water for Injection, Bacteriostatic
Water for Injection	SOLID CARRIER
Water for Injection, Sterile	Sugar Spheres
Water for Irrigation, Sterile	
Water, Purified	

From the United States Pharmacopeial Convention Inc. USP 30/ NF 25. 2006: Front Matter—NF: Excipients. Rockville, MD: Author, 2007, with permission.  
 Source: 2007 USP 30/ NF 25. Rockville, MD: The United States Pharmacopeial Convention Inc., 2006: Front Matter—NF: Excipients.

*Id.*

**B. Claims 12-15 and 31**

***12. The composition of claim 11, wherein the fluid comprises an alcohol.***

***13. The composition of claim 12, wherein the alcohol comprises ethanol.***

113. As discussed above, Ahmad teaches that its composition of (Z)-endoxifen can include an alcoholic vehicle. Ex. 1003, 20:63-65 (“In another preferred embodiment[,] the composition of [the] invention containing endoxifen may also contain one or more nonaqueous vehicles, such as alcoholic vehicles.”).

114. de Villiers likewise teaches that alcohols are common vehicles for suspensions. For example, de Villiers explains “solvent-vehicles frequently used as ingredients in drug products and compounded preparations include alcohol....” Ex. 1007 at 190. de Villiers further teaches that ethanol is a common alcohol used in pharmaceutical preparations. *Id.* at 195. For example, de Villiers explains that “[ethanol] is used as a solvent-vehicle for the preparation of pharmaceutical dosage forms for internal or external use.” *Id.*

115. It would have been routine and within the skill of a POSA to formulate a suspension of highly-pure (Z)-endoxifen as taught by Ahmad with an alcohol, such as ethanol, as taught by de Villiers. Formulating a suspension of highly-pure (Z)-endoxifen as taught by Ahmad with an alcohol such as ethanol as taught by de Villiers would have been nothing more than a routine design choice for a POSA.

**14. The composition of claim 9, wherein the suspension comprises an alcohol, a plant oil, a mineral oil, a glycol, an agar, or a mixture thereof.**

**15. The composition of claim 9, wherein the suspension comprises ethanol, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.**

**31. The method of claim 30, wherein the fluid comprises an alcohol, ethanol, a plant oil, a mineral oil, a glycol, an agar, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.**

116. As discussed above, Ahmad teaches that its composition of (Z)-endoxifen can include an alcoholic vehicle, and provides an example of ethanol as such an alcoholic vehicle. Ex. 1003, 20:63-67. Ahmad further teaches the use of “sodium lauryl sulfate” as a “pharmaceutically acceptable carrier.” Ex. 1003, 8:31-40.

117. All of the claimed substances are routinely used in pharmaceutical compositions, including as vehicles for a suspension. As such, a POSA would understand that any of the claimed substances could be used in the formulation of a suspension as described by Ahmad. Indeed, de Villiers lists common liquid vehicles, including many of those claimed, that would be used for a pharmaceutical suspension. Ex. 1007 at 191, Table 15.1 (listing common liquid vehicles). For example, as discussed, de Villiers teaches the use of alcohols, such as ethanol, as a liquid vehicle for pharmaceutical use. As shown below, de Villiers additionally teaches the use of sorbitol, mineral oil, plant oils, and vegetable oils as vehicles. *Id.*

**Table 15.1****USP AND NF EXCIPIENTS CATEGORIZED AS SOLVENTS AND VEHICLES**

SOLVENT	VEHICLE
Acetone	FLAVORED AND/OR SWEETENED
Alcohol	Aromatic Elixir
Alcohol, Diluted	Benzaldehyde Elixir, Compound
Amylene Hydrate	Dextrose
Benzyl Benzoate	Peppermint Water
Butyl Alcohol	Sorbitol Solution
Canola Oil	Syrup
Caprylocaproyl Polyoxylglycerides	OLEAGINOUS
Corn Oil	Alkyl (C12-15) Benzoate
Cottonseed Oil	Almond Oil
Diethylene Glycol Monoethyl Ether	Canola Oil
Ethyl Acetate	Corn Oil
Glycerin	Cottonseed Oil
Hexylene Glycol	Ethyl Oleate
Isopropyl Alcohol	Isopropyl Myristate
Lauroyl Polyoxylglycerides	Isopropyl Palmitate
Linoleoyl Polyoxylglycerides	Mineral Oil
Methyl Alcohol	Mineral Oil, Light
Methylene Chloride	Octyldodecanol
Methyl Isobutyl Ketone	Olive Oil
Mineral Oil	Peanut Oil
Oleoyl Polyoxylglycerides	Safflower Oil
Peanut Oil	Sesame Oil
Polyethylene Glycol	Soybean Oil
Polyethylene Glycol Monomethyl Ether	Squalane
Propylene Glycol	STERILE
Sesame Oil	Sodium Chloride Injection, Bacteriostatic
Stearoyl Polyoxylglycerides	Water for Injection, Bacteriostatic
Water for Injection	SOLID CARRIER
Water for Injection, Sterile	Sugar Spheres
Water for Irrigation, Sterile	
Water, Purified	

From the United States Pharmacopeial Convention Inc. USP 30/ NF 25. 2006: Front Matter—NF: Excipients. Rockville, MD: Author, 2007, with permission.  
 Source: 2007 USP 30/ NF 25. Rockville, MD: The United States Pharmacopeial Convention Inc., 2006: Front Matter—NF: Excipients.

*Id.*

118. It would have been routine and within the skill of a POSA to formulate a suspension of highly-pure (Z)-endoxifen as taught by Ahmad with an alcohol, ethanol, of sorbitol, mineral oil, plant oils, and/or vegetable oils, as taught by de Villiers. Formulating a suspension of highly-pure (Z)-endoxifen as taught by

Ahmad with the claimed vehicles would have been nothing more than a routine design choice for a POSA.

**XVI. Claim 16 Over Ahmad and Liu in View of the Knowledge of a POSA**

**A. Claim 16**

***16. The composition of claim 1, wherein the compound of Formula (III) is stable in the composition for at least 10 days at about 25° C.***

119. A POSA would understand “stable” as used in claim 16 to mean “the continued presence of at least 90% (Z)-endoxifen in a composition...measurable by (Z)-endoxifen conversion to (E)-endoxifen starting from the date of synthesis.” Ex. 1001, 81:14-18. As discussed above, the (Z)-endoxifen disclosed by Ahmad is the same composition claimed in the 391 patent and therefore Ahmad inherently teaches the claimed stability.

120. Even if not inherent in Ahmad in view of Liu, a POSA would understand that it is desirable for a pharmaceutical composition to be stable. As such, a POSA would have been motivated to obtain a composition of (Z)-endoxifen that was stable. A POSA would be familiar with different ways to improve the stability of a pharmaceutical composition by using formulation strategies and/or packaging solutions amongst others. *See* Ex. 1030 at 102-163. Formulation strategies are specific to the type of degradation mechanism and API, but could include for example: use of stabilizers, coatings, pH optimization, solubilization techniques, polymorph selection, lyophilization etc. *See id.* Packaging solutions are dependent

on the type of dosage form, but could include for example: desiccants and/or moisture barriers, oxygen scavengers, light-resistant containers, air-tight or inert gas packaging. *See id.* Utilizing such techniques to improve the stability of the (Z)-endoxifen composition would have been nothing more than utilizing known, conventional, and predictable processes, and a POSA would have had a reasonable expectation of success in doing so.

**XVII. Claims 21-25 Over Ahmad and Stegemann/HPE in View of the Knowledge of a POSA**

**A. Claims 21-25**

121. Claims 21-25 present identical issues of patentability to claims 9-13 of the 334 patent that were found unpatentable by the Board. For example, the claims from both patents recite common, well-known pharmaceutical excipients. *Compare* Ex. 1001, Claims 21-25, *with* Ex. 1023, Claims 9-13. A comparison chart showing the similarities of the claims is below.

391 Patent	334 Patent (Unpatentable)
21. The composition of claim 1, wherein the composition further comprises a filler.	9. The oral formulation of claim 1, wherein the endoxifen composition further comprises a filler.
22. The composition of claim 21, wherein the filler comprises a sugar, salt, talc, calcium carbonate, microcrystalline cellulose, methyl cellulose, carboxymethyl cellulose, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinized starch, or combinations thereof.	10. The oral formulation of claim 9, wherein the filler comprises talc, calcium carbonate, a sugar, a salt, microcrystalline cellulose, methyl cellulose, carboxymethyl cellulose, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinized starch, or combinations thereof.
23. The composition of claim 1, wherein the composition further comprises a disintegrant.	11. The oral formulation of claim 1, wherein the endoxifen composition further comprises a disintegrant.
24. The composition of claim 1, wherein the composition further comprises a lubricant.	12. The oral formulation of claim 1, wherein the endoxifen composition further comprises a lubricant.
25. The composition of claim 24, wherein the lubricant comprises calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, ethyl oleate, ethyl laureate, agar, or combinations thereof.	13. The oral formulation of claim 12, wherein the lubricant comprises calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, ethyl oleate, ethyl laureate, agar, or combinations thereof.

***21. The composition of claim 1, wherein the composition further comprises a filler.***

122. As a POSA would know, a filler is sometimes referred to as a diluent.

A filler/diluent is a common pharmaceutical excipient that increases the volume of a pharmaceutical formulation, which helps make the ingredients easier to process,

stabilizes the formulation, and makes the formulation a suitable size for consumption. *See* Ex. 1020 at 184.

123. Fillers/diluents are well known in the pharmaceutical industry. For example, Stegemann teaches that several excipients function as fillers at higher volumes. Ex. 1008 at 7-8 (“Talcum, for instance, serves as a lubricant in concentrations below 5%. At higher concentrations, it is mainly considered a filler.... And besides being an excellent filler, microcrystalline cellulose also serves as a disintegrant.... Starch, which is commonly added to tablets as a disintegrant owing to its macerating properties of 5% to 10%, might be used as a filler in hard gelatin capsules....”); *see also* Ex. 1009 at 900 (“Fillers *see* Diluents (tablet/capsule)”), 897 (listing “Diluents tablet/capsule” including talc, calcium carbonate, sugar spheres, microcrystalline cellulose, kaolin, mannitol, sorbitol, starch, pregelatinized starch, and others). Ahmad also teaches formulations including substances that can act as a filler/diluent. *See, e.g.*, Ex. 1003, 9:57-61 (sucrose, glucose, lactose, sorbitol, mannitol), 8:37-38 (starch).

124. The use of a filler in a pharmaceutical formulation was a routine and common practice in the formulation arts. A POSA would have been motivated to use a filler and/or diluent for its normal use—to make the ingredients easier to process, stabilize the formulation, and/or make the formulation a suitable size for

consumption. A POSA would have had a reasonable expectation of success, as fillers and diluents were common excipients in the art.

**22. The composition of claim 21, wherein the filler comprises a sugar, salt, talc, calcium carbonate, microcrystalline cellulose, methyl cellulose, carboxymethyl cellulose, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinized starch, or combinations thereof.**

125. As discussed above, fillers are a common pharmaceutical excipient. The fillers recited in claim 22 were well-known and common examples of fillers. For example, Ahmad describes sucrose, glucose, lactose, sorbitol, mannitol, and starch; Stegeman describes “[t]alcum,” “microcrystalline cellulose” and “[s]tarch;” the HPE describes talc, calcium carbonate, sugar spheres, microcrystalline cellulose, kaolin, mannitol, sorbitol, starch, pregelatinized starch, and others; and Ansel describes “lactose, microcrystalline cellulose and starch.” Ex. 1003, 9:57-61(sucrose, glucose, lactose, sorbitol, mannitol), 8:37-38 (starch); Ex. 1008 at 7-8; Ex. 1009 at 897; Ex. 1020 at 184. Accordingly, the selection of these fillers would be nothing more than an obvious and routine formulation decision for a POSA.

**23. The composition of claim 1, wherein the composition further comprises a disintegrant.**

126. Disintegrants were well known in the pharmaceutical industry. A disintegrant is a common pharmaceutical excipient that increases dissolution of a formulation once it is in a proper medium. It helps ensure that the active ingredient

is made available quickly and absorbed by the body in the proper location. *See* Ex. 1020 at 184.

127. As discussed above, Ahmad teaches that its compositions can include “disintegrants [sic] (e.g., potato starch or sodium starch glycolate)...” Ex. 1003, 8:31-38. Similar to Ahmad, Stegemann teaches use of the following ingredients as disintegrants:

**Disintegrants**

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→ To ensure disintegration of powder mixture

- Croscarmellose
- Corn starch
- Crospovidone
- Starch 1500
- Sodium glycyll starch
- Alginic acid

Ex. 1008 at 8; *see also* Ex. 1009 at 897-98 (listing disintegrants); Ex. 1020 at 184 (same).

128. As taught by these references and as was known in the art, the use of a disintegrant in a formulation was a routine and common practice in the formulation arts. A POSA would have been motivated to use a disintegrant for its normal use—to ensure that the active ingredient is made available quickly and absorbed by the body in the proper location. A POSA would have had a reasonable expectation of success as disintegrants were commonly used excipients.

**24. The composition of claim 1, wherein the composition further comprises a lubricant.**

129. A lubricant is also a common pharmaceutical excipient. A lubricant is used to decrease the friction between pharmaceutical formulations and the tableting equipment contact surface. Lubricants help make processing and manufacturing more efficient.

130. Lubricants were well known in the pharmaceutical industry. For example, Stegemann teaches the use of lubricants in capsules:

## **Lubricants**

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→ Improved flow properties and reduced powder adhesion to metal parts

- Magnesium stearate
- Glyceryl monostearate
- Stearic acid

Ex. 1008 at 8; *see also* Ex. 1009 at 905 (listing “Lubricants (tablet/capsule)”).

Ahmad likewise discloses the use of compounds that have lubricating properties.

*See, e.g.*, Ex. 1003, 13:15-25 (stearic acid).

131. As taught by these references, the use of a lubricant in the formulation was a routine and common practice in the formulation arts. A POSA would have been motivated to use a lubricant for its normal use—to make processing and manufacturing more efficient.

**25. The composition of claim 24, wherein the lubricant comprises calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, ethyl oleate, ethyl laurate, agar, or combinations thereof.**

132. As described above, the use of lubricants was common in the pharmaceutical arts. The claimed lubricants were also well-known. *See, e.g.*, Ex. 1008 at 8; *see also* Ex. 1009 at 905 (listing “Lubricants (tablet/capsule)” including calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, and others); Ex. 1003, 13:15-25 (stearic acid).

133. As such, the use of these common lubricants with Ahmad’s (Z)-endoxifen would have been nothing more than a well-known, routine design choice, and a POSA would have had a reasonable expectation of success in arriving at formulating the (Z)-endoxifen taught by Ahmad with the lubricants disclosed in Stegemann and/or the HPE.

#### **XVIII. Claims 17-19, 38, and 39 Over Ahmad and Cole in View of the Knowledge of a POSA**

##### **A. Claims 17-19, 38, and 39**

134. Claims 17-19, 38, and 39 present identical issues of patentability to claims 5-7 of the 334 patent that were found unpatentable by the Board. For example, the claims from both patents recite properties of enteric/delayed-release

drugs. *Compare* Ex. 1001, Claims 17-19, 38, 39, *with* Ex. 1023, Claims 5-7. A comparison chart showing the similarities of the claims is below.

<b>391 Patent</b>	<b>334 Patent (Unpatentable)</b>
17. The composition of claim 1, formulated such that the composition is resistant to dissolution in an acidic environment for at least 2 hours, as measured in a dissolution test performed according to a method of USP 711.	5. The oral formulation of claim 1, formulated such that the oral formulation is resistant to dissolution in an acidic environment for at least 2 hours, as measured in a dissolution test performed according to a method of USP 711.
18. The composition of claim 1, formulated such that the composition releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.	6. The oral formulation of claim 1, formulated such that the oral formulation releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.
19. The composition of claim 1, formulated such that the composition releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.	7. The oral formulation of claim 1, formulated such that the oral formulation releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.
38. The method of claim 32, further comprising releasing no more than 10% of the (Z)-endoxifen in a stomach of the subject within 2 hours following the administering of the composition.	6. The oral formulation of claim 1, formulated such that the oral formulation releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.
39. The method of claim 32, further comprising releasing at least 50% of the (Z)-endoxifen in a small intestine of the subject within 8 hours following the administering of the composition.	7. The oral formulation of claim 1, formulated such that the oral formulation releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.

***17. The composition of claim 1, formulated such that the composition is resistant to dissolution in an acidic environment for at least 2 hours, as measured in a dissolution test performed according to a method of USP 711.***

135. As discussed above, Ahmad teaches that the purpose of an enteric coating is to prevent release of drug in the stomach. Ex. 1003 at 18:19-21. Enteric coatings are resistant to dissolution in an acidic environment (at a low pH).

136. Like Ahmad, Cole teaches enteric coated capsules. Cole teaches that its enteric coating prevents drug release for at least two hours under strongly acidic conditions. Ex. 1010 at 89 (“No paracetamol<sup>8</sup> was released over 2 h at pH 1.2 from the capsules coating with 6 and 8 mg cm<sup>-2</sup> Eudragit® L 30 D-55.”). While Cole does not disclose explicitly that the method used was USP 711, USP 711 is the most common method for dissolution testing. Therefore, a POSA would understand from Cole’s methodology that Cole was using USP 711.

137. As such, Cole teaches that enteric coated capsules, such as those taught in Ahmad, would be “formulated such that the oral formulation is resistant to dissolution in an acidic environment for at least 2 hours, as measured in a dissolution test performed according to a method of USP 711.” Indeed, resistance to dissolution would be the purpose of enteric coating. A POSA would have been motivated to

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<sup>8</sup> Paracetamol is the sample active ingredient used in Cole. The identity of the active ingredient is immaterial as to whether it is released from a capsule, because it is entirely contained in the capsule until the capsule breaks open.

formulate Ahmad's (Z)-endoxifen to be resistant to dissolution in an acidic environment for at least 2 hours to ensure that the endoxifen was released in the small intestine, rather than in the stomach where it may be degraded by acid, as taught by Ahmad. Cole teaches a method of achieving the claimed release rate and a POSA would have had a reasonable expectation of success in achieving the claimed release rate by using the teachings of Cole.

***18. The composition of claim 1, formulated such that the composition releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.***

***38. The method of claim 32, further comprising releasing no more than 10% of the (Z)-endoxifen in a stomach of the subject within 2 hours following the administering of the composition.***

138. As discussed above, an enteric coating, such as that disclosed in Cole, is designed to resist degradation in acid. As such, the enteric coating described by Cole would not release the (Z)-endoxifen over at least 2 hours. The pH of the human stomach is 1.5. Ex. 1021 at 8. Thus, the conditions described above in Cole using a pH of 1.2 show that its enteric coatings would not release any drug for 2 hours in gastric fluid or in the stomach.

139. Thus, Cole teaches that enteric coated capsules, such as those taught in Ahmad, would be “formulated such that the oral formulation releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution

test performed according to a method of USP 711.” As discussed above, a POSA would understand from Cole’s methodology that Cole was using USP 711.

140. A POSA would have been motivated to achieve such a formulation, and methods of using such formulations, to ensure that the endoxifen was released in the small intestine, rather than in the stomach where it may be degraded by acid, as taught by Ahmad. A POSA would have had a reasonable expectation of success in achieving this release rate as taught by Cole.

***19. The composition of claim 1, formulated such that the composition releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.***

***39. The method of claim 32, further comprising releasing at least 50% of the (Z)-endoxifen in a small intestine of the subject within 8 hours following the administering of the composition.***

141. Ahmad teaches that the purpose of its enteric coating is to prevent release of medication before it reaches the small intestine. Ahmad further teaches that enteric coatings work by breaking down rapidly at the relatively higher pH of the small intestine and resist degradation in the lower pH of the stomach. Ex. 1003 at 18:19-26. Similarly, Cole teaches that at “pH 6.8,<sup>9</sup> release of the paracetamol was rapid....” Ex. 1010 at 89; *see also id.* at 91, Fig. 4 (showing 50% release in pH 6.8

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<sup>9</sup> The pH of the proximal small intestine has been measured to be about 6.6. Ex. 1017.

by about 2.5-3 hours). Thus, Ahmad's formulation coated according to Cole would be made "such that the oral formulation releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711." Again, a POSA would understand from Cole's methodology that Cole was using USP 711.

142. A POSA would have been motivated to achieve such a formulation and method of using it to ensure that the endoxifen was released in the small intestine where it would be absorbed into the body and have pharmaceutical effect. As discussed above, Ahmad describes the use of enteric coatings and cautions against acid degradation of endoxifen by stomach acids. A POSA would have had a reasonable expectation of success in formulating and using Ahmad's composition coated according to Cole because the use of enteric materials was well known in the art and Cole describes the use of such coatings.

## **XIX. Claim 30 Over Ahmad and Gandhi in View of the Knowledge of a POSA**

### **A. Claim 30**

***30. A method of making the composition of claim 9, the method comprising suspending the endoxifen and the enteric material in a fluid.***

143. As discussed, Ahmad teaches an enteric coating to prevent release of medication before it reaches the small intestine. Ahmad does not specifically disclose the use of an enteric material in a suspension. However, as discussed above,

Ahmad describes both the use of suspensions of endoxifen and the use of enteric materials to prevent release of the endoxifen in the stomach.

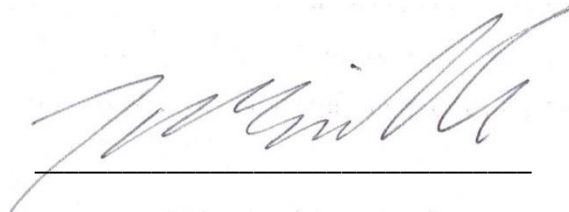
144. The use of enteric materials in suspensions was well known in the art before the date of 391 patent. For example, Gandhi teaches the use of a “rate controlling polymer” in an oral suspension to create a “stable, sustained release oral liquid suspension dosage.” Ex. 1022 at Abstract. Gandhi describes “sustained-release dosage forms” as a dosage designed to release “an active agent over an extended period of time.” *Id.* at 4:15-16. The “rate controlling polymers” described by Gandhi are enteric materials. *See id.* at 4:16-18 (synonymizing “sustained-release” with “controlled-release” and “delayed release”). Both Gandhi and the 391 patent describe the same substances for use as a “rate controlling polymer” and “enteric material.” *Compare* Ex. 1022 at 7:20-8:22 (listing EUDRAGIT L and S as hydrophobic rate controlling polymers), *with* Ex. 1001 at 39:22-51 (describing EUDRAGIT L and S copolymers as “pH dependent polymers” that “target upper small intestines and colon”); *see also* Ex. 1001 at 84:61-67, 85:45-49 (examples using Eudragit FS D30 and Eudragit L30 D55 as enteric materials).

145. A POSA would have been motivated to formulate a suspension of (Z)-endoxifen, as described by Ahmad, with an enteric material, as described by Gandhi, to ensure that the endoxifen was released in the small intestine where it would be absorbed into the body and have a pharmaceutical effect. Indeed, as discussed

above, Ahmad describes the use of enteric materials for its (Z)-endoxifen formulations. A POSA would have had a reasonable expectation of success as this is taught in Gandhi.

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146. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further 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.



Jason McConville, Ph.D.

04/03/2025

Date

# **APPENDIX A**

CURRICULUM VITAE  
Jason T. McConville, Ph.D.  
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I. Personal

Born July 13, 1971 in Coventry, United Kingdom.  
Married.

Citizen of The United Kingdom of Great Britain and Northern Ireland.  
Citizen of The United States of America.

II. Education

Oct 91 – Jun 94            Bachelor of Science with Honors, Applied Chemistry  
Coventry University, Coventry, United Kingdom

Jul 99 – Sep 02            University of Strathclyde, Glasgow, United Kingdom.  
Doctor of Philosophy, Pharmaceutics

Dissertation:            “Pulsed-Release Drug Delivery and Development of the  
Time-Delayed Capsule”

III. Positions Held

September 1994 to July 1999 –Research Technician in Pharmaceutics,  
Centre for Drug Formulation Studies, University of Bath, Bath, United Kingdom.

July 1999 to September 2002 – Ph.D. Student/Candidate,  
Department of Pharmacy, University of Strathclyde, Glasgow, United Kingdom.

October, 2002 to August 2006 – Post Doctoral Fellow/ Research Associate,  
College of Pharmacy, University of Texas at Austin, Austin, TX.

August, 2006 to May 2012 – Assistant Professor of Pharmaceutics,  
College of Pharmacy, University of Texas at Austin, Austin, TX.

July, 2012 to Present – Associate Professor of Pharmaceutics,  
College of Pharmacy, University of New Mexico, Albuquerque, NM.

August, 2012 to Present – Adjunct Professor  
Department of Pharmaceutical Technology and Biopharmacy,  
University of Bonn, Germany.

July, 2021 to Present – Vice Chair of Education in Pharmaceutical Sciences,  
College of Pharmacy, University of New Mexico, Albuquerque, NM.

IV. Professional Memberships

American Association of Pharmaceutical Scientists <i>Sections: Formulation Design &amp; Development</i> <i>Physical Pharmacy &amp; Biopharmaceutics</i>	1997 - present
Aerosol Society	1997 - present
Controlled Release Society	2002 – present
Canadian Society for Pharmaceutical Sciences	2004 – present
American Association of Colleges of Pharmacy	2006 – present
American Association of Pharmaceutical Scientists <i>Inhalation and Nasal Community Leadership Member</i>	2020 - present

V. Professional Training

Short course: *Particle Characterization using Low Angle Laser Light Scattering*,  
Malvern Instruments, Limited, Malvern, Worcestershire, UK, June, 1996.

The Royal Institute of Biology, *Accredited Training for Personnel Working under the  
Animals (Scientific Procedures) Act 1987* (Modules 1, 2, 3, and 4),  
Guy's, King's and St Thomas' Medical School, London, UK, April, 1997.

Short course: *Advances in Controlled Release and Drug Delivery Technologies*.  
The Center for Microencapsulation and Drug Delivery, Texas A&M University,  
College Station, TX, October, 2004.

Short course: *Particle Engineering Technologies: Theory and Practice*,  
American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.

Short course: *Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist*,  
University of Minnesota, College of Pharmacy, Minnesota, MN, July, 2005.

Workshop: *Tablet Coating Technologies, International Pharmaceutical Excipients Council  
(IPEC Americas 2008)*, San Juan, Puerto Rico, April, 2008.

The Royal Institute of Biology, *Accredited Training for Personnel Working under the Animals (Scientific Procedures) Act 1987* (Modules 1, 2, 3, 4, and 5), Vesalius, London, UK, June, 2009.

Joint American Association of Pharmaceutical Scientists/Controlled Release Society Workshop: *Developing Pharmaceutical Products for Controlled Pulmonary Delivery*, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington, DC, October, 2011.

Workshop: *Setting Release Specifications for in vitro Testing of Controlled Release Dosage Forms*, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.

Short Course: *Macromolecule Drug Delivery: Challenges and Triumphs*, AAPS National Biotechnology Conference, San Diego, CA, May, 2014.

National Association for Biomedical Research (NABR), *Reducing Burden: Options and Opportunities*, November, 2017.

Collaborative Institutional Training Initiative, *Planning Research and Completing the Protocol Form*, December, 2018.

Office of Laboratory Animal Welfare (OLAW), *21st Century Cures Act*, December, 2019.

## VI. Current Research Interests

New technologies to improve patient compliance and health outcomes with inhalation, oral, thin film, and 3D printed drug delivery technologies.

## VII. Honors and Awards

1. Annual Research Day Award for “Design and Evaluation of Pulsatile Drug Delivery Capsule”, *University of Strathclyde*, Glasgow, May, 2001.
2. Outstanding Presentation Award: “Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets”, *138th British Pharmaceutical Conference*, Glasgow, United Kingdom, September, 2001.
3. Editor’s Choice Award: “Design and Evaluation of a Restraint-Free Small Animal Inhalation Dosing Chamber”. *LeadDiscovery*, February, 2005.

4. Innovative Aspects of Oral Drug Delivery and Absorption Graduate/Post-Doc Award: “Improved Dissolution Rate and Bioavailability through the Formation of a Highly Miscible Binary Mixture”, *32nd International Symposium on Controlled Release of Bioactive Materials*, Miami, FL, June, 2005.
5. Best Resident and Research Presentation Award: “Aerosolized Itraconazole (ITZ) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*”, *27th American College of Clinical Pharmacy Annual Meeting*, St. Louis, MS, October, 2006.
6. Invited article: J.T. McConville, N.P. Wiederhold, Antifungal Prophylaxis to the Lung Using Itraconazole, *Inhalation*, 1(2007) 6-9.
7. Invited article: J.T. McConville, Targeted Lung Delivery of Antifungals: Preclinical Studies Using Itraconazole Nanoparticles, *RDD Europe 2007*, 1(2007) 43-50.
8. Invited article: D.A. Miller, J.T. McConville, W. Yang, R.O. Williams III, J.W. McGinity, Hot-Melt Extrusion for Enhanced Delivery of Drug Particles, *Journal of Pharmaceutical Sciences*, 96(2007) 361-76. Invited Article.
9. Featured News Article: “University of Texas at Austin Pharmacy Researcher Works to Lower Carbon Footprint of Pharmaceuticals”, *www.BiobasedNews.com*, August, 2008.
10. Featured News Article in Carbon Market News: “Research Reveals Pharmaceuticals Can Cut Carbon Footprint with Organic Solvent”, *www.carbonoffsetsdaily.com*, August, 2008.
11. Guest Editor: Innovative Inhalation Technologies: Special Edition: *Drug Development and Industrial Pharmacy*, 34(2008).
12. Invited article: Y-J. Son, J.T. McConville, Advancements in Dry Powder Delivery to the Lung, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 948-959.
13. Invited article: A.B. Watts, J.T. McConville, R.O. Williams III, Current Therapies and Technological Advances in Aqueous Aerosol Drug Delivery, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 913-922.
14. Invited article: W. Yang, J. Tam, D.A. Miller, J. Zhou, J.T. McConville, K.P. Johnston, R.O. Williams III, High Bioavailability from Nebulized Itraconazole Nanoparticle Dispersions with Biocompatible Stabilizers, Special Edition: Pharmaceutical Nanotechnology, *International Journal of Pharmaceutics*, 361(2008) 177–188.

15. Session Judge: Poster on the Podiums, *Respiratory Drug Delivery (RDD2008)*, Scottsdale, Arizona, 2008.
16. Research Presentation Award: “Manufacture and Characterization of Natural Polymer Based Films as Buccal Delivery Systems”, *International Pharmaceutical Excipients Council (IPEC Americas 2009)*, San Juan, Puerto Rico, April, 2009.
17. Invited article: S. Thitinan, J.T. McConville, Interferon Alpha Delivery Systems for the Treatment of Hepatitis C, *International Journal of Pharmaceutics*. 369(2009) 121-135.
18. Invited article: J.T. McConville, S.A. Kucera, T.C. Carvalho, E.M. Hurley, Ethyl Lactate as a Pharmaceutical-Grade Excipient and Development of a Sensitive Peroxide Assay, *Pharmaceutical Technology*, 33(2009) 74-84.
19. Invited article: Y-J Son, J.T. McConville, Dissolution Testing for Inhalation Formulations, *Inhalation*, 2:6(2009) 8-11.
20. Invited article: Y-J. Son, M. Horng, M. Copley, J.T. McConville, Optimization of an *In Vitro* Dissolution Test Method for Inhalation Formulations, *Dissolution Technologies*, 17(2010), 6-13.
21. Member of the Society for Teaching Excellence, *University of Texas at Austin*, September, 2011.
22. Corresponding author for the most downloaded article in *European Journal of Pharmaceutics and Biopharmaceutics*: “Manufacture and Characterization of Mucoadhesive Buccal Films”, January-March 2011.
23. Invited article: T.C. Carvalho, S.R. Carvalho, J.T. McConville, Formulations for Pulmonary Administration of Anticancer Agents to Treat Lung Malignancies, *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 24 (2011), 61-80.
24. Nomination: University of Texas System Regents' Outstanding Teaching Award, December 2011.
25. Research Presentation Award: Influence of particulate API in Eudragit® RS and RL films for buccal delivery, *International Pharmaceutical Excipients Council (IPEC Americas 2012)*, San Juan, Puerto Rico, 2012.
26. Invited article: S. Thitinan, J.T. McConville, Development of a Gastroretentive Pulsatile Drug Delivery Platform, *Journal of Pharmacy and Pharmacology*, 64 (2012), 505-516.
27. Invited article: Y-J. Son, J.T. McConville, Preparation of Sustained Release Rifampicin Microparticles for Inhalation, Special Edition: *Journal of Pharmacy and Pharmacology*, 64 (2012), 1291-1302.

28. Research Presentation Award: “Antisolvent Co-Precipitation Synthesis of D,L-Valine/Lysozyme”, *International Pharmaceutical Excipients Council (IPEC Americas 2014)*, Raleigh-Durham, NC, April, 2014.
29. Invited article: J.O. Morales, J.T. McConville, Novel Strategies for the Buccal Delivery of Macromolecules, *Drug Development and Industrial Pharmacy*, 40 (2014), 579–590.
30. Best Inter-Departmental Collaborative Research Award: “Polymeric Coating of Endotracheal Tubes for Local Drug Delivery”, *University of New Mexico College of Pharmacy Research and Scholarship Day*, Albuquerque, NM, September, 2015.
31. Invited article: J.E. Hasted P. Bäckman, A.R. Clark, W. Doub, A. Hickey, G. Hochhaus, P.J. Kuehl, C-M. Lehr, P. Mauser, J. McConville, R. Niven, M. Sakagimi and J.G. Weers, Scope and relevance of a pulmonary biopharmaceutical classification system AAPS/FDA/USP Workshop March 16-17th, 2015 in Baltimore, MD, *AAPS Open*, 2 (2016), 1-20.
32. Invited article: T.C. Carvalho, J.P. McCook, N.R. Narain, J.T. McConville, Development of Aqueous Dispersions of Coenzyme Q10 for Pulmonary Delivery and the Dynamics of Active Vibrating-Mesh Aerosolization, Special Issue: Staniforth Festschrift, *International Journal of Pharmaceutics*, 514 (2016), 514(2), 407-419.
33. Invited article: J.O Morales, K.R. Fathe, A. Brunaugh, S. Ferrati, S. Li, M. Montenegro-Nicolini, Z. Mousavikhamene, J.T. McConville, M.R. Prausnitz, H.D.C. Smyth, Challenges and Future Prospects for the Delivery of Biologics: Oral Mucosal, Pulmonary, and Transdermal Routes, *The AAPS Journal*, 2017, 1-17.
34. Guest Editor: Formulation and Delivery of Macromolecules, Special Edition: *AAPS PharmSciTech* 18 (2017).
35. Abstract Reviewer and Publication Coordinator for the Taylor & Francis Group and ExcipientFest 2017, Providence, RI.
36. Invited Article: I. Rossi, F. Sonvico, J. McConville, F. Rossi, E. Fröhlich, S. Zellnitz, A. Rossi, E. Del Favero, R Bettini, F. Buttini, Nebulized Coenzyme Q10 Nanosuspensions: A Versatile Approach for Pulmonary Antioxidant Therapy, *European Journal of Pharmaceutical Sciences*, 113 (2017), 159-170.
37. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2017)*, Edinburgh, UK, December, 2017.
38. Session Judge: Pat Burnell Young Investigator Prize, *Drug Delivery to the Lungs (DDL2017)*, Edinburgh, UK, December, 2017.
39. Inducted as a member of the Tom L. Popejoy Society, *University of New Mexico*, 2018.

40. Elected: Member at Large Faculty Senate Health Sciences Center Council, *University of New Mexico*, July, 2018.
41. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2018)*, Edinburgh, UK, December, 2018.
42. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2018)*, Edinburgh, UK, December, 2018.
43. Keynote Speaker, *4th World Congress & Expo on Pharmaceuticals and Drug Delivery Systems*, Milan, Italy, March, 2019.
44. Special Issue Guest Editor, Thin Film Technologies, *International Journal of Pharmaceutics*, November, 2019.
45. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2019)*, Edinburgh, UK, December, 2019.
46. Elected: Faculty Senator for the College of Pharmacy, *University of New Mexico*, July, 2020.
47. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2021)*, Edinburgh (Virtual), UK, December, 2021.
48. Re-Elected: Faculty Senator for the College of Pharmacy, *University of New Mexico*, July, 2022.
49. Session Judge: Academic and Industrial Posters, *Drug Delivery to the Lungs (DDL2022)*, Edinburgh, UK, December, 2022.
50. Supervisor: 2023 Pharmaceutical Sciences P-2 Award for Maydelin Santiesteban, *University of New Mexico, College of Pharmacy*, April, 2023
51. Supervisor: 2023 Pharmaceutical Sciences Pharm.D. Research Award for Haya Albazzaz, *University of New Mexico, College of Pharmacy*, April, 2023
52. 2023 Rainforest Inventor Innovation Award, *UNM Rainforest Innovations*, Albuquerque, NM, April, 2023.
53. 2025 Rainforest Inventor Innovation Award, *UNM Rainforest Innovations*, Albuquerque, NM, April, 2025.

VIII. University Service and Committees Served

1. Chemical, Radiological, & Biohazard Safety Committee, University of Texas at Austin, College of Pharmacy, 2006 – 2008.
2. Pharmacokinetics Task Force, University of Texas at Austin, College of Pharmacy, 2006 – 2008.
3. Curriculum Committee, University of Texas at Austin, College of Pharmacy, 2009 – 2010.
4. Program Assessment Team, University of Texas at Austin, College of Pharmacy, 2009 – 2010.
5. Financial Aid Committee (Professional Student), University of Texas at Austin, College of Pharmacy, 2006 – 2012.
6. Admissions Committee, University of Texas at Austin, College of Pharmacy, 2008 – 2012.
7. Cultural Proficiency Committee, University of Texas at Austin, College of Pharmacy, 2008 – 2012.
8. Pharmaceutics Division Graduate Advisor, University of Texas at Austin, College of Pharmacy, 2008 – 2012.
9. Promotion and Tenure Committee, Department of Pharmaceutical Sciences, University of New Mexico, 2012 – Present.
10. Web Re-Design Committee, College of Pharmacy, University of New Mexico, 2012 – 2013.
11. Staff Excellence Award Committee, College of Pharmacy, University of New Mexico, 2012 – 2013.
12. Faculty Development Committee, College of Pharmacy, University of New Mexico, 2012-Present. (Vice Chair: 2014 – 2015; Chair: 2015 – 2017).
13. Institutional Animal Care and Use Committee (IACUC), Health Science Center, University of New Mexico, 2013 – Present.
14. Accreditation Committee, College of Pharmacy, University of New Mexico, 2014 – 2016.
15. Graduate and Postdoctoral Affairs Committee, College of Pharmacy, University of New Mexico, 2015 – 2017.

16. Student Pharmacist Research Interest Group (SPRIG), College of Pharmacy, University of New Mexico, 2015 – 2017.
17. Pharmacy Year 1 Faculty Advisor, College of Pharmacy, University of New Mexico, Academic year 2017 – 2018.
18. Pharmacy Year 2 Faculty Advisor, College of Pharmacy, University of New Mexico, Academic year 2018 – 2019.
19. Pharmacy Year 3 Faculty Advisor, College of Pharmacy, University of New Mexico, Academic year 2019 – 2020.
20. Graduate Affairs Committee, College of Pharmacy, University of New Mexico, 2018 – 2019.
21. Office of Research and Compliance Academic Misconduct Special Investigation Committee, University of New Mexico, 2018 – 2019.
22. Research and Scholarship Committee, College of Pharmacy, University of New Mexico, 2018 – 2020.
23. Curriculum Learning and Assessment Committee, College of Pharmacy, University of New Mexico, Member: 2018 – 2021; Co-Chair: 2021 – Present.
24. Faculty Senate Health Sciences Center Council, University of New Mexico, 2018 – 2020.
25. Faculty Senate, University of New Mexico, 2020 – 2024.
26. Undergraduate Affairs Committee, 2021 – Present.
27. UNM 2040 Steering Committee, University of New Mexico, 2021 – 2024.
28. Faculty Advisor Industrial Pharmacists Organization (IPhO), University of New Mexico, 2021 – 2024.

#### IX. Scientific Advisory Roles

1. Editorial Board Member of *Drug Development and Industrial Pharmacy*, 2007 – Present.
2. Editorial Advisory Board Member of *Inhalation*, 2007 – Present.
3. Prosolv<sup>®</sup> Advisory Board, JRS Pharma, Patterson, NY, 2009-2012.

4. Review Panel Member (*Ad-hoc*): National Institutes of Health, Center for Scientific Review, Nanotechnology Study Section, 2011.
5. Scientific Advisor for Respiratory Drug Delivery 2012, Phoenix, AZ, 2012.
6. American Association for the Advancement of Science, Research Competitiveness Program Review Committee (*Ad-Hoc*), New York Ave NW, Washington, DC, 2014.
7. Associate Editor of Special and Themed Issues for *Drug Development and Industrial Pharmacy*, 2015 – 2019.
8. Review Panel Member (*Ad-hoc*): National Institutes of Health, Center for Scientific Review, Special Emphasis Panel Study Section, 2017.
9. Scientific Advisor for the Aerosol Society, Drug Delivery to the Lungs (DDL), 2016 – Present.
10. Scientific Advisor for the International Pharmaceutical Excipients Council (IPEC) of the Americas, 2017 – 2019.
11. Editorial Board Member of the *Journal of Biopharmaceutics and Therapeutic Challenges*, 2017 – Present.
12. Review Panel Member (*Ad-hoc*): National Institutes of Health, Center for Scientific Review, Preclinical Services for HIV Therapeutics Special Emphasis Panel Study Section, 2020.
13. Associate Editor for *Drug Development and Industrial Pharmacy*, 2019 – Present.
14. Editorial Board Member of *Pharmaceutics*, 2020 – Present.

#### X. Teaching Experience

1. PHR352C (Lecture), Biopharmaceutics and Pharmacokinetics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2007 - 2009.
2. PHR152P (Laboratory), Biopharmaceutics and Pharmacokinetics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2007 - 2009.
3. PHR390S, Applied Pharmacokinetics, Course Coordinator, University of Texas at Austin, College of Pharmacy, 2007-2009.

4. PHR382R, Recent Advances in Pharmaceutics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2007.
5. PHR380Q, Advanced Pharmaceutical Processing, Course Instructor, University of Texas at Austin, College of Pharmacy, 2008.
6. PHR380M, Drug Development, Course Instructor, University of Texas at Austin, College of Pharmacy, 2008.
7. PHR252C, Biopharmaceutics, Course Instructor, University of Texas at Austin, College of Pharmacy, 2009-2011.
8. PHR386Q, Preclinical and Clinical Drug Development, Course Instructor, University of Texas at Austin, College of Pharmacy, 2010-2012.
9. PHRM593, Pharmaceutical Sciences and Toxicology Seminar, Instructor of the Record (IOR), University of New Mexico, College of Pharmacy, 2014.
10. PHRM726, Biopharmaceutics and Pharmacokinetics, Course Instructor/Instructor of the Record (IOR), University of New Mexico, College of Pharmacy, 2012 – 2017.
11. PHRM702, Pharmaceutics II, Course Instructor, University of New Mexico, College of Pharmacy, 2013 – 2017.
12. PHRM598, Pharmaceutics & Drug Delivery Course Instructor/Instructor of the Record (IOR), University of New Mexico, College of Pharmacy, 2014.
13. PHRM701, Pharmaceutics I, Course Instructor, University of New Mexico, College of Pharmacy, 2016-2017.
14. PHRM802, Physical Pharmacy and Biopharmaceutics, University of New Mexico, College of Pharmacy, Instructor of the Record: 2017 – 2021; Course Instructor 2017 – Present.
15. PHRM824, Dosage Forms, Course Instructor, University of New Mexico, College of Pharmacy, 2017 – Present.
16. PHRM576, Molecular and Cellular Pharmacology, IOR, University of New Mexico, College of Pharmacy, (Instructor 2017 – 2022; IOR 2022 – Present).

## XI. Mentoring

### *Graduate Students and Postdoctoral Fellows*

1. Yoen-Ju Son, Ph.D., Pharmaceutics Graduate Program, 2006-2010.  
*Post-Doctoral fellow under supervision of Dr. Michael Hindle, Virginia Commonwealth University, 2011-2013.*
2. Sumalee Thitinan, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2007-2011. Funded by a Thailand Government Pharmaceutical Organization Scholarship,  
*Employer: Thailand Government Pharmaceutical Organization, 2011-present.*
3. Thiago Carvalho Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin, 2007-2011.  
*Employer: Bristol-Myers Squibb, New Brunswick, New Jersey, 2011-present.*
4. Matt Herpin, Pharmaceutics Graduate Program, University of Texas at Austin, 2011-2012.
5. Ping Du, Pharmaceutics Graduate Program, University of Texas at Austin, 2011-2012.
7. Ashkan Yazdi. Pharm.D./Ph.D Student Rotation, Pharmaceutics Graduate Program, University of Texas at Austin, 2011-2012.
8. Shih-Fan Jang, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2007-2013.
9. Javier Morales, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2008-2012. Funded by a Fulbright Organization Scholarship.  
*Assistant Professor, Department of Pharmaceutical Sciences and Technology, University of Chile, 2013-present.*
10. Simone Carvalho, Ph.D., Pharmaceutics Graduate Program, University of Texas at Austin 2009-2013.
11. Audrey Smith, Biomedical Sciences Graduate Program (BSGP) Student Rotation, University of New Mexico, Spring, 2013.
12. Dominique Perez, Biomedical Sciences Graduate Program (BSGP) Student Rotation, University of New Mexico, Spring, 2013.
13. Joseph Castillo, Biomedical Sciences Graduate Program (BSGP) Student Rotation, University of New Mexico, Fall, 2013.
14. Kai Berkenfeld Ph.D., Graduate Student, Department of Pharmaceutical Technology Graduate Program, University of Bonn, 2012-2019.
15. Anh-Le Dung, Nanoscience and Microsystems Engineering Graduate Program, University of New Mexico, 2013-2016.
16. Kristina Schönhoff M.S., Graduate Student, Department of Pharmaceutical Technology Graduate Program, University of Bonn, 2014-2016.
17. Sudha Ananthakrishnan M.S., Nanoscience and Microsystems Engineering Graduate Program, University of New Mexico, 2013-2016.

18. Elnaz Sadeghi M.S., Biomedical Engineering Graduate Program, University of New Mexico, 2016-2018.
19. Rikhav Gala, Ph.D., Research Scientist I, University of New Mexico, 2017-2018.
20. Madelyn Dankocsik, UNM Pharm.D./MS. Dual Degree Student, 2023 – Present.

*Pharm.D Students*

1. Ashkan Yazdi, UT Pharm.D./Ph.D Student Rotation, 2008. (Honors Project)
2. Michelle Horng, UT Pharm.D. Student, 2008-2011.
3. Rajesh Peddaiahgari, UT Pharm.D. Student, 2009.
4. Yi Guo, UT Pharm.D. Student, 2009.
5. Tian Tian, UT Pharm.D./Ph.D Student Rotation, 2010/2011. (Honors Project)
6. Ashley Jewitt, UT B.S. Student, 2011-2012.
7. Nicole Wesley, UT Pharm.D. Student, Fall 2011.
8. Lessel Lamkin, UNM Pharm.D. Student, Spring 2012 – Spring 2014.
9. Colin Williams, UNM Pharm.D. Student, Spring 2012.
10. Michael Bernauer, UNM Pharm.D. Student, Spring 2013-Fall 2015.
11. Maria Gabriela Cabanilla, UNM Pharm.D. Student, Fall 2014 – Spring 2016.
12. Christina Clise, UNM Pharm.D. Student, Spring 2012 – Spring 2016.
13. Meghan Bass, UNM Pharm.D. Student, Spring 2016 – Spring 2017.
14. Jarrid Young, UNM Pharm.D. Student, Fall 2016 – Fall 2017.
15. Jason Solano, UNM Pharm.D. Student, Spring 2017-2018.
16. Joseph Dinallo, UNM Pharm.D. Student, Spring 2016-2017.
17. Anh Le, UNM Pharm.D. Student, Summer 2018 – Summer 2019.
18. Victoria Lopez, UNM Pharm.D. Student, Summer 2018 – Spring 2019.
19. Aaron Rodriguez, UNM Pharm.D. Student, Summer 2018 – Spring 2019.
20. Haya Albazzaz, UNM B.S./Pharm.D. Student, Fall 2018 – Fall 2022.
21. Erena Hovhannisyan, UNM Pharm.D. Student, Spring 2020 – 2021.
22. Madison Robinette, UNM BSPS Student, Summer 2021 – Spring 2022.
23. Maydelin Rives Santiesteban, UNM Pharm.D. Student, Fall 2022 – Spring 2024.
24. Nahla K Ismael, UNM Pharm.D. Student, Spring 2023 – Fall 2023.
25. Ansley Battle, UNM Pharm.D. Student, Fall 2022 – Spring 2024.
26. Madelyn Dankocsik, UNM Pharm.D. Student, Spring 2023 – Spring 2024.

27. Gabriella Rodriguez, UNM Pharm.D. Student, Fall 2023 – Present.
28. Ariyana LaCour, UNM Pharm.D. Student, Fall 2023 – Present.
29. Dana Atencio, UNM Pharm.D. Student, Fall 2024 – Present.
30. Daniel Anderson, UNM Pharm.D. Student, Fall 2024 – Present.
31. Trish Ngyuen, UNM Pharm.D. Student, Fall 2024 – Present.

*Visiting Scholars*

1. Simone Dietz, Pharmaceutics Intern from University of Bonn, Germany. Fall/Spring 2010/2011.
2. Christine Joseph, Pharmaceutics Intern from University of Bonn, Germany. Spring/Summer 2011.
3. Gero Joks, Pharmaceutics Intern from University of Bonn, Germany. Summer 2011.
4. Professor Alf Lamprecht, Visiting Professor from University of Bonn, Germany. Fall 2016.
5. Ian Morales, Pharmaceutics Intern from Department of Chemistry, University of Puerto Rico. Summer 2017.
6. Yousef Abugalyon, National Institute of Health (NIH) The University of Texas at El Paso BUILDing Scholars Program. Summer 2017.
7. William Mclain, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2017.
8. Adnan Hassan, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2017.
9. Liam Wade, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2018.
10. Haya Albazzaz, Volunteer Pre-Pharmacy Undergraduate Student, UNM, Fall 2018 – Summer 2019.
11. Hannah Avery, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2019.
12. Chrystabel Chinye, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2019.
13. Maddi Barnaby, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2023.
14. Effie McGregor, Visiting Scholar from Master of Pharmacy degree programme in the Department of Pharmacy & Pharmacology at the University of Bath. Fall 2024.

*Dissertation Committees Served*

1. Justin Tolman, Ph.D., UT Pharmaceutics Graduate Program, 2009.
2. Piynauch Wonganan, Ph.D, UT Pharmaceutics Graduate Program, 2010.
3. Yoen-Ju Son, Ph.D., UT Pharmaceutics Graduate Program, 2010. (Chair)
4. Sumalee Thitinan, Ph.D., UT Pharmaceutics Graduate Program, 2011. (Chair)
5. Nicole Nelson, Ph.D, UT Pharmaceutics Graduate Program, 2011.
6. Martin Donovan, Ph.D, UT Pharmaceutics Graduate Program, 2011.
7. Shayna McGill, Ph.D, UT Pharmaceutics Graduate Program, 2011.
8. Nicole Nelson, Ph.D., UT Pharmaceutics Graduate Program, 2011.
9. Loti David King'ori, M.Sc., Pharmacy, Rhodes University, South Africa, 2011.
10. Thiago Carvalho Ph.D., UT Pharmaceutics Graduate Program, 2011. (Chair)
11. Helen Lirolla, Ph.D., UT Pharmaceutics Graduate Program, 2012.
12. Prinda Wanakule, Ph.D., UT BME Graduate Program, 2012.
13. Mehra Haghi, Ph.D., Pharmacy, University of Sydney, 2012.
14. Letty Rodriguez, Ph.D., UT Pharmaceutics Graduate Program, 2012.
15. Javier Morales, Ph.D., UT Pharmaceutics Graduate Program, 2012. (Chair)
16. Shih-Fan Jang, Ph.D., UT Pharmaceutics Graduate Program, 2013. (Chair)
17. Eileen Dawson, Ph.D., UT BME Graduate Program, 2013.
18. Amit Kumar, Ph.D., UT Pharmaceutics Graduate Program, 2013.
19. Simone Carvalho, Ph.D., UT Pharmaceutics Graduate Program, 2013. (Co-Chair)
20. Amber McBride, Ph.D., UNM NSME Graduate Program, 2014.
21. Kristina Schönhoff, M.S., Pharmaceutical Technology Graduate Program, University of Bonn, 2014. (Co-Chair)
22. Ashmita Ramanah, Pharmacy, Rhodes University, 2016.
23. Elnaz Sadeghi, M.S. UNM Biomedical Engineering Graduate Program, 2018. (Chair)
24. Kai Berkenfeld Ph.D., University of Bonn, Pharmaceutical Technology Graduate Program, 2019. (Co-Chair)
25. Sudha Ananthkrishnan M.S., UNM NSME Graduate Program, 2019. (Chair)
26. Annika Rautenberg, Ph.D., University of Bonn, Pharmaceutical Technology Graduate Program, 2024.

XII. Peer Reviewing

1. Drug Development and Industrial Pharmacy, Taylor & Francis Group, Abingdon, UK.
2. European Journal of Pharmaceutical Sciences, Elsevier, Amsterdam, Netherlands.
3. European Journal of Pharmaceutics and Biopharmaceutics, Elsevier, Amsterdam, Netherlands.
4. International Journal of Pharmaceutics, Elsevier, Amsterdam, Netherlands.
5. Journal of Controlled Release, Elsevier, Amsterdam, Netherlands.
6. Journal of Pharmaceutical Sciences, Elsevier, Amsterdam, Netherlands.
7. Pharmaceutical Research, Springer Nature, Basel, Switzerland.
8. Molecular Pharmaceutics, American Chemical Society, Washington, DC.
9. Ashley Publications Ltd., London, UK.
10. Drug Delivery, Taylor & Francis Group, Abingdon, UK.
11. Journal of Pharmacy and Pharmaceutical Sciences, Edmonton, Alberta, Canada.
12. Informa Healthcare USA, New York, NY
13. Pharmaceutical Press, London, UK
14. Journal of Pharmacy and Nutrition Science, Lifescience Global, Mississauga, Ontario, Canada.
15. Inhalation, CSC Publishing, St. Paul, MN.

XIII. Publications

1. J.T. McConville, N. Patel, N. Ditchburn, P. Woodcock, M.J. Tobyn, J.N. Staniforth, Use of a Novel Modified TSI for the Evaluation of Controlled-Release Aerosol Formulations, *Drug Development and Industrial Pharmacy*, 26(2000) 1191-1198.
2. J.T. McConville, A.C. Ross, A.R. Chambers, G. Smith, A.J. Florence, H.N.E. Stevens, The Effect of Wet Granulation on the Erosion Behavior of an HPMC–Lactose Tablet, Used as a Rate-Controlling Component in a Pulsatile Drug Delivery Capsule Formulation, *European Journal of Pharmaceutics and Biopharmaceutics*, 57(2004) 541-549.
3. J.T. McConville, A.C. Ross, A.J. Florence, H.N.E. Stevens, Erosion Characteristics of an Erodible Tablet Incorporated in a Time-Delayed Capsule Device, *Drug Development and Industrial Pharmacy*, 31(2005) 79-89.

4. J.T. McConville, Recent Trends in Oral Drug Delivery, *The Drug Delivery Companies Report*, PharmaVentures, Oxford, UK, Autumn/Winter (2005) 24-27.
5. J.T. McConville, T.C. Carvalho, A.N. Iberg, R.L. Talbert, D.S. Burgess, J.I. Peters, K.P. Johnston, R.O. Williams III, Design and Evaluation of a Restraint-Free Small Animal Inhalation Dosing Chamber, *Drug Development and Industrial Pharmacy*, 31(2005) 35-42.
6. B.J. Hoeben, D.S. Burgess, J.T. McConville, L.K. Najvar, R.L. Talbert, J.I. Peters, N.P. Wiederhold, B.L. Frei, J.R. Graybill, R. Bocanegra, K.A. Overhoff, P. Sinswat, K.P. Johnston and R.O. Williams III, *In Vivo* Efficacy of Aerosolized Nanostructured Itraconazole Formulations for the Prevention of Invasive Pulmonary Aspergillosis, *Antimicrobial Agents and Chemotherapy*, 50(2006) 1552-1554.
7. J.M. Vaughn, J.T. McConville, X. Gao, M.T. Crisp, K.P. Johnston, R.O. Williams III, Supersaturation Produces High Bioavailability of Amorphous Danazol Particles Formed by Evaporative Precipitation into Aqueous Solution and Spray Freezing into Liquid Technologies, *Drug Development and Industrial Pharmacy*, 32(2006) 559-567.
8. J.T. McConville, K.A. Overhoff, P. Sinswat, J.M. Vaughn, B.L. Frei, D.S. Burgess, R.L. Talbert, J.I. Peters, K.P. Johnston, R.O. Williams III, Targeted High Lung Concentrations of Itraconazole Using Nebulized Dispersions in a Murine Model, *Pharmaceutical Research*, 23(2006) 901-911.
9. J.M. Vaughn, J.T. McConville, D.S. Burgess, J.I. Peters, K.P. Johnston, R.L. Talbert, R.O. Williams III, Single Dose and Multiple Dose Studies of Aerosolized Itraconazole Nanoparticles, *European Journal of Pharmaceutics and Biopharmaceutics*, 63(2006) 95-102.
10. T. Purvis, J.M. Vaughn, T.L. Rogers, X. Chen, K.A. Overhoff, P. Sinswat, J. Hu, J.T. McConville, K.P. Johnston, R.O. Williams III, Cryogenic liquids, Nanoparticles, and Microencapsulation, *International Journal of Pharmaceutics*, 324(2006) 43-50.
11. J.T. McConville, N.P. Wiederhold, Antifungal Prophylaxis to the Lung Using Itraconazole, *Inhalation*, 1(2007) 6-9.
12. J.T. McConville, Targeted Lung Delivery of Antifungals: Preclinical Studies Using Itraconazole Nanoparticles, *RDD Europe 2007*, 1(2007) 43-50.
13. D.A. Miller, J.T. McConville, W. Yang, R.O. Williams III, J.W. McGinity, Hot-Melt Extrusion for Enhanced Delivery of Drug Particles, *Journal of Pharmaceutical Sciences*, 96(2007) 361-76.
14. J.M. Vaughn, N.P. Wiederhold, Jason T. McConville, J.J. Coalson, R.L. Talbert, D.S. Burgess, K.P. Johnston, R.O. Williams III, Murine Airway Histology and Alveolar

- Macrophage Uptake of Inhaled Amorphous Itraconazole, *International Journal of Pharmaceutics*, 338(2007) 219-224.
15. C.A. Alvarez, N.P. Wiederhold, J.T. McConville, J.I. Peters, L.K. Najvar, J.R. Graybill, J.J. Coalson, R.L. Talbert, D.S. Burgess, R. Bocanegra, K.P. Johnston, R.O. Williams III, Aerosolized Nanostructured Itraconazole as Prophylaxis Against Invasive Pulmonary Aspergillosis, *Journal of Infection*, 55(2007) 68-74.
  16. M. T. Carvajal, D. Cipolla, M. Copley, J.T. McConville, Highlights from RDD 2008: *Inhalation* Reports on Some of the Most Interesting Research Presented at the Most Recent Respiratory Drug Delivery Meeting, *Inhalation*, 2:3(2008) 18-20.
  17. K.A. Overhoff, J.T. McConville, W. Yang, K.P. Johnston, J.I. Peters, R.O. Williams, Effect of Stabilizer on the Maximum Degree and Extent of Supersaturation and Oral Absorption of Tacrolimus Made by Ultra-Rapid Freezing, *Pharmaceutical Research*, 25(2008) 167-175.
  18. W. Yang, J. Tam, D.A. Miller, J. Zhou, J.T. McConville, K.P. Johnston, R.O. Williams III, High Bioavailability from Nebulized Itraconazole Nanoparticle Dispersions with Biocompatible Stabilizers, Special Edition: Pharmaceutical Nanotechnology, *International Journal of Pharmaceutics*, 361(2008) 177-188.
  19. J. Tam, J.T. McConville, R.O. Williams III, K.P. Johnston, Amorphous Cyclosporin-A Nanodispersions for Enhanced Pulmonary Deposition and Dissolution, *Journal of Pharmaceutical Sciences*, 97(2008) 4915-4933.
  20. P. Sinswat, K.A. Overhoff, J.T. McConville, K.P. Johnston, Robert O. Williams III, Nebulization of Nanoparticulate Amorphous or Crystalline Tacrolimus – Single-Dose Pharmacokinetics Study in Mice, *European Journal of Pharmaceutics and Biopharmaceutics*, 69(2008) 1057-1066.
  21. Y-J. Son, J.T. McConville, Advancements in Dry Powder Delivery to the Lung, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 948-959.
  22. A.B. Watts, J.T. McConville, R.O. Williams III, Current Therapies and Technological Advances in Aqueous Aerosol Drug Delivery, Special Edition: Innovative Inhalation Technologies, *Drug Development and Industrial Pharmacy*, 34(2008) 913-922.
  23. S. Thitinan, J.T. McConville, Interferon Alpha Delivery Systems for the Treatment of Hepatitis C, *International Journal of Pharmaceutics*. 369(2009) 121-135.
  24. J.T. McConville, S.A. Kucera, T.C. Carvalho, E.M. Hurley, Ethyl Lactate as a Pharmaceutical-Grade Excipient and Development of a Sensitive Peroxide Assay, *Pharmaceutical Technology*, 33(2009) 74-84.

25. Y-J Son, J.T. McConville, Dissolution Testing for Inhalation Formulations, *Inhalation*, 2:6(2009) 8-11.
26. J.T. McConville, L. Hodges, T. Jones, J.P. Band, B. O'Mahony, B. Lindsay, A.C. Ross, A.J. Florence, A.J. Stanley, M.J. Humphrey, C.G. Wilson, H.N.E. Stevens, A Pharmacoscintigraphic Study of Three Time-Delayed Capsule Formulations in Healthy Male Volunteers, *Journal of Pharmaceutical Sciences*, 98(2009) 4251-4263.
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#### XIV. Published Abstracts

1. An *In Vitro* Method for Evaluation of Dry Powder Inhaler Formulations using a Novel Modified Twin Stage Impinger, Annual Meeting of the American Association of Pharmaceutical Scientists, Boston, MA, November, 1997.
2. A Novel *Ex Vivo* Method for Determining Diffusion Rates of Dry Powder Inhaler Formulations using an Isolated Perfused Guinea Pig Lung Model, Annual Meeting of the American Association of Pharmaceutical Scientists, Boston, MA, November, 1997.
3. The Comparison of Two Delivery Techniques for Dosing an Isolated Perfused Guinea Pig Lung (IPGPL), Annual Meeting of the American Association of Pharmaceutical Scientists, San Francisco, CA, November, 1998
4. An *In Vitro* Method for Evaluation of Lung Deposition and Drug Diffusion from Dry Powder Formulations using a Modified Twin Stage Impinger, Annual Meeting of the American Association of Pharmaceutical Scientists, San Francisco, CA, November, 1998.
5. Preclinical Evaluation of an Isotretinoin (iso) Powder Formulation for Aerosol Administration in Lung Cancer Chemoprevention, 90th American Association of Cancer Research, Philadelphia, PA, April, 1999.
6. Effect of Process Variables on the Time-delayed Release from a Capsule Based Delivery Device, 23rd Joint Research Seminar, Dublin, Ireland, June, 2000.
7. Effect of Process Variables on Drug Release from a Time-Delayed Capsule Delivery System, 137th British Pharmaceutical Conference, Birmingham, United Kingdom, September, 2000.
8. Processing Induced Variability of Time-delayed Delivery from a Pulsatile Capsule Device, Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October, 2000.
9. Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets, 138th British Pharmaceutical Conference, Glasgow, United Kingdom, September, 2001.

10. The use of Microwave Analysis to Describe the Effect of a Wet Granulation Processing Technique, Annual Meeting of the American Association of Pharmaceutical Scientists, Denver, CO, October, 2001.
11. Gamma Scintigraphic Visualisation of Drug Release from a Time-Delayed Capsule, 6th US-Japan Drug Delivery Symposium, Honolulu, HI, November, 2001.
12. Gamma Scintigraphic Investigation of Drug Release from a Time-Delayed Capsule, 29th International Symposium on Controlled Release of Bioactive Materials, Seoul, Korea, June, 2002.
13. Preparation of Water-impermeable Capsule Bodies for a Pulsatile Drug Delivery System, 139th British Pharmaceutical Conference, Manchester, United Kingdom, September, 2002.
14. Time Delayed Delivery of Theophylline, 139th British Pharmaceutical Conference, Manchester, United Kingdom, September, 2002.
15. The Suitability of a Capsule Component for use with a Pulsed Release Drug Delivery Device, Annual Meeting of the American Association of Pharmaceutical Scientists, Toronto, Canada, November, 2002.
16. Gastrointestinal Transit and Release of Time-Delayed Delivery Capsules, Annual Meeting of the American Association of Pharmaceutical Scientists, Toronto, Canada, November, 2002.
17. A Study to Investigate the effects of Food Administration Post-Gastric Emptying on a Time-delayed Formulation in Healthy Volunteers using Gamma Scintigraphy, 30th International Symposium on Controlled Release of Bioactive Materials, Glasgow, United Kingdom, June, 2003.
18. Physicochemical Properties of Itraconazole Produced by Spray-Freezing into Liquid Process, 1st European Federation for Pharmaceutical Sciences Conference on Optimizing Drug Delivery and Formulation: New Challenges in Drug Delivery, Versailles, France, September, 2003.
19. Controlling Particle Characteristics of Itraconazole Powders Produced by Spray-freezing into Liquid - Organic Solution Versus Emulsion Liquid Feed Solutions, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2003.
20. Nebulization of a Suspension Containing Itraconazole Prepared by Evaporative Precipitation into Aqueous Solution, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2003.
21. Spray Freezing into Liquid of Itraconazole for Pulmonary Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2003.
22. Enhanced Solubility and Dissolution of Itraconazole Prepared by the Spray Freezing into Liquid Technique, 31st International Symposium on Controlled Release of Bioactive Materials, Honolulu, HI, June, 2004.
23. The Use of Antioxidants to Stabilize Ethyl Lactate, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
24. Design of a Restraint-Free Small Animal Dosing Chamber for Inhalation and Investigation of Drug Distribution Within the Chamber, Annual Meeting of the

- American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
25. Miscibility of Hydrophilic Polymers and Surfactants with Polyethylene Oxide in Hot-melt Extruded Tablets Containing Poorly Water Soluble Drug, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
  26. Delivery of Poorly Water Soluble Drugs using Nebulization, 15th Drug Delivery to the Lungs Conference, London, United Kingdom, December, 2004.
  27. Improved Dissolution Rate and Bioavailability through the Formation of a Highly Miscible Binary Mixture, 32nd International Symposium on Controlled Release of Bioactive Materials, Miami, FL, June, 2004.
  28. Delivery of Nebulized Itraconazole Nanoparticles in the Murine Model, Respiratory Drug Delivery Europe 2005, Paris, France, May, 2005.
  29. Particle Engineering for Rapid Dissolution Rates of Poorly Water Soluble Drugs, American Institute of Chemical Engineers (AIChE) Annual Meeting, Cincinnati, OH, October, 2005
  30. Investigation of Dissolution Properties of Microcrystalline or Stabilized Amorphous Particles of Itraconazole in Melt Extruded Solid Dispersions, Joint Symposium on the Future Prospects of Pharmaceutical Sciences, Hoshi University, Tokyo, Japan, October, 2005.
  31. Characterization of Nebulized Itraconazole Nanoparticles and Delivery to the Murine Lung, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
  32. Treatment of Acute Pulmonary Aspergillosis with Nebulized Itraconazole in the Murine Model, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
  33. Improved Danazol Supersaturation and Oral Bioavailability via Formulation into an Amorphous Solid Solution, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
  34. Investigation of Dissolution Properties of Microcrystalline or Stabilized Amorphous Particles of Itraconazole in Melt Extruded Solid Dispersions, Annual Meeting of the American Association of Pharmaceutical Scientists, Nashville, TN, November, 2005.
  35. Treatment of Pulmonary Aspergillosis using Nebulized Itraconazole Nanoparticles prepared using Particle Engineering Technologies, 16th Drug Delivery to the Lung Conference, London, United Kingdom, December, 2005.
  36. *In Vivo* Efficacy of Aerosolized Nano-structured Itraconazole (ITZ) Formulations for the Prevention of Invasive Pulmonary Aspergillosis (IPA), 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, DC, December 2005 (originally scheduled for New Orleans, September, 2005).
  37. Single Dose Variability and Multi-Dose Studies of Nebulized Itraconazole in a Murine Model, Respiratory Drug Delivery (RDD X) Conference, Boca Raton, FL, April, 2006.
  38. Murine Airway Histology and Alveolar Macrophage Uptake of Inhaled Amorphous Itraconazole (Itra), American Thoracic Society International Conference, San Diego, CA, May, 2006.

39. Particle Engineering and Formulation for Enhanced Bioavailability of Poorly Water Soluble Drugs, Particles 2006 Conference, Orlando, FL, May, 2006.
40. Sustained Lung Concentrations of Itraconazole using Nebulized Dispersions in a Murine Model, 32nd International Symposium on Controlled Release of Bioactive Materials, Vienna, Austria, July, 2006.
41. Aerosolized Itraconazole (ITZ) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*, American College of Clinical Pharmacy Annual Meeting, St. Louis, MS, October, 2006.
42. *In-vitro* and *In-vivo* Comparison of Melt Extruded Particulate Dispersions of PVP and HPMC-Stabilized Nano-Structured Amorphous Itraconazole Particles, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
43. Antisolvent Precipitation of Cyclosporin A Nanoparticles for Enhanced Pulmonary Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
44. Immunological Response and Alveolar Macrophage Uptake of Inhaled Amorphous ITZ, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
45. *In Vitro* and *In Vivo* Validation of a High-Concentration Pre-Clinical Rodent Dosing Apparatus for Inhalation, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, October, 2006.
46. A Novel *In Vitro* Pulmonary Dissolution Testing Method for Controlled Release Inhalation Formulations, 34th International Symposium on Controlled Release of Bioactive Materials, Long Beach, CA, July, 2007.
47. The Swelling Properties of Walocel-HM (Hypromellose) in 100% Ethanol, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2007.
48. A Novel *In Vitro* Dissolution Testing Method for Inhalation Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2007.
49. *In Vitro* Determination of Gastric Mucoadhesion for Hypromellose Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2007.
50. Development of a Standardized *In Vitro* Pulmonary Dissolution Testing Method, 6th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Barcelona, Spain, April 2008.
51. Development of a Standardized Dissolution Test for Inhalable Formulations, Respiratory Drug Delivery (RDD XI) Conference, Scottsdale, AZ, May, 2008.
52. *In Vitro* Determination of Gastrointestinal Mucoadhesion Formulations, 35th International Symposium on Controlled Release of Bioactive Materials, New York, NY, July, 2008.
53. Aerosolized Voriconazole (VRC) as Prophylaxis against Invasive Pulmonary Aspergillosis (IPA) due to *Aspergillus fumigatus*, 48th Interscience Conference on Antimicrobial Agents and Chemotherapy/Infectious Diseases Society of America 46th Annual Meeting, Washington, DC, October, 2008.

54. Preliminary Studies for Rapidly Disintegrating Mini-Tablets for Enteric Coated Oral Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
55. Gender and Race-Based Disparities in the Proportion of Hepatitis C Patients that are Co-Infected with HIV/AIDS in The 1996-2005 US National Hospital Discharge Survey, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
56. Low Concentration Range Determination of API 31510 using High Performance Liquid Chromatography (HPLC), Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
57. Major Sites of Pulmonary Malignancy and Associated Health Outcomes for Lung Cancer Patients in the 1996-2005 National Hospital Discharge Survey (NHDS), Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
58. Improvements of an *In Vitro* Dissolution Test Method For Dry Powder Inhalation Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
59. Aerosol Characterization and Single-Dose Pharmacokinetic Analysis of Nebulized Voriconazole Solution, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
60. Investigation of Nebulized Dose and Inhaled Dose of Itraconazole Dispersions in a Nose-Only Rodent Dosing Chamber, Annual Meeting of the American Association of Pharmaceutical Scientists, Atlanta, GA, November, 2008.
61. Characterization of Saccharide Derived Fast Disintegrating Tablets, ExcipientFest 2009, San Juan, PR, May, 2009.
62. Manufacture and Characterization of Natural Polymer Based Films as Buccal Delivery Systems, ExcipientFest 2009, San Juan, PR, May, 2009.
63. Development of Fast Disintegrating Tablets using Starch and Starch Derivatives, 36th International Symposium on Controlled Release of Bioactive Materials, Copenhagen, Denmark, July, 2009.
64. An Investigation of Natural Based Films Suitable for Buccal Delivery, 36th International Symposium on Controlled Release of Bioactive Materials, Copenhagen, Denmark, July, 2009.
65. Effect of Oral Candidiasis Co-Infection in HIV/AIDS and Hepatitis C Patients Admitted to Hospitals in The United States, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
66. Effect of Cooling Rate on the Particle Size of API31510 Emulsions, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
67. Investigation of nebulized itraconazole dispersions: *in-vitro-in-vivo* comparison of dose administered to mice in a nose-only dosing apparatus, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.

68. Nanostructured Tacrolimus Produced by Ultra-Rapid Freezing for Dry Powder Inhalation, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
69. Development and Evaluation of a Manufacturing Process for Xanthan Gum-Based Films, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
70. Optimization of an In Vitro Dissolution Test Method for Inhalation Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
71. Low Density Chitosan-Based Particles Prepared by Spray Drying as a Pulmonary Drug Delivery Vehicle, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
72. Particle Manufacture for Targeted Oral Delivery in a Rodent Model, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
73. Development of Submicron Aqueous Formulations of API31510, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
74. Manufacture and characterization of Fast Disintegrating Tablets, Annual Meeting of the American Association of Pharmaceutical Scientists, Los Angeles, CA, November, 2009.
75. Optimization of an In Vitro Dissolution Test Method for Inhalation Formulations, Proceeding of the Drug Delivery to the Lungs Conference (DDL20), Edinburgh, UK, December 2010.
76. The Use of Silicified Microcrystalline Cellulose and Fructose in the Development of Orally Disintegrating Tablets, 37th International Symposium on Controlled Release of Bioactive Materials, Portland, OR, July, 2010.
77. Rapidly Disintegrating Tablets for Targeted Oral Delivery, 37th International Symposium on Controlled Release of Bioactive Materials, Portland, OR, July, 2010.
78. Assessment of Student Performance in Biopharmaceutics using the TurningPoint Audience Response System, Proceedings of AACP Annual Meeting and Seminars, Seattle, WA, 2010.
79. Development and Characterization of Films for Buccal Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
80. Time Dependent Aerosolization Stability of Vibrating-Mesh Nebulizers with Submicron Lecithin Aqueous Dispersions of API31510, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
81. Nebulization Performance of Submicron Aqueous Dispersions of API 31510 prepared using High Pressure Homogenization, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
82. Measurement of Surface Tension of Liquids using Texture Analyzer, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.

83. Manufacture of BSA Microcrystals by a Co-Precipitation Method, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
84. Stabilized Buoyancy and Optimal Loading Capacity of a Floating Gastric Device, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
85. Size Exclusion and Gastric Emptying in Rodent Models, Annual Meeting of the American Association of Pharmaceutical Scientists, New Orleans, LA, November, 2010.
86. Fighting Dysphagia with Orally Disintegrating Tablets, 8th International Conference on Functional Foods for Chronic Diseases: Science and Practice, Las Vegas, NV, March 2011.
87. Time Dependent Aerosolization Stability of a Vibrating-Mesh Nebulizer using API31510, Respiratory Drug Delivery Europe 2011, Berlin, Germany, May, 2011.
88. The Influence of Physicochemical Properties of Aqueous Dispersions on Active Vibrating-Mesh Nebulization, 18th Congress of International Society for Aerosols in Medicine, Rotterdam, Netherlands, June, 2011.
89. Orally Disintegrating Dietary Supplement Tablets, Institute of Food Technology Annual Meeting, New Orleans, LA, June, 2011.
90. A Gastric Retention Modeling Study of Floating Devices, 38th International Symposium on Controlled Release of Bioactive Materials, National Harbor, MD, July, 2011.
91. Impact of Drying Conditions on the Physicochemical and Aerodynamic Properties of Rifampicin Dihydrate (RFDH) Microcrystals, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
92. BSA Microcrystals by a Co-Precipitation Method: The Effect of Solvent Type and Presence of Surfactant, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
93. The Influence of Particles on Physical Properties of Films, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
94. *In Vitro* Evaluation of Adhesion Properties of Mucoadhesive Pellets Using Artificial Agar/Mucin Gel, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
95. The Influence of Physicochemical Properties of Aqueous Dispersions on Active Vibrating-Mesh Nebulization, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington DC, October, 2011.
96. Dissolution Rate Comparison of Micronized and Spray-Dried Budesonide, Respiratory Drug Delivery 2012, Phoenix, AZ, May, 2012.
97. A Novel Method for the Manufacture of Protein-Coated Nanoparticles, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.
98. Dissolvable Strip for Treatment of Oral Thermal Burns, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.

99. The Effect of pH on Protein-coated Submicron Particles Obtained by Antisolvent Co-precipitation, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
100. Manufacture and Characterization of Films for Buccal Delivery of Protein-coated Submicron Particles, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
101. Influence of Particulate API in Eudragit® RS and RL Films for Buccal Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
102. Controlled Release Properties of Cellulose Processed by Rapid Freezing Technology, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
103. Prediction of *In Vitro* Aerosolization Profiles Based on Rheological Behaviors for Aqueous Dispersions of API 31510, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
104. Acoustic Levitation to Simulate Rifampicin Spray Drying Kinetics, Annual Meeting of the American Association of Pharmaceutical Scientists, Chicago, IL, October, 2012.
105. Multiple Dose Platforms for Once-Daily Administration of Ciprofloxacin or Verapamil, 3rd International Conference and Exhibition on Pharmaceutics & Novel Drug Delivery Systems, Northbrook, IL, April, 2013.
106. Effect of Time Between Actuation on the Dose Variability for Three Metered Dose Inhalers, Respiratory Drug Delivery Europe 2013, Berlin, Germany, May, 2013.
107. Controlled Release Mucoadhesive Films Containing Nanoparticles of Lysozyme, 40th International Symposium on Controlled Release of Bioactive Materials, Honolulu, HI, July, 2013.
108. Determination of Thermodynamic Characteristics of A Rifampicin Solvate Recrystallized from Ethanol, 31st Annual Meeting of the Mountain West Society of the Society of Toxicology, Albuquerque, NM, September, 2013.
109. Bioadhesive Films Containing Nanoparticles of Lysozyme, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
110. Development of Films of Insulin-coated Nanoparticles for Use in Buccal Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
111. Gastroretentive Capsules for Once-daily Administration of Ciprofloxacin or Verapamil, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
112. Preformulation Development Studies of Respirable Rifampicin Particles through Crystal Modification, Annual Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX, November, 2013.
113. Inhaled Therapeutics for Lung Cancer, Drug Delivery to the Lungs Conference (DDL24), Edinburgh, UK, December, 2013.
114. Antisolvent Co-Precipitation Synthesis of D,L-Valine/Lysozyme, ExcipientFest 2014, Raleigh, NC, April, 2014.

115. Antisolvent Co-precipitation Synthesis of D,L-Valine/Lysozyme (Encore Presentation), Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2014.
116. Core Forming Antisolvent Co-precipitation of Protein Loaded Crystals, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2014.
117. Investigating of Protein-Coated Nanoparticles for Controlled Release Films, 42nd International Symposium on Controlled Release of Bioactive Materials, Edinburgh, UK, July, 2015.
118. Enhancing Macrophage Uptake of Rifampicin, 3rd International TB-Meeting, October, 2015 Parma, Italy
119. Development of Coenzyme Q10 Nano-emulsions for a Nebulization Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
120. Formulation and Characterization of Dextromethorphan Thin Films, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
121. Manufacture and Characterization of Rifampicin Particles for Aerosolization, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
122. Polymeric Coating of Endotracheal Tubes for Local Drug Delivery, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
123. Stability Characterization of Nano-Emulsions Intended as a Vehicle for Aerosol Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2015.
124. Preparation and Evaluation of Dextromethorphan Containing Thin Films, ExcipientFest 2015, Baltimore, MD, April, 2015.
125. Development of Coenzyme Q10 Nano-Emulsions for Nebulization Delivery, 43rd International Symposium on Controlled Release of Bioactive Materials, Seattle, WA, July, 2016.
126. Polyethylene Glycol Coating of Endotracheal Tubes for Local Delivery, 43rd International Symposium on Controlled Release of Bioactive Materials, Seattle, WA, July, 2016.
127. Manufacture and Assessment of a Novel 3D Printed Induction Port for Cascade Impactor Analysis, ExcipientFest 2017, Providence, RI, April, 2017.
128. Effect of Drug Concentration on Viscosity of Submicron Dispersions of Coenzyme Q10, ExcipientFest 2017, Providence, RI, April, 2017.
129. Investigating ACI Performance of a Salbutamol pMDI Formulation Using a Modified 3D Printed Induction Port, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2017.
130. Effect of Drug Concentration on surface tension and the rheology of Submicron Dispersions of CoenzymeQ10, Annual Meeting of the American Association of Pharmaceutical Scientists, San Diego, CA, November, 2017.
131. Reducing the Sol-Gel Transition of Hypromellose 2910 with Highly Electronegative Ion Containing Gelling Aids, ExcipientFest 2018, San Juan, PR, May, 2018.

132. Oral Gelling Liquid Formulations for Dental Remineralization, ExcipientWorld 2019, National Harbor, MD, May, 2019.
133. Preparation of Drug Containing Core Microparticles for use in Taste Masking Applications, 43th International Symposium on Controlled Release of Bioactive Materials, Las Vegas, NV, June, 2020.
134. Determining the design space of intermediate core microparticles obtained from spray dried acrylic polymers for taste masking bitter drugs, Annual Meeting of the American Association of Pharmaceutical Scientists, Virtual Meeting, October, 2020.
135. Enhanced Dissolution of a Poorly Soluble Drug Using a Spray Drying Technique, Annual Meeting of the American Association of Pharmaceutical Scientists, Philadelphia, PA, October, 2021.
136. The Effect of 3D Printed Mimetic Human Induction Ports on the Deposition of Inhalation Aerosols, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2022.
137. Variability in 3D Print Weight for Novel Solid Oral Dosage Form Components, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2022.
138. Modifying Drug Release from Microparticles Prepared by Spray Drying Using a 3-Fluid Nozzle, Annual Meeting of the American Association of Pharmaceutical Scientists, Boston, MA, October, 2022.
139. 3D Printed Mimetic Human Induction Ports Effects the Deposition of Inhalation Aerosols, American Society of Health-System Pharmacists (ASHP) Midyear Meeting, Las Vegas, NV, December, 2022.
140. Tortuous Control of Drug Release from 3D Printed Tablets, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2023.
141. Thermally Gelling Liquid Sprays for Oropharyngeal Targeting, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2023.
142. Impact of Solubility Parameters on Particle Coating Using a 3-Fluid Spray Drying Process for Modified Drug Release, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2023.
143. Thermally Gelling Hypromellose Liquid Sprays for Oropharyngeal Targeting, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2023.
144. Improved Distribution of Water Insoluble Components in Soluble Thin Film Formulations, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2023.
145. Influence of Polymer Miscibility on Drug Release from Microparticles Prepared using a 3-Fluid Spray Drying Process, Annual Meeting of the American Association of Pharmaceutical Scientists, Orlando, FL, October, 2023.
146. Self Emulsifying Nanoemulsion Aerosol Formulations, UNM College of Pharmacy Annual Research Day, Albuquerque, NM, April, 2024.
147. Leveraging 3D Printed Anatomical Features to Improve In Vitro Test Methods for Pharmaceuticals, 3D Printing & Additive Manufacturing Meeting, Rome, Italy, November, 2024.

148. Formulation Design of Thermally Gelling Liquid Sprays for Oropharyngeal Targeting of MEK Inhibitors, Annual Meeting of the American Association of Pharmaceutical Scientists, Salt Lake City, UT, October, 2024
149. Oropharyngeal Targeting using a Novel Thermally Gelling Liquid Spray, Drug Delivery to the Lungs Conference (DDL35), Edinburgh, UK, December, 2024.

XV. Book Contributions and Editorials

1. J.T. McConville, Preface for *Advanced Drug Formulation Design to Optimize Therapeutic Outcomes*, (Eds.) Robert O. Williams III, David R. Taft, J.T. McConville, Informa Healthcare, New York, NY, September, 2007.
2. J.T. McConville, N.P. Wiederhold, Invasive Pulmonary Aspergillosis: Therapeutic and Prophylactic Strategies, In *Advanced Drug Formulation Design to Optimize Therapeutic Outcomes*, (Eds.) Robert O. Williams III, David R. Taft, J.T. McConville, Informa Healthcare, New York, NY, September 2007.
3. J.T. McConville, F.J. McInnes, A.C. Ross, Preface for Innovative Inhalation Technologies: Special Edition, *Drug Development and Industrial Pharmacy*, 34(2008) 1-2.
4. S. Thitinan, J.T. McConville, Pulsatile Drug Delivery, In *Controlled Release: Oral Dosage Forms*, Eds. Patrick Crowley, Clive Wilson, Controlled Release Society Books, St. Paul, MN, 2011.
5. Y-Ju Son, J.T. McConville, In Vitro Performance Testing for Pulmonary Drug Delivery, In *Controlled Release Science and Technology: Pulmonary Delivery*, (Eds.) Hugh Smyth, Anthony Hickey, Controlled Release Society Books, St. Paul, MN, 2011.
6. J.O. Morales, A.B. Watts, J.T. McConville, Mechanical Particle Size Reduction Techniques, In *Formulating Poorly Water Soluble Drugs*, (Eds.) Dave Miller, Alan Watts, Robert O. Williams III, Springer Publishing Company, New York, NY, 2011.
7. J.O. Morales, J.T. McConville, Polymer Drug Delivery Systems for Sustained Mucoadhesion in the Respiratory Tract. In *Polymers for Pulmonary Drug Delivery*, (Eds.) H.D.C. Smyth, I. Saleem, J.T. McConville, iSmithers, Shrewsbury, UK, 2013.
8. P. Du, J.T. McConville, Regulatory Aspects of Pulmonary Delivery of Polymers. In *Polymers for Pulmonary Drug Delivery*, (Eds.) H.D.C. Smyth, I. Saleem, J.T. McConville, iSmithers, Shrewsbury, UK, 2013.
9. J.T. McConville, Polymer Drug Delivery Systems Targeting the Alveolar Macrophages. In *Polymers for Pulmonary Drug Delivery*, (Eds.) H.D.C. Smyth, I. Saleem, J.T. McConville, iSmithers, Shrewsbury, UK, 2013.

10. J.O. Morales, J.T. McConville, Preface for Buccal Drug Delivery Theme Issue, *Drug Development and Industrial Pharmacy*, 40(2014), 577–578.
11. J.T. McConville, Preface for Special Focus: Pharmaceutical Dosage Form Design Influence on Drug Pharmacokinetics, *Drug Development and Industrial Pharmacy*, 41(2015), 1921.
12. J.T. McConville, Preface for Special Focus: Transdermal, Topical and Folicular Drug Delivery Systems, 42(2016), 845.
13. J.T. McConville, Preface for Special Focus: Ocular and Ophthalmic Drug Delivery Systems, 42(2016), 513.
14. J.T. McConville, Preface for Special Focus: Current developments in oral drug administration, *Drug Development and Industrial Pharmacy*, 43 (2017), 699.
15. J.T. McConville, J.O. Morales, Preface for Selected abstracts from Excipient Fest 2017, *Drug Development and Industrial Pharmacy*, 44 (2018), 868.
16. J.T. McConville, R. Gala, J.O. Morales, Preface for Special Issue: Thin Film Technologies, *International Journal of Pharmaceutics*, November, 2019.
17. J.O. Morales, A.B. Watts, J.T. McConville, Mechanical Particle-Size Reduction Techniques, In *Formulating Poorly Water Soluble Drugs*, Eds. R.O. Williams III, D.A. Davis Jr., D.A. Miller, Springer Publishing Company, New York, NY, 2022.

XVI. Invited Talks, Sessions, and Workshop Presentations

1. *Microwave Dielectric Analysis of Wet Granulations for Erodible HPMC Tablets*, Proceedings of the 138th British Pharmaceutical Conference, Glasgow, United Kingdom, September, 2001.
2. *Chronopharmaceutical Drug Delivery*, University of Texas at Austin, Austin, TX, October, 2001.
3. Workshop Presenter: *Particle Engineering Technologies: Theory and Practice*, Annual Meeting of the American Association of Pharmaceutical Scientists, Baltimore, MD, November, 2004.
4. *Capsule Filling and Topical Formulations*, Science Camp Presentation, Priscilla Pond Flawn Child and Family Laboratory, University of Texas at Austin, Austin, TX, June, 2005.

5. *Pre-Clinical Development Studies with Poorly Water-Soluble Drugs*, Universidade Federal de Minas Gerais, Belo Horizonte, Brasil, June, 2005.
6. *Targeted High Lung Concentrations of Itraconazole using Nebulized Dispersions in a Murine Model*, 1<sup>st</sup> Joint Symposium on the Future Prospects of Pharmaceutical Sciences, Hoshi University, Tokyo, Japan, October, 2005.
7. *Pre-Clinical Development Studies with Poorly Water-Soluble Drugs*, University of Louisiana at Monroe, Monroe, LA, January, 2006.
8. *The Effective Delivery of Itraconazole for the Treatment of Acute Fungal Infections*, University of Mississippi, Oxford, MS, January, 2006.
9. *Targeted High Lung Concentrations of Itraconazole using Nebulized Dispersions in a Murine Model*, University of Texas at Austin, Austin, TX, February, 2006.
10. *Enhanced Therapeutic Outcomes using Targeted Itraconazole Delivery in a Murine Model*, Long Island University, Brooklyn, NY, February, 2006.
11. *Targeted Treatment of Infectious Diseases to the Lung*, Virginia Commonwealth University, February, 2007.
12. *Targeted Lung Delivery of Antifungals: Preclinical Studies using Itraconazole Nanoparticles*, Respiratory Drug Delivery Europe 2007, Paris, France, April, 2007.
13. *Preclinical Studies with Poorly Water Soluble Drugs*, University of Strathclyde, Glasgow, UK, July, 2007.
14. *Antifungal Prophylaxis to Treat Pulmonary Aspergillosis*, GEA-NUS 10th Anniversary Celebration & Pharmaceutical Technology Seminar, Singapore, December, 2007.
15. *Novel In Vitro Dissolution Testing Methods for Inhalation Formulations*, Dissolution Testing, Bioequivalence & Bioavailability Strategies Meeting, London, United Kingdom, June 2008.
16. *Dissolution Testing of Inhalation Products*, Copley Scientific Ltd, London, United Kingdom, June 2008.
17. *Modification of the USP Type II Dissolution Testing Apparatus for Powder Formulations*, Novartis, Basel, Switzerland, July 2008.
18. *The Use of Renewable Ingredients for Pharmaceutical Formulations*, Tate & Lyle, Decatur, September 2008.

19. *Improved Therapy by Direct Lung Targeting for the Treatment of Pulmonary Aspergillosis*, Purdue University, September, 2008.
20. Attendee/Observer at the Aerosol Advisory Board Meeting, United States Pharmacopeia Headquarters, Rockville, MD, January, 2009.
21. *Formulation and Characterization of Prosolv<sup>®</sup> Fast Disintegrating Tablets*, Prosolv<sup>®</sup> Advisory Board Meeting, San Juan, Puerto Rico, April, 2009.
22. Workshop Presenter: Advances in the Development of Oral Controlled Release Pharmaceutical Forms and/or Site Specific Gastrointestinal Tract Delivery and Pulmonary Delivery Systems: *An Introduction to Pulmonary Drug Delivery*, Santiago, Chile, October, 2009.
23. *Formulation and Characterization of Fast Disintegrating Tablets Containing Renewable Ingredients*, 2<sup>nd</sup> Joint Symposium on the Future Prospects of Pharmaceutical Sciences, Hoshi University, Tokyo, Japan, October, 2009.
24. *Dissolution Testing of Aerosol Powder Formulations*, Novartis, Horsham, UK, December 2009.
25. Workshop Presenter: *An Introduction to Buccal Drug Delivery*, Advances in Pharmaceutical Technology and Pharmaceutical Engineering, Santiago, Chile, October, 2010.
26. *Fighting Dysphagia with Orally Disintegrating Tablets*, Functional Foods for Chronic Diseases: Science and Practice, Las Vegas, March, 2010.
27. *Formulation of Rapidly Disintegrating Tablets to Combat Dysphagia*, Prosolv<sup>®</sup> Advisory Board Meeting, Miami, FL, April, 2011.
28. Workshop Moderator and Presenter: *Developing Pharmaceutical Products for Controlled Pulmonary Delivery*, Annual Meeting of the American Association of Pharmaceutical Scientists, Washington, DC, October, 2011.
29. Workshop Presenter and Panel Discussion Member: *Dissolution Testing to Meet Formulation Challenges*, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.
30. Speaker and Panel Discussion Member: *A Prospective Dissolution Test Design: Controlling the Important Variables*, Respiratory Drug Delivery 2012, Phoenix, AZ, 2012.
31. Workshop Presenter and Panel Discussion Member: *Setting Release Specifications for in vitro Testing of Controlled Release Dosage Forms: Dissolution Testing to meet*

- Formulation Challenges*, 39th International Symposium on Controlled Release of Bioactive Materials, Quebec City, Canada, July, 2012.
32. Visiting Professor and Workshop Presenter: *An Introduction to Pulmonary Drug Delivery*, Advances in Pharmaceutical Technology and Pharmaceutical Engineering, Santiago, Chile, April, 2013.
  33. *Trans-Mucosal Buccal Drug Delivery*, New Mexico Society of Health-System Pharmacists (NMSHSP) Balloon Fiesta Symposium, Albuquerque, NM, October, 2013.
  34. *Inhaled Therapeutics for Lung Cancer*, Drug Delivery to the Lungs Conference (DDL24), Edinburgh, UK, December, 2013.
  35. *Development of a Single Capsule Multiple Dose Regimen*, (New Mexico Pharmacist Association (NMPHA) Mid-Winter Meeting, January, 2014.
  36. Session Chair and Moderator: *Macromolecule Drug Delivery: Challenges and Triumphs*, AAPS National Biotechnology Conference, San Diego, CA, May, 2014.
  37. *Use of Cationic Polymethacrylate Derivatives for Oral Mucosa Drug Delivery*, 1st International Society for Biomedical Polymers and Polymeric Biomaterials Conference, Washington DC, July, 2014.
  38. *Enhancing Macrophage Uptake of Rifampicin*, 3rd International TB-Meeting: Inhaled Therapies for Tuberculosis and Other Infectious Diseases, October, 2015, Parma, Italy.
  39. Session Chair and Moderator: *Challenges and Future Prospects of Alternative Delivery of Biologics*, American Association of Pharmaceutical Sciences Annual Meeting, Orlando, FL, October, 2015.
  40. *Development of a Buoyant Gastroretentive Dosage Form*, University of Sarajevo, Sarajevo, Bosnia and Herzegovina, June, 2016.
  41. *Cascade Impactor Performance using 3D Printed Induction Port Designs*, American Association of Pharmaceutical Scientists Rocky Mountain Discussion Group 5th Annual Meeting, Albuquerque, NM, October, 2017.
  42. *Using Highly Electronegative Gelling Aids with Hypromellose 2910*, 4th World Congress & Expo on Pharmaceutics and Drug Delivery Systems, Milan, Italy, March, 2019.
  43. *Cascade Impactor Performance using Anatomically Appropriate 3D Printed Induction Port Designs*, University of Cork, Cork, Ireland, August, 2019.

44. *Taking it Slow: Reduced Velocity Aerosols*, Inspire Me, San Francisco, CA, June, 2019.
45. *Oral Gelling Liquid Formulations*, Rainforest Innovations, Albuquerque, NM, August, 2021.
46. *STEM Presentation: Gastroretentive Pharmaceuticals*, Sandia High School, Albuquerque, NM, September, 2022.
47. *STEM Presentation: 3D Printed Tablets*, Sandia High School, Albuquerque, NM, February, 2023.
48. *STEM Presentation: Pharmaceuticals of Oral Medications*, Sandia High School, Albuquerque, NM, May, 2023
49. *Targeted Oropharyngeal Therapy for HPV Infections*, University of Bonn, February, 2024.
50. *STEM Presentation: 3D Printed Tablets Update*, Sandia High School, Albuquerque, NM, February, 2024.
51. Session Chair and Moderator: 3rd International Conference on 3D Printing & Additive Manufacturing, Rome, Italy, November, 2024.
52. *Leveraging 3D Printed Anatomical Features to Improve In Vitro Test Methods for Pharmaceuticals*, 3rd International Conference on 3D Printing & Additive Manufacturing, Rome, Italy, November, 2024.
53. *Oropharyngeal Targeting of MEK Inhibitors Using a Thermally Gelling Spray*, UNM Comprehensive Cancer Center, Albuquerque, NM, November, 2024.
54. *Dispersion of Poorly Soluble Components in Thin Film Formulations*, University of Bonn, February, 2025.

## XVII. Intellectual Property

1. Enhanced Delivery of Drug Compositions to Treat Life Threatening Infections, United States Patent US9061027 B2 (WO2006026502A1), Issue date: Jun 23, 2015.
2. Enhanced Delivery of Immunosuppressive Drug Compositions for Pulmonary Delivery, United States Patent US9044391 B2, Issue Date: Jun 2, 2015.

3. Stabilized Hot Melt Extrusion Composition with Small Drug Particles, United States Patent US9504658 B2 (WO2007001451A9), Issue date: Nov 29, 2016.
4. Enhanced Delivery of Immunosuppressive Drug Compositions for Pulmonary Delivery, United States Patent US10231955 B2, Issue Date: Mar 19, 2019.
5. Treatment of Pulmonary Fungal Infection with Voriconazole via Inhalation, Non-Provisional Patent Application (PCT/US2009/043027), filed: May 6, 2009.
6. Bioadhesive Films for Local and/or Systemic Delivery: Non-Provisional Patent Application (PCT/US2013/032490 - WO 2014/065870), filed: March 15, 2013.
7. Wireless Dispensing Device Monitor: Provisional Application (US62/796,678), filed: Jan 25, 2019.
8. Drug-eluting medical devices coatings: Provisional Application (US62/948,469), filed: Dec 16, 2019.
9. Oral Gelling Liquid Formulations, United States Patent US11369631 B1, Issue date: Jun 28, 2022.
10. Thermally Gelling Drug Formulations, United States Patent US11464736 B2, Issue date: Oct 11, 2022.
11. Topical Formulations for Targeted Delivery of Therapeutics: Provisional Application (US63/411,027), filed: Sep 28, 2022.
12. Coenzyme Q10 Aerosol, United States Patent US11369631, Issue Date: April 2, 2024.